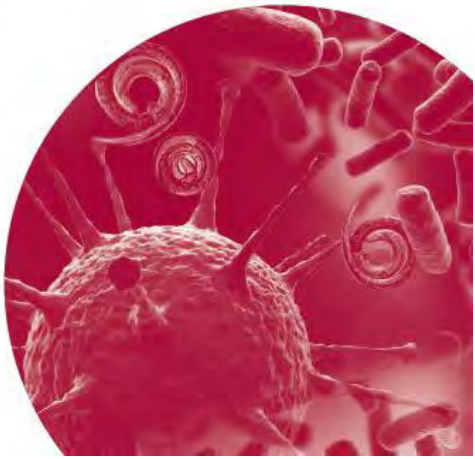
Nationale Forschungsplattform für Zoonosen

National Symposium on Zoonoses Research

15 – 16 October | Berlin 2015

Program and Abstracts



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Nationale
Forschungsplattform
für Zoonosen

Editor
German Research Platform for Zoonoses

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Welcome Address of the German Research Platform for Zoonoses

Dear colleagues,

We are delighted to welcome you to the *National Symposium on Zoonoses Research 2015*. The focus of this year's conference is "Research meets Public Health."

Over the past year, the German Research Platform for Zoonoses has worked hard to close the gap between research and practical application, forging links between representatives from both sides. Against this background, we are very pleased that Ute Teichert (Akademie für öffentlichen Gesundheitsdienst Düsseldorf) and Jürgen Rissland (Fachausschuss Infektionsschutz im Bundesverband der Ärztinnen und Ärzte des öffentlichen Gesundheitsdienstes e.V. - BVÖGD) contributed to the planning of the symposium's agenda and will moderate several sessions. Both Dr. Teichert and Dr. Rissland play an active role in public health services in Germany.

This year's program structure is intended to attract the attention of researchers and public health professionals alike (in human and in veterinary medicine). It will intensify exchange between these two stakeholder groups and encourage discourse among participants. To ensure the event is accessible to everyone, some segments will be held in English and others in German.

Zoonoses and related research are key topics within public health services (including veterinary health services). And this year's conference again offers an exciting and appealing program of keynotes and accompanying sessions. A particular highlight is the Public Health-Session on Thursday afternoon (to be held in German) that will address antibiotic resistance.

Our Young Scientists Breakfast will take place on Friday morning. Early-stage researchers are invited to take advantage of this relaxed setting to talk with experienced colleagues about possible career paths and other topics.

The conference is designed as a platform for exchanging up-to-date knowledge, meeting new partners and developing existing partnerships that span scientific disciplines and geographical boundaries. Let's join forces and bring the One Health idea to life!

We would like to take this opportunity to thank all those who have submitted abstracts, and prepared posters and presentations, some of whom have travelled a great distance to join us. All of you are making a positive contribution to the success of this conference.

We hope you enjoy and benefit from the *National Symposium on Zoonoses Research 2015*.

Stephan Ludwig
(Münster, Germany)

Martin H. Groschup
(Isle of Riems, Germany)

Sebastian C. Semler
(Berlin, Germany)

Directors of the German Research Platform for Zoonoses

Welcome Note of the Federal Ministries

For years, the scientific promotion of zoonoses control has been a priority of the federal government. For some time, we have been aware that a one-sided approach to human and animal health, food safety or the environment does not produce the comprehensive success in zoonoses control we are aiming for and which the citizens expect.
Consequently, the motto of this year's symposium is „Research meets Public Health".
According to the World Organization for Animal Health in Paris, about 60 to 70 % of all (new) diseases occurring in humans are caused by pathogens first recognized in animals. This alarming development has many reasons:

- The close association of livestock and their keepers.
- The increasing constriction of the natural habitat of wild animals causes an increasingly close contact between humans and animals - even in urban areas.
- The arrival and spread of suitable live vectors for highly pathogenic and novel zoonotic pathogens, particularly exacerbated by climate change.
- The vehement increase of international trade and tourism.
- Change of climatic factors in the context of climate change.

All together, enough reasons why zoonotic pathogens may colonize and multiply in animal and human populations and spread across continents within a day. As a result, the health of humans and animals is threatened. It also has a significant negative impact on society.
In a highly developed country like ours, we must conquer these challenges. This is the responsibility of Public Health bodies, Public Veterinary authorities and Public Health services. Thus, it is imperative to put scientific results to practical use.
To this end, the scientific clearing of unanswered questions, the development of efficient diagnostic and therapeutic methods, preventive measures and, finally, informing the public as well as surveillance of zoonotic pathogens are important steps.
For an effective control and efficient political measures, it takes a comprehensive and interdisciplinary approach:

"One health" – health cannot be divided - the responsibility for maintaining the health of humans and animals, however, is administratively divided and often also in science. This must be overcome. In order to achieve our goal according to the "One health" principle, health and veterinary authorities, agriculture, food industry, well informed consumers and science must work together.
The scientists of national zoonoses research lay the foundation for this. Now, their scientific results must be put to practical use.
Therefore, we wish all participants interesting discussions, new insights, creative ideas for future research initiatives and a successful conference!

Dr. Joachim Klein

Federal Ministry of Education and Research

Dr. Antina Ziegelmann

Federal Ministry of Health

Dr. Ralf Rotheneder

Federal Ministry of Food and Agriculture

Welcome Note of Public Health Representatives

Sehr geehrte Damen und Herren,
liebe Kolleginnen und Kollegen,

zum diesjährigen Nationalen Symposium für Zoonosenforschung heiße ich Sie als Vorsitzende des Bundesverbandes der Ärztinnen und Ärzte des Öffentlichen Gesundheitsdienstes gemeinsam mit meinem Kollegen, Herrn Dr. Jürgen Rissland, der Sprecher für den Fachausschuss Infektionsschutz im BVÖGD ist, herzlich willkommen.
Wir erleben heute und auch morgen eine Besonderheit. „Research meets Public Health". So lautet in diesem Jahr der Untertitel für diese Veranstaltung. Und man könnte einen Ihnen vielleicht noch vertrauten, ehemaligen Spitzenpolitiker zitieren, der 1989 gesagt hat: „es wächst zusammen, was zusammengehört!". Das Zitat stammt von Willy Brand und bezog sich ursprünglich auf die beiden deutschen Staaten nach der Wiedervereinigung vor nun rund 26 Jahren. „Es wächst zusammen, was zusammengehört" – diese Aussage gilt aber auch für das Thema Zoonosen und öffentliche Gesundheit. Fast 70 % der heute für den Menschen bedeutsamen Infektionskrankheiten sind ursprünglich zunächst beim Tier aufgetreten und dann auf den Menschen übergegangen. Darunter so bedeutsame wie das humane Immunschwächevirus oder auch lebensmittelbedingte Infektionen, aber in jüngerer Vergangenheit vor allem Coronaviren als Auslöser des Middle East Respiratory Syndrome, abgekürzt (MERS), oder 2009 das pandemische Influenzavirus.
Was macht die Bedeutung dieser und anderer Zoonosen für die öffentliche Gesundheit aus? Zum einen sicherlich, dass die Überwindung der Speziesbarriere auf eine wichtige Eigenschaft der Erreger hinweist: sie sind in der Lage, sich auf neue Wirte einzustellen, und allein diese Flexibilität ist bereits ein alarmierendes Signal. Zum anderen bedeutet der Übergang von Mensch auf Tier ein Infektionsrisiko, dessen Folgen für die Menschheit nur sehr bedingt abschätzbar sind. Manche Infektionserreger sind in der Lage, sich binnen wenigen Wochen über den gesamten Erdball zu verbreiten (Stichwort: pandemisches Influenzavirus), bei anderen ist das epidemiologische Geschehen deutlich schwieriger aufzudecken (Stichwort: multiresistente Enterobakterien).

In jedem Fall führen solche Zoonosen zu zwei unmittelbaren Konsequenzen: zu einem Bedarf an erhöhter Surveillance, oder gar zu direkten Interventionen, wie z. B. Ausbruchsuntersuchungen oder Impfaktionen. Beide Aufgaben haben neben der individualmedizinischen auch bevölkerungsmedizinische Bedeutung: und hier liegt die Schnittstelle zwischen der ambulanten bzw. stationären Versorgung und dem dritten Pfeiler des deutschen Gesundheitswesens: dem öffentlichen Gesundheitsdienst. Dessen Kernaufgaben sind eben genau die Überwachung der epidemiologischen Situation und das Eingreifen bei Infektionshäufungen bis hin zum Management von infektiologischen Krisensituationen.
Rund 400 Gesundheitsämter, Landesbehörden und Bundesinstitutionen bilden den „ÖGD" und arbeiten in Deutschland an der Aufdeckung und Bewältigung von Influenzapandemien, Ausbrüchen von EHEC-Bakterien oder lebensmittelbedingten Infektionen. Dabei ist ein wesentliches Element für erfolgreiches Handeln die Vernetzung zwischen Human- und Veterinärmedizin. Und das nicht nur auf dem Gebiet der Mikrobiologie oder auch der Epidemiologie, sondern ganz konkret auch bei der Zusammenarbeit zwischen Bundes- und Landesbehörden, und ganz besonders bedeutsam: zwischen kommunalen Behörden. Man könnte auch sagen: die Idee von „One Health" als interdisziplinärer Kollaboration und Kommunikation für alle Aspekte der gesundheitlichen Versorgung von Mensch, Tier und Umwelt in praktischer Umsetzung.
Damit diese Zusammenarbeit gefördert wird und das Handeln aller Beteiligten „evidenzbasiert" ist, braucht es darüber hinaus die enge Verzahnung zwischen Wissenschaft und Praxis. Und damit sind wir wieder bei der eingangs erwähnten Besonderheit des diesjährigen Nationalen Symposiums für Zoonosenforschung und dem Zitat von Willy Brand. Wie Sie aus dem Programm erkennen können, gibt es dieses Jahr verschiedene Plenarvorträge und Sessions, bei denen die Kongresssprache Deutsch ist. Dies sind die auch bereits nach außen wirkenden Zeichen für die Programmteile, bei denen der BVÖGD sowohl bei der Planung eingebunden war, als auch bei der Moderation beteiligt ist. Wir sind dafür sehr dankbar und hoffen darauf, dass die Themen und Referenten auf Ihr reges Interesse stoßen.
Dankbar ist der BVÖGD auch für die gute Zusammenarbeit mit dem Internen Beirat sowie der Nationalen Forschungsplattform Zoonosen insgesamt. Namentlich hervorheben möchten wir an dieser Stelle Frau Dr. Ilia Semmler und Frau Dr. Friederike Jansen, die uns als Ansprechpartner in allen organisatorischen Angelegenheiten mit Rat

und Tat zur Seite standen. Danken möchten wir auch sehr herzlich den Referentinnen und Referenten, die auf unsere Anfrage gerne bereit waren, Plenar- und Impulsreferate zu übernehmen.
Wir wünschen nun uns allen eine spannende Veranstaltung und interessante Diskussionen, auf dass der Untertitel „Research meets Public Health" oder auf Deutsch: Forschung trifft öffentliche Gesundheit" mit Leben erfüllt wird.

Ute Teichert

Vorsitzende des Bundesverbandes der Ärztinnen und Ärzte des Öffentlichen Gesundheitsdienstes (BVÖGD)

Jürgen Rissland

Sprecher für den Fachausschuss Infektionsschutz im Bundesverband der Ärztinnen und Ärzte des Öffentlichen Gesundheitsdienstes (BVÖGD)

Program

Thursday, October 15, 2015

08:00	**Registration (Poster Mounting)**
10:00 – 12:00	**Plenary Session** **(Room Ballsaal)** *Language English / German* Chair: *Stephan Ludwig*
10:00	Opening Remarks
10:30	**Keynote 1:** **MERS - a zoonotic disease disguised as a pandemic threat** Christian Drosten, Bonn, Germany
11:15	**Keynote 2:** **Luftgetragenen Mikroorganismen aus der Nutztierhaltung – Umweltmedizinische Risikobewertung aus Sicht der Öffentlichen Gesundheit** Caroline Herr, Munich, Germany
12:00	*Lunch and Poster Viewing*

14:00 – 15:30 Session 1: Epidemiology and modelling (Room Ballsaal)
Language: English
Chairs: *Anton Aebischer and Susanne Röhrs*

14:00 **Highly Pathogenic Avian Influenza H5N8 in Germany: Outbreak investigations**
F.J. Conraths, C. Sauter-Louis, A. Globig, K. Dietze, G. Pannwitz, K. Albrecht, D. Höreth-Böntgen, M. Beer, C. Staubach, T. Homeier-Bachmann

14:15 **Epidemiology and surveillance of acute febrile illnesses in southwestern Tanzania**
B. Flach, C. Mangu, H. Msila, L. Maboko, M. Hoelscher, N. Heinrich, G.Dobler

14:30 **Considering sheep movements when predicting human Q fever cases**
S. O. Brockmann, C. Wagner-Wiening, M. Eichner

14:45 **Assessing the potential health care and economic burden of Chikungunya across Europe**
S. M. Thomas, K. Kaiser, E. Schorling, N. B. Tjaden, C. Beierkuhnlein, K. H. Nagels

15:00 **Distribution of individual members of the *Anopheles maculipennis* complex in Germany known as vectors for zoonotic**
R. Lühken, C. Czajka, S. Steinke, H. Jöst, J. Schmidt-Chanasit, E. Kiel, A. Krüger, E. Tannich

15:15 **Geographical distribution of Tick-borne encephalitis virus in Central Europe**
S. Frey, S. Eßbauer, G. Dobler

14:00 – 15:30 Session 2: Pathogen-cell interaction (Room Zehlendorf)
Language: English
Chairs: *Christian Menge and Linda Brunotte*

14:00 **NFkappaB signalling pathway inhibition impairs Puumalavirus propagation**
O. Planz, U. Wulle, C. Hartmayer, P. Witkowski, D. H. Krüger

14:15 **TMPRSS11a activates influenza viruses and emerging coronaviruses**
P. Zmora, A.-S. Moldenhauer, S. Pöhlmann

14:30 **The chicken reproductive tract as a possible target tissue for H1N1 and H9N2 influenza viruses**
H. Sid, S. Hartmann, S. Rautenschlein

14:45 **Streptococcus suis affects the replication of swine influenza virus in porcine tracheal cells**
N.-H. Wu, F. Meng, M. Seitz, P. Valentin-Weigand, G. Herrler

15:00 **Quantitative proteomic analysis of protein signatures in permissive vs. non-permissive influenza A virus infections in human host cells**
A. Sadewasser, K. Paki, K. Eichelbaum, B. Bogdanow, M. Selbach, T. Wolff

15:15 **Functional relatedness between the surface glycoproteins of human and bat-derived mumps viruses**
N. Krüger, M. Hoffmann, M.A. Müller, J.F. Drexler, C. Drosten, C. Sauder, S. Rubin, C. Örvell, G. Herrler

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14:00 – 15:30 **Session 3: Risikobewertung (Room Steglitz)**
Language: German
Chairs: *Sandra Eßbauer and Jürgen Rissland*

14:00 **Impulsvortrag: Risikobewertung neu und wieder auftretender Zoonosen**
A. Ammon

14:20 **Risk of cross-contamination with ESBL E. coli and MRSA during handling of fresh chicken meat in household kitchens**
A. Fetsch, B.-A. Tenhagen, C. Thoens, Y. Kelner-Burgos, A. Kaesbohrer

14:35 **Analysis of environmental factors associated with the success of LA-MRSA in healthcare settings**
S. van Alen, B. Ballhausen, E.A. Idelevich, R. Köck, G. Peters, K. Becker

14:50 **Improving animal health - combining different sets of existing information in a Public-Private Partnership Information System (PPP-InfoS)**
A. Wendt, D. Meemken, G. Klein, T. Blaha, K. N. Knöll, T. May, L. Kreienbrock

15:05 Discussion

15:30 *Coffee Break and Poster Viewing*

16:00 – 17:30 **Public Health-Session: Antibiotika – Einsatz und Resistenzen**
(Room Ballsaal)
Language: German
Chairs: *Ute Teichert, Jürgen Rissland and Martin H. Groschup*

16:00 – 16:10 Antibiotika-Resistenz-Monitoring in Niedersachsen (ARMIN)
J. Dreesman

16:10 – 16:20 Aufgaben der Kommission *Antiinfektiva, Resistenz und Therapie*
M. Abele-Horn

16:20 – 16:40 Bekämpfung von Antibiotikaresistenzen in Tierhaltung und Lebensmittelproduktion
B.-A. Tenhagen

16:40 – 16:55 Antibiotika-resistente Erreger in Deutschland: die Rolle von zoonotischen Ansteckungsquellen
R. Köck

16:55 Discussion

17:30 – 19:30 **General Assembly German Research Platform for Zoonoses**
Room: Ballsaal
Language: German
Chair*: Sebastian C. Semler*

19:30 *Welcome Reception/Social Dinner*
Room: Ballsaal

Friday, October 16, 2015

07:30 – 09:00 **Young Scientists Breakfast**
Room: Restaurant

09:00 – 10:30 **Session 4: Antimicrobial use and resistance (Room Steglitz)**
Language: English
Chairs: *Peter Valentin-Weigand and Robin Köck*

09:00 **Potential of Artemisinin derivatives and trioxolanes as anti-Leishmania chemotherapy**
S. Cortes, A. Albuquerque, L. Cabral, L. Lopes, M.L. Cristiano, L. Campino

09:15 **Epidemiological relationship of ESBL-/AmpC-producing Enterobacteriaceae in the broiler cvproduction chain**
M. Projahn, K. Dähre, P. von Tippelskirch, S. Orquera, T. Alter, A. Friese, U. Rösler

09:30 **Identification of the novel oxazolidinone/phenicol resistance gene optrA and its distribution in Enterococcus faecalis and Enterococcus faecium of human and animal origin**
J. Li, A. T. Feßler, Y. Wang, Y. Lv, J. Cai, L.Cui, Z. Hu, R. Zhang, Q. Zhao, T. He, D.Wang, Z. Wang, Y. Shen, Y. Li, C.Wu, H. Yu, X. Deng, S. Schwarz, J. Shen

09:45 **Antimicrobial usage in human and veterinary medicine in Germany**
F. Lieke, M. Hemme, L. Kreienbrock

10:00 **Spread of antimicrobial resistance in the tropical setting – experiences from Mali**
R. M. Hagen, **R. Hinz**, S. Priesnitz, H. Frickmann

10:15 **The NF-κB inhibitor LG-ASA exhibits anti-pathogenic activity against influenza A virus and *S. aureus* co-infection *in vitro* and *in vivo***
I.L. Gieselmann, A. van Krüchten, S. Ludwig, **C. Ehrhardt**

09:00 – 10:30 Session 5: Public Health relevant zoonoses (Room Zehlendorf)
Language: English
Chairs: *Martin Pfeffer and Hendrik Scheinemann*

09:00 **Ebola Diagnostic Preparedness in Côte d'Ivoire**
C. Kohl, B. Diane, A. Kurth, R. Bärmann, D. Bourquain, S. Brödel, M. Collier, H. Ellerbrok, A. Etilé, J. Hinzmann, H. Laraway, A. Meerbach, A. Merckelbach1, J. Michel, P. Raab, M. Richter, C. Yue, C. Uhlenhaut, W. Biederbick, F. Leendertz, L. Schaade, C. Akoua-Koffi, F. B. Yapo, A. Nitsche

09:15 **Host association of Leptospira species in small mammals in Germany**
S. Fischer, A. Mayer-Scholl, N. Kratzmann, E. Heuser, S. Schmidt, U.M. Rosenfeld, K.

09:30 **Revelations from vaccination trials against anthrax in large animals: Improvement of diagnostic procedures and practical implications on the predicability of the outcome of an ongoing infection with *B. anthracis***
S.M. Koehler, O.C. Ndumnego, F. Buyuk, O. Celebi, S. Otluc, M. Doganay, M. Sahin, H. van Heerden, W. Beyer

09:45 **Infectious MERS-Coronavirus excretion and serotype variability based on live virus isolates from patients in Saudi Arabia**

D. Muth, V. M. Corman, M. A. Müller, B. Meyer, A. Assiri, M. Al-Masri, M. Farah, J. A. Al-Tawfiq, A. Albarrak, Z. A. Memish, C. Drosten

10:00 **Gorilla adenoviruses: cross-species transmission and recombination**
E. Hoppe, M. Pauly, G. Schubert, F. H. Leendertz, D. Sébastien-Calvignac-Spencer, B. Ehlers

10:15 **Sub-lethal sodium hypochlorite concentrations trigger antibiotic resistance in S. aureus *in vitro***
F. Kirchner, A.Feßler, C. Kopetz, M. Reinhardt, S. Schwarz, U. Truyen, **S. Speck**

09:00 – 10:30 Session 6: New and emerging zoonoses (Room Ballsaal)
Language: English
Chairs: *Gudrun Wibbelt and Isabella Eckerle*

09:00 **Crimean Congo hemorrhagic fever virus neutralizing antibodies in African bats**
M.A. Müller, S. Devignot, E. Lattwein, V. M. Corman, G.D. Maganga, F. Gloza-Rausch, T. Binger, P. Vallo, P. Emmerich, V. M. Cottontail, M. Tschapka, S. Oppong, J. F. Drexler, F. Weber, E.M. Leroy, C. Drosten

09:15 **Discovery of a novel zoonotic bornavirus: A One Health approach of awareness, modern diagnostics and multi-disciplinary networking**
B. Hoffmann, D. Tappe, D. Höper, Ch. Herden, K. Schlottau, A. Bolt, Ch. Mawrin, O. Niederstraßer, T. Müller, M. Jenckel, E. van der Grinten, Ch. Lutter, B. Abendroth, J.P. Teifke, K. Tauscher, Ch. Fast, S. Herzog, Ch. Frank, K. Stark, D. Cadar, J. Schmidt-Chanasit, R.G. Ulrich, **M. Beer**

09:30	**Identification and functional characterization of TMPRSS2 cleavage sites in the spike protein of SARS-coronavirus** **L. Reinke**, H. Hofmann-Winkler, S. Gierer, M. Winkler, S. Pöhlmann
09:45	**Origin and Evolution of Usutu virus, a neglected emerging arbovirus in Europe and Africa** D. Engel, H. Jöst, M. Wink, J. Börstler, S. Bosch, M-M. Garigliany, A. Jöst, C. Czajka, U. Ziegler, M. H. Groschup, M. Pfeffer, N. Becker, J. Schmidt-Chanasit, **D. Cadar**
10:00	**Hepatitis E virus genotype 3 induces infection dose dependent incubation times in domestic pigs** **L. Dähnert**, J. Schlosser, M. Eiden, A. Vina-Rodriguez, C. Schröder, A. Gröner, W. Schäfer, M. H. Groschup
10:15	**Cowpox virus virulence factors - genetic definition and *in vivo* testing** **A. Franke**, D. Hoffmann, A. Tamošiūnaitė, M. Jenckel, B. Hoffmann, N. Osterrieder, M. Beer
10:30	*Coffee Break and Poster Viewing*

11:00 – 12:30 **Session 7: Innate and adaptive immune response**
(Room Steglitz)
Language: English
Chairs: *Veronika von Messling and Stephan Ludwig*

11:00 **Targeted gene deletion in chickens as a powerful tool to dissect immune responses to zoonotic pathogens and vaccination in chickens**
B. Schusser, D. Aumann, M. Laparidou, K. Sutton, Rob Etches, B. Kaspers

11:15 **Immunopathology in a new model of haemorrhagic fever caused by hantavirus infection**
M.J. Raftery, L. Kobak, G. Schönrich

11:30 **Comparative analysis of Mycobacterium (M.) avium-complex (MAC) infections in a goat model**
H. Köhler, A. Zigan, J. Schinköthe, S. Fischer, P. Reinhold, P. Möbius, E. M. Liebler-Tenorio

11:45 **Inhibition of host cell entry of ebolaviruses by interferon-induced transmembrane proteins**
F. Wrensch, C.B. Karsten, K. Gnirß, M. Hoffmann, K. Lu, G. Simmons, M. Winkler, S. Pöhlmann

12:00 ***Campylobacter jejuni*** **colonization is influenced by genotype and feed composition in chicken.**
H. Zifeng, C. Pielsticker, T. Willer, L. Li, S. Rautenschlein

12:15 **Collagen VI harbors antimicrobial properties against oral pathogens**
M. N. Langer, M. von Köckritz-Blickwede, M. Mörgelin

11:00 – 12:30 **Session 8: Novel methods, diagnostics, NGS, and bioinformatics**
(Room Zehlendorf)
Language: English
Chairs: *Karsten Nöckler and Jens Hammerl*

11:00 **Development of pen-side methods for quick and easy detection of rabies**
K. Schlottau, E. Eggerbauer, C. Freuling, T. Müller, M. Beer, B. Hoffmann

11:15 **Detection of zoonotic bacteria in food by fluorescence in situ hybridization**
A. Rohde, J.A. Hammerl, B. Appel, R. Dieckmann, S. Al Dahouk

11:30 **Analysis of vaccine-induced rabies cases using deep sequencing**
F. Pfaff, C. Freuling, T. Müller, M. Beer, T. C. Mettenleiter, D. Höper

11:45 **Comparison of the infection of porcine precision-cut lung slices by porcine influenza virus H3N2 and porcine respiratory coronavirus PRCoV**
T. Krimmling, C. Schwegmann-Weßels

12:00 **Microevolution of Burkholderia mallei studied during a deliberate infection within its natural host**
E. Georgi, U. Wernery, M.H. Antwerpen, R. Werner, H.C. Scholz

12:15 **Separation of foreground and background reads in mixed NGS datasets**
S. Tausch, B. Y. Renard, A. Nitsche, **P. W. Dabrowski**

11:00 – 12:30 **Session 9: One Health und neue Zoonosen (Room Ballsaal)**
Language: German
Chairs: *Ute Teichert and Rainer Ulrich*

11:00 **Impulsvortrag: Exotische Zoonosen – eine Herausforderung für Forschung, Diagnostik und Gesundheitsdienste**
J. Schmidt-Chanasit

11:20 **Leptospirosis outbreak in field workers in Lower Saxony, Germany, 2014**
J. Dreesman, **S. Toikkanen**, M. Runge, L. Hamschmidt, B. Lüsse, J. Freise, J. Ehlers, K. Nöckler, C. Knorr, B. Keller, A. Mayer-Scholl

11:35 **Detection of hepatitis E virus in meat products from retail in Germany**
E. Trojnar, K. Szabo, H. Anheyer-Behmenburg, A. Binder, U. Schotte, L. Ellerbroek, G. Klein, R. Johne

11:50 **Survey for zoonotic pathogens in Norway rat populations from European cities**
J E. Heuser, **R. Ryll**, S. Fischer, M. Pépin, G. Müller, A-C. Heiberg, J. Lang, D. Hoffmann, S. Drewes, H. Ansorge, J. Freise, S. Guenther, R. Johne, A. Mayer-Scholl, K. Nöckler, S. Eßbauer, R.G. Ulrich

12:05 Discussion

12:30 *Lunch and Poster Viewing*

14:30 – 16:00 **Plenary Session**
(Room Ballsaal)
Language: English/German
Chair: *Martin H. Groschup*

14:30 **Keynote 3: Wild rodents in Europe – a reservoir for infectious agents?**
Heikki Henttonen, Vantaa, Finland

15:15 **Keynote 4: Die Rolle internationaler Großflughäfen bei der Verbreitung hochpathogener Krankheitserreger**
René Gottschalk, Frankfurt, Germany

16:00 **Poster Awards**

16:20 **Farewell**

General Information

Date and Venue
October 15-16, 2015
Best Western Plus Hotel Steglitz International
Albrechtstraße 2, 12165 Berlin
www.si-hotel.com

Conference Languages
The official conference languages are English and German.

Steering Committee
Martin H. Groschup (Greifswald - Isle of Riems)
Stephan Ludwig (Münster)
Sebastian C. Semler (Berlin)

Ute Teichert, Düsseldorf
Jürgen Rissland, Homburg

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Office of the German Research Platform for Zoonoses

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Greifswald - Isle of Riems:
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Björn Kaesz
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The poster awards are selected by the members of the Internal Advisory Board of the German Research Platform for Zoonoses.

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Young Scientists Breakfast
The Young Scientists Breakfast is going to take place at the "Pavillon" room of the hotel on Friday, October 16, at 7:30 am.
The attending senior scientists are:

Anton Aebischer, Berlin, Germany
Jan Felix Drexler, Bonn, Germany
Annemarie Käsbohrer, Berlin, Germany
Carolin Sauter-Louis, Riems, Germany
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Lunch Set-up
Due to the capacity of the venue premises, lunch will be served in two consecutive shifts. Please exercise some patience while seating yourself accordingly.

Continuous Medical Education
The National Symposium on Zoonoses Research 2015 is registered for 6 CME points of category A per day by the Berlin Chamber of Physicians (Ärztekammer Berlin). You will receive your certificate during the lunch breaks. Please note that you will need one barcode label per day for the confirmation of participation.

Continuous Veterinary Education
The National Symposium on Zoonoses Research 2015 is registered for 9 hours (ATF-Stunden) by the Federal Chamber of Veterinarians (Bundestierärztekammer). You will receive your certificate during the lunch break on the second day of the symposium.

Poster Presentations
Posters will be presented during both days of the conference. Poster presenters should refer to this booklet to find the poster session and board number assigned to them. Please use the poster board with the designated number. Poster presenters are responsible to remove the posters at the end of the conference.

Oral Presentations
Oral presentations should be handed over on a common data carrier at the registration desk on Thursday, October 15, between 8.00 am and 1.00 pm. All session rooms will be equipped with a PC computer

and a LCD projector. Apple computers are not available. Please make sure, that you use either a powerpoint or a pdf file format.

Internet Access
For internet access you are pleased to register at the hotel reception in the ground floor. WLAN will be provided without charge.

Funding
The National Symposium on Zoonoses Research is funded by the Federal Ministry of Education and Research.

This year´s symposium is organized in close cooperation with:

Akademie für öffentliches Gesundheitswesen in Düsseldorf

BbT
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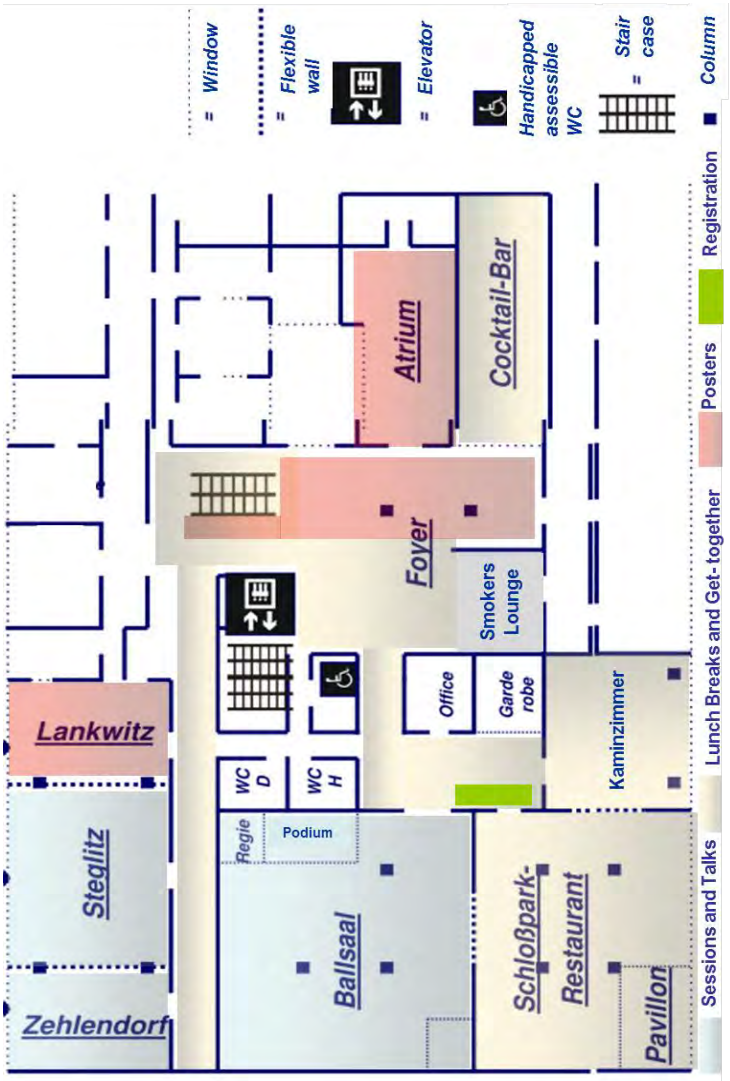
BVÖGD Bundesverband der Ärztinnen und Ärzte des Öffentlichen Gesundheitsdienstes e.V.

AG TT Arbeitsgruppe Tiergesundheit und Tierseuchen - eine AG der Länderarbeitsgemeinschaft Verbraucherschutz

Floor Plan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Zehlendorf
Ballsaal
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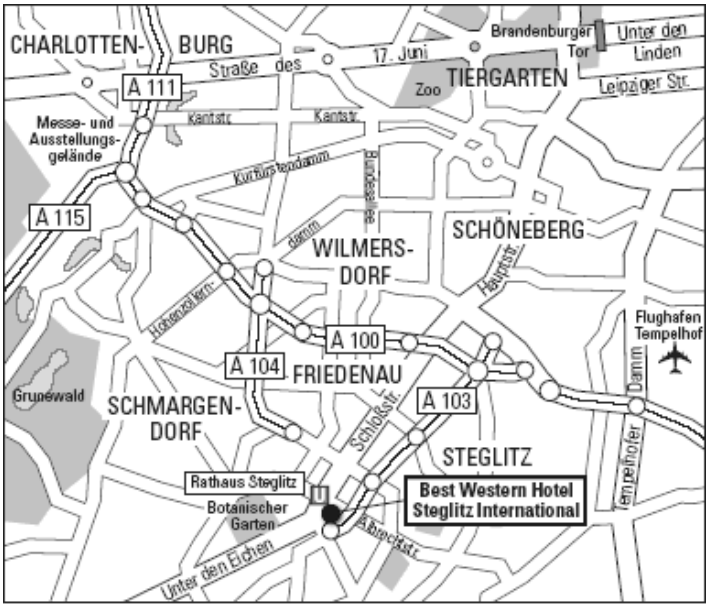
Smokers Lounge
Office
Garde robe
Kaminzimmer
Schloßpark-Restaurant
Pavillon

Site Plan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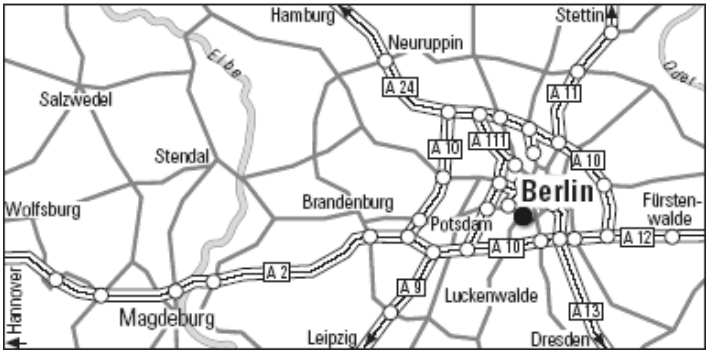
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Dresden

About the German Research Platform for Zoonoses

The German Research Platform for Zoonoses is a central information and service network, initiated and funded by the German Federal Ministry of Education and Research (BMBF) in 2009, for all working groups operating in Germany in the field of zoonoses research.

The objective of the platform and its currently over 600 members is to increase the exchange of professional experiences and knowledge at national and international levels and thus intensify research activities in the field of zoonoses research, promoting broad horizontal cross-linking of human and veterinary medicine as well as other scientific disciplines related to zoonotic disease research and public and veterinary health services. To develop and maintain sustainable and flexible solutions strengthening research, prevention and therapy of zoonotic infectious diseases in Germany, the Research Platform offers the following measures:

- Organization and realization of joint events that support interdisciplinary exchange and interaction.
- Encouragement of communication as well as national, European and international collaboration.
- Registration, harmonization and standardization of existing resources, including the setting up of both real and virtual specimen databases (i.e. the Database Internet Portal)
- Providing information about zoonotic infectious diseases for the general public
- Initiation and realization of innovative and interdisciplinary pilot projects of a cross-sectional nature
- Support and counseling for the design and implementation of zoonotic funding schemes
- Furtherance of junior scientists in the field of zoonosis research

Acting as a central service point that provides fact-oriented, transparent information relating to research on zoonoses both for politics and the general public, the German Research Platform aims to be the definite voice of German zoonosis research. Additionally,

the platform also promotes a continuous and intensive exchange of expertise between scientists from all over the world.

As part of these activities, the German Research Platform for Zoonoses organizes every year the National Symposium on Zoonoses Research with up to 350 participants.

Furthermore, scientific workshops, also for researchers at the beginning of their career, are organised, where specific topics are presented and discussed.

All researchers working on zoonoses in Germany are welcomed to join the German Research Platform for Zoonoses.

For further information please visit our website www.zoonosen.net.

Oral Presentations

Plenary Sessions

October 15, 2015
10:30 – 12:00
Room: Ballsaal
Chair: Stephan Ludwig

and

October 16, 2015
14:30-16:00

Room: Ballsaal
Chair: Martin H. Groschup

MERS - a zoonotic disease disguised as a pandemic threat

C. Drosten, University of Bonn, Germany

The Middle East respiratory syndrome coronavirus (MERS-CoV) was first isolated in 2012 from a man who died of viral pneumonia in Saudi Arabia. Due to the relatedness of the MERS virus with the agent of SARS (severe acute respiratory syndrome), public health authorities around the globe urged on assessments of the pandemic risk associated with the new agent. After the standards for MERS detection and diagnostics had been defined, work was initiated to understand the etiology, transmission and spread of MERS-CoV in the region of emergence. Based on the exposure history of a patient treated in Munich/Germany, samples from several livestock species were tested, identifying dromedary camels as carrier of specific MERS-CoV antibodies. Direct infection of humans from camels has since been documented in several cases. MERS-CoV was found in a series of studies to exist at high prevalence in camels across the Arabian Peninsula and Eastern/Subsaharan Africa. Earliest samples investigated in these studies dated back to 1983. During an investigation of 26 human household contact clusters across KSA, secondary infections including subclinical transmissions from index cases to any household contact were seen in less than half of all cluster, suggesting human-to-human transmission chains cannot be maintained. A national serosurvey in the Kingdom of Saudi Arabia based on >10,000 persons matching the age structure and geographic distribution of the Saudi population yielded antibodies in 0.15% of people, suggesting seroprevalence far below what is expected for a virus that is continuously transmitted in the population. Cohorts of subjects with occupational exposure to camels had up to 23-fold higher seroprevalence against MERS-CoV. These data in summary suggest humans across the region have been exposed to MERS-CoV for decades without evidence for further spread of the virus. In spite of a high case fatality proportion associated with infection, MERS must be considered a classical zoonosis that is directly acquired by contact with livestock.

Luftgetragenen Mikroorganismen aus der Nutztierhaltung – Umweltmedizinische Risikobewertung aus Sicht des Öffentlichen Gesundheitsdienstes

C. Herr, Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit, Germany

Die Ansiedlung großer Tierhaltungsanlagen führt insbesondere bei Anwohnern in der Nachbarschaft solcher Anlagen zu Akzeptanzproblemen. Im Rahmen von Baugenehmigungs- und Nachbarklageverfahren wird hierzu häufig Stellung genommen. Für Bioaerosole im Außenluftbereich sind weder Dosis-Wirkungs-Beziehungen bekannt noch existieren Grenzwerte. Die umweltmedizinische Bewertung erfolgt auf Basis der VDI-Richtlinie 4250 Blatt 1 „Bioaerosole und biologische Agenzien – Umweltmedizinische Bewertung von Bioaerosol-Immissionen – Wirkungen mikrobieller Luftverunreinigungen auf den Menschen". Nach dem Bewertungsschema dieser Richtlinie ist es aus präventiver Sicht unerwünscht, dass die ortsübliche natürliche Hintergrundkonzentration in der Nachbarschaft durch anlagenspezifische Immissionen deutlich überschritten wird. Beispielsweise können in der Stallluft enthaltene Staphylokokken und resistente Mikroorganismen, die nicht im Hintergrund zu erwarten sind, mit der Abluft aus den Ställen freigesetzt werden. Besonders für Risikogruppen wie immuneingeschränkte Personen, Allergiker und Atemwegsvorgeschädigte kann eine zusätzliche Bioaerosolimmission mit einem zusätzlichen Gesundheitsrisiko verbunden sein. Die umweltmedizinische Bewertung erfolgt auf Basis von Immissionsprognosen (Ausbreitungsrechnung). Da die Ergebnisse der Ausbreitungsrechnung erheblich von den realen Messergebnissen vor Ort nach Inbetriebnahme der Anlagen abweichen können, kann es aus umweltmedizinischer Sicht notwendig sein, Immissionsmessungen anlagenspezifischer Bioaerosole im Einwirkungsbereich von Ansiedlungen in der Nachbarschaft sowie Messungen der Hintergrundkonzentration durchzuführen.

Wild rodents in Europe – a reservoir for infectious agents

H. Henttonen, Natural Resources Institute Finland

I will first review the general occurrence and distributions of important rodent-borne pathogens in Europe. I consider rodents *sensu lato* including also pathogens hosted by insectivores. These include hantaviruses, cowpox, arenaviruses, possible Ljungan-type viruses, tularemia and yersinias. I will clarify the epidemiology of well-studied systems, using hantas and tularemia as examples, showing how environmental factors greatly impact the transmission and epidemiologic outcome in rodents and humans, and they do it in different ways in different biomes. Hence our slogan, *biome spefific epidemiologies*. I use the Puumala hantavirus in Europe as the important model. Hantaviral epidemiological patterns are related to the dynamics of reservoir rodent species. In temperate Europe masting is the important driver of bank vole (*Myodes glareolus*) fluctuations and hence hanta epidemics (mostly due to Puumala virus, PUUV), and it has been suggested that warm summers induce masting. In contrast, in boreal northern Europe, specialist predation is thought be the main driver. Consequently, the underlying top-down or bottom-up causes of rodent fluctuations are different depending on the biome. When survey periods are long enough, in addition to short-term fluctuations (3-4 y), long-term trends can be observed, superimposed on the shorter "cycles", possibly due to the climatic changes. There are clear seasonal differences in the transmission dynamics of PUUV between biomes, affecting seasonality of human epidemics. Landscape structure and changes affect host/pathogen spread in the environment. New findings on the transmission of PUUV and the impacts of PUUV on voles will be reviewed.

Session 1: Epidemiology and modelling

October 15 2015
14:00 – 15:30

Room Ballsaal
Chairs: Anton Aebischer and Susanne Röhrs

Highly Pathogenic Avian Influenza H5N8 in Germany: Outbreak investigations

F. J. Conraths[1], C. Sauter-Louis[1], A. Globig[1], K. Dietze[1], G. Pannwitz[2], K. Albrecht[2], D. Höreth-Böntgen[1], M. Beer[1], C. Staubach[1], T. Homeier-Bachmann[1]

[1]Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Greifswald-Insel Riems, Germany; [2]Landkreis Vorpommern-Greifswald, Greifswald, Germany

Keywords: avian influenza, emerging diseases, epidemiology

Background and objectives: In November 2014, highly pathogenic avian influenza virus H5N8 was first detected in Europe in a turkey farm in Mecklenburg-Western Pomerania, Germany, followed by outbreaks in the Netherlands, the United Kingdom, Italy, Hungary and another five outbreaks in Germany. Epidemiological investigations were conducted in affected poultry holdings and a zoo to identify potential routes of entry of the pathogen via water, feedstuffs, animals, people, bedding material, other fomites (equipment, vehicles etc.), and the presence of wild birds near affected holdings.

Materials and methods: Data were obtained by on-site visits to the holdings and structured interviews with farm managers and veterinarians. Additional data were extracted from invoices, trade documents (purchase of poultry and feed) and stable records.

Results: The highest mean risk scores were observed for the factor 'wild birds' with low uncertainty. The risk of introduction into the commercial poultry farms via indirect contact with materials (e.g. bedding material) contaminated by infected wild bird feces used on the affected premises was estimated to be highest.

Conclusion: Indirect introduction of HPAIV H5N8 by material infected wild bird feces seems to be the most reasonable explanation for the outbreaks in the affected commercial holdings. The introduction into small free-range poultry holding and the zoo was probably caused by direct introduction through wild birds.

Epidemiology and surveillance of acute febrile illnesses in southwestern Tanzania

B. Flach[1,2], C. Mangu[2,3], H. Msila[2,3], L. Maboko[2,3], M. Hoelscher[4,5], N. Heinrich[4,5], G. Dobler[1,2]

[1]Bundeswehr Institute of Microbiology, Munich, Germany; [2]German Partnership Program for Excellence in Biological and Health Security, Munich, Germany; [3]NIMR-Mbeya Medical Research Center, Mbeya, Tanzania; [4]Division for Infectious Diseases and Tropical Medicine, Medical Center of the University of Munich, Germany; [5]German Center for Infection Research, Munich Partner Site, Munich, Germany

Keywords: Epidemiology, Infection, Zoonoses

Background and objectives: To study and diagnose the cause of acute febrile diseases in vulnerable patients in southwestern Tanzania. Febrile illness is one of the major contributions of hospital admissions and death.
Materials and methods: Individuals with >37.5°C fever were enrolled into the study. Individuals were tested for HIV and Malaria using governmental rapid test kits. RNA was isolated using QIAGEN viral RNA kit and assessed for nucleic acid testing by RPA (TwistDX). Blood culture bottles (BD) were inoculated at visit 1 and evaluated for bacterial growth.
Results: 189 patients have been enrolled to this point. 67.8% of all enrolled patients were <18 years, and 54,3% were female. Body temperature ranged from 38.5°C to 41.1°C (Median 38.6°C). 12,2% of all patients tested positive for HIV. 55.4% of patients tested positive for Malaria, of which 53.6% identified as *Plasmodium falciparum*. 115 subjects were so far tested for detection of viral nucleic acid but remained negative for the following viruses: Yellow Fever, Rift Valley Fever, Dengue 1-3 and 4, West Nile and Chikungunya Virus. 15 % of all enrolled patients showed a positive blood culture and the preliminary identification of bacterial species revealed a high number of *Salmonella ser typhi,* along with *Staphylococcus spp*.
Conclusion: Understanding the cause of acute febrile illness may help to target prevention and disease transmission and improve treatment interventions.

Considering sheep movements when predicting human Q fever cases

S. O. Brockmann[1], C. Wagner-Wiening[2], M. Eichner[3]

[1]Regional Health Office, Reutlingen, Germany; [2]Baden-Württemberg State Health Office, Stuttgart, Germany; [3]Department of Clinical Epidemiology and Applied Biometry, University of Tübingen, Germany

Keywords: Q fever, epidemiology, sheep

Background and objectives: Human Q fever cases are frequently associated with ungulate contact. In this study, we analyze risk factors for human Q fever cases.

Methods: Detailed information on notified human Q fever cases from 2001 to 2008 were collected from local health offices. Using 3 hierarchically organized maximum likelihood models, we predicted the number of notified human Q fever cases on municipality level. Independent variables included the actual presence of sheep on municipality level (220,000 resident animals corrected for time and place of pasture, documented by 205,063 movement applications), drought index, number of cattle (1,050,000 animals), and human population density on municipality level.

Results: In the study period, 259 human Q fever events (single cases and outbreaks) with a total number of 422 cases were reported from 191 municipalities (whereby 13 outbreaks caused 41% of cases). Sheep density was an important predictor: the predicted relative risk of a disease increased from 1 (0 sheep/km^2) to 2.8 (1/km^2), 19.2 (10/km^2) and 182.6 (100/km^2), respectively. Drought and the prevalence of cattle were of minor importance.

Conclusion: Considering temporal positioning of sheep proved to be an important model feature to predict the number of human cases. To prevent further outbreaks we recommend strengthening of Q fever-monitoring in sheep. Veterinary Health authorities and sheep owners may consider vaccination of female sheep as a preventive measure.

Assessing the potential health care and economic burden of Chikungunya across Europe

S. M. Thomas[1], K. Kaiser[2], E. Schorling[2] Nils B. Tjaden[1], C. Beierkuhnlein[1], K. H. Nagels[2]

[1]Department of Biogeography, University of Bayreuth, Bayreuth, Germany; [2]Institute for Healthcare Management and Health Sciences, University of Bayreuth, Bayreuth, Germany

Keywords: Chikungunya, cost-of-illness, burden of disease

Background and objectives: Due to climate change vector-transmitted diseases like Chikungunya gain importance as public health risks in previously unaffected areas. Former Chikungunya outbreaks were focused on Africa, India and the Caribbean. The first European epidemic in 2007 could be limited to 200 cases due to isolation of affected areas. In the light of ongoing climate change, rapid spread of pathogens represents an emerging public health risk across Europe. Chikungunya can serve as a case study to assess health and economic burden.

Materials and methods: The following models have been applied: 1. bioclimatic envelope modelling for both vector and disease as a whole, to project future areas at risk under climate change, 2. extrapolation of Chikungunya cases by combining bioclimatic models with epidemiological data, 3. modelling the course of disease, 4. analysing and predicting clinical and economic outcomes across Europe.

Results: Bioclimatic envelope modelling shows that vector mosquito *Ae. albopictus* is able to survive in certain areas of Europe. Cost-of-illness studies reveal medical costs ranging from €60 to €120 per case and higher costs at persistent complications, which occur in 12% of cases. This implies a potentially high economic burden in case of a Chikungunya outbreak in Europe.

Conclusion: Our results show that an outbreak of Chikungunya in Europe is possible and the economic and health burden is relevant for public health.

Distribution of individual members of the *Anopheles maculipennis* complex in Germany known as vectors for zoonotic pathogens

R. Lühken[1], C. Czajka[1], S. Steinke[2], H. Jöst[1,3], J. Schmidt-Chanasit[1,3], E. Kiel[2], A. Krüger[4], E. Tannich[1,3]

[1]Bernhard Nocht Institute for Tropical Medicine, WHO Collaborating Centre for Arbovirus and Haemorrhagic Fever Reference and Research, Hamburg, Germany; [2]Research group Aquatic Ecology and Nature Conservation, Carl von Ossietzky University Oldenburg, Oldenburg, Germany; [3]German Centre for Infection Research, partner site Hamburg-Lübeck-Borstel, Hamburg, Germany; [4]Bundeswehr Hospital Hamburg, Hamburg, Germany

Keywords: Anopheles maculipennis complex, species distribution modelling

Due to their role as vectors of malaria parasites, species of the *Anopheles maculipennis* complex were intensively studied in the past, but with the disappearance of malaria in Germany in the middle of the last century, interest in this field of research declined. Although members of the *An. maculipennis* complex (*An. atroparvus*, *An. daciae*, *An. maculipennis* s.s., *An. messeae*) were recently identified to be potential vectors of *Dirofilaria* ssp. and Batai virus in Germany, a comprehensive ecological analysis of the current species distribution of all four members is lacking. Between 2010 and 2013, a total of 722 individuals and 90 pools comprising another 723 imagines of the *An. maculipennis* complex were collected at 72 different sites distributed over Germany and the various members were distinguished by newly developed molecular methods. The results indicated highest prevalence for *An. messeae* representing 69.53% of all individuals followed by *An. maculipennis* s.s. (13.30%), *An. daciae* (6.93%), and *An. atroparvus* (1.80%). Most remarkable was the low prevalence of *An. atroparvus* compared to historic data, which might be explained by the specific requirements for overwintering of this species. This is one of the first studies, which demonstrated that environmental data are useful to predict the spatial distribution of German mosquito species. These models could, for example, be incorporated into risk models for mosquito-borne diseases.

Geographical distribution of Tick-borne encephalitis virus in Central Europe

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[1]Bundeswehr Institute of Microbiology, Munich, Germany

Keywords: Tick-borne encephalitis virus, distribution

Tick-borne encephalitis (TBE) is the most important tick-borne virus disease in humans in Central Europe. The causative agent is a virus of the genus *Flavivirus* within the family of Flaviviridae. So far no efforts were conducted to sub-type the European subtype of TBE virus and finally to sub-classify into genetic clades or genotypes to clarify the geographic distribution of this subtype and also to construct possible ways of spread.
In an effort to identify the TBE virus strains circulating in Central Europe we sequenced the E genes of more than 100 TBE virus strains and compared the sequences with TBE virus E gene sequences which were available in the data base.
The analyzed E genes of the TBE viruses could be distinguished in more than 10 different genotypes. Some of the genotypes could be only detected in single TBE foci or in TBE natural foci close to each other. Some other genotypes included strains which were originally located over whole countries or even were distributed over the whole European continent. Although the E gene homologies were high, viruses from each focus could be distinguished from viruses from other foci. So far, it cannot be understood exactly how the geographic distribution might have happened but our data give some ideas to carve out some possible ways of spread.
More phylogenetic data are needed to finally get a complete picture of the distribution of TBE virus and then again try to establish models on the spread of TBE virus in Europe.

Session 2: Pathogen-cell interaction

October 15 2015
14:00 – 15:30

Room Zehlendorf
Chairs: Christian Menge and Linda Brunotte

NFkappaB signalling pathway inhibition impairs Puumalavirus propagation

O. Planz[1], U. Wulle[1], C. Hartmayer[1], P. Witkowski[2], D. H. Krüger[2]

[1]Interfaculty Institute for Cell Biology, Department of Immunology, Eberhard Karls University of Tübingen, Tübingen, Germany; [2]Institute of Virology, Campus Charite Mitte, Berlin, Germany

Keywords: Hantavirus, Antivirals, Signaling pathway

Background and objectives: Puumalavirus (PUUV), the most prevalent hantavirus in Europe is causing hemorrhagic fever with renal syndrome often called nephropathia epidemica. PUUV is transmitted by bank voles (*Myodes glareolus*) and infections of humans are common in endemic areas such as the Swabian Alb in Southern Germany. Antivirals against PUUV are not available; nevertheless reports have shown that ribavirin can be useful in the very early stage of the disease. Thus, there is an urgent need to develop antivirals. Based on our work with influenza virus the objective of the present study was to investigate whether PUUV replication is dependent on intracellular signalling pathways.
Materials and methods: Vero cells and Vero cells with impaired and active NFkappaB were used for PUUV-infections (strain: Sotkamo). PUUV-infected Vero cells were also treated with different drugs inhibiting the NFkappaB and the Raf/MEK/ERK signalling pathway.
Results: We were able to improve PUUV-infection of Vero cells in order to perform our antiviral-assays. PUUV replication is drastically reduced in Vero cells with impaired NFkappaB signalling. NFkappaB-inhibitors and MEK-inhibitors are able to reduce viral titers in PUUV-infected Vero cells.
Conclusion: PUUV replication is dependent on the activation of the NFkappaB and Raf/MEK/ERK signalling pathways. Inhibition of theses pathways leads to strongly reduced virus production. Pre-clinical *in vivo* experiments are needed as a next step.

TMPRSS11a activates influenza viruses and emerging coronaviruses

P. Zmora[1], A.-S. Moldenhauer[1], S. Pöhlmann[1]

[1]Infection Biology Unit, German Primate Center, Göttingen, Germany

Keywords: TMPRSS11a, protease, influenza

Type II transmembrane serine proteases (TTSP) have been implicated in the proteolytic activation of the surface proteins of influenza A viruses (FLUAV) and coronaviruses (CoV). However, it is incompletely understood which members of the TTSP family can activate these viruses. Our study focussed on TMPRSS11a, a TTSP previously reported to be expressed in the respiratory system.

We found that ectopically expressed TMPRSS11a cleaves and activates the surface proteins of FLUAV and emerging CoVs and that TMPRSS11a activity can be suppressed by the serine protease inhibitors camostat and serpin1. Moreover, endogenous TMPRSS11a facilitated trypsin-independent FLUAV spread in HepG2 cells and PCR analysis showed that TMPRSS11a mRNA is expressed in the human respiratory tract, indicating that this protease could contribute to viral spread *in vivo*. Finally, we obtained evidence that TMPRSS11a can counteract the host cell-encoded antiviral factor tetherin, suggesting that this protease might promote viral spread via two mechanisms: activation of viral surface proteins and inactivation of cellular factors with antiviral activity. Collectively, our results identify TMPRSS11a as an activator of respiratory viruses and suggest that this protease could support viral spread in the host.

The chicken reproductive tract as a possible target tissue for H1N1 and H9N2 influenza viruses

H. Sid[1], S. Hartmann[1], S. Rautenschlein[1]

[1]Clinic for Poultry, University of Veterinary Medicine Hannover, Foundation, Hannover, Germany

Keywords: Influenza A virus, Chicken, reproductive tract

Background and objectives: Most of Influenza A viruses target the respiratory and intestinal tract in poultry, little is known regarding the interaction of these viruses with other epithelial surfaces. Pandemic H1N1 influenza virus was shown to induce a drop in egg production in turkeys, while a recent study demonstrated replication of H9N2 avian Influenza virus (AIV) in the chicken oviduct. Therefore, we investigated *in vitro* the virus-host interaction, especially the innate antiviral responses, in the reproductive tract of poultry.
Materials and methods: We used explant cultures of the juvenile chicken oviduct. The replication pattern and induction of interferons (IFN) including IFN type I (IFN-alpha) as well as IFN type III (IFN-lambda) were determined at 24 and 48 h after inoculation with A/chicken/Saudi Arabia/CP7/1998 (H9N2) or A/Giessen/06/09 (H1N1).
Results: Both viruses replicated in the oviduct without the need for exogenous proteolytic activation, while higher titers were achieved after H9N2-infection. A significant up-regulation of IFN-lambda mRNA expression ($p<0.05$) was observed after infection with H9N2 at both investigated time points.
Conclusion: This study demonstrates the susceptibility of the chicken oviduct for AIV and may suggest a possible role of the oviduct in virus distribution to the progeny as well as the environment.

Streptococcus suis affects the replication of swine influenza virus in porcine tracheal cells

N.-H. Wu[1], F. Meng[1], M. Seitz[2], P. Valentin-Weigand[2], G. Herrler[1]

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Keywords: co-infection, swine influenza virus, Streptococcus suis

Secondary infection by *Streptococcus suis* may enhance the severity of disease in piglets infected by Swine influenza viruses (SIV) resulting in substantial economic losses. In order to understand the interaction between SIV and *S. suis*, we established an *in vitro* co-infection model based on newborn pig trachea cells (NPTr).
Two SIV variants A/sw/Bad Griesbach/IDT5604/2006 H1N1 and A/sw/Herford/IDT5932/2007 H3N2 were used to compare subtype differences. Wild type *S. suis* serotype 2 strain 10 (wt) and a noncapsulated mutant strain (Δcps) were used as secondary infectious agents in this study. NPTr cells were first inoculated with SIV, followed by bacterial inoculation. The course of infection was monitored by immunofluorescence microscopy and by determining the virus titers at different time points.
Our results show that the viral hemagglutinin expressed on the surface of virus-infected cells interacted with the capsular polysaccharide and thus enhanced the binding of *S. suis* and facilitated bacterial infection. The release of H1N1 and H3N2 SIV were delayed when NPTr cells were co-infected with *S. suis*.
These findings indicated that *S. suis* and SIV affect each other in the infectious behavior in NPTr cell. This interaction is mediated by hemagglutinin of influenza viruses that recognizes α2,6-linked sialic acid on the capsular polysaccharide of *S. suis.*

Quantitative proteomic analysis of protein signatures in permissive vs. non-permissive influenza A virus infections in human host cells

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Keywords: Influenza A Virus, Quantitative Proteomics, Host Specificity

Background and objectives: Influenza A virus (IAV) infections are the major cause for respiratory disease in humans. Most avian and human IAV strains differ in their replication efficiency in and activation of human cells despite successful cell entry. We hypothesize that the distinct outcome of an IAV infection with a given virus strain is determined by the differential interplay between specific host and viral factors, which remain to be defined entirely.
Materials and methods: We used a "Spike-in SILAC" approach in human A549 cells that are highly permissive for seasonal H3N2 IAV, but restrict replication of avian H3N2 virus. This setup allows the definition and quantitative comparisons of changes in host cell proteomes in response to infections with these two viruses.
Results: We quantified about 3500 proteins and identified distinct sets of cellular factors influenced by infections with the human or avian strain, respectively. Rapid apoptotic cell death was excluded as restriction factor for impaired avian IAV replication. Ongoing studies involve the validation of differentially regulated proteins as well as functional analyses to elucidate their roles in IAV infection and their potential contributions to IAV adaptation to human cells.
Conclusion: Here, we present results of a comprehensive analysis of host pathogen interaction networks by using systems biology tools. We expect to identify key parameters related to efficient IAV replication and host specificity.

Functional relatedness between the surface glycoproteins of human and bat-derived mumps viruses

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Keywords: mumps virus, bats, viral entry

Background and objectives: Mumps is a highly contagious childhood disease with usually mild symptoms caused by mumps virus (MuV), a member of the family *Paramyxoviridae*. So far, humans are the only known host of MuV. The detection of RNA of a MuV-related virus (BatPV/Epo_spe/AR1/DCR/2009, batMuV) in African flying foxes raises the question if bats may serve as an intermediate or reservoir host for MuV.
Materials and methods: The ORFs of the fusion (F) and hemagglutinin-neuraminidase (HN) protein of batMuV and a human MuV isolate (hMuV) were cloned into expression plasmids. The F and HN proteins were coexpressed in different mammalian cell lines to analyze their ability to mediate syncytium formation. The biological activities of the HN were investigated in hemadsorption and neuraminidase activity assays.
Results: The coexpression of batMuV F and HN resulted in cell-to-cell fusion in chiropteran, simian, rodent, and human cells. Those syncytia were smaller compared to that induced by hMuV F and HN. The phenotype of syncytia could be attributed to different surface expression levels of the F proteins which were determined by the signal peptide. Further, it could be demonstrated that batMuV HN exhibits neuraminidase activity and interacts with cellular sialic acids.
Conclusion: Our results indicate that there is a high relatedness between the glycoproteins of the human and bat-derived MuV, not only based on the highly conserved sequences, but also on the functional activity.

Session 3: Risikobewertung

October 15 2015
14:00 – 15:30

Room Steglitz
Chairs: Sandra Eßbauer and Jürgen Rissland

Risk of cross-contamination with ESBL *E. coli* and MRSA during handling of fresh chicken meat in household kitchens

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Keywords: cross-contamination, ESBL- E. coli, MRSA

Background and objectives: Extended-spectrum beta-lactamases (ESBL) producing *Escherichia (E.) coli* and Methicillin-resistant *Staphylococcus aureus* (MRSA) frequently enter household kitchens via food, e.g. chicken meat. The level of cross-contamination in the kitchen currently remains unknown hindering reliable risk assessments for both bacteria. The aim of this study was to quantify the transfer of ESBL-*E. coli* and MRSA from chicken meat to hands, and the kitchen equipment and from there onto ready-to-eat foods.
Materials and methods: In two different scenarios each with ten repetitions realistic situations in household kitchens were simulated. Fresh chicken breast filets were contaminated with log 5-7 CFU per 20cm^2 of either ESBL- *E. coli* or MRSA and stored overnight at +4^{0}C. Scenario 1 simulated the transfer of bacteria to consumer's hands. In the same scenario, cutting of chicken meat and the reuse of the same knife and cutting board without cleaning for slicing of bread were simulated. In scenario 2, transfer from contaminated plates to grilled chicken meat, not previously contaminated, was investigated. The numbers of bacteria were estimated by colony counting techniques using selective agar plates.
Results: Results of the two scenarios were highly homogenous with low standard deviations per step. Surprisingly high CFU counts were seen. Transfer rates for each of the handling step retrieved significant differences between the handling steps and between ESBL- *E. coli* and MRSA.
Conclusion: Cross-contamination with ESBL- *E. coli* and MRSA during handling of fresh chicken meat in household kitchens occur. Raw chicken meat may contribute to the exposure of consumers. Data will be used to feed quantitative risk assessment models.

Analysis of environmental factors associated with the success of LA-MRSA in healthcare settings

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Keywords: LA-MRSA CC398, Minimum inhibitory concentration, heavy metals

In the past 15 years, livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) of clonal complex CC398 emerged in regions with high livestock density. To date, little is known about the underlying conditions of the successful spread of this zoonotic *S. aureus* lineage in healthcare settings. Here, we studied whether external environmental factors present in healthcare settings offer a selective advantage for LA-MRSA.

The minimum inhibitory concentrations (MICs) of heavy metal ions (zinc chloride, copper sulphate, nickel chloride) of LA-MRSA CC398 isolates were determined in comparison to HA-MRSA. For that purpose, CC398 strains covering the period from their first detection in the North-West German Münsterland area in 2000 until today were included. The zinc-resistance phenotype was confirmed by a PCR-based analysis of the *czrC* gene.

Overall, 142 CC398 strains as well as 142 HA-MRSA strains have been included. Interestingly, the MICs of zinc chloride were considerably higher in LA-MRSA (MIC_{50}, 2 mM; MIC_{90}, 4 mM) in comparison to HA-MRSA (MIC_{50}, 0.5 mM; MIC_{90}, 1 mM). No differences between LA-MRSA and HA-MRSA were found for copper sulphate (MIC_{50} and MIC_{90}, each 8 mM) and nickel chloride (MIC_{50} and MIC_{90}, each 8 mM).

In summary, the results of this study reveal decreased sensitivity of LA-MRSA to zinc chloride. The co-selection of methicillin resistance by zinc resistance could be linked to the success of this zoonotic *S. aureus* lineage in the healthcare environment.

Improving animal health - combining different sets of existing information in a Public-Private Partnership Information System (PPP-InfoS)

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Keywords: data integration, health indicators, animal welfare

Improving animal health has profound impact on public health, for example through better food supply and food security, the reduction of zoonotic and animal diseases or as social good. Throughout the lifetime of a farm animal, many sets of information are collected and documented by farmers and their practitioners, official veterinarians and slaughterhouse operators. Some of them might serve as animal health indicators to describe animal health on herd level. Aiming at improving animal health, it is expected to get a better insight into animal health by combining relevant sets of information from the private and the public sector within the food chain.
Funded by the Federal Office for Agriculture and Food (BLE) and the Landwirtschaftliche Rentenbank, the PPP-InfoS project has started, to first view the existing data which might serve as possible indicators. Then, relevant variables will be selected and integrated into the system to finally provide a tool for the prevention and early warning of health and welfare deficiencies. As this project addresses many new topics in this area, there will be challenges arising from data integration, secondary use and data sharing, but also from confidentiality issues. Dealing with them will produce valuable insight and a data protection concept for integrating public and private data along the food chain.

Session 4: Antimicrobial use and resistance

October 16 2015
09:00 – 10:30

Room Steglitz
Chairs: Peter Valentin-Weigand and Robin Köck

Potential of Artemisinin derivatives and trioxolanes as anti-*Leishmania* chemotherapy

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Keywords: Leishmania, chemotherapy, trioxolanes

Background and objectives: Leishmania infantum is the causative agent of human and canine leishmaniasis in the Mediterranean basin. It affects canines and is an opportunistic and emerging disease in humans. The few available drugs have high cost, toxic side effects, declining efficacy and increasing drug resistance.
Artemisinin, derivatives and synthetic peroxides have demonstrated efficacy against protozoan parasites such as Plasmodium sp. The aim of this work was to access susceptibility of L. infantum in both life stage forms and cytotoxicity to selected semi-synthetic and synthetic peroxides.
Materials and methods: Different concentrations of a small library of artemisinin-derived trioxanes and synthetic trioxolanes was tested against promastigote, and intramacrophage amastigote forms of a L. infantum strain (MHOM/PT/88/IMT151). Inhibitory concentrations (IC50) were calculated. Cytotocitity was also accessed in the THP-1 cell line and selectivity index (SI) calculated. Currently in use anti-Leishmania drugs were used as controls.
Results: Some of the trioxolanes (LC50 and LC95) presented good activity with inhibitory concentrations (IC50) ranging between 3.51 µM and 1.25 mM, for promastigote, and between 79.76 µM and 1.20 mM, for intramacrophage amastigote forms, close to those of control drugs. Concerning cytotoxicity LC50 and LC95 showed comparable or higher SI values than control drugs.
Conclusion: These first results and the easy access to this chemotypes by chemical synthesis, demonstrate the potential for further studies in the context of leishmanial therapy.

Epidemiological relationship of ESBL-/AmpC-producing Enterobacteriaceae in the broiler production chain

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Keywords: ESBL, Antibiotic resistance, Broiler

Background and objectives: Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBL) or AmpC beta-lactamases are occurring in many herds on broiler farms in Germany. Little is known about the origin of these resistant bacteria in fattening farms and the vertical and horizontal transfer of ESBL-/AmpC producing strains along the broiler production chain. In our study we, therefore, investigate for the first time batch depending transmission routes in the entire broiler production chain.
Materials and methods: We collect faecal and environmental samples from seven parent flocks, their eggs and the environment in the hatchery and take samples from fattening farms and finally the slaughter house tracking each flock separately. Suspicious enterobacteria were investigated concerning their phylogenetic groups and ESBL/AmpC genes to determine first potential epidemiological relationships.
Results: *Escherichia coli* isolates originating from the first analysed production chain were assigned to Phylogroup A harbouring a TEM-52 gene (parent flock), to Phylogroup A, B1, F or E/D which were positive tested for CMY-2 genes (fattening farm) and Phylogroup A, B1, E, E/D harbouring gene combinations of CMY-2, TEM-52 and CTX-M15 (slaughterhouse).
Conclusion: First comparisons of ESBL-/AmpC-Genes and phylogenetic groups of isolates show that an exclusively vertical transfer of ESBL-/AmpC producing enterobacteria seems to be not very likely but further investigations will be done.

Identification of the novel oxazolidinone/phenicol resistance gene *optrA* and its distribution in *Enterococcus faecalis* and *Enterococcus faecium* of human and animal origin

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Keywords: antibiotics of last resort, plasmid, interspecies transfer

Background and objectives: Oxazolidinones are antibiotics of last resort to control MRSA and VRE infections. Here, we report the identification of a novel oxazolidinone resistance gene *optrA* and a study of the extent to which this gene is present in enterococci from humans, pigs and chickens. The gene *optrA* was detected by whole plasmid sequencing and subsequent cloning and expression in a susceptible host. *E. faecalis* (n=438) and *E. faecium* (n=447) isolates of human and animal origin (pigs, chickens) were screened by PCR for *optrA* and the 58 *optrA*-positive isolates were analysed for their MICs, their genotype, and the location of *optrA*. The novel plasmid-borne ABC transporter gene *optrA* conferred combined resistance to oxazolidinones (linezolid, tedizolid) and phenicols (chloramphenicol, florfenicol). The conjugative plasmid pE349, on which *optrA* was located, had a size of 36,331 bp. The *optrA* gene was functionally expressed in *E. faecalis, E. faecium*, and *Staphylococcus aureus*. It was detected more frequently in *E. faecalis* and *E. faecium* from food-producing animals (20.3% and 5.7%, respectively) than from humans (4.2% and 0.6%, respectively). An animal reservoir and selection of *optrA* by the use of florfenicol in food-producing animals was assumed.

The dissemination of *optrA* will reduce the efficacy of oxazolidinones in the control of serious infections with Gram-positive bacteria and thereby pose a major threat to public health.

Antimicrobial usage in human and veterinary medicine in Germany

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Keywords: antimicrobial resistance, consumption of antibiotics, surveillance systems

It is assumed that a high consumption of antibiotics causes bacterial resistances. In order to minimize the development of bacterial resistance, the usage of antibiotic needs to be reduced.
Currently, many surveillance systems have been implemented in human and veterinary medicine. For example, the scientific institute of the German health insurance company "AOK" collects the prescriptions of antibiotics for non-privately insured persons. This information is evaluated in DDD, a statistical unit per 1,000 persons. The in-patient surveillance is realized in the ADKA-if-RKI, a voluntary system which describes DDD/100 care days.
For veterinary antibiotic consumption there is a national database, in which farmers enter their farm-animal antibiotic usage. The treatment frequency, defined as single dose per animal is being published biannual, dividing the farmers in three groups: below the median, between the median and the third quartile and above. These categories are used for consulting action to help the farmers to reduce the usage of antibiotics.
Although the DDD/1000 Inhibitions and the treatment frequency are based on different systems in details, it will be possible to compare human and veterinary consumption of antibiotics. This presentation will give a first insight in comparing antibiotic consumption in human and animals in Germany.

Spread of antimicrobial resistance in the tropical setting – experiences from Mali

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Keywords: antimicrobial resistance, foodborne transmission

Background and objectives: Recent observations of antimicrobial resistance in tropical and subtropical countries especially in conflict or post-conflict szenarios are of major public health concern. Data from epidemiological studies in the tropical setting are scarce.
Materials and methods: During a nine-months-intervall stool samples of deployed European soldiers with diarrhoea from the European Union Training Mission (EUTM) in Mali were analyzed for surveillance purposes with PCR for stool pathogens as well as for resistance by cultural methods.
Results: Beside a broad variety of foodborne pathogens dominated by diarrhoea-associated E. coli we found Enterobacteriaceae with extended spectrum beta-lactamases (ESBL) in 25 % of the patients.
Conclusion: Even in low income countries with limited access to modern antibiotics a relative high percentage of isolates from patients with diarrhoea could be demonstrated. The explanation of this phenomenon is still speculative. Probable routes of transmission i.e. importation of livestock and food should be further investigated.
Regarding the limited ressources for an appropriate antibiotic treatment efforts should be initiated to take countermeasures and to stop further spread.

The NF-κB inhibitor LG-ASA exhibits anti-pathogenic activity against influenza A virus and *S. aureus* co-infection *in vitro* and *in vivo*

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Keywords: influenza virus, staphylococcus aureus, anti-pathogen therapy

Background and objectives: Infections with influenza A viruses (IAV) are still amongst the major causes of highly contagious severe respiratory diseases. One specific problem concerns increased fatality rates, linked to secondary bacterial pneumonia, caused by pathogens such as *Staphylococcus aureus* (*S. aureus*). Occurrence of resistant IAV- as well as *S. aureus* strains against the currently licensed medications points to the urgent need for new and amply available anti-infective strategies targeting both pathogens.
In different studies we have identified virus-supportive cellular signaling modules (e.g. NF-κB) as potential targets for antiviral intervention. Here we examined the anti-pathogen effect of the NF-κB inhibitor LG-ASA against IAV and/or *S. aureus* infection.

Materials and methods: We established *in vivo* and *in vitro* co-infection models using serial infection with IAV and *S. aureus*. The effect of LG-ASA was determined on viral and bacterial load as well as inflammatory responses.

Results: We demonstrate that targeting NF-κB signaling by LG-ASA inhibits IAV replication and intracellular *S. aureus* upon singular as well as co-infection. Interestingly, LG-ASA is able to block *S. aureus* internalisation.
Further, we provide evidence that treatment of mice with LG-ASA results in reduced pathogen load and enhanced survival during IAV/*S. aureus* coinfection.

Conclusion: The NF-κB inhibitor LG-ASA may serve as a potential agent against IAV and/or *S. aureus* infection.

Session 5: Public Health relevant zoonoses

October 16 2015
09:00 – 10:30

Room Zehlendorf
Chairs: Martin Pfeffer and Hendrik Scheinemann

Ebola Diagnostic Preparedness in Côte d'Ivoire

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Keywords: capacity building, Ebola virus, diagnostic

The German Partnership Program for Excellence in Biological and Health Security was launched in 2013 and is funded by the German Federal Foreign Office. As a consequence of the current Ebola virus outbreak in West Africa, the German Federal Foreign Office allocated additional funding in order to strengthen diagnostic capacities in Côte d'Ivoire.

The Institut Pasteur in Abidjan is the reference laboratory for Ebola virus Disease (EVD) diagnostic in Côte d'Ivoire. It had to be expected that cases of EVD might also occur far from Abidjan, close to the border region of affected neighboring countries. We established a regional laboratory in Bouaké. In case larger specimen numbers would have to be tested, this laboratory in Bouaké could also serve as a support backup for the capacities at the Institut Pasteur, especially for specimens from the Central or Northern region of Côte d'Ivoire. As the actual outbreak has shown, aside from mere equipment and consumables that are needed for safe handling and diagnostic testing, it is crucial to have trained personnel available that is able to perform reliable diagnostics.

Therefore, our goal is to train about 54 local individuals in nine lab courses over a period of two weeks for each course. Further and specialized training of the already existing cadre of qualified life science personnel in CIV could allow for vital support in other African regions affected by EVD. Evaluation and experiences from the ongoing training will be presented.

Host association of *Leptospira* species in small mammals in Germany

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Keywords: Leptospira spp., small mammals, reservoir

Amongst wildlife species, rodents are considered to be an important reservoir for various zoonotic viruses, endoparasites and bacteria, such as *Leptospira* spp..

To characterize the reservoir for *Leptospira* spp. and other rodent-borne pathogens a rodent monitoring was performed between 2010 and 2014 in forest and grassland habitats in four German states in Mecklenburg-Western Pomerania, Thuringia, Baden-Wuerttemberg and North Rhine-Westphalia. A total of 3951 small mammals could be analyzed, including different rodent and shrew species. As expected, bank voles and yellow-necked mice were mainly trapped in forest habitats. In contrast, trapping in grassland habitats resulted mainly in capturing of common voles.

Kidney tissues were analyzed by PCR targeting the *lipl32* gene which only amplifies DNA of pathogenic *Leptospira* species. Using this initial screening PCR, 524 of 3951 small mammals were tested positive for *Leptospira* spp.. Subsequently, a partial *secY* gene-specific PCR and sequencing was used to identify the *Leptospira* species. For 244 of the 524 PCR-positive samples the presence of *Leptospira kirschneri* (63.0%), *Leptospira borgpetersenii* (9.5%) and *Leptospira interrogans* (27.5%) was determined.

In conclusion, this investigation confirmed that leptospires infect a broad spectrum of small mammal species and are geographically widely distributed. The results did not indicate any obvious reservoir specificity of the different *Leptospira* species.

Revelations from vaccination trials against anthrax in large animals: Improvement of diagnostic procedures and practical implications on the predicability of the outcome of an ongoing infection with *B. anthracis*

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Keywords: Anthrax, Clinical data, Serology, Goat

Background and objectives: In a veterinary context few vaccination studies against anthrax in large animals such as goats, sheep and cattle are conducted, especially if the protective effect is to be assessed with a fully virulent challenge. Additionally, detailed clinical observations with implications on the progress of the disease in connection with a full spectrum on serological data are close to non-existent, making the setup and realization of such a trial a vague endeavour. Materials and methods: We completed several vaccination trials including challenge with spores of fully virulent field strains in goats in comparison to the Sterne spore live vaccine. Here we summarize the gathered clinical data of these trials in correlation to the serological results and the outcome of the infection. Data concerning the assessment of the vaccine strategies are presented in detail elsewhere.
Results: On-sight monitoring and assessment of the status of the progressing disease were improved due to defining temperature thresholds, objective assessment of behaviour and the determination of a time frame in which bacteria in the blood can be detected before death. Furthermore, we were able to show significant correlations between antibody titres, the development of fever, and survival.
Conclusion: The acquired data enables a higher level of predictability and a qualitative differentiation of the immune responses to vaccination from survivors after the challenge.

Infectious MERS-Coronavirus excretion and serotype variability based on live virus isolates from patients in Saudi Arabia

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Keywords: MERS-CoV, virus isolation, serotype variability

Background: Middle East respiratory syndrome coronavirus (MERS-CoV) has infected at least 1082 people, including 439 fatalities. So far no empirical virus isolation study has been done to elucidate infectious virus secretion as well as serotype variability.
Materials and Methods: 51 respiratory samples from 32 patients, age 24 to 90, diagnosed with MERS between February and June 2014 at the Prince Sultan Military Medical City (Riyadh, KSA) were used for virus isolation in VeroB4 and Caco2 cells. Plaque reduction neutralization assays using representative virus strains and patient sera were done to assess serotype variability.
Results: We found CaCo2 cells to significantly enhance isolation success over routinely used Vero cells. Isolation success correlated with viral RNA concentration and time after diagnosis, as well as the amount of IgA antibodies secreted in respiratory samples used for isolation. There were no obvious differences in neutralization efficiency, neither between virus strains nor between sera.
Conclusion:
This study showed that Caco2 cell should be preferred for MERS-CoV isolation from clinical samples, IgA antibodies are produced in respiratory tract secretions and protect against MERS-CoV, and all MERS-CoV variants currently circulating in the human population form only one serotype.

Gorilla adenoviruses: cross-species transmission and recombination

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Keywords: Adenovirus; cross-species transmission; recombination

Background and objectives: Human adenoviruses (AdV) of species *Human mastadenovirus B* (HAdV-B) are genetically highly diverse and comprise several pathogenic types. AdV closely related to HAdV-B infect African great apes (gorillas, chimpanzees). In particular, gorillas frequently shed a high diversity of HAdV-B. The aim of the study was to search for mastadenoviruses in humans and great apes in 6 African countries and to identify signs of AdV cross-species transmission and recombination.
Materials and methods: Mastadenoviruses were identified with different PCR methods and sequencing. Several software modules were used for determination of (i) genetic diversity and species delineation of HAdV species, (ii) ancestral host reconstruction and host change counts, and (iii) timing of HAdV evolution, and to identify signs of recombination.
Results: We determined that the evolutionary origin of HAdV-B is in ancient gorillas and chimpanzees and that two independent HAdV-B transmission events to humans occurred more than 100,000 years ago. In addition, phylogenomic analysis of several HAdV-B infecting wild gorillas revealed evidence for recombination.
Conclusion: Since zoonotic AdV have been reported to cause respiratory outbreaks both in humans and monkeys, and humans in West and Central Africa frequently hunt and butcher primates thereby increasing the chance of zoonotic transmission, such HAdV-B recombinants might widen the pool of potential human pathogens.

Sub-lethal sodium hypochlorite concentrations trigger antibiotic resistance in *S. aureus in vitro*

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Keywords: S. aureus, sodium hypochlorite

Background and objectives: Exposure to selective biocides triggers bacterial antibiotic (AB) resistance *in vitro*. This has been shown for triclosan, chlorhexidine, and quaternary ammonium compounds. Hence, there is an understandable concern that the improper use of disinfectants could select for AB-resistant bacteria. We tested, whether the sequential growth of *S. aureus* in sub-inhibitory concentrations of sodium hypochlorite (NaOCl) would have an effect on antimicrobial susceptibility.
Materials and Methods: *S. aureus* ATCC® 29213 and 6538 were grown in sub-lethal NaOCl concentrations at 37°C for 24 h (trial 1) and 72 h (trial 2), respectively. From all NaOCl concentrations permitting growth, passages were performed after the respective time (24 h or 72 h). Each trial included 10 passages. Antibiotic susceptibility was tested prior and after these experiments using the Vitek®2 technology and broth microdilution according to CLSI.
Results: After NaOCl-treatment, *S. aureus* ATCC® 29213 revealed marked resistance against oxacillin (≥4 mg/l vs. ≤0.25 mg/l afore). The presence of the genes *mecA* and *mecC* was excluded by PCR. Other mechanisms are currently under investigation.
Conclusions: We selected a borderline-resistant *S. aureus* by NaOCl-treatment. This adds NaOCl to the list of biocides known to trigger AB resistance *in vitro* and underlines the necessity of research regarding this topic.

Session 6: New and emerging zoonoses

October 16 2015
09:00 – 10:30

Room Ballsaal
Chairs: Gudrun Wibbelt and Isabella Eckerle

Crimean Congo hemorrhagic fever virus neutralizing antibodies in African bats

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Keywords: Crimean Congo hemorrhagic fever virus (CCHFV), serology, bat

Bats can be infested by soft and hard ticks making them putative hosts for tick-borne viruses. African *Hipposideros gigas* bats were recently shown to carry nairoviruses distinct from human pathogenic Crimean Congo hemorrhagic fever virus (CCHFV). To assess the putative presence of CCHFV in bats, a large serosurvey using bat serum samples was conducted. We tested 1,136 sera from 16 different bat species accumulated in Ghana, Gabon, Germany and Panama between 2005 and 2010. Samples were analyzed by molecular and serological methods including a recombinant glycoprotein (GP)-based immunofluorescence assay (IFA) for screening purposes and two different virus neutralization tests for confirmation. In total 114/1,136 (10.0%) bat sera reacted with recombinant CCHFV GP (range 0.6% to 42.9%). In 6 samples we confirmed presence of neutralizing antibodies (titer range 1:40 to 1:160) that correlated with high IFA-based endpoint titers (160-1,280). Seroprevalence was highest in migratory cave-dwelling African bats. All tested serum samples were negative for nairovirus nucleotide sequences. The detection of neutralizing antibodies in bat sera suggests circulation of CCHFV or a closely related virus in African bat populations that may pose a potential public health risk. Increased seroprevalence in migratory bats could indicate a possible role of bats in the geographic dispersal of CCHFV.

Discovery of a novel zoonotic bornavirus: A One Health approach of awareness, modern diagnostics and multi-disciplinary networking

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Keywords: zoonotic bornavirus, next-generation sequencing, variegated squirrel, one-health approach

Background and objectives: Three breeders of variegated squirrels developed a progressive and finally fatal meningoencephalitis within a few months after symptom onset. Lesions with mononuclear infiltration were suggestive for a viral infection, and veterinary and human health institutes and officials worked together to find the causative agent.

Materials and methods: Standard diagnostics, and subsequently a metagenome pipeline using next-generation sequencing (NGS) and the RIEMS analysis workflow, were used for pathogen identification and characterisation.

Novel molecular diagnostics and serology tests were developed and evaluated for the newly discovered virus. Public health measures were implemented.
Results: No infectious agent was detected by extensive standard laboratory investigations, but NGS analysis revealed the presence of a novel bornavirus in a contact squirrel. Subsequent intensive analysis including novel RT-qPCR and antigen staining confirmed its presence in samples of the deceased patients and the squirrel. Whole-genome analyses demonstrated that this novel virus forms a separate lineage within the bornavirus species. Additional positive animals could be identified and high bornavirus-specific antibody titers were detected. A test procedure for live animals was established.
Conclusion: This discovery of a bornavirus with zoonotic potential demonstrated the power of novel diagnostic methods and the need of effective awareness systems in a One Health approach.

Identification and functional characterization of TMPRSS2 cleavage sites in the spike protein of SARS-coronavirus

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Keywords: SARS-coronavirus, spike, protease

The SARS-coronavirus (SARS-CoV) is an emerging zoonotic agent which poses a substantial threat to human health. The spike protein of SARS-CoV (SARS-S) mediates viral binding and entry into target cells. Cleavage and activation of SARS-S by a cellular protease is a prerequisite to infectious entry and serine proteases, in particular TMPRSS2, were shown to activate SARS-S in cell culture and in the infected host. The present study determined which residues in SARS-S are required for cleavage and activation by TMPRSS2.
Mutation of amino acids K543/R544 or K563/K566, which were previously not implicated in proteolytic processing of SARS-S, abrogated processing by TMPRSS2 but was not compatible with robust S protein incorporation into virions. Unexpectedly, our preliminary data indicate that R667, which is required for S protein processing by trypsin, might also play a role in S protein cleavage by TMPRSS2. Thus, differences in the molecular weight of SARS-S fragments generated by TMPRSS2 and trypsin were shown to be due to differential glycosylation and mutation of R667 reduced S protein cleavage by trypsin and processing by TMPRSS2. The ability of the S protein mutants to drive TMPRSS2-dependent cell-cell and/or virus-cell fusion is currently under investigation and results will be presented. Collectively, these studies provide insights into S protein determinants controlling activation by TMPRSS2 and, in the long term, might contribute to the development of novel antivirals.

Origin and Evolution of Usutu virus, a neglected emerging arbovirus in Europe and Africa

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Keywords: Phylogeography; Evolution; genetic traits

Usutu virus (USUV), one of the most neglected mosquito-borne encephalitic flavivirus causes epizootics among wild and captive birds and sporadic infection in humans. We determined the evolutionary rate and important features for host adaptation of USUV. Phylogeography traced the origin of the recent epizootics and identified patterns of spread among countries of endemicity. An evolutionary rate of 4.05×10^{-4} subs site^{-1} year^{-1} was estimated, and the currently circulating strains have an ancestor that existed within the last 200 years. Epizootics in Europe appear to have origins in Senegal, whereas the common ancestor of all USUV emerged from South Africa. A total of six phylogenetic lineages were found, with 4 apparently contributing to the current epizootics in Europe. We also observed an increase in relative genetic diversity during the 2000s, which correlates with the emergence of USUV in Europe. Our results suggest likely ship- or aircraft-borne transportation of USUV-infected mosquitoes between Africa and Europe than long-distance movements of viremic birds. Most amino acid changes in the polyprotein are deleterious polymorphisms removed by purifying selection. However, evidence for adaptive evolution was found in NS5 gene, and a large number of sites in the polyprotein may be subjected to positive pressure evolving under episodic directional

selection as possible results of adaptive evolution to the naïv host populations from different geographic regions.

Hepatitis E virus genotype 3 induces infection dose dependent incubation times in domestic pigs

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Keywords: Hepatitis E virus, genotype 3, pig

Background and objectives: Rising numbers of detected autochthonous human hepatitis E virus (HEV) genotype 3 (gt3) cases in developed countries recently have drawn attention to this infection. Wild boar and domestic pigs are infected world-wide and can cause zoonotic infections by foodborne transmission. The lack of efficient cell culture systems for HEV makes animal challenge studies necessary. Therefore, we performed a serial HEV endpoint titration study in domestic pigs to understand HEV pathogenesis and to determine the minimal infectious dose.

Materials and methods: 36 store pigs housed separately in nine different isolation stables under BSL3** conditions were challenged intravenously with liver homogenate dilutions (tenfold up to 10^{-9}) of an experimentally HEV gt3 infected wild boar. Animals were checked clinically daily up to 92 dpi. Serum and faecal samples were taken regularly and analysed by HEV qRt-PCR and ELISA.

Results: None of the animals developed substantial clinical symptoms; however, animals in the groups up to a dilution of 10^{-7} (corresponding to 5 copies/2 ml inoculum) displayed a productive virus replication and shed HEV in their faeces.

Conclusion: Interestingly, the beginning of virus shedding as indicator of infection was dependent on the challenge dose itself, higher doses caused early whereas lower doses caused very delayed onsets. It remains to be clarified whether similar phenomena also occur in humans.

Cowpox virus virulence factors - genetic definition and *in vivo* testing

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Keywords: Cowpox virus (CPXV), virulence, pathogenicity

The pathogenic potential of different cowpox virus (CPXV) strains is rather variable. The knowledge about virulence factors of CPXV field strains is crucial to allow a risk assessment for the viruses circulating in voles and infecting accidental hosts like rats, cats or humans. Therefore, the objective of our study was the identification and confirmation of CPXV virulence markers in a rodent host model.
Here, two representative CPXV isolates, from a rat and a cell culture-adapted virus, were compared. Whole genomes were analyzed and by the use of single gene mutants as well as several chimeric viruses, genotypic differences were investigated *in vitro* and *in vivo* using a rat model.
The genome of the CPXV from a rat specifies more open reading frames (ORF) compared to the laboratory strain, especially sequences for the genes ati, p4c NMDAr, 7tGP, D7L kelch-like protein, and CrmE. *In vitro* growth analyses revealed no differences between the CPXV strains. Furthermore both virus strains exhibited V^- phenotype of the A-type inclusion bodies (proteinaceous intracellular aggregates). In contrast, morbidity and mortality rates in the animal model were quiet different. The chimeric viruses and the single gene mutant viruses demonstrated that ati, p4c and D7L are important virulence factors.
Genotypic differences of the characterized CPXV could be related to different phenotypes and important virulence markers were defined.

Session 7: Innate and adaptive immune response

October 16 2015
11:00 – 12:30

Room Steglitz
Chairs: Veronika von Messling and Stephan Ludwig

Targeted gene deletion in chickens as a powerful tool to dissect immune responses to zoonotic pathogens and vaccination in chickens

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Keywords: chicken, reverse genetics, antibody

Avian immunology has made considerable progress since the discovery of the function of the bursa of Fabricius. However, at a functional level progress has been slow which is largely due to a lack of *appropriate in vitro* and *in vivo* techniques to investigate adaptive immune responses.

While gene targeting technology is available for mammals, knockout technology has not previously been available in chickens. However, the ability to culture chicken primordial germ cells (PGCs), and the ability of genetically modified PGCs to colonize the embryonic gonad and give rise to fully transgenic progeny in the next generation created the opportunity to introduce site-specific changes into the avian genome.

Here we used, for the first time, cell-based homologous recombination in a non-mammalian vertebrate to successfully generate a targeted deletion in chickens. The target of the gene knockout was the JH segment of the immunoglobulin heavy chain. Although B cells colonized the epithelial buds in the bursa of the knockout and proliferated without a B-cell receptor they failed to survive after hatch. Serum antibodies were absent in JH knockout chickens and the birds failed to produce antibodies after immunization.

The knockout chicken with a block in post-bursal B cell development will be a valuable tool in infectious disease research. Additional knockout birds lacking T-cell subpopulations are under development and will be used to gain insides into cell mediated immune defence mechanisms.

Immunopathology in a new model of haemorrhagic fever caused by hantavirus infection

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Keywords: Hantavirus, Disease model, Immunopathology

Background and objectives: Zoonotic hantaviruses are a cause of renal and pulmonary failure in humans worldwide. The pathogenesis of hantavirus-induced human disease is a matter of debate, however. Although human pathology would suggest an immune component, current rodent models of hantavirus infection surprisingly indicate that CD8+ T cells are not involved. In order to resolve this point we have developed humanized mouse models of hantavirus infection based on NSG and NSG-HLA-A2 mice that harbour functional HLA-A2-restricted CD8+ T cells.
Materials and methods: The course of infection in these mice was followed by qRT-PCR, flow cytometry and immunohistochemistry.
Results: In the absence of CD8+ cells lethal infection was accompanied by induction of cellular neutrophilic infiltrates. In accordance, we have shown that overproduction of neutrophil extracellular traps is a characteristic of clinical hantavirus infection. The presence of CD8+ T cells, however, induced a much stronger and more rapidly lethal infection, with widespread inflammatory infiltrates despite the same quantity of viral replication. Further experiments demonstrated that infection of hematopoietic cells was a central feature unique to highly pathogenic hantaviruses, and that infection of antigen presenting cells (APC) resulted in widespread and unspecific activation of T cells.
Conclusion: We propose that the capacity to activate neutrophils and to infect APC thereby inducing widespread activation of T cells is central to hantavirus-induced disease in humans.

Comparative analysis of *Mycobacterium (M.) avium*-complex (MAC) infections in a goat model

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Keywords: MAC, goat model, host response

Background and objectives: MAC members cause infections in man and livestock with growing incidence. Large animal models allow insights into host-pathogen interaction, a prerequisite for the design of intervention strategies. Here, kinetics and intensity of systemic and local host responses of goats to *M. avium* subsp. *hominissuis* (MAH) and subsp. *paratuberculosis* (MAP) were compared.
Materials and methods: Goat kids were orally inoculated with MAH or MAP. Clinical symptoms, cell mediated immunity (specific IFN-γ response [IFNR]) and specific antibody response (AR) were monitored regularly until necropsy (4, 7 and 13 mpi) in inoculated animals and controls. Bacterial organ burden (BOB) and gene expression of immune modulatory cytokines was examined in organized gut associated lymphatic tissue and intestinal lymph nodes.
Results: MAP-inoculated (MAPG) and control goats stayed healthy. Half of MAH-inoculated goats (MAHG) developed severe disease at 2-3 mpi; the others only mild transient fever and depression. A high initial antigen induced IFNR and an early AR was noted in MAHG. Onset of both responses was delayed in MAPG. Despite moderate to high BOB at 2-3 mpi, MAH was almost eliminated from animals at 13 mpi while MAP was still frequent. Immune modulatory cytokines were differentially regulated in the course of MAH and MAP infection.
Conclusion: MAP and MAH interact differently with the host. Comparative studies will allow insights into protective mechanisms against MAC members.

Inhibition of host cell entry of ebolaviruses by interferon-induced transmembrane proteins

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Keywords: IFITMs, Ebola, Restriction factor,

Ebolaviruses are highly pathogenic in humans and nonhuman primates and pose a severe threat to public health. The interferon-induced transmembrane (IFITM) proteins can restrict entry of Ebola virus (EBOV, formerly Zaire ebolavirus), influenza A viruses, and other enveloped viruses. However, the breadth and mechanism of the antiviral activity of IFITM proteins are incompletely understood. It has been proposed that IFITM-dependent modulation of endosomal cholesterol content contributes to the inhibition of virus entry but this concept is controversial.
We employed ebolavirus glycoprotein–pseudotyped vectors and ebolavirus-like particles to study the antiviral effects of IFITMs. We found that IFITMs inhibit the cellular entry of diverse ebolaviruses and demonstrate that type I interferon induces IFITM protein expression in macrophages, major viral targets. Moreover, we show that the IFITM-mediated block of influenza A virus but not EBOV entry can be overcome by Amphotericin B, suggesting that IFITMs inhibit cellular entry of these viruses by two different mechanisms. Finally, we provide evidence that antibodies and IFITM proteins can synergistically inhibit cellular entry of EBOV. These results provide interesting insights into the role of IFITM proteins in ebolavirus infection and suggest a mechanism how antibodies, which are weakly neutralizing *in vitro*, might still contribute to viral control *in vivo*.

Campylobacter jejuni colonization is influenced by genotype and feed composition in chicken

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Keywords: Campylobacter jejuni, genotype, feeding strategy

Background and objectives: As an enteric microorganism, *Campylobacter jejuni* (*C.j.*) has been recognized as a commensal of poultry. On the other hand, it may induce mild inflammatory responses and in some cases may also lead to disease in avian species. We may speculate that genotype and feeding strategy may influence the outcome of *C.j.* infection, possibly due to differences in the immune response and the gut flora composition. So far, little is known about the local and systemic immune responses in chicken colonized by *C.j.* The objectives of our study were to investigate the influence of the genotype and feed composition on the outcome of *C.j.* colonization and infection.

Materials and methods: *C.j.*-free commercial broilers and layer pullets were fed either with broiler or layer feed. Subgroups were inoculated with *C.j.* or *C.j.*-free medium at the one and 22 days post hatch. Six birds per subgroup were necropsied at one, two, seven and 14 days post infection. T cells subpopulations and expression of different cytokines were detected by flow cytometry, immunohistochemistry and qRT-PCR, respectively.

Results: In broilers, *C.j.* colonization is not significantly affected by the feeding strategy ($p > 0.05$). Layers feed with broiler feed showed significant higher colony forming units (CFU) of *C.j.* at seven days post inoculation (dpi) than layers fed with layer feed ($p < 0.05$).

Conclusion: Overall, broilers mount a more vigorous immune response after inoculation compare to layers. Feeding strategy may significantly affect *C.j.* colonization. Further studies have to elucidate of modification of genotype and feeding strategy may reduce the risk of *C.j.* colonization of commercial chicken flocks.

Collagen VI harbors antimicrobial properties against oral pathogens

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After the surgical application of dental implants, patients may suffer from severe infections at the implant site. Usually harmless bacteria like oral Streptococci are able to infiltrate the damaged tissue in the fresh wound. Here they may develop a highly pathogenic potential and establish persistent infections in the oral cavity, compromising implant integration. Therefore new strategies including bioactive antimicrobial implant surfaces might be beneficial for the patient. In this study the bacterial killing properties of collagen VI against human oral pathogens were investigated. Scanning electron microscopy and different bacterial killing assays were used to detect bacterial killing of four different bacterial species present in dental plaque. Thereby antimicrobial properties of collagen VI were confirmed, due to formation of membrane vesicles, disruption of the bacterial membrane and ejection of bacterial cytoplasmic contents. Furthermore, the persistence of collagen VI's antimicrobial properties was tested and the *in vivo* situation was simulated by incubating bacteria with collagen VI in the presence of neutrophils. Taken this together, these data show that collagen VI exhibits bacterial killing properties. This leads to the suggestion that coating of oral dental implants with collagen VI may protect patients against infections during the first time after an operation.

Session 8: Novel methods, diagnostics, NGS and bioinformatics

October 16 2015
11:00 – 12:30

Room Zehlendorf
Chairs: Karsten Nöckler and Jens Hammerl

Development of pen-side methods for quick and easy detection of rabies

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Keywords: rabies, pen-side

Background and objectives:
Rabies is a lethal zoonotic disease caused by lyssaviruses, a member of the family *Rhabdoviridae*. Although the most European countries are free of rabies, it represents a severe public threat with thousands of deaths per year in the developing countries. At present the fluorescent antibody test is the "gold standard test" for rabies diagnosis, but there is an increasing demand for rapid and simple diagnostic tools for the use in the field (pen-side tests). Some rapid immunodiagnostic assays are commercially available, but have to be further evaluated. In the last years other molecular pen-side tests were developed and could be suitable for the integration into mobile systems.
Materials and methods:
Candidates for molecular pen-side assays were designed and validated in comparison to routine diagnostic tests for rabies virus. Published assays were converted into a high-speed RT-qPCR and two isothermal amplification systems (recombinase polymerase amplification, helicase-dependent amplification) were new developed.
Results:
All designed tests were able to detect different rabies strains in much less time than the standard diagnostic, but are slightly less sensitive. However, the viral loads appearing in nature are much higher than the limit of detection, which makes the methods suitable for application in the field.
Conclusion:
In general, the development of new molecular pen-side methods, for rapid rabies diagnosis outside of laboratories was successful.

Detection of zoonotic bacteria in food by fluorescence *in situ* hybridization

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Keywords: fluorescence in situ hybridization, food microbiology, rapid detection

Background and objectives:
The dietary intake is not only closely connected to the ingestion of nutrients, but also involves the uptake of considerable numbers of bacteria. Most foodborne bacteria are innocuous; however, some of them are known to be pathogenic, resulting in a substantial amount of zoonotic infections. Fluorescence *in situ* hybridization (FISH) is a promising tool to identify viable bacteria in a culture-independent manner. The purpose of this study was to establish a comprehensive set of FISH tests suitable for the detection of important zoonotic bacteria in food.
Materials and methods:
Fluorescent probes targeting the ribosomal RNAs of a large set of pathogens, e.g. *Campylobacter*, *Salmonella* and *Yersinia*, were developed and designed in a way that they can be employed simultaneously for multiplex detection by microscopy. Pure cultures and spiked food products were used to assess the suitability of FISH.
Results:
The developed FISH probes proved to be highly specific and allowed the detection of low amounts of the target pathogens in the presence of an abundant accompanying flora. Different food matrices showed variable levels of background fluorescence, but the bacteria could still be reliably detected.
Conclusion:
FISH offers unique advantages for food microbiology and the detection of zoonotic agents since it has the capacity to detect only viable bacteria and yields quantitative results while keeping the high discriminatory power of molecular detection methods.

Analysis of vaccine-induced rabies cases using deep sequencing

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Keywords: Next generation sequencing, vaccine-induced rabies, low frequency variants

Since the early 1980s much effort was made to eradicate terrestrial rabies in Europe. During large-scale vaccination programs of foxes, millions of oral rabies vaccine virus baits were outlaid. Notably, most of them contained one of the live-attenuated SAD (Street Alabama Dufferin) strains. Post vaccination surveillance detected at least seven possible vaccine-induced fatal rabies cases in red foxes (*Vulpes vulpes*) and in a stone marten (*Martes foina)*.
In order to determine the genetic relationship of these viruses with the vaccine strains used for the campaigns in the respective region, we conducted deep sequencing of brain and salivary gland tissue, as well as SAD vaccine batches, using the Ion Torrent platform. For data analysis we calculated the frequency of each nucleotide at each position of the viral genome in order to identify low frequency variants, hiding beyond the consensus. Subsequently, the nucleotide frequencies of all strains were compared using Manhattan distance analysis and non-metric multidimensional scaling for visualization.
Results show that most of the analyzed strains exist as diverse population of variants, also referred to as quasi species. Furthermore we were able to show that vaccine virus-associated isolates were nearly indistinguishable from their parental vaccine strains at consensus level, but showed significant changed spectra of variants. Further investigations will analyze if the detected variants are a trigger for vaccine-induced rabies.

Comparison of the infection of porcine precision-cut lung slices by porcine influenza virus H3N2 and porcine respiratory coronavirus PRCoV

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Keywords: Coronavirus, porcine lung, influenza virus

Ex vivo systems are useful tools to analyze virus infection. Here, we established coronavirus infection studies in porcine precision cut lung slices (PCLS). Porcine coronaviruses as well as porcine influenza A viruses (SIV) can be involved in the porcine respiratory disease complex (PRDC). PRDC is caused by a combined infection of several viruses and/or bacteria. We compared single infection by SIV H3N2 and porcine respiratory coronavirus (PRCoV), as well as co-infection of the PCLS with both viruses. PCLS were infected for two days and analyzed by confocal microscopy after staining for viral antigen. The ciliary activity of infected PCLS was compared with uninfected controls over a time period of 7 days. PCLS infected with SIV H3N2 showed a clear decrease in ciliary activity two days post infection. In contrast, in PCLS infected with SIV H3N2 and PRCoV as well as with PRCoV alone ciliary activity was reduced 4-5 days post infection. Virus titration on NPTr cells showed lower infectious titers of PCLS supernatants after co-infection with SIV H3N2 and PRCoV than after mono-infection with PRCoV. Titration of the supernatants on MDCKII cells showed higher virus titers of the supernatants of co-infected PCLS compared to H3N2 alone. These results suggest an interaction of both viruses that is not fully understood and highly dependent on time and infection conditions. Further studies will show in what extend the viruses influence each other during infection of the lung epithelium.

Microevolution of *Burkholderia mallei* studied during a deliberate infection within its natural host

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Keywords: glanders, experimental infection, genomic rearrangement

Background and objectives: Glanders is a notifiable epizootic disease caused by *Burkholderia mallei*. The infection mainly affects horses and donkeys, but sporadic cases in humans have been reported. The pathogen is a host-adapted lineage of *B. pseudomallei* and developed by genome reduction, rearrangements and elimination of prophages. Both species are recognized biothreat agents.
Materials and methods: Donkeys and goats were infected intranasally with *B. mallei* strain Dubai7 and monitored for clinical signs of illness. Subsequent genomic analyses comprised the initial strain used for infection and 47 isolates that have been re-isolated either from lesions or carcasses of 9 experimentally infected animals. Whole genome sequencing (WGS) was applied to selected strains using PacBio RS II and Ion PGM platforms.
Results: All typical manifestations of the disease like mucopurulent discharge could be observed. We found 30 closely related but different clusters by MLVA23-typing, suggesting genomic alterations within repeat regions. By WGS extensive deletions of up to 250k bp with the involvement of IS elements as well as a series of single and multiple nucleotide exchanges were determined.
Conclusion: This study provides insights into microevolution of a zoonotic pathogen with a narrow ecological niche within its natural host. Our findings reveal the enormous structural flexibility of the genome, challenge the meaning of *in-vitro* studies, and will have a strong impact on bioforensics.

Separation of foreground and background reads in mixed NGS datasets

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Keywords: NGS, bioinformatics

NGS is a valuable technology for rapid and in-depth analysis of clinical samples, as it allows sequencing of a pathogen's whole genome directly from patient material within as little as 26 hours. However, the follow-up analysis is severely slowed down by the abundance of reads originating from the host. Thus, in order to leverage the full potential of the technology for rapid diagnostics, a method for rapid *in silico* removal of host reads is necessary. Commonly, a mapping-based approach is used: either reads mapping to a background reference or reads not mapping to a foreground reference are discarded. However, while the former approach is highly specific in discarding only true background reads and the latter is highly sensitive in only keeping foreground reads, neither offers a good balance.

We have developed a novel tool geared towards both specific and sensitive separation of foreground and background reads. We achieve this by training markov chains of an order k from 4 to 12 on user-provided sets of foreground and background reference sequences and then assigning each read to foreground or background based on which of the two markov chains it fits better.

We have tested our tool on several datasets, including Cowpoxvirus sequenced from a human host. In all cases, our tool was faster than any competing tool while consistently achieving the best F-Score. We believe that this tool is highly useful as an initial filtering step for anyone analyzing viral sequences via NGS.

Session 9: One Health und neue Zoonosen

October 16 2015
11:00 – 12:30

Room Ballsaal
Chairs: Ute Teichert and Rainer Ulrich

Leptospirosis outbreak in field workers in Lower Saxony, Germany, 2014

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Keywords: mice, field fever, strawberry harvesters

Background and objectives: Between June and August 2014, 45 cases of leptospirosis were notified among predominantly Polish seasonal workers on two strawberry farms in North-West Germany. We describe the actions taken by the German authorities to investigate this outbreak and prevent further cases. Materials and methods: The activities of the local, federal and national public health and veterinary institutions included collection of case data, laboratory testing of cases and mice trapped on the fields, investigation of weather data and information of farmers, field workers and the authorities in Poland and Romania.
Results: Of 45 notified cases (27 male, median age 22), 47% were hospitalised. Characteristic symptoms were high fever (>38.5°C), generalised muscle pain and an increase in renal or liver enzymes. Fifteen cases could be confirmed by serological and/or molecular methods. The probable causative agent was identified as *L. kirschneri* serovar Grippotyphosa. *Leptospira*-specific DNA found from kidneys of 67% of 64 trapped rodents was further identified as *L. kirschneri* sequence type 110. During the estimated period of infection, the affected region faced warm weather with heavy rainfalls. Conclusions
The investigations confirmed the chain of infection from mice to field workers. In 2015, a campaign was initiated to inform physicians, farmers and workers, and to establish prevention measures, such as the use of personal protective equipment and early consultation of a physician in case of illness.

Detection of hepatitis E virus in meat products from retail in Germany

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Keywords: Hepatitis E virus, detection method, real-time RT-PCR

Hepatitis E virus (HEV) is a pathogen of increasing importance, which can be zoonotically transmitted from domestic pigs, wild boar, and deer to humans. Foodborne transmission by consumption of raw and undercooked liver, meat, or sausages prepared from infected animals has been documented. The aim of this study was to investigate the distribution of HEV in meat products in Germany. As no standardized methods for HEV detection in food exists, a sensitive and reliable technique for HEV detection in raw and liver sausages should be developed and thereafter applied to samples from retail. Different methods for sample homogenization and virus extraction followed by real-time RT-PCR detection of HEV were compared using artificially contaminated sausages. Since a location of HEV within the tissue can be expected, the efficient disruption of the food matrix during the homogenization process was controlled by detecting the release of pig DNA. A method using TRI Reagent® Solution showed the best efficacy of matrix disruption. Treatment of the lysate with chloroform followed by a silica-based RNA extraction method resulted in the highest HEV detection rates. The detection limit of the method was 2.9×10^3 and 5.3×10^4 genome equivalents per 5 g raw and 2 g liver sausage, respectively. A total of 120 food samples (pork and wild boar sausages) were analyzed for the presence of HEV. By this, the HEV genome was detected in 15 out of 70 (21%) raw pork sausages and in 12 out of 50 (24%) liver sausages. The study shows that HEV is broadly distributed among meat products in Germany. Further studies should analyze the infectivity of the detected viruses in order to assess the risk of virus transmission from the food to the consumer.

Survey for zoonotic pathogens in Norway rat populations from European cities

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Keywords: Rattus norvegicus, zoonotic pathogens, Europe

Rattus norvegicus represents an important reservoir of various zoonotic pathogens. Previous studies have demonstrated infections with Seoul hantavirus (SEOV), multi-drug resistant bacteria, *Leptospira*, *Yersinia, Rickettsia, Bartonella* and *Streptobacillus* spp. in wild Norway rats. A recent next-generation sequencing-based investigation indicated several zoonotic viruses and novel viruses with unknown zoonotic potential (Sachsenröder et al., 2014, J. Gen. Virol. 95, 2734). Our survey in 440 rats from five different European countries focused on *Leptospira* spp., *Rickettsia* spp., Orthopox viruses (OPV) and SEOV. PCR-based investigation of the *lipl32* gene from kidney tissue revealed *Leptospira* DNA in rats collected at nine sites in three countries. *SecY* sequencing and MLST analysis of five samples identified *Leptospira interrogans* (serovar Icterohaemorrhagiae). Rickettsia DNA was detected only in one of the 286 rat ear tissue samples investigated. Sequencing of the partial *ompB* gene revealed *Rickettsia helvetica*. Additionally this rat was also positive for *Leptospira interrogans*. PCR-based analysis failed to detect any OPV-specific DNA and SEOV-specific RNA.

In conclusion, our study results indicate a broad geographical distribution of *Leptospira* infections in rats within Europe underlining the need for further investigation to assess the public health relevance. In contrast, *Rickettsia*, OPV and SEOV infections seem not or only very rarely to occur in the present rat populations.

Poster Presentations

Poster Session Epidemiology and modelling

E01

Contact to non-human primates and risk factors for zoonotic disease emergence in the Taï region, Côte d'Ivoire

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Keywords: bushmeat; non-human primates; zoonotic pathogen transmission

Background and objectives: Elevated exposure levels to non-human primates (NHP) and NHP bushmeat represent major risk factors for zoonotic disease transmission in sub-Saharan Africa. Demography can affect personal nutritional behavior, and thus risk of contact to NHP bushmeat. We examined this in detail in the Taï region in Western Côte d'Ivoire, where respective zoonotic pathogens are prevalent and have been transmitted from NHP to humans before.
Materials and methods: NHP contact data from 504 participants of differing demographic and ethnic backgrounds were collected through a standardized questionnaire. We employed descriptive statistics in order to summarize contact rates to NHP, and Generalized Linear Mixed Models to examine demographic risk factors.
Results: Overall, participants' contact rates to NHP were high, and increased along a gradient of bushmeat processing (e.g., 8 % hunted, but 62 % consumed monkeys). Individuals' sex, country of birth and ethnicity significantly affected rates of NHP contact, with male participants from Côte d'Ivoire being at particular risk of exposure to NHP.
Conclusion: In view of the continuing difficulties to control and prevent zoonotic infectious disease outbreaks, the information gathered here contributes to the understanding of factors facilitating contact to potential NHP hosts. This allows to formulate prevention recommendations and develop acceptable economic alternatives to bushmeat trade and consumption.

E 02

Forecasting the incidence of human Puumala virus cases in South West Germany

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Keywords: hantavirus, epidemiology, modelling

Background and objectives: Puumala virus (PUUV) is endemic in Germany. Since 2001, the State of Baden-Württemberg has been reporting the highest number of cases with a fluctuation from 22 (2006) to 1,694 (2012) cases per year. Aiming for an early warning tool to optimize public health response, we developed a predictive model for human PUUV cases in Baden-Württemberg.
Materials and Methods: Data on PUUV cases (onset of disease, site of infection) were extracted from the mandatory system. We developed generalized linear models (Poisson distributed residuals), using climate factors, beech mast-data and data on forest coverage with different types of trees as independent factors to explain reported PUUV cases for 2006–2012. Model selection was based on the goodness of fit to reported cases.
Results: The selected model contains beech mast, beech tree and other broadleaf tree coverage, September sunshine duration, August and September temperature, and county. It qualitatively predicts 86% (252/290) of data points, given by a combination of county and year. The selected parameters are available from October and allow predicting PUUV cases of the following year. Supplementary, a model which extrapolates newly reported cases has been developed.
Conclusion: A predicted PUUV outbreak allows for early information of the public and for planning observational and interventional studies. Results of such studies are urgently needed to target public health recommendations and interventions.

E 03

Risk factors for human Leptospira infection

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Keywords: leptospirosis, epidemiology, risk factors

Background and objectives: Leptospirosis is a notifiable disease in Germany, yet only 1,209 cases were reported from 2001 to 2014 (median 74/year). We investigated whether infection incidence is as low as indicated by these reports, and determined risk factors for seropositivity.
Materials and Methods: We evaluated population-based cross-sectional data of 1007 people in Baden-Württemberg, collected as random samples from 9 municipalities in 2008, comprising exposure questionnaires and IgG antibody examinations by immunofluorescence assay covering different serovars. We calculated relative risks (RR) of seropositivity and 95% confidence intervals (CI).
Results: 42 participants (4.2%) had antibodies against *Leptospira* serovars. People reporting frequent pet rat contacts had a significantly increased risk for seropositivity (RR=13.1 [95% CI: 5.7-23.1]). Other factors like frequent contact with cattle (6.3 [2.5-13.8]), pet mice (5.7 [1.8-13.4] poultry (3.0 [1.2-6.8]), or occupation as forester (7.4 [2.4-16.3]) were not statistically significant after Bonferroni correction. Other occupational and environmental factors (i.e. contact to surface water) did not consistently increase RR.
Conclusion: The high seroprevalence contrasts with the number of reported cases. This is consistent with the hypothesis of underdiagnosis of clinical and asymptomatic cases. Mild forms may be caused by certain serovars. Leptospirosis should be considered among rodent owners with unclear symptoms.

E 04

Incidence of Rotavirus and cryptosporidium gastroenteritis among a sample of children attended Raparin Pediatrics Hospital in Erbil, Iraqi Kurdistan Region

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Background and objectives: Cryptosporidiosis caused by obligate intracellular parasites *Cryptosporidium spp*. are a frequent cause of diarrheal illness in human, particularly in children younger than 5 years old and in immunocompromised individuals such as AIDS patients and individuals with organ transplant. The infection is mostly self-limiting in immunocompetent individuals, while it is life threatening in immunocompromised patients. Rotavirus is the most common cause of severe diarrhea among infants and young children, nearly every child in the world have been infected with Rotavirus at least once by the age of five. Since both infections cause profuse watery diarrhea in young children that are usually misdiagnosed because both infections can not be detected by routine stool examination, the current study was aimed to explore the incidence of Rotavirus and cryptosporidium gastroenteritis among children in Erbil in relation to demographic parameters and seasonal distribution and to evaluate the efficacy of Rotavirus vaccine and vaccination procedure that applying in Erbil. Methods and patients: This is an analytical cross sectional study. Fecal specimens were collected from 500 children of both genders with ages ranged between one month to five years old and who attended Raparin Pediatrics Hospital in Erbil for severe gastroenteritis. The sampling method was simple random sampling. Modified Ziehl Neelsen technique was used for detection of cryptosporidium oocysts and fifty samples of those were subjected to nested PCR (targeting 18S rRNA gene). The samples that were chosen for PCR were from children with gastroenteritis and shown negative results in both modified Ziehl Neelsen and for Rotavirus. Rotavirus infection was detected by Certest immunochromatography. Ethical acceptance was issued from the Researches Ethical Committee in the college of Medicine, Hawlere Medical University and informed consent was obtained from the parents. The data were Statistically analyzed using SPSS version 17.0. The association

between two or more categorical variables was assessed by Chi-square test. Count and percentages were used to describe the frequency of different variables. P-value P≤0.05 was considered statistically significant. Results: The infection rate of Cryptosporidiosis was 0 % and 6.0 % by modified Ziehl-Neelsen stain and PCR, respectively. The incidence of cryptosporidiosis was non-significantly higher among boys (6.25%) than girls (5.55%) and children with age group ≤2 years (11.7 %) were more susceptible to infection. The rate of infection was significantly (P<0.05) higher among children from rural areas (13.3%) than those from urban areas (3.7%) and sub urban (0%). The highest number of cryptosporidiosis was recorded over March and April (9.5%), and was significantly (P<0.05) higher than that detected over January, February, May and June. The overall infection rate of Rotavirus in the study groups was (32.0%) and was non-significantly higher in females (34.4%) than males (30.0%). Rotavirus infection was significantly (P<0.05) higher among children with ages from 1 to 3 years old (39.3%). The infection rate was significantly (P<0.05) higher among children from urban areas (34.5%) than those from rural areas (26.8%) and sub urban areas (0%). The highest number of Rotavirus infection was observed over January and February (38.6%). The infection rate was significantly (P<0.05) increased among non-vaccinated children (65.9%) than vaccinated group (14.1%) and was also significantly (P<0.05) higher among children who received single dose of Rotavirus vaccine (60.4 %) comparing with those received two (55.2 %) or three (14.1 %) doses of vaccine. Conclusion: The incidence of cryptosporidiosis is suggested to be reduced comparing with previous studies that carried out in Erbil and polymerase chain reaction is more efficient for detection of Cryptosporidiosis comparing with modified Ziehl Neelsen technique. Rotavirus is a common cause of diarrhea in young children in Erbil, thus it should be considered in the laboratory investigations for all children suffering from gastroenteritis. Vaccination procedures that applying in Erbil is effective to reduce and even prevent Rotavirus infection in young children.

E05

Development of a model for the spread of ESBL/AmpC E.coli in broiler production

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Keywords: ESBL/AmpC E.coli, Broiler chain, Risk assessment

Background and objectives: Consumption of chicken meat has been suggested as a cause of transmission of ESBL/AmpC-producing E.coli. All stages in the production of broilers are significant with regards to the contamination of the final chicken products. The objective of this work is to create a model for the spread of ESBL/AmpC producing E.coli involving the "farm stage" of the supply chain.
Materials and methods: Markov Chain principle implying that the percentage positive flocks at a particular point in the chain depend on the percentage in the previous point of the chain is applied.
Results: The model developed here describes the effects of vertical and horizontal transmission, as well as effects of inactivation and removal of bacteria and the dynamic of growth and cross-contamination in terms of the transfer of ESBL/AmpC producing E.coli from other infected broilers (in the same flock, in other flock within the same farm and in the previous production cycle). Three main steps are considered here: parent flocks; one-day old chicks; broilers. The same basic considerations are applied in each consecutive stage taking into account the different factors affecting each stage.
Conclusions: The output values of this "farm model" will be used as input for the poultry processing model for quantitative risk assessment. Moreover, knowledge about the epidemiology of ESBLs/AmpC at the farm level may be of great value for the design of effective prevention and control strategies.

E 06

House mice dominate small mammal communities in Northern Afghan military camp sites

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Keywords: Rodents, rodent-borne diseases, phylogeography

Military personnel serving in camp sites all over the world are often confronted with tropical diseases, many of which are rodent-borne. This study aimed at investigating the small mammal communities at three Northern Afghan military bases, determining the risk of rodent transfer to and from the bases and ultimately to define the risk of zoonotic infection in such installations.

Rodents were trapped in three military camp sites and investigated by analysis of mitochondrial *cytochrome b* gene and D loop control region. The phylogeography was further determined by genetic analysis of a murine rhadinovirus infecting Afghan and European house mice.

Small mammals consisted mainly of Eastern house mice. Genetic analysis of mice and murine rhadinovirus points towards a recruitment of indigenous house mice in the bases.

The import of small mammals and their subsequent pathogens into Afghan military bases is unlikely. A detailed analysis of pathogens in these mammals with DNA microarray/next generation sequencing work-flow is in progress.

E 07

ESBL-producing *E. coli* in cattle farms – A cross-sectional study in Germany

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Keywords: antibiotic resistance, prevalence, risk factors

Extended spectrum beta-lactamases (ESBL) belong to the most widely disseminated resistance mechanisms in *Enterobacteriacae*. In a cross-sectional study in livestock, among broiler and fattening pig farms, also 42 cattle farms were sampled in 2011 and 2012. Data on potential risk factors were collected by means of a questionnaire. The aim of the study was to investigate the prevalence of ESBL-producing *E. coli* and potential risk factors for their occurrence.

Dairy and beef cattle farms were located in Bavaria as well as in the middle, the east and the north-west of Germany. On each farm samples were taken from two animal groups, three collective faecal samples one boot swab and one dust sample. The growth of *E. coli* on MacConkey agar plates containing 1 mg/l cefotaxime was investigated and the bacterial species was confirmed using MALDI TOF. Supplemental data on management, feeding, hygiene and the use of antimicrobial substances were collected using a questionnaire. The laboratory results of the samples and the data derived from the questionnaire were basis for the risk factor analyses.

In 80% of the cattle farms, positive samples were found. The explorative risk factor analyses identified factors from the areas hygiene (cleaning) and management (feeding period), for which a higher number of positive samples was found.

Overall factors indicating a more traditional farm management were associated with a lower number of positive samples.

E 08

Coxiella burnetii seroprevalence and associated risk factors in Acute Febrile patients in Wajir County, Kenya

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Keywords: Seroprevalence, Coxiella burnetii, Febrile-patients

Background and objectives: Q fever is a zoonosis caused by bacterium *Coxiella burnetii*. Q fever in Kenya is highly neglected and the epidemiology is unknown with no attention to control and prevention.The study aimed to determine the seroprevalence of *C. burnetii* in febrile patients from a pastoralist population in Kenya and investigate predictors for seropositivity using multivariable logistic regression modelling.
Materials and methods: blood was obtained from 504 subjects and tested for IgG antibodies against *C. burnetii* phase 1 and 2 antigens by ELISA method. The questionnaire was filled for each subject to obtain epidemiological and clinical history.
Results: Phase 1 antibodies were detected in 60(12.0%) and phase 2 in 74(14.7%) subjects. Fifty two (10.3%) were positive to both phase 1 and 2 antigen, but 22(4.4%) and 8(1.6%) were reactive to only phase 2 and 1 respectively. Q fever was not clinically suspected in any subject but were mainly treated for common tropical fevers. Majority (79% and 88.2%) reported risky occupational or dietary practices and only 2 subjects had prior knowledge of Q fever. Identified factors predisposing to *Coxiella* infection included increasing age, exposure to cattle and slaughter of animals. Dietary factors were consumption of raw cattle milk and traditionally prepared milk.Conclusion: Many cases of Q fever are misdiagnosed. Exposure is potentially influenced by occupational and cultural factors. Physician and community awareness and febrile patient screening for Q-fever to allow timely diagnosis is crucial. This is the first study of Q fever in febrile patients in Kenya providing data on predictors for Q-fever infection and baseline evidence for policy development for control and prevention.

E 09

Staphylococcus stepanovicii harboring the methicillin resistance encoding gene *mec*C isolated from a bank vole (*Myodes glareolus*)

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Keywords: mecC, rodents, resistome

Background and objectives: In 2011, a novel *mec*A homologue (*mec*C) harbored by SCC*mec*XI was described for methicillin resistant *Staphylococcus aureus* (MRSA). To gain deeper insights into the chromosomal integration site (*att*BSCC) of a *mec*C-positive *S. stepanovicii*, we conducted whole genome sequencing (WGS).
Materials and methods: The *Staphylococcus stepanovicii* strain IMT27065 (ODD4) was isolated in 2011 from wild bank vole as part of a screening study of the Network "Rodent-Borne Pathogens". WGS was carried out on a HiSeq (Illumina, USA). Annotation of ORFs and prediction of (protein) coding sequences (CDS) was performed by The RAST Server. For comparative genomic analyses Geneious 7.1.5 was employed.
Results: Genome sequencing revealed that IMT27065 harbors a *mec*C gene which shares 99.2% nucleotide sequence identity with *mec*C from *S. aureus* strain LGA251. In addition, the *mec*C encoding region harbors the typical class E *mec* complex, but lacked transposases as well as *ccr* recombinase homologues. Analysis of the 15bp direct repeats (DR) flanking *att*BSCC revealed similar DRs widely distributed downstream of *orfX* within the genus *Staphylococcus*, including SCC*mec* elements, indicating the possibility of a broad genetic exchange.
Conclusion: Our data highlights the necessity of research on putative transmission routes of resistance encoding factors from the environmental resistome in terms of wildlife reservoirs to opportunistic bacteria such as *S. aureus*.

Poster Session Pathogen-cell interaction

P 01

Functional characterization of the poxvirus host range factor p28 in macrophages

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Keywords: cowpox virus, cytosolic DNA sensing, macrophages

The poxviral p28 protein was first described as a virulence and host range factor of Ectromelia virus that allows its replication in macrophages. Previously, we were able to show that a Δp28 cowpox virus (CPXV-Δp28) exhibits a similar host range restriction in macrophages.

In this study, we analysed the function of p28 via heterologous expression of different variants of CPXV p28 in J774A.1 macrophage-like cells.

Expression of full-length p28 was sufficient to rescue CPXV-Δp28 replication in J774A.1 cells, while expression of truncated p28-variants lacking either its KilA-N or RING finger domain had no such effect. Interestingly, deletion of the KilA-N domain led to a highly increased expression of p28, which might be attributed to the deletion of three specific lysine residues. Mutation of these lysine residues also boosts the expression of full-length p28, most likely through reduced ubiquitination and proteasomal degradation of p28. As p28 co-localizes with viral DNA in infected cells, we analysed if p28 modulates the innate immune sensing of cytosolic DNA. We could show that heterologous expression of p28 reduced the phosphorylation of IRF3 and NF-κB in J774A.1 cells following stimulation with dsDNA.

In conclusion, we were able to extend the understanding of the function of p28 by demonstrating that both the KilA-N and the RING finger domains are necessary for p28's host range function and by showing a putative role of p28 during innate immune sensing of cytosolic DNA.

P 02

Neutrophil extracellular traps (NETs) in the *Streptococcus suis*-infected cerebrospinal fluid compartment

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Keywords: S. suis, NETs, CNS

Streptococcus (S.) suis is a major pathogen in pigs and an emerging zoonotic agent, causing severe meningitis and other pathologies. Infiltrations with neutrophils are typical for lesions induced by *S. suis* infection. Recently, NETs have been identified as a defense mechanism against different pathogens, but its function during meningitis has not been studied so far. Here, we studied *in vitro* and *in vivo* NET formation in the infected cerebrospinal fluid (CSF) compartment. Furthermore, the role of the *S. suis* DNases SsnA and EndAsuis in NET-escape was investigated. For this we infected comparatively with *S. suis* wt and *in frame ssnA* and *endAsuis* deletion mutants in a model of a blood-CSF barrier formed from a human choroid plexus papilloma cell line. Formation of NETs and bacterial survival were monitored in the CSF compartment after transmigration of neutrophils through epithelial cells. To correlate these *in vitro* results with *in vivo* findings, the CSF of infected piglets was analyzed using immunofluorescence microscopy. Our results indicate the NET-formation and subsequent entrapment of bacteria in the infected CSF compartment *in vitro* and *in vivo*. Interestingly, differences in NET-formation and bacterial survival were not recorded when comparing infections with *S. suis* wt and mutants *in vitro*. In conclusion, our preliminary results lead to the hypothesis that NET-formation contributes to the host-pathogen interaction in the CSF during *S. suis* meningitis.

P 03

Role of the surface unit of the Ebola virus glycoprotein in tetherin counteraction

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Keywords: Ebola, Tetherin

Tetherin is a host cell encoded antiviral factor that can inhibit release of several enveloped viruses from infected cells. The Ebola virus (EBOV) glycoprotein (GP) antagonizes tetherin's antiviral activity via a so far unknown mechanism. It was previously shown that the transmembrane subunit of EBOV-GP, GP2, is necessary but not sufficient for tetherin counteraction. In the present study, we assessed whether residues in the surface unit, GP1, contribute to tetherin counteraction. For this, we determined whether mutations in GP1 compromised the ability of GP to rescue the release of HIV-1 Gag- and EBOV-VP40-based virus-like particles from inhibition by tetherin.

We found that the mucin-like domain is largely dispensable for tetherin counteraction and for transduction of target cells, in keeping with published data. In contrast, mutation of the furin cleavage site slightly diminished tetherin antagonism. More impressively, mutations in the receptor binding domain (RBD) of EBOV-GP, which reduced host cell entry, largely abrogated tetherin antagonism. Finally we discovered that glycan processing in the Golgi apparatus, while dispensable for GP-mediated entry, is required for efficient tetherin antagonism by GP but not by HIV-1 Vpu. In sum, our results show that the integrity of the RBD and adequate GP glycosylation are essential for tetherin counteraction. Agents targeting the RBD might thus disrupt the viral life cycle at the stage of entry and release.

P 04

Regulation of cell death mechanisms after influenza A virus and *Staphylococcus aureus* super-infection

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Keywords: Influenza A virus, staphylococcus aureus, cell death

Background and objectives: Most of the fatal cases during an influenza A virus (IAV) epidemic are a result of secondary pneumonia caused by bacteria such as *Staphylococcus aureus (S. aureus)*. Here, cell death mechanisms play an important role. While these processes are very well analyzed during infections by IAV or *S. aureus* alone, much less is known for the coinfection situation. Here, we focussed on apoptosis and necroptosis mechanisms.
Materials and methods: In an *in vitro* coinfection model human lung epithelial cells (A549) were infected with different IAV and *S. aureus* strains. Induction of cell death was monitored by detection of various cellular factors on protein and mRNA level.
Results: We were able to show that IAVs induce the expression of pro-apoptotic factors such as TRAIL or the cleavage of caspases and PARP. Although in the presence of *S. aureus* the activation of apoptosis-markers was reduced, cell-morphology was changed and cell-viability seemed to be decreased. Concomitantly, a marker of necroptosis, the mixed lineage kinase domain-like protein (MLKL), was strongly activated in presence of bacteria.
Conclusion: Our results indicate that *S. aureus* is able to inhibit the IAV-induced apoptotic cellular response. We hypothesize that the *S. aureus*-mediated switch from apoptosis to necroptosis supports intracellular bacterial survival and spread. Thus we introduce a novel mechanism that might contribute to increased pathogenicity upon IAV and *S. aureus* coinfection.

P 05

Impact of the Raf-MEK-ERK signaling cascade during influenza virus and *Staphylococcus aureus* coinfection *in vitro* and *in vivo*

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Keywords: coinfection, Raf-MEK-ERK pathway

Background and objectives: Influenza A virus (IAV) infections are one of the major causes of severe respiratory diseases. Secondary bacterial pneumonia can increase pathogen load, resulting in higher morbidity and mortality. During coinfection, antivirals and antibiotics lack efficiency and the risk of emerging resistances is high. Thus, new pathogen-inhibiting strategies are required and targeting cellular factors might minimize the risk of resistance induction. Here we analyse the virus-supportive cellular Raf-MEK-ERK signaling pathway as a potential target for anti-pathogenic therapies.
Materials and methods: Human lung epithelial cells (A549) were infected with different IAV strains and the *Staphylococcus aureus* strain 6850 in the presence or absence of specific MEK-inhibitors (U0126, CI-1040). Further, Balb/c mice were infected with both pathogens and treated with solvent or U0126.
Results: Inhibition of MEK led to reduced viral titers, which was independent of the viral strain. Moreover, bacterial growth was reduced in the presence of U0126 and inhibition of MEK resulted in reduced chemokine levels. Administration of U0126 *in vivo* led to significantly reduced lung bacterial titers.
Conclusion: Our data provide evidence that the activation of ERK plays an important role in pathogensis during coinfection. Therefore, targeting the Raf-MEK-ERK pathway as a new therapeutic approach seems to be promising and will be further investigated.

P 06

The effect of *Streptococcus suis* co-infection on the infection of well-differentiated porcine respiratory epithelial cells by swine influenza viruses

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Keywords: respiratory epithelium, porcine influenza viruses, Streptococcus suis

Background and objectives: Respiratory diseases in swine are responsible for high economic losses in pig industry worldwide. A major factor responsible for severe virus infections may be viral-bacterial co-infections. Influenza A viruses are a major cause of acute respiratory disease in pigs which may play an important role in the interspecies transmission of influenza viruses. *Streptococcus suis (S. suis)* is an emerging zoonotic agent. It is one of the most important bacterial pathogens affecting the porcine airways causing invasive diseases.
Materials and methods: Precision-cut lung slices (PCLS) were co-infected by SIV followed by co-infection with *S. suis*. The effect of co-infection was evaluated.
Results: The results show that (i)Primary infection by SIV facilitates adherence and colonization of encapsulated *S. suis*. (ii)Airway epithelium damage induced by infection of SIV promotes colonization and invasion of both encapsulated and non-encapsulated *S. suis*. (iii)Encapsulated *S. suis* affects infection by SIV and reduce the amount of infectious virus released into the supernatant.
Conclusion: We observed that adherence and invasion of *S. suis* on PCLS was efficiently promoted by SIV pre-infection. The PCLS model shows much promise for investigating microbial and host factors to determine the complex mechanisms and dynamics involved in bacterial-viral co-infections.

P 07

Proteomic analysis of bovine udder epithelial cell responses to *Coxiella burnetii* infection

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Keywords: Coxiella burnetii, bovine udder epithelial cell, proteome

The obligate intracellular bacterial pathogen *Coxiella burnetii (C. b.)* is the causative agent of Q fever in humans. The most important infection source is ruminants which may shed the agents in high numbers via placental fluids, feces and milk. *C. b.* replicates in the acidic parasitophoric vacuoles of eukaryotic cells. To identify host cell metabolic processes affected by *C. b*. infection, we investigated the proteome of bovine udder epithelial cells infected with *C. b.*-strains Nine Mile I RSA 943 and Nine Mile Phase II by two-dimensional gel electrophoresis using fluorescent detection dyes (DIGE) of whole cell lysate proteins. With this approach, 25 differentially regulated proteins were identified in Nine Mile Phase II infected cells and 26 proteins in Nine Mile I infected cells. Both strains induced an increased activity in cell (energy) metabolism, cell compartment formation and signaling, protein processing and regulation, stress and immune responses. Three proteins, dipeptidylpeptidase III, annexin A3 and bovine keratin, were differentially regulated after infection with both strains. The virulent Nine Mile I strain induced a more pronounced upregulation of proteins implicated in cell signaling and regulation processes as well in stress and immune reactions as compared to low-virulent Phase II strain. Our results provide first insights into the impact of *Coxiella* strains which exhibit different levels of virulence on host cell molecular processes in cattle.

P 08

Identification of APRIL as a novel host protein interacting with influenza virus ribonucleo-proteins

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Keywords: Influenza A Virus, APRIL, RNP

During infection, influenza A viruses (IAV) are highly dependent on the interaction with cellular proteins to manipulate the host intracellular environment and allow viral replication and evasion of the intracellular antiviral response system. In this study we aimed to identify cellular proteins that interact with the IAV replication machinery.
Materials and methods: Using a recombinant IAV carrying a strep-tag at the PB2 Protein and mass spectrometry, we were able to identify novel host proteins that interact with IAV vRNPs 4 hours p.i.
Results: Aside from known vRNP interaction partners, we identified the host protein APRIL. APRIL is involved in diverse cellular processes like mRNA export, apoptosis, and gene expression. Knock down of APRIL enhanced viral replication, indicating a potential inhibitory property. Overexpression of APRIL resulted in a concentration dependent down-regulation of reporter protein expression in the minireplicon assay. Strikingly, primer extension analysis revealed that reduced reporter expression is not accompanied by a reduction in reporter mRNA synthesis. Mutation of the nuclear export signal (NES) suggests that the nuclear export function of APRIL is not required for this phenomenon.
Conclusion: We suggest that APRIL is a cellular interaction partner of influenza A virus replication machinery with an inhibitory effect on viral replication. Inhibition might be mediated by a posttranslational inhibition of viral protein expression.

P 09

Comparative analysis of filovirus entry into human, primate and bat cell lines

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Keywords: Bats, filoviruses, entry

The *Filoviridae* family includes viruses, which cause severe disease in humans and non-human primates and constitute a severe health threat, as underlined by the ongoing Ebola virus (EBOV) epidemic in Western Africa. Although being known for almost 50 years, the ecology of filoviruses is poorly understood. Molecular and serological studies suggest that bats constitute a filovirus reservoir and it is of high interest to determine whether filoviruses interact differently with cells of human and bat origin. The filovirus glycoprotein (GP) drives viral binding and entry into host cells and several cellular factors required for efficient GP-driven entry into human cells have been identified. Here, we asked whether GP uses the same factors for entry into bat cell lines.

We investigated GP-mediated transduction of human, non-human primate and bat cell lines using rhabdoviral vectors pseudotyped with the GPs of all known filoviruses. The GPs were able to facilitate transduction of all cell lines tested, but bat cells were markedly less susceptible than cells of human and non-human primate origin. At present we are comparing whether GP-driven entry into primate and bat cell lines is differentially susceptible to blockade by a panel of inhibitors targeting discrete steps of the entry process and the results will be presented.

Poster Session Antimicrobial use and resistance

A 01

Characterization of livestock-associated methicillin-susceptible Staphylococcus aureus

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Keywords: MSSA, zoonosis, antimicrobial resistance, spa typing, ST 9

Background and objectives: Methicillin-resistant *Staphylococcus aureus* have emerged among livestock (LA-MRSA) and their impact for colonization and infection of farmers has been demonstrated. In contrast, little is known about the occurrence of methicillin-susceptible *S. aureus* (MSSA) among these animals and zoonotic transmission.
Materials and methods: Five dust samples each were collected at 51 pig holdings and nasal swabs were obtained of farmers from the same holdings. Samples were enriched (MH broth with 6.5% NaCl), then streaked onto colistin-aztreonam agar. Absence of *mecA* was confirmed by PCR. Susceptibility testing was done by broth microdilution. MSSA isolates were *spa* typed.
Results: Overall, 28 MSSA isolates (20 from dust and 8 from farmers) were found on 18 farms. Isolates from dust were associated with *spa* types t337 (n=8), t1430 (4), t034 (2), t1334 (2), t8893, t037, t011, t1333 (each n=1); those of farmers with *spa* types t337 (2), t012, t2413, t034, t728, t1430, t190 (each n=1), respectively. Tetracycline and clindamycin resistance both involved 25% of the isolates.
Conclusion: MSSA of *spa* types associated with sequence type (ST) 9 (t337, t1430) predominated. Farmers were partly colonized with these MSSA. Some TET-resistant isolates exhibiting *spa* types t034 and t011 corresponded to typical LA-MRSA suggesting a loss of *mecA*. Considering the risk of LA-MRSA for farmers, further studies should assess the role of LA-MSSA for infections in this group of persons.

A 02

Comparison of extended-spectrum beta-laktamase (ESBL)-producing *Escherichia coli* isolates from hospitals, ambulatory settings and the community

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Keywords: antibiotic resistance, ST131, CTX-M-15

Background and objectives: Here we report the results of the molecular characterization of ESBL-producing *Escherichia coli* isolates from different studies in the interdisciplinary research project "RESET". Materials and methods: We analyzed 524 ESBL-*E. coli* Isolates from 3 studies: 124 nosocomial and 104 *E. coli* isolates from outpatient departments, 211 *E. coli* from healthy participants (community) and 85 community-acquired *E. coli* from a case-control study. The presence of ß-lactamase genes (bla_{ESBL}) was tested by PCR and sequencing. Phylogenetic grouping by PCR was performed for all isolates and 264 isolates (50%) were further analyzed by Multilocus-Sequence-Typing (MLST). Results: The ESBL-*E. coli* from hospital and outpatients mainly harbored CTX-M-15 (ambulant 58%; nosocomial 48%) and CTX-M-1 (ambulant 24%; nosocomial 37%). *E. coli* from healthy persons showed a high proportion of CTX-M-15 (46%) and CTX-M-1 (24%). *E. coli* from the case-control study mainly harbored CTX-M-1 (42%) and CTX-M-15 (29%). Sequence type ST131 was determined for 92% (ambulant) and 86% (nosocomial) of the *E. coli* with CTX-M-15. Within the case-control-study and the community study the proportion of ST131 among CTX-M-15-producing *E. coli* was 50% and 15%, respectively.
Conclusion: CTX-M-15 and CTX-M-1 are the most frequent ESBL-types in *E. coli* from humans. In all settings we found the worldwide successful clonal group *E. coli* ST131 in high proportions.

A 03

Positive predictive value of isolation of potentially ESBL-producing Escherichia coli on MacConkey agar containing 1 mg/l cefotaxime

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Keywords: ESBL, positive predictive value, isolation

Extended spectrum beta-lactamases (ESBL) belong to the most widely disseminated resistance mechanisms in *Enterobacteriacae*. According to a common isolation protocol, also recommended by the European Food Safety Authority (EFSA), the isolation starts with an enrichment culture followed by cultivation on MacConkey agar plates containing 1 mg/l cefotaxime. ESBL-production is then confirmed by antimicrobial susceptibility testing with specific panels and PCR of the ESBL-genes.

We were interested in the positive predictive value (PPV) of the cultural isolation on MacConkey agar plates containing 1 mg/l cefotaxime for ESBL-production. Therefore ESBL-producing *E. coli* samples from broiler, fattening pig and cattle farms were first isolated culturally. Subsequently ESBL suspicious isolates were confirmed by antimicrobial susceptibility testing and PCR of ESBL-genes.

From samples collected on fattening pig farms 121 isolates growing on MacConkey agar plates containing 1 mg/l cefotaxime were obtained. Of these isolates 107 could be confirmed by PCR. It follows a PPV of 87%. In the presentation, the results of PPV for the different sample sources will be reported. The calculation of the sensitivity and specificity from these data and the possible limitations of this method will be explained.

A 04

Occurrence of ESBL-/AmpC-producing *Enterobacteriaceae* along the broiler production chain

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Background and objectives: Previous studies showed the occurrence of extended-spectrum ß-lactamase (ESBL) and plasmid-mediated AmpC ß-lactamase-producing *Enterobacteriaceae* in broiler fattening farms, even in day-old chicks. Therefore we assume an early entry or emergence of these resistant bacteria in the broiler production chain, which is investigated in this ongoing study.
Materials and methods: Seven broiler fattening flocks, preselected by positive initial testing of the parent flocks, are tracked along the entire production chain. The hatchery, as suspected bottleneck for bacteria transmission, is sampled intensively. In the farms the chicken and their environment are investigated from arriving until leaving, also their carcasses and packed meat in the slaughterhouse.
Results: ESBL-/AmpC-producing *Enterobacteriacea* in the hatchery were found on some egg surfaces in one flock only. At the chickens' arrival in their fattening farms the bacteria were not detected in cloacal swabs, but in a few samples from the environment inside the barn. However, during the fattening period several samples of animals and environment were positive, which was the same for slaughterhouse.
Conclusion: Mostly negative samples from hatcheries and arriving at fattening farms but findings of antibiotic resistant bacteria in the course of fattening period do not support the hypothesis of a vertical ESBL-transfer in broiler herds. Further molecular characterizations will be considered.

A 05

MRSA in chicken meat at retail in Germany – changes between 2009 and 2013

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Keywords: MRSA, chicken meat, antimicrobial resistance

Livestock associated Methicillin-resistant *S. aureus* are considered an emerging problem. We aimed to find out, if the prevalence of MRSA in chicken meat as a potential vehicle for MRSA into the household of consumers was increasing and if the characteristics of the isolates were changing over time.
Samples of chicken meat were collected at retail according to a national sampling plan based on the distribution of the human population in Germany. MRSA detection was conducted according to a previously described highly sensitive method including selective enrichment. Isolates from positive samples were *spa* and SCC*mec* typed and tested for antimicrobial resistance by broth microdilution. Minimum inhibitory concentrations were evaluated according to epidemiological cut off values provided by EUCAST for *S. aureus* or, whenever available for MRSA.
Prevalence of MRSA in chicken meat samples was similar in all three years (2009, 2011 and 2013). Besides resistance to beta-lactams, MRSA isolated were resistant to tetracycline, clindamycin, and erythromycin (>80 %). Quinupristin/dalfopristin resistance was less prevalent in 2009 (65 % vs. 80 % in 2011 and 2013). Differences were also observed for the prevalence of resistance to kanamycin (11.7 % in 2013 vs. 35 % in 2009 and 2011) and ciprofloxacin (25.8 % in 2013 vs. 33 % in 2011 and 2009). The proportion of non CC398 MRSA decreased over time in the three years (26.6, 17.2 und 7.7 %).

A 06

Systematic review of observational studies on ESBL-producing E. coli in pigs

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Keywords: reporting, data extraction, summary

Data on the prevalence and the characteristics of resistant bacteria are the basis for the development of surveillance programs or mathematic models like risk analyses. In most studies on ESBL-producing bacteria *E. coli* are investigated as common intestinal colonisers and indicators for the presence of resistances. The aim of this study is, to summarise the present publications on the prevalence and the characteristics of these bacteria.
For this systematic review a search strategy was defined and in August 2014 applied to three literature databases which are free of charge and available online (CAB abstracts, PubMed and Web of Knowledge). Through this search 102 relevant publications were identified. To extract and manage the published data, a structured data sheet with 118 input fields was developed.
Within this presentation a summary of the laboratory diagnostic methods and the results published in observational studies on ESBL-producing E. coli in pigs will be given. Preliminary analyses show considerable heterogeneity between the designs of the published studies and the way of reporting, e.g. of statistical analyses used.
The stricter application of reporting guidelines and the implementation of study registers for observational studies could help to improve the comparableness of published results.

A 07

Detection of virulence genes in multi-resistant CTX-M-14-producing *Escherichia coli* isolates from cattle

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Keywords: Microarray, plasmids, ESBL

Background and objectives: ESBL-producing *Escherichia coli* have emerged during recent years. The aims of this study were to characterize multi-resistant CTX-M-14-producing *E. coli* for additional resistance and virulence genes.
Materials and methods: Twenty-seven multi-resistant CTX-M-14-producing *E. coli* isolated during 2010-2014 from healthy and diseased cattle and farm environment were characterized by susceptibility testing, XbaI-PFGE, MLST, phylotyping, replicon typing, S1-nuclease PFGE, PCRs and DNA microarray.
Results: Most of the $bla_{\text{CTX-M-14}}$-positive isolates were resistant to phenicols, aminoglycosides, tetracyclines, sulphonamides, trimethoprim and quinolones. The phylogenetic groups A, B1 and D were detected. MLST type ST10 was most common (n=7) and 15 isolates showed unrelated XbaI-patterns. The $bla_{\text{CTX-M-14}}$ genes were located on plasmids (IncF, IncB/O, IncK or IncI) of 60-100 kb. These plasmids encoded solely resistance to β-lactam antibiotics (n=11) or to one (n=3) or two (n=13) additional classes of antimicrobial agents. The co-located resistance genes *aac(3)-IIa* (gentamicin) and/or *floR* (chloramphenicol/florfenicol) were identified. The virulence genes *pfrB*, *f17A*, *f17G*, *iss* and *ireA* were most common. No virulence genes were detected on the $bla_{\text{CTX-M-14}}$-carrying plasmids.
Conclusions: Plasmids play an important role in the dissemination of antimicrobial resistance. Virulence genes of the $bla_{\text{CTX-M-14}}$-carrying isolates increase their pathogenic potential.

Poster Session Novel methods, diagnostics and NGS

D 01

The bank vole (*Myodes glareolus*) – the small animal model for novel Hepaciviruses

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Keywords: novel hepacivirus, bank vole, animal model, bank vole hepaci virus

The recent discovery of novel non-primate hepaciviruses (NPHV) in different mammal species, such as rodents, dogs, horses and cattle, allow the development of disease and/or reservoir models for human Hepatitis C. In this study (funded by German Research Platform for Zoonoses - "Vole-Infection-Model"), we demonstrated that bank voles are susceptible for experimental infection with a NPHV found in bank voles (bank vole hepacivirus = BvHV). In contrast, IFN-receptor-deficient mice were found to be resistant against BvHV infection. The highest viral genome loads were measured in the liver and viral RNA was visualized by in situ hybridization (ISH) in hepatocytes, clearly confirming a marked hepatotropism. Different patterns of the course of infection were observed suggesting clearance or alternatively long-term infection, most likely depending on the virus strain used. Histopathological inspection and ISH of liver slides of all investigated infected animals showed high load of viral RNA and electron microscopy showed signs of chronical inflammation and lymphocytic infiltration respectively. We conclude that bank voles are a promising small animal model for novel Hepacivirus. Furthermore it is a perfect topic-overlapping-example for appropriation of a pathogen/host model in human medicine research, that originated from "virus hunting" and zoonoses research.

D 02

Invertebrates as neglected zoonosis research assistants

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Keywords: invertebrates, biodiversity, zoonotic pathogens

Research on zoonosis usually only considers invertebrates as vectors. Typically, invertebrates would be screened for those pathogens they potentially vectorise and the host DNA they sometimes carry would be used to investigate their host ranges. Here, we argue that any invertebrate ingesting or getting in contact with vertebrate tissues and/or droppings may be considered as a sampler of both local vertebrate biodiversity and their microorganisms. To illustrate this concept, we present a large body of data derived from molecular analyses of dipterans.

We collected flying insects attracted to carcass smells at nine rainforest and savannah sites in sub-Saharan Africa and one urban site in Germany. DNA extracts were screened by PCR for mammal DNA and a next-generation sequencing-based metabarcoding approach was used to identify mammal species. At all sites, numerous mammal species known to occur in the area could be readily detected. We also used PCR to look for microorganism nucleic acids at one of these sites. By doing so, we could detect a carcass-borne pathogen (*Bacillus cereus* biovar *anthracis*) as well as a feces-borne pathogen (Adenovirus).

We conclude that invertebrates not known to vectorise any pathogen can also provide information relevant to zoonosis research. We suggest that many other invertebrates could be suitable for similar analyses and that vector invertebrate diet analyses should also be considered relevant to biodiversity research.

D 03

Using Full Genome SNP Analysis as a tool to investigate the Epidemiology and Ecology of *Bacillus cereus* biovar *anthracis*

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Keywords: Anthrax, Population Dynamics, Ecology

The sudden death of chimpanzees and gorillas in Côte d'Ivoire (Tai National Park) and Cameroon (Dja Reserve) in 2001 and 2004 was caused by a new *Bacillus anthracis*- like bacterium. The pathogen was named *Bacillus cereus* biovar *anthracis (Bcbva)* because it combines the chromosomal background of *Bacillus cereus* with the virulence plasmids of *Bacillus anthracis* and displays characteristics of both species on bacteriological level. The virulence of *Bcbva* was studied in small animal models and shown to be comparable to that of classical *Bacillus anthracis.*

Until today *Bcbva* has only been found in tropical rain forests and many questions regarding its epidemiology and ecology still need to be addressed. In an ongoing long-term study in Tai National Park autopsies on all deceased wildlife have been conducted with samples dating back to 1996. *Bcbva* was identified as a frequent cause of death for a number of large mammal species. To reveal possible transmission pathways and reservoirs various environmental samples were collected and tested. All samples were analyzed using molecular methods and positive PCR results were confirmed by bacterial culture. The genomes of >200 *Bcbva* isolates are currently being determined by next generation sequencing and will be used for SNP-based phylogenomic analyses; to further inform the latter we also performed *in vitro* experiments to determine the whole genome mutation rate of *Bcbva*. This unique set of data will help us understand the population dynamics of *Bcbva* in Tai National Park, and possibly highlight plausible routes of transmission.

D 04

Real-time multiplex polymerase chain reaction for the detection of enterohemorrhagic *Escherichia coli* O26:H11 and differentiation of strains belonging to the new *E. coli* O26:H11 clone

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Enterohemorrhagic *Escherichia coli* (EHEC) of serotype O26:H11/H$^-$ are the most common non-O157 EHEC causing human diseases worldwide. Strains harboring *stx*$_{1a}$ gene prevail among isolates from patients, but strains harboring *stx*$_{2a}$ as the sole Shiga toxin (Stx)-encoding gene have been emerging and are significantly associated with a severe clinical outcome of the infection such as hemolytic uremic syndrome (HUS). The *stx*$_{2a}$-harboring strains consist of two phylogenetically distinct groups defined by sequence types ST21 and ST29. The ST29 strains represent a new virulent clone of EHEC O26 that emerged in Germany in the 1990s and accounted for ~50% of all *stx*$_{2a}$-harboring EHEC O26 strains isolated from patients with HUS in Europe during 1996 to 2012. Despite the clinical significance of strains of the new clone, reservoirs of this pathogen and sources of the infection for humans are unknown. The improvement of this situation requires an availability of a reliable and rapid method for identification of EHEC O26 of the new clone, which is at present based on multilocus sequence typing which is not routinely performed. In this study, we developed a rapid and specific real-time multiplex PCR (rtMPCR), which allows a stepwise identification of EHEC O26:H11/H$^-$ and distinguishing of strains of the new clone. 50 human *stx*$_{2a}$-harboring O26:H11/H$^-$ strains whose multilocus sequence typing (MLST) had been determined were tested. The real-time PCR results demonstrated 100% concordance with MLST typing. Of the 50 human EHEC O26:H11/H$^-$ strains, 26 (52%) belonged to ST29. Introducing this rtMPCR into routine microbiological laboratories will improve our understanding the epidemiology of this important pathogen.

D 05

Defining hidden traits of successful pathogenic E. coli lineages in sequence type 10 strains

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Keywords: Escherichia coli, population genetics, microevolution

The ancestral Escherichia coli sequence type (ST) 10 harbors commensal and pathogenic isolates, thus presenting a valuable population for studying E. coli microevolution.
Whole-genome sequencing and population genetic analyses of a representative ST10 E. coli collection of 96 strains defined three phylogenetic subgroups as well as host and pathotype-specific recombination patterns.
Biolog analyses revealed differences in the metabolic pathways for certain pathotypes. This enabled us to identify pathtotype-specific biomarkers, possibly enabling future new anti-infective strategies.

D 06

Usefulness of MinION in Orthopoxvirus Sequencing

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Keywords: Orthopoxvirus, Next generation sequencing, MinION

Background and objectives:
Aim of the study was to test the usefulness of Oxford nanopore's MinION next generation sequencing platform in Orthopoxvirus (OPV) sequencing.
Materials and methods:
DNA from cell culture propagation or DNA from patient material was used/will be used for MinION sequencing.
Results:
Initial experiments produced reads of up to 16,065 bases in length. The longest OPV read so far was 10,908 bases long. A mapping of OPV reads or assembly was not possible with standard bioinformatics tools. Only a local blast search of the reads to the NCBI nr/nt database showed a low pairwise identity (76.6%) to the corresponding OPV sequence.
Conclusion: The MinION is an ultraportable device that generates reads that are up to 16 kb long. These two features in combination, as well as the easy library generation procedure that only needs 6 hours, makes this device a promising next generation sequencing tool for the future.

D 07

Brucellosis in small mammal populations – a natural reservoir of novel *Brucella* species in Germany?

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Keywords: Brucella, small mammals, detection, Germany

Background and objectives: Brucellosis is a widespread zoonotic disease transmitted from animal reservoirs to humans. In Germany, bovine and ovine/caprine brucellosis were eradicated more than a decade ago and mandatory measures in livestock have been implemented. In contrast, surveillance of wildlife is still challenging, and reliable data do not exist. To assess the role of small mammals as a potential reservoir or vector for *Brucella* spp. a molecular survey was carried out.
Materials and methods: Large scale rodent monitoring data were used to identify potential host species of *Brucella* in small mammal populations, to describe the spatial distribution of brucellosis in small mammals, and to determine effects on the means of transmission.
Results: A total of 537 small mammals which were trapped in four federal states located throughout Germany were investigated for the presence of *Brucella.* Using a two-step molecular assay based on *Brucella*-specific sequences, 14.2 % (n=76) of the tested animals were positive. These originated mainly from Western and Southwestern Germany, where preliminary analyses indicate population density-dependent *Brucella* prevalence. *recA* typing revealed a close relationship to a potentially novel species recently isolated from red foxes.

D 08

Efficient cloning of complete NNSV full-length genomes by RecE/RecT mediated recombination to create genetically modified field isolates.

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Keywords: Rabies, reverse genetics, RedET cloning

Reverse genetics for NSVs let to an outstanding boost in virus research as targeted mutagenesis of virus genomes allowed direct proof of concepts in virus replication and pathogenesis. Although reverse genetics technology had been further developed over time, still a bottleneck in many systems is the limited number of cloned cDNA genomes. In particular, in the case of non-segmented NSVs used cDNA clones are often generated from cell culture adapted or attenuated vaccine strains, leading to a limited usability in pathogenesis research. In case of rabies virus (RABV) most reverse genetics work has been performed with recombinant viruses derived from attenuated vaccine strains or mouse adapted virulent virus.

Here we developed a system in which cDNA copies of complete virus genomes from field RABV strains (from dog, fox and raccoon) were directly cloned into reverse genetics vectors by RedE/T mediated recombination. The use of Rac phage derived recombination enzymes RedE and RedT allowed rapid and highly efficient cloning with up 80-90% correctly recombined virus cDNAs. Because the RedE/T recombination approach works independently of genome size and needs no restriction endonucleases, no a priori sequence information about the clone is required except for the 50 terminal nucleotides. Hence, the system is highly flexible, can be easily adapted to other NSVs and allows not only efficient cDNA cloning but also rapid recovery of different recombinant viruses strains. Exemplary, we show the rescue of different field RABV strains that now enable us to perform pathogenesis research with genetically modified field virus strains in their respective hosts. This may be an important step in the identification of pathogenesis factors, host adaptive mutations and attenuation strategies beyond conventional mouse models.

D 09

Comparison of the infection of porcine precision-cut lung slices by porcine influenza virus H3N2 and porcine respiratory coronavirus PRCoV

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Keywords: Coronavirus, porcine lung, influenza virus

Ex vivo systems are useful tools to analyze virus infection. Here, we established coronavirus infection studies in porcine precision cut lung slices (PCLS). Porcine coronaviruses as well as porcine influenza A viruses (SIV) can be involved in the porcine respiratory disease complex (PRDC). PRDC is caused by a combined infection of several viruses and/or bacteria. We compared single infection by SIV H3N2 and porcine respiratory coronavirus (PRCoV), as well as co-infection of the PCLS with both viruses. PCLS were infected for two days and analyzed by confocal microscopy after staining for viral antigen. The ciliary activity of infected PCLS was compared with uninfected controls over a time period of 7 days. PCLS infected with SIV H3N2 showed a clear decrease in ciliary activity two days post infection. In contrast, in PCLS infected with SIV H3N2 and PRCoV as well as with PRCoV alone ciliary activity was reduced 4-5 days post infection. Virus titration on NPTr cells showed lower infectious titers of PCLS supernatants after co-infection with SIV H3N2 and PRCoV than after mono-infection with PRCoV. Titration of the supernatants on MDCKII cells showed higher virus titers of the supernatants of co-infected PCLS compared to H3N2 alone. These results suggest an interaction of both viruses that is not fully understood and highly dependent on time and infection conditions. Further studies will show in what extend the viruses influence each other during infection of the lung epithelium.

D 10

In silico validation of diagnostic PCR assays

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Keywords: Diagnostic PCR, software, validation

Who has never asked themselves in a diagnostic setting whether their favourite PCR assay was still up to date and thus reliably detected every known pathogen discovered and sequenced so far? To make scientists sleep well, we developed a bioinformatics tool for the automated *in silico* validation of diagnostic PCR assays.

The tool called PCRater was developed using Java. Degenerated bases are resolved and an automated NCBI BLAST search – with the option to include own unpublished sequences in the search via local BLAST – is performed to test primers and probes for specificity to pathogen sequences. All BLAST hits are evaluated for specific binding of primers/probes, generation of product and/or signal and meeting the selected taxonomy criteria. The program can be run routinely and even in batch mode. Results are presented in a graphic interface, and can be filtered and exported as Excel file.
In order to demonstrate the usability of PCRater, we evaluated Ebolavirus assays recently published. According to the PCRater results, some of the assays showed a higher risk of failing in the detection of individual Ebolavirus strains available in GenBank.

We believe that this tool will be of great advantage in keeping diagnostic PCR assays up to date and thus will help to keep up with the rapidly growing number of sequences in sequence databases. PCRater is open-source and platform-independent.

Poster Session New and emerging zoonoses

N 01

Close interface between humans and animals as a breeding ground for interspecies transmission of viruses in rural Africa and Asia

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Keywords: Zoonoses, developing countries, livestock (max. 3)

Background and objectives: Intensification of land-use, bushmeat trade, and migration are among the main drivers for emergence of infectious (zoonotic) diseases (EID) in sub-Saharan Africa and South-East Asia, recognized EID hotspots. In rural Côte d`Ivoire and Laos, the overlapping habitats of the local population, domestic and wild animals create many opportunities for cross-species transmission of pathogens. In this study, we investigated whether this propitious environment facilitates the inter-species transmission of environmentally stable and mainly host-specific viruses (e.g. adenovirus, AdV) and of other viruses with zoonotic potential (e.g. hepatitis E virus).
Materials and methods: Fecal samples collected from humans and domestic animals in the study regions were tested by PCR and ELISA. Circulating viruses were characterized by sequencing and subsequent phylogenetic and species delineation analyses.
Results: In livestock, AdV shedding was highly prevalent and diverse, and some of the identified AdV might represent novel types. Despite the pronounced human-livestock-wildlife interface, only anthropozoonotic and cross-species, but no zoonotic transmission of AdV was observed. Moreover, circulation of other potentially zoonotic viruses was revealed.
Conclusion: These findings underline the thus far underestimated importance of reverse zoonotic transmission of viruses and of the role of domestic animals as pathogen reservoirs or intermediate hosts.

N 02

Absence of an appropriate receptor rather than lack of proteolytic activation prevents entry of bat-borne SARSr-CoV into human cell lines

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Keywords: Bats, SARS-CoV, entry

At the beginning of this century, the severe acute respiratory syndrome (SARS) pandemic caused by a novel coronavirus (SARS-CoV) caused 774 death and wrecked enormous economic havoc. In the aftermath of SARS, bats have been shown to harbour a variety of related viruses (SARSr-CoV) and have recently been confirmed as the natural reservoir of SARS-CoV. However, with one single exception, no SARSr-CoV could be isolated, leaving a gap of knowledge about their zoonotic potential. We investigated the ability of the spike glycoproteins (S) of non-cultivatable SARSr-CoV for their ability to mediate virus entry into target cells, as a predictor of zoonotic potential.

Employing S protein pseudotyped vectors, we could show that SARSr-S proteins were unable to mediate entry into cell lines, despite robust expression and particle incorporation of the S proteins. Ectopic expression of human or bat ACE2 rendered target cells susceptible to SARS-S but not SARSr-S-driven transduction and analysis of chimeric S proteins revealed that SARSr-S proteins can drive membrane fusion. Furthermore, human proteases known to activate SARS-S for entry were able to process SARSr-S proteins. These results indicate that the S proteins of SARSr-CoVs utilize a different/additional entry receptor than SARS-CoV but can be readily activated by human proteases.

N 03

Virulence Determinants within the Hemagglutinin of H5N1 HPAIV.

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Keywords: H5N1 HPAIV, hemagglutinin, virulence

Highly pathogenic avian influenza viruses (HPAIV) cause rapid and fatal disease in chicken leading to enormous losses in poultry world-wide. Moreover, repeated zoonotic infections have raised serious concerns of a novel pandemic. Beside their essential polybasic hemagglutinin cleavage site (HACS), we previously demonstrated the existence of further virulence determinants required for a lethal phenotype in chicken. In this study, we aimed to reveal those determinants within the HA.

To this end, we used the reverse genetics systems from the HPAIV A/Swan/Germany/R65/01 (H5N1) (R65) and the low-pathogenic strain A/Teal/WV632/2005 (H5N1) to exchange the entire HA or the HA1 and HA2 regions. Moreover, we modified the amino acids 123 and 124 at the HA1/HA2 interface. Then, we investigated the HA activation pH versus virulence of those HA mutants in chicken.

Mainly, we found that the R65 HA variants with exchanged HA1 and/or introduced the point mutations S123R or I124T display a notable decrease of activation pH up to one pH magnitude paralleled by considerably reduced virulence in chicken.

Therefore even in the complete HPAIV R65 background, the elevation of the HA activation pH predominantly mediated by amino acids at residues 123 and 124 is essential for high virulence in chicken. Overall, the transformation of low-pathogenic strains into HPAIV mediated by acquisition of the essential polybasic HACS requires co-adaptation of the HA.

N 04

Transmission of Ebola virus: Facts and Issues

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Keywords: Ebola, transmission, zoonosis

Background and objectives: Whilst transmission of Ebola virus primarily occurs by direct contact with bodily fluids of infected humans, index cases are generally linked to animal contacts. Regarding the dynamic of the ongoing and first Ebola virus disease (EVD) epidemic in West Africa, further potential transmission routes should be taken into account.
Materials and methods: The current literature has been screened for eligible transmission routes of Ebola virus.
Results: Non-human primates, duikers, fruit bats, small rodents, and shrews are considered potential hosts of Ebola virus. Whilst indirect or direct contact with body fluids, e.g., urine, faeces or saliva of fruit bats or non-human primates might cause EVD, data on virus transmission by rodents or shrews and their role as mechanical vectors are scarce. The same applies for mechanical transmission of contaminated bodily fluids to healthy individuals by houseflies, which are known to transmit several viruses and bacteria. For airborne transmission, Ebola virus is considered to require genotypic changes, however, experimentally produced aerosols are capable of causing EVD.
Conclusion: Though currently applied measures finally seem to reduce the spread of the Ebola virus, some questions considering its transmission still remain unclear. Further studies should evaluate the role of aerosol-borne transmission, insects as mechanical vectors and rodents and shrews for biological or mechanical virus transmission.

N 05

Astrovirus and coronavirus transmissibility in insectivorous bats depends on species identity rather than spatial proximity of the host

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Keywords: insectivorous bat species, astrovirus, species specificity

Background and objectives: In recent years, bats moved into the focus of research in infectiology, after a number of infectious agents with a zoonotic potential were detected in different bat species. However, there is still a lack of knowledge on the transmission dynamics in bats, as well as from bats to other mammals.
Materials and methods: We analysed more than 950 urine, feces and oral swab samples collected from 653 bats of mainly four species (*M. nattereri*, *M. bechsteinii*, *M. daubentonii*, and *P. auritus*) in three regions in Germany Bavaria, Mecklenburg Western Pomerania and North Rhine Westphalia. Using hemi-nested reverse transcriptase (RT)-PCR amplification of fragments within the highly conserved regions of the respective RNA dependent RNA polymerase (RdRp) genes, we screened for the presence of coronavirus, paramyxovirus and astrovirus related nucleic acids.
Results: We detected astrovirus sequences in up to 65% of the individual animals per local population, while the detection rates for coronaviruses and paramyxoviruses were distinctly lower. The sequence similarities in samples collected from the same bat species in different geographical areas were noticeably larger than the sequence similarities between samples from different species sampled at the same location.

N 06

Hendra virus attachment protein expressed in the protozoan host *Leishmania tarentolae* displays interaction with Ephrin-B2 receptor

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Keywords: Hendra virus, attachment protein,. Leishmania tarentolae

Background and objectives: *Hendra virus* (HeV) is an emerging zoonotic paramyxovirus that has caused several outbreaks with high morbidity and mortality in human and horses in Australia since 1994. HeV infection is mediated by the attachment (G) glycoprotein that is essential for receptor binding of the virus to the host cell membrane. Recently, vaccine strategies against HeV infection centred upon the G protein, eliciting a potent neutralizing antibody response under experimental settings. The unicellular parasite *Leishmania tarentolae* (*L.tarentolae*) has been introduced as a novel tool to express recombinant proteins with mammalian-type glycosylation. Only a few viral proteins have been expressed in this system so far. Here we show the expression and purification of a truncated soluble HeV G protein (sHeV G).
Materials and Methods: *Strep*-tag affinity chromatography was used to purify the recombinant protein. A potential binding between the sHeVG and Ephrin-B2, the cellular entry receptor of HeV, was investigated by ELISA, immunoprecipitation and functional cell adhesion assays.
Results: Total protein amount was about 0,5mg per litre of cell culture. Mass spectrometry confirmed the authenticity of the recombinant protein. Furthermore, sHeV G interacted with Ephrin-B2 in all conducted assays indicating proper folding of the recombinant protein. Conclusion: Taken together, these experiments confirm the suitability of *L.tarentolae* for the expression of viral proteins.

N 07

Arcobacter butzleri induce inflammatory responses in gnotobiotic IL-10 deficient mice

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Keywords: Arcobacter butzleri, immune-pathological properties

Background and objectives: Acute gastroenteritis with abdominal pain and acute or prolonged watery diarrhoea has been described for humans infected with *Arcobacter* (*A.*) *butzleri*. Adhesive, invasive and cytotoxic capacities have been described for *A. butzleri in vitro*. So far, only limited information is available about the immune-pathogenic mechanisms of infection *in vivo*.
The aim of this study was to investigate the immune-pathological properties of *A. butzleri* in a well-established murine infection model.
Methods: Gnotobiotic IL-10$^{-/-}$ mice were orally infected with two *A. butzleri* strains and clinical signs as well as fecal shedding were determined over time. At day 6 and day 16 post-infection apoptotic and proliferating cells, intestinal infiltration with immune cells and cytokine expression patterns were determined.
Results: Despite no overt macroscopic signs of disease, stable infection of gnotobiotic IL-10$^{-/-}$ mice with *A. butzleri* led to increased numbers of apoptotic cells, influx of immune cells and higher expression of pro-inflammatory cytokines in the intestine, depending on the respective *A. butzleri* strain.
Conclusion: Even though no overt clinical signs have been observed we could clearly show that *A. butzleri* is able to stably colonize and induce apoptosis paralleled by induction of pro-inflammatory immune responses in the intestine of infected gnotobiotic IL-10$^{-/-}$ mice, pointing towards an immune-pathogenic potential of *A. butzleri in vivo.*

N 08

Phenotypic analysis and genome sequence of a new *Francisella species* (W12-1067) isolated in Germany

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Background: *Francisella* isolates from patients suffering from tularemia in Germany are generally strains of the species *F. tularensis* subsp. *holarctica*. Furthermore, to our knowledge, no other *Francisella* species are known for Germany. Recently, we isolated a new *Francisella* species from a water reservoir of a cooling tower in Germany. Results: *Francisella* strain W12-1067 was isolated from a water reservoir of a cooling tower of a hospital in Germany. The closest homolog of this strain is the recently published new strain *F. guangzhouensis*, isolated in China. The 16S rDNA of W12-1067 is 99% identical to the respective nucleotide sequence of *F. guangzhouensis.* The overall sequence identity of both genome is approximately 89%, indicating that strain W12-1067 is not identical to *F. guangzhouensis*. The whole genome of the strain W12-1067 was sequenced (~1.7 mbp, 32.2% G+C content) and the draft genome was annotated. Whereas various virulence genes common to the genus *Francisella* are present, the major virulence factor, the *Francisella* pathogenicity island (FPI), is missing. Instead, another putative type-VI secretion system is present within the genome of strain W12-1067 and the strain was able to replicate within a mouse-derived macrophage-like cell line.
Conclusions: Isolate W12-1067 is closely related to the recently described *F. guangzhouensis* species and is able to replicate within eukaryotic host cells. Interestingly, it exhibits a putative new type-VI secretion system. Obviously, *F. tularensis* subsp. *holarctica* is not the sole species in Germany. Therefore, additional research is needed to

further investigate the epidemiology, ecology and pathogenicity of *Francisella* species present in Germany.

N 09

Detection of diverse novel bat astrovirus sequences in the Czech Republic

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Keywords: astrovirus, bat, phylogenetic analysis, novel viruses

Background: Bats (Chiroptera) are important reservoirs of viruses, including zoonotic viruses. Astroviruses are a major cause of gastroenteritis in humans and animals. Recently, novel groups of astroviruses were identified in apparently healthy insectivorous bats.
Materials and methods: A total of 43 fecal or intestinal content samples from different European bat species were collected in 2008-2014 in South Moravia, Czech Republic. Total RNA was extracted with the QIAamp Viral RNA Mini Kit, followed by reverse transcription (Transcriptor First Strand cDNA Synthesis Kit) and seminested PCR. Resulting amplicons were purified with the Wizard SV Gel and PCR Clean-Up System and sequenced commercially.
Results: We report the detection of diverse novel astrovirus sequences in nine different European bat species: *Eptesicus serotinus, Hypsugo savii, Myotis emarginatus, Myotis mystacinus, Nyctalus noctula, Pipistrellus nathusii* or *Pipistrellus pygmaeus, Pipistrellus pipistrellus, Vespertilio murinus*, and *Rhinolophus hipposideros*. In six bat species, astrovirus sequences were detected for the first time. One astrovirus strain, detected in *Rhinolophus hipposideros*, clustered phylogenetically with Chinese astrovirus strains originating from bats of the families *Rhinolophidae* and *Hipposideridae*. All other Czech astrovirus sequences from vesper bats formed, together with one Hungarian sequence, a separate monophyletic lineage within the bat astrovirus group.

Conclusion: These findings provide new insights into the molecular epidemiology, ecology, and prevalence of astroviruses in European bat populations.

N 10

Virulence of emerging *Bacillus cereus* biovar *anthracis* is determined by toxins and two types of capsules.

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Keywords: anthrax, virulence plasmids, capsule

Untypical bacteria causing anthrax-like disease were isolated from chimpanzees and other animals in African rain forest areas. The bacteria exhibit bacteriological features typical for either *B. anthracis* or *B. cereus* and possess plasmids with high similarity to the toxin and capsule plasmids of *B. anthracis* (*Ba*) in a chromosomal background of *B. cereus*. Therefore, they were designated as *B. cereus* biovar *anthracis* (*Bcbva*). In our study we wanted to analyse the regulation of the virulence factors and their effect in appropriate *in vivo* models.

Gene expression was studied from bacteria grown under different conditions. Virulence was tested by cutaneous and intranasal delivery of *Ba* and *Bcbva* spores in mice and guinea pigs. Bacterial mutants were constructed to assess the influence of different factors separately.

Virulence of wild type strains of *Ba* and *Bcbva* was comparable, but in contrast to *Ba*, where lack of the capsule plasmid results in considerable loss of virulence, a corresponding *Bcbva* mutant was not attenuated. This fact can be ascribed to production of a second capsule composed of hyaluronic acid in *Bcbva* which is impeded in *Ba* due to a mutation in the corresponding gene cluster located on the toxin plasmid. Regulation of toxins and both capsule types is induced by growth in elevated CO_2 atmosphere.

Bcbva strains might be considered as a new lineage in the *B. cereus* group with a similar co-evolution process between chromosome and plasmids as supposed for *B. anthracis*.

N 11

Borna disease virus 1 in the red fox (*Vulpes vulpes*)?

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Keywords: borna disease virus 1, red fox, encephalitis

Background and objectives: Bicolored white-toothed shrews act as reservoir for Borna disease virus 1 (BoDV-1). The red fox (*vulpes vulpes*) mainly feeds on small mammals including shrews and is susceptible for viruses of the order *Mononegavirales* which comprises many neurotropic and zoonotic viruses. The aim of the study was to investigate whether foxes can be infected by BoDV-1 in case of contact to BoDV-1 shedding bicolored white-toothed shrews.
Materials and methods: Blood and brain samples from 232 red foxes originating from Bavaria, Baden-Württemberg and Hesse have been screened for anti-BDV antibodies, BDV-RNA and BDV-antigen by indirect immunofluorescence test, RT-PCR, immunohistochemistry and histology. A pan-Borna-RT-PCR detecting strains from five bornavirus species and including the new zoonotic variegated squirrel strain was applied.
Results: 37/225 foxes displayed anti-BoDV-1 antibodies. 7/63 foxes originated from Bavaria, 23/131 from Baden-Württemberg and 7/31 from Hesse. Titers reached from 1:40 to 1:2560. 16 foxes displayed a non-purulent encephalitis. Neither BoDV-1-RNA nor -antigen has been found in the brain samples, also not by the use of the pan-Borna-RT-PCR.
Conclusion: So far only anti-BoDV-1 antibodies could be detected in foxes. Further investigations on non-purulent encephalitis of unknown origin in red foxes are currently in progress.

N 12

Detection of potentially zoonotic enterovirus A119 in healthy people living in Côte d'Ivoire

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Keywords: enteroviruses, Côte d´Ivoire, zoonotic transmission

Background and objectives: Enteroviruses (EVs) infect numerous mammalian species, including humans and Non-Human Primates (NHP). Data from Cameroon reported a high frequency among captive NHP of EV serotypes already isolated in humans, including EV-A119, just recently identified in humans in sub-Saharan Africa. We investigated enterovirus presence in healthy people living in Côte d´Ivoire and identified a potential zoonotic enterovirus serotype.
Materials and methods: The study was based on 105 stool samples obtained from healthy individuals collected between June 2013 and December 2014 in the Sud-Comoé Region of Côte d´Ivoire. After shipment to Germany, the samples were analyzed by real-time PCR for the presence of EVs. Molecular typing and virus isolation of all samples were performed.
Results: Out of 105 samples, 24 (22.8%) were detected EV positive by real-time PCR. Twenty-one EV positive samples could be characterized with serotypes belonging to EV groups A – C. Several rarely described serotypes were identified, e. g. EV-C99, EV-B93, EV-C116 and EV-A119. Interestingly, the full-length VP1 sequence of the EV-A119 isolate displayed a sequence similarity of 94% with the EV-A119 strain isolated from a captive chimpanzee in Cameroon (KF541634).
Conclusion: This study provided the first available data about the presence of potentially zoonotic EV serotypes in Côte d´Ivoire.

N 13

Leptospira spp. in shrews and rodents from locations with low and high hantavirus incidence rates in Baden-Wuerttemberg, Germany

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Keywords: Leptospira spp., rodent-borne pathogen, reservoir

Leptospirosis is a worldwide distributed, zoonotic disease caused by pathogenic *Leptospira* spp.. Small mammals, mainly rodents, are considered as most important maintenance reservoir hosts in nature. This is likewise the case for hantaviruses which may cause similar clinical symptoms. We were interested whether or not the prevalence for *Leptospira* spp. in rodents and shrews differed between study sites with high (10-100 cases per 100.000 per year) and low (≤1) hantavirus incidence rates.

During a study for the epidemiology of Puumala hantavirus, small mammals were collected in 2012 and 2013 at four sites with high hantavirus incidence rates and at four other sites with low rates. Small mammals were dissected and kidneys were removed. DNA was extracted from the kidneys and a real-time PCR targeting the *lipl 32* gene was performed to detect *Leptospira* spp.. In total 736 small mammals were collected, 660 *Myodes glareolus*, 68 *Sorex* spp., 4 *Microtus* spp. and 4 *Apodemus flavicollis*. Altogether 43 of all small mammals were positive for *Leptospira* spp. (5.8%), 27 of those were *M. glareolus*, 12 *Sorex* spp., 2 *Microtus* spp. and 2 *A. flavicollis*. Although 31 of those animals were from sites with high hantavirus incidence rates and only 12 from low incidence sites, the prevalences did not differ significantly. However shrews were significantly more often infected then rodents suggesting a more prominent role as reservoirs for *Leptospira* spp.

N 14

Geographic distribution and diversity of Hepatitis E virus in dromedary camels, 1983-2013

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Keywords: Hepatitis E virus, camels, HEV

Hepatitis E virus (HEV) is a major cause of hepatitis globally. Major animal reservoirs for zoonotic infection of humans are swine and deer. A recent study reported 2 HEV genomic sequences in dromedary camels sampled in the United Arab Emirates (UAE).
Here, we investigate camels sampled in Africa and the Arabian Peninsula as reservoir hosts for potentially zoonotic HEV.
A total of 1824 fecal and serum samples from camels were collected during 1983-2013 in five Arabian and African countries. Specimens were tested for HEV RNA by broadly reactive HEV RT-PCR, sequenced and phylogenetically analyzed. Seroprevalence was determined using an Enzyme Linked Immunosorbent Assay (ELISA).
HEV was detected in 0.3 % of serum samples and 1.9 % of fecal samples. The oldest positive sample dated back to 1983. Positive samples originated from the UAE, Kenya and Somalia. Camel HEVs from this and the preceding study clustered monophyletically in sister relationship to all other known HEVs. The HEV nucleotide diversity found in camel was high with 21.6 %.
The percentage of samples ranked positive in the ELISA was high in all sampling sites with 65-90 %. Viral RNA concentration was up to 1.94×10^8 copies per gram feces and up to 2.51×10^6 copies per ml of serum. Conclusion: HEV is a common pathogen in camels. High viral loads may facilitate zoonotic transmission.

N 15

Co-infections of *Neoehrlichia mikurensis* or *Anaplasma* spp. with particular Lyme borreliae in questing *Ixodes ricinus* ticks

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Keywords: Lyme borreliosis, Neoehrlichia mikurensis, Anaplasma spp.

Ixodes ricinus ticks serve as vector for pathogens, including *Borrelia burgdorferi* s.l., *Neoehrlichia mikurensis* and *Anaplasma* spp. Each of the European species of Lyme borreliae is associated with a group of reservoir hosts. The reservoir associations perpetuating *N. mikurensis* and *Anaplasma* spp. are less well defined. If certain Anaplasmatacean species are adapted to a reservoir host, co-infections of that pathogen and particular Lyme borreliae would be more frequent in questing ticks than expected by chance. Thus, we determined rates of co-infection to identify potential reservoir hosts. Questing *I. ricinus* ticks which we had previously characterized for the presence and species of Lyme borreliae were examined for Anaplasmataceae by high-resolution melting PCR. We compared the rates of single and multiple infections by χ^2-test and determined the index of co-infection (I_c, after Ginsberg). Of 994 ticks, 9.7% harbored *N. mikurensis,* 3.1% a particular variant of *Anaplasma* spp. and 30.6% Lyme borreliae. 13.1% and 6.6% were infected by rodent-associated *B. afzelii* and lizard-associated *B. lusitaniae*, respectively. Nymphal ticks co-infected by *B. afzelii* and *N. mikurensis* were significantly more frequent than expected (I_c 4.6). Similarly, rates of co-infection by *B. lusitaniae* and a novel *Anaplasma* variant in nymphal and adult ticks were significantly higher than expected (I_c 14). We conclude that *N. mikurensis* is associated with rodents and this *Anaplasma* variant with lizards.

N 16

Potentially Zoonotic Novel Phlebovirus in Northern Bats, Germany

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Keywords: phleboviruses, bats, phylogeny

Bats are reservoir hosts for several emerging and re-emerging viral pathogens, causing morbidity and mortality in wildlife, animal stocks and humans. Various phleboviruses within the family *Bunyaviridae* have been documented as such viral pathogens, including the highly pathogenic Rift Valley fever virus and Malsoor virus, a novel phlebovirus with close genetic relation to severe fever with thrombocytopenia syndrome (SFTSV) and Heartland virus, which have both caused encephalitis and haemorrhagic fevers with fatal casualties in human.
For the identification of novel bat viruses in European bats, organs of moribund or dead-found microchiropteran bats with potentially virus-related histo-pathological changes were pooled and further processed for deep-sequencing of the bat virome. Within this study, a novel virus belonging to the genus *Phlebovirus* was detected in the virome of several Northern bats (*Eptesicus nilssonii*). Phylogenetic analysis of the polymerase protein of this virus showed the closest relation to the recently isolated Malsoor virus, Heartland virus and SFTSV.
In this study we present the detection of a novel phlebovirus revealed through deep-sequencing of the *Eptesicus nilssonii* bat virome. So far, no other phlebovirus has been detected in bats of the family Vespertilionidea. Considering the phylogenetic relation to pathogenic Heartland virus and SFTSV, a potential zoonotic impact to public health should be considered.

N 17

The role of integrins in Flavivirus infection

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Keywords: Integrins, Flavivirus

Background and objectives: Dengue virus, Japanese encephalitis virus and West Nile Virus (WNV) belong to the Flavivirus genus and are responsible for large outbreaks throughout the world with high rates of mortality and morbidity. Up to now, few molecules including integrins were characterized as candidates for Flavivirus receptors. Integrins are heterodimeric molecules with important functions in cell biology like cell adhesion and migration, cell signalling and apoptosis. Previous studies from our group using WNV as model showed that the β3 integrin subunit may be involved in WNV infection. The aim of the present study is to elucidate the role of integrins in Flavivirus infection.
Materials and methods: Mouse cell lines deficient for β1, αV, β3 or αV/β3 integrin subunits were established previously. In this study their integrin expression was rescued and together with integrin gene transfected CHO cells (a Flavivirus non permissive cell line) the rescued cells are used in infection experiments to evaluate the potential role of integrins in Flavivirus infection.
Results: The integrin expression in mouse and hamster cell lines has been successfully rescued. RT-PCR, FACS, adhesion assay and immunofluorescence analysis showed high level of integrin expression.
Conclusion: Further analyses of short- and long-term infection experiments with deficient and rescued cells will reveal a profound insight into the potential use of integrins in flavivirus interaction with the host cell.

Poster Session Free topics

F 01

Arthropod origin of a pathogenic RNA virus family

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Keywords: virus evolution, ancestral reconstruction, arbovirus

Background and objectives:
The evolutionary origins of arboviruses are unknown because their typical dual host tropism is paraphyletic within viral families. Here we studied one of the most diversified and medically relevant RNA virus families, the *Bunyaviridae*, in which four of five established genera are arboviruses.
Materials and methods: Viruses were isolated in mosquito cells and ability to infect vertebrates was assessed by temperature gradient studies. Ancestral host reconstructions were performed using Mesquite and Bayestraits.
Results: We define two cardinally novel bunyavirus groups based on isolation of two novel viruses from mosquitoes. Both viruses were incapable of replicating at vertebrate-typical temperatures but replicated efficiently in insect cells. Replication involved formation of vRNA and mRNA including cap snatching activity. SDS-PAGE, mass spectrometry and Edman degradation identified translation products corresponding to virion-associated RNA-dependent RNA polymerase (RdRp), glycoprotein precursor, Gn, Gc, as well as putative NSs and NSm proteins. Both viruses were genetically equidistant from all other bunyaviruses, showing <15% amino acid identity in the RdRp palm domain. The viruses define two novel sister taxons to the superclade of orthobunyaviruses, tospoviruses and hantaviruses. Phylogenetic ancestral state reconstruction of bunyavirus hosts for major virus lineage bifurcations suggested ancestral associations with arthropods at deep nodes throughout the bunyavirus tree.
Conclusion: Our findings suggest that the vertebrate-infecting viruses evolved from arthropod-specific progenitors.

F 02

Does host evolution limit the distribution of Central European *Puumala virus*?

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Keywords: Puumala virus, bank vole, evolutionary lineages

Puumala virus (PUUV) is a hantavirus causing a mild to moderate form of hemorrhagic fever with renal syndrome in humans. Its reservoir host, the bank vole (*Myodes glareolus*), is widely distributed in Europe. PUUV outbreaks mainly affect western and southern Germany. In contrast, very low numbers of human cases have been recorded in Northeastern Germany.
The objective of our study is to find out potential reasons for the inhomogeneous distribution of PUUV infections in Central Europe. Our hypothesis is that the presence of different evolutionary lineages of the rodent host represents a major reason.
For this purpose, bank voles from relevant regions of Germany and the neighbouring parts of Poland were tested for PUUV infection. Serological and molecular analyses demonstrated a usually medium to high PUUV prevalence in endemic areas. In contrast, bank voles from various sites in the northeastern part of Germany were seronegative. Similarly, the investigations showed an absence or low prevalence of PUUV in the Polish bank vole populations. Initial *cytochrome b* analyses of bank voles suggested the presence of the Eastern and Carpathian evolutionary lineages at the sites in Poland and the Northeast of Germany, but the Western evolutionary lineage in the endemic regions.
Future investigations will have to prove if the different genetic lineages of the bank vole differ in susceptibility to PUUV and might be a cause of the inhomogeneous distribution of this hantavirus in Central Europe.

F 03

Clinical characterization of two severe cases of HFRS caused by hantaviruses Puumala and Dobrava-Belgrade virus genotype Sochi

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Keywords: Dobrava-Belgrade virus, Puumala virus, clinical course

Background: Hantavirus disease belongs to the emerging infections. The clinical picture differs between patients, hantavirus species and may even vary between hantavirus genotypes. The mechanisms that lead to the broad variance of clinical symptoms and severity are not completely understood. Host- and virus-specific factors were discussed.
Methods: We analyzed two severe cases of hantavirus diseases in two young women by comparing clinical signs, laboratory parameters and organ involvement.
Results: One case was caused by Puumala virus (PUUV) in Germany; the second case describes the infection with Dobrava-Belgrade virus genotype Sochi (DOBV) in Russia. The kind of symptoms did not differ between both infections. However, severity and deterioration of laboratory parameter values was stronger in infection caused by DOBV. Dialysis was required once in PUUV and six times in DOBV infection. Hospitalization was much longer (18 days) for DOBV than for PUUV (9 days) disease. In addition to acute renal failure, pleural effusion, pulmonary congestion and acute pancreatitis were observed in DOBV infection. In both cases, normalization of laboratory values was paralleled with the mobilization of circulating endothelial progenitor cells.
Conclusion: Hantavirus disease caused by PUUV and DOBV does not vary in the symptoms but in the severity. Hantaviruses share the same pattern of pathogenesis and repair. However, severity may depend on the replication capacity of hantavirus species.

F 04

Intra-host diversity of canine distemper virus

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Keywords: canine distemper virus, tissue-specific populations

Background and objectives: Morbilliviruses, including measles and canine distemper virus (CDV), cause devastating diseases in their respective hosts. Time course analyses with eGFP-expressing viruses have revealed a sequential dissemination with an initial amplification in immune tissues followed by spread to epithelia and transmission to a new host. While the consensus sequence of these viruses is stable across multiple passages, little is known about the overall diversity and changes associated with replication in different tissues.
Materials and methods: To gain insights in the virus population dynamics over the course of the disease, we sacrificed ferrets at different times after infection with wild type CDV and isolated virus from immune and epithelial tissues. The replication efficiency and growth characteristics of viruses from the different tissues are then compared in cell lines of immune and epithelial origin, and the genetic diversity is determined by deep sequencing.
Results: An initial characterization of the viruses isolated from the different tissues revealed little differences in cell lines of immune cell origin, but there was a slightly improved replication of epithelia-origin virus in epithelial cell lines. We are currently investigating the genetic diversity in each group.
Conclusion: Spread to epithelia results in alteration of virus characteristics.

F 05

Husbandry of insectivores as new animal model

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Keywords: insectivores, husbandry, shrews

Background and objectives: Mostly, rodents are used as animal models, models of other animal species are rare. *Eulipotyphla* (formerly *Insectivora*) are promising model systems for reservoir hosts of emerging infectious diseases and related immunologic issues due to their phylogenetic relation to bats and their primitive mammal characteristics. Shrews are a large family of *Eulipotyphla* and are already known reservoirs of leptospira, hantaviruses and bornaviruses. Data about successful husbandry and breeding of shrews are rare.
Materials and methods: A husbandry of bicolored white-toothed shrews was established with successful breeding.
Results: Shrews were kept in adapted laboratory cages. Food consisted of a mixture of chicken heart, chicken liver and insects. Mating shrews were kept together for 2-3 weeks in a special mating cage. Birth and weaning are performed separately from the male.
Conclusion: Husbandry and breeding of shrews need adapted husbandry conditions. Shrews are promising insectivore models for issues of infection studies, pathobiology and physiology.

F 06

Production of recombinant IFN-γ of *Myodes glareolus* for use in cell culture following *Toxoplasma gondii* infection

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Keywords: Interferon-γ, Myodes sp., Toxoplasma gondii

Background and objectives: *Toxoplasma gondii* is the causative agent of one of the most common parasitic zoonoses world-wide. Recently, it has been shown that field strains of *Mus musculus* have highly polymorphic IFNγ-induced IRG proteins that confer them resistant to *T. gondii* strains normally lethal for laboratory mice. This is believed to allow mouse-virulent *T. gondii* strains to survive in nature and are thus able to reach the definitive host, the cat. However, since wild rodents are the major prey for cats we postulate that *e.g.* voles, *Myodes sp.* are more important for transmission of mouse-virulent strains in nature. To evaluate the relationship between polymorphic IRGs in *Myodes sp.* and *T. gondii* susceptibility in culture systems active IFN-γ is required. Since IFN-γ activity is known to be highly species-specific, the production of the autologous protein for a given species is a prerequisite.
Materials and methods: We cloned and expressed codon optimized IFN-γ from *Myodes glareolus* in *E. coli* and purified it.
Results: Soluble MgIFN-γ was purified to homogeneity in high yield. Dimerization was confirmed by gel filtration implying functional protein.
Conclusion: MgIFN-γ activity on growth of virulent and avirulent *T. gondii* strains can now be tested in *M. glareolus* cells, like the kidney cell line BVK168. Due to high sequence similarity with *Microtus sp.* (~95%) MgIFN-γ is expected to be a valuable tool also for other closely related host-parasite systems like Hanta virus.

F 07

Occurence of *Yersinia enterocolitica* in wild boars in Lower Saxony, Germany

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Keywords: swine, enteropathogenic Yersinia, bioserotype

Background and objectives: In Europe, enteropathogenic *Y. enterocolitica* of bioserotype 4/O:3 and 2/O:9 are the causing agent of Yersiniosis, which is the 4th most frequently reported zoonoses. Slaughter pigs are the most important reservoir, carrying *Y. enterocolitica* mainly in the tonsils.
In recent years, wild boar population has exploded all over Europe leading to increased hunting activities and consumption of their meat. The objective of the study was to get knowledge about the occurrence of *Y. enterocolitca* in wild boars hunted in Northern Germany.
Materials and methods: Tonsils were sampled from shot wild boars. For isolation the standardized ISO 10273:2003 method was used. Presumptive colonies were sub-cultured on LB agar plates and identified by MALDI-TOF. Identified *Y. enterocolitica* strains were serotyped using commercial antisera. Biotyping was performed according to the ISO 10273 method. The chromosomal genes *ail*, *ystA,* and *ystB* and the plasmid-borne virulence genes *yadA*, *virF*, and *yopT* were investigated by PCR.
Results: Tonsils from 17.1% of 111 tested wild boars were positive for *Y. enterocolitica*. All but two isolates belonged to BT 1A, with the majority bearing an *ystB* nucleotid sequence. Two isolated carried the *ail* gene. The remaining *Y. enterocolitica* were identified as BT 1B without carrying the virulence plasmid.
Conclusion: Most *Y. enterocolitica* isolates from wild boars belonged to BT 1A. Typical enteropathogenic *Y. enterocolitica*, usually harboured by slaughtered pigs in Europe, could not be identified.

F 08

Characterization of *Vibrio cholerae* non-O1, non-O139 isolates from the environment and from food in Germany

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Keywords: virulence factors, antibiotic resistance, MLST

Vibrio cholerae bacteria of non-O1, non-O139 serogroups are present in German coastal waters and are found regularly in seafood. These bacteria can cause gastroenteritis and extraintestinal infections. However, so far infections are rare in Germany. In the present study, we investigated German isolates to find out if such isolates could pose a risk for public health.

We selected 100 environmental strains from the North Sea and Baltic Sea and 30 isolates from seafood. The strains were characterized by MLST and examined for the presence of cholera toxin gene and other virulence associated factors including haemolysins, RTX toxins, pandemic islands and type III secretion system. Phenotypic assays for haemolytic activity and antibiotic resistance pattern were also performed.

Genotyping results showed that none of the isolates contained the cholera toxin (*ctxA*) and genes of the *ctx* associated element. The presence of other toxins showed a strain specific pattern. Antibiotic resistance revealed that some *V. cholerae* strains were non-susceptible to aminopenicillins and sporadically resistances towards carbapenems, quinolones and folate pathway inhibitors occurred. Based on MLST analyses, the phylogenetic relationship of strains was characterized. Nearly all strains showed clear haemolytic activity against human and sheep erythrocytes.

Our study indicates the need for continued surveillance of *Vibrio* spp. in Germany as *Vibrio* infections are predicted to increase due to global warming.

F 09

Occurrence of *Giardia* assemblages in seven South Eastern European countries

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Keywords: Giardia duodenalis, assemblages, dogs

Giardia duodenalis is an intestinal parasite infecting various mammals including humans worldwide. *Giardia* comprises the zoonotic assemblages A and B and the non-zoonotic assemblages C to H, harboured by different host species. In order to identify *Giardia* assemblages in dogs from South Eastern Europe, 1645 canine faecal samples from Albania, Bulgaria, Hungary, Macedonia, Romania and Serbia were tested for *Giardia* coproantigen by enzyme-linked immunosorbent assay (ELISA). DNA was extracted from a subset of 107 faecal samples demonstrating *Giardia* cysts by direct immunofluorescence assay (IFA) or microscopy plus 26 IFA-positive canine faecal samples from Croatia. Multilocus sequence typing with nested PCRs was performed targeting five different gene loci: SSU rRNA, ITS1-5.8S-ITS2, beta giardin (bg), glutamate dehydrogenase (gdh) and triosephosphate isomerase (tpi). The ELISA detected *Giardia* infections in 33.7 % of all dogs. Shelter dogs had a significantly higher prevalence compared to household dogs (57.2 vs. 29.7 %, $p < 0.01$). The amplification rate at the different gene loci ranged from 1.5 (tpi) to 82.0 % (SSU rRNA). Sequencing revealed the dog-specific assemblages C and D in 50 and 68 samples, respectively. The results of the study demonstrate that *G. duodenalis*

should be considered as a common parasite in dogs from South Eastern Europe. However, there was no evidence for zoonotic *Giardia* assemblages in the investigated canine subpopulation.

F10

Different disease outcomes in goats experimentally infected with *Mycobacterium avium* subsp. *hominissuis* (MAH) and their potential relevance for zoonotic infection

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Keywords: non-tuberculous mycobacteria (NTM), granuloma, fecal shedding

Background and objectives: MAH elicits granulomatous infection in humans and animals. This study presents two different disease outcomes in goats and discusses their potential relevance for public health.
Materials and methods: Eighteen goat kids were orally inoculated with MAH. Unexpectedly, 2-3 month post first inoculation (mpi) nine goats died or had to be euthanized for animal welfare reasons. The remaining goats were healthy until necropsy 13 mpi. Fecal cultivation was done every 4 weeks. At necropsy tissues were sampled for histology, immunohistochemistry (IHC) and bacterial cultivation. Lesions were evaluated in HE-stained paraffin sections followed by detection of MAH by IHC.
Results: Until 2 mpi all inoculated goats excreted moderate amounts of MAH via feces. Goats necropsied at 2-3 mpi had severe ulcerations with granulomatous infiltrates in organized gut associated lymphatic tissue (oGALT) and extensive granulomas in intestinal lymph nodes (ILN). Variable amounts of MAH were labelled by IHC. Many MAH were cultivated from lesions and peripheral organs. Surviving goats had multiple granulomas in oGALT an ILN. MAH was detected in low amounts by IHC in few granulomas (3/9) and by culture (6/9).
Conclusion: Environmental contamination with MAH via feces is conceivable and might pose a risk for human health. MAH in granulomas of healthy animals might cause meat contamination during slaughter. Further epidemiological research is needed to verify these assumptions.

F 11

The role of integrins in Flavivirus infection

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Keywords: Integrins, Flavivirus

Background and objectives: Dengue virus, Japanese encephalitis virus and West Nile Virus (WNV) belong to the Flavivirus genus and are responsible for large outbreaks throughout the world with high rates of mortality and morbidity. Up to now, few molecules including integrins were characterized as candidates for Flavivirus receptors. Integrins are heterodimeric molecules with important functions in cell biology like cell adhesion and migration, cell signalling and apoptosis.
Previous studies from our group using WNV as model showed that the β3 integrin subunit may be involved in WNV infection. The aim of the present study is to elucidate the role of integrins in Flavivirus infection.
Materials and methods: Mouse cell lines deficient for β1, αV, β3 or αV/β3 integrin subunits were established previously. In this study their integrin expression was rescued and together with integrin gene transfected CHO cells (a Flavivirus non permissive cell line) the rescued cells are used in infection experiments to evaluate the potential role of integrins in Flavivirus infection.
Results: The integrin expression in mouse and hamster cell lines has been successfully rescued. RT-PCR, FACS, adhesion assay and immunofluorescence analysis showed high level of integrin expression.
Conclusion: Further analyses of short- and long-term infection experiments with deficient and rescued cells will reveal a

profound insight into the potential use of integrins in flavivirus interaction with the host cell.

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