Understanding bacterial genome plasticity

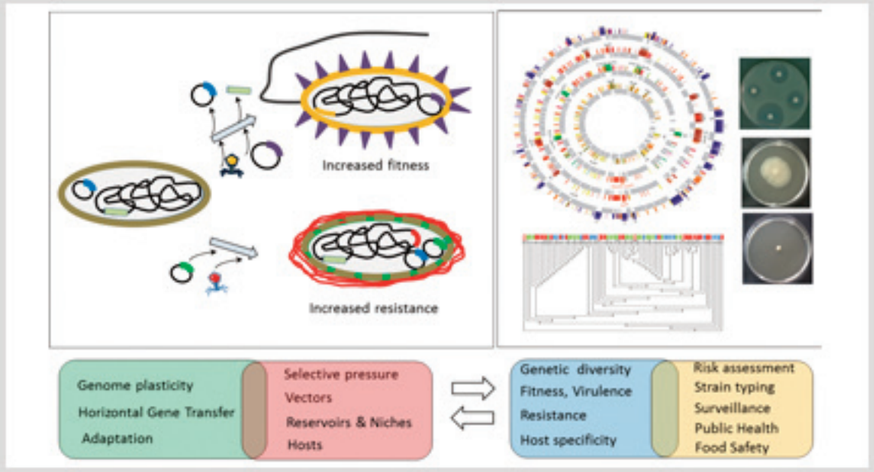

Fig 1

The emergence and spread of extended spectrum beta-lactamase- (ESBL-)producing enterobacteria from poultry to the human population, but also the sprout-associated enterohaemorrhagic *Escherichia coli* (EHEC) outbreak in 2011, demonstrate that new variants of bacterial pathogens can constantly arise and cause outbreaks. The genes for virulence and resistance-related traits are mainly located on mobile genetic elements which can be easily spread by horizontal gene transfer between bacteria. If we aim for a better understanding of the mechanisms underlying the emergence of new zoonotic pathogens and antibiotic resistance traits, we have to study their evolution and the underlying mechanisms. We need to comprehensively analyse (i) the variability of vectors contributing to the exchange of virulence and resistance genes, and (ii) their reservoirs and transfer.

Zoonoses pose a major threat to public health in the European Community (EC), and the resistance of zoonotic bacteria to (multiple) antibiotics is of particular concern, because zoonotic pathogens are transmitted from animals to humans and food, and may thus interfere with an efficient treatment of infections in humans. In particular, resistance to beta-lactam antibiotics, fluoroquinolones and macrolides seriously limits the therapeutic possibilities of human medicine. Unfortunately, the same or very similar antibiotics are used to treat infections in animals which are kept for food production. For example, *Campylobacter* and *Salmonella* isolates from humans, animals and food are often resistant to ciprofloxacin as well as non-pathogenic *E. coli* fecal isolates from healthy poultry. Identical plasmids harbouring resistance-encoding genes can be found in unrelated *E. coli* isolates from poultry and humans, indicating horizontal plasmid transfer.[1-3]

Many infections caused by zoonotic pathogens are emerging infectious diseases. According to the Centers for Disease Control and Prevention, it is estimated that about 75% of recently emerging infectious diseases affecting humans are diseases of animal origin and that approximately 60% of all human pathogens are zoonotic. These microbes can be new organisms that have been previously been unknown. They can also represent already known organisms for which a pathogenic role has not yet been identified. Furthermore, well-known pathogens can also acquire new traits and exhibit altered phenotypes, such as antibiotic-resistant micro-organisms.

At the source

The sources of and reasons for the spread of antibiotic resistance and zoonotic pathogens are manifold. Zoonotic pathogens can be directly transmitted between humans, the environment and foods of plant and animal origin. Enterobacteria, for example, belong to the normal intestinal microbiota of humans and animals. ESBL-producing enterobacteria colonise different animal species. They occur in the environment and food, as well as in the human population and are transmitted within and between them.

Nevertheless, the transmission mechanisms of zoonotic pathogens and resistance genes are not yet comprehensively understood. Although many studies have investigated the development of antibiotic resistance and its spread, the evolutionary mechanisms and the vectors involved as well as the multifaceted interactions between hosts and zoonotic pathogens, their reservoirs and transmission routes are not fully understood. We have to comprehensively analyse the epidemiology, adaptability and virulence of zoonotic pathogens if we want to obtain a more complete picture of their ability to efficiently colonise different hosts, survive in the environment, and cause epidemics.

Outbreaks

During outbreaks, molecular typing of isolates is important to determine the clonal distribution and identify clusters of cross-transmission or clusters linked to an environmental source. Next-generation sequencing (NGS), together with the huge amount of bacterial genome sequence data generated by these approaches, is extremely valuable for the comprehensive identification of food pathogens and contaminating multiresistant enterobacterial pathogens. The use of (meta-)genomic data and NGS tools, and its integration into pathogen detection and risk assessment, will facilitate monitoring of the different sources of food-borne infections.

EHEC is an important cause of diarrhoea in humans. In the last years, the number of EHEC infections in humans in EC member states increased. Ruminants are the natural reservoir of EHEC. The public health impact of EHEC infections is high because of their systemic complications and late sequelae, as well as their ability to cause large foodborne outbreaks. Some EHEC clones are truly emerging pathogens. Besides the most commonly isolated serogroups from human disease cases, other less frequently observed variants can cause severe infections in humans.

The O104:H4 EHEC isolate responsible for the large outbreak in central Europe in 2011 was surprising because it had only been rarely detected as a pathogen before. The natural reservoir is still unknown. In addition, this clone exhibited a new combination of virulence traits of EHEC and of enteroaggregative *E. coli*, another human diarrhoeagenic pathogen. The lack of knowledge of this pathogenic clone (its virulence, genome content, reservoir) hindered the fast detection and risk assessment of the pathogen, as well as outbreak surveillance and patient treatment.

Extraintestinal pathogenic *E. coli* (ExPEC) are a major source of sepsis/bacteremia and urinary tract infections in humans. In poultry, avian pathogenic *E. coli* (APEC) is one of the major opportunistic pathogens causing colibacillosis, a systemic infection that causes heavy economic losses. (Multi-)Resistance in ExPEC and APEC increases. Certain human ExPEC and APEC cannot be clearly distinguished, and they share a common virulence and resistance-associated gene pool. APEC is considered a reservoir of virulence and resistance-associated genes for human ExPEC, and a zoonotic risk cannot be excluded. The ability of APEC and ExPEC to accumulate multiple virulence and resistance-associated genes determines their potential to cause disease.

An increased understanding of bacterial genome plasticity and the underlying mechanisms will support the development of preventive, therapeutic and diagnostic strategies to specifically interfere with relevant virulence or colonisation mechanisms in the animal reservoir, the food chain and the infected patient.

References

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Prof Dr Ulrich Dobrindt
Institute of Hygiene
University of Münster
Mendelstr. 7
48149 Münster
Germany
tel: +49 (0)251 980-2875
dobrindt@uni-muenster.de
http://campus.uni-muenster.de/hyg_forschungsgebiete.html?&L=1

Contact Info

Author
Prof Dr Ulrich Dobrindt

Organisation
Institute of Hygiene

Telephone
+49 (0)251 980-2875

Email
dobrindt@uni-muenster.de

Website
http://campus.uni-muenster.de/hyg_forschungsgebiete.html?&L=1

UKM Universitätsklinikum Münster
Westfälische Wilhelms-Universität Münster