



Prevalence and optimised detection of resistance to antibiotics vital for animal and human health (Uni Fribourg)

Laurent Poirel¹

¹University of Fribourg, Department of Medicine, 1700, Fribourg, Switzerland

Key words

Antibiotic, resistance, mechanism, rapid test, colistin, aminoglycosides

Aim of the study

The study was performed to; i) identify emerging antibiotic resistance determinants in animals, ii) decipher the genetic mechanisms of acquisition of antibiotic resistance genes in those isolates, and iii) develop rapid diagnostic tests for detection of some specific resistance determinants either in humans or in animals.

Material and methods

The initial surveillance of antibiotic resistance included collections of *Escherichia coli*, *Salmonella enterica*, *Klebsiella pneumoniae*, *Pseudomonas* sp. and *Acinetobacter* sp. isolated from the gut microbiomes of pigs and cattle. Existing collections of isolates collected as part of the routine diagnostics have been analysed, in addition to isolates collected prospectively from healthy animals from the national surveillance laboratories as well as from animals which were treated with colistin or aminoglycosides. In addition, we have developed rapid diagnostic tests (screening media and rapid biochemical tests) to isolate and characterize bacterial isolates resistant to those compounds.

Results and significance

We have developed a selective screening medium for polymyxin resistance, as well as a rapid colorimetric test for categorizing susceptible/resistant enterobacterial isolates. That selective medium as well as this rapid test are currently being used by the University of Fribourg and other partners to identify colistin-resistant Gram-negative isolates.

In addition, we have characterized a series of mechanisms leading to acquired resistance to polymyxins, among isolates recovered from human, environmental and animal isolates.

The development of diagnostic tests and media has been realized. In particular, rapid detection tests for polymyxin resistance and pan-aminoglycoside resistance have been developed, and are used for rapid screening of the corresponding resistances in Enterobacteriaceae. They can be used directly on isolated bacteria, but also directly from clinical samples such as urines or blood cultures

In addition, two screening media have been developed in parallel, being the SuperPolymyxin aiming to select for polymyxin-resistant isolates, and the SuperAminoglycoside medium aiming to select for isolates being resistant to almost all aminoglycosides. Those media are now used for prospective surveillances using rectal swabs recovered from patients or from animals.

Our epidemiological surveys allowed to identify some important reservoirs of colistin-resistant isolates.

Ongoing epidemiological surveys are now conducted as part of other project using as bases our selective media and rapid diagnostic tests. The technology has been transferred to colleagues in Switzerland (Pr V. Perreten, Bern and Pr R. Stephan, Zürich) in order to easily implement prospective epidemiological surveys in animals and also in food products.

Publications, posters and presentations

We have published a series of articles in relation with that project, in which the ANIWhA project has been acknowledged.

- Zurfluh, K.; Stephan, R.; Widmer, A.; Poirel, L.; Nordmann, P.; Nüesch, H.J.; Hächler, H.; Nüesch-Inderbinen, M. (2017) Screening for fecal carriage of MCR-producing Enterobacteriaceae in healthy humans and primary care patients. *Antimicrobial Resistance and Infection Control* 6:28.
- Poirel, L.; Kieffer, N.; Nordmann, P. (2017) In Vitro Study of ISAp1-Mediated Mobilization of the Colistin Resistance Gene mcr-1. *Antimicrobial Agents and Chemotherapy* 61:e00127-17.
- Kieffer, N.; Nordmann, P.; Poirel, L. (2017) Moraxella Species as Potential Sources of MCR-Like Polymyxin Resistance Determinants. *Antimicrobial Agents and Chemotherapy* 61:e00129-17.
- Poirel, L.; Kieffer, N.; Fernandez-Garayzabal, J.F.; Vela, A.I.; Larpin, Y.; Nordmann, P. (2017) MCR-2-mediated plasmid-borne polymyxin resistance most likely originates from Moraxella pluranimalium. *Journal of Antimicrobial Chemotherapy* 72:2947-9.
- Poirel, L.; Larpin, Y.; Dobias, J.; Stephan, R.; Decousser, J.W.; Madec, J.Y.; Nordmann, P. (2018) Rapid Polymyxin NP test for the detection of polymyxin resistance mediated by the mcr-1/mcr-2 genes. *Diagnostic Microbiology and Infectious Diseases* 90:7-10.
- Kieffer, N.; Aires-de-Sousa, M.; Nordmann, P.; Poirel, L. (2017) High Rate of MCR-1–Producing Escherichia coli and Klebsiella pneumoniae among Pigs, Portugal. *Emerging Infectious Diseases* 23 :2023-2029.
- Haenni, M.; Poirel, L.; Kieffer, N.; Châtre, P.; Saras, E.; Métayer, V.; Dumoulin, R.; Nordmann, P.; Madec, J.Y. (2016) Co-occurrence of extended spectrum β lactamase and MCR-1 encoding genes on plasmids. *Lancet Infect Dis.* 16:281-2.
- Poirel, L.; Kieffer, N.; Brink, A.; Coetze, J.; Jayol, A.; Nordmann, P. (2016) Genetic features of MCR-1-producing colistin-resistant Escherichia coli isolates, South Africa. *Antimicrob Agents Chemother.* 20;60:4394-4397.
- Bontron, S.; Poirel, L.; Nordmann, P. (2016) Real-time PCR for detection of plasmid-mediated polymyxin resistance (mcr-1) from cultured bacteria and stools. *J Antimicrob Chemother.* 71:2318-2320.
- Zurfluh, K.; Poirel, L.; Nordmann, P.; Nüesch-Inderbinen, M.; Hächler, H.; Stephan, R. (2016) Occurrence of the plasmid-borne mcr-1 colistin resistance gene in ESBL-producing Enterobacteriaceae in river water and imported vegetable samples in Switzerland. *Antimicrob Agents Chemother.* 60:2594-2595.
- Gudeta, D.D.; Bortolaia, V.; Jayol, A.; Poirel, L.; Nordmann, P.; Guardabassi, L. (2016) Chromobacterium spp. harbour Ambler class A β -lactamases showing high identity with KPC. *J Antimicrob Chemother.* 71:1493-1496.
- Poirel, L.; Jayol, A.; Bontron, S.; Villegas, M.V.; Ozdamar, M.; Türkoglu, S.; Nordmann, P.; (2015) The mgrB gene as a key target for acquired resistance to colistin in Klebsiella pneumoniae. *J Antimicrob Chemother.* 70:75-80.
- Poirel, L.; Kieffer, N.; Liassine, N.; Thanh, D.; Nordmann, P. (2018) Plasmid-mediated carbapenem and colistin resistance in a clinical isolate of Escherichia coli. *Lancet Infect Dis.* 16:281.

Project 1.15.08

Project duration March 2015 – May 2018