**SUMMARY**

**Title:** Molecular approaches to integrate surveillance: study of the genetic bases of extended-spectrum cephalosporins resistance in bacteria of animal origin in Italy.

Key words: ESBL, AmpC, ESC-R, *Enterobacteriaceae, E.coli*, Salmonella

Extended-spectrum cephalosporins (ESCs) resistance is a major Public Health issue from both human and animal health perspectives. Extended-spectrum β-lactamases (ESBL) and AmpC-producing *Enterobacteriaceae* have emerged globally during the last decades in humans and animals, with the burning concern of animals being a possible source of ESBLs/AmpCs for humans.
The aim of this project was to characterize ESC-R pathogens and commensal *Enterobacteriaceae* (Salmonella and *E.coli*) collected in the frame of population-based studies (e. g. National Control Programmes, monitoring activities at farm or at retail level, food) and surveillance activities, by using a variety of molecular techniques. A subset of relevant isolates (N=50 ESC-R, MDR up to 8 antimicrobial classes) were also processed by using Whole Genome Sequencing (WGS) protocols. The WGS data analyzed with bioinformatics tools, were interpreted for the detection of the many different molecular markers used for further characterization of pathogens and their accessory genome (e. g. housekeeping genes for MLST, Plasmid Typing based on Replicons, PlasmidMLST), virulence markers and molecular mechanisms leading to AMR (point mutations, acquired resistance genes).
Overall, a total of N=1009 ESC-R isolates collected during 2013-2015 were screened by ad hoc end-point PCRs to identify ESC-R families (ESBL or plasmid-borne AmpC). Most of Salmonella isolates (106/114, 93.0%) and commensal *E. coli* (728/895, 81.3%) tested positive for ESBL CTX-M family. Results of WGS analysis identified the genetic basis of all ESC-R, MDR isolates.
All isolates tested positive for different plasmids (replicons), potentially associated to horizontal AMR genes transfer. Another subset of *E.coli* ESC-R isolates collected in 2016-2018 (negative for ESBL/ plasmid-borne AmpC genes), were also analyzed by WGS and all of them tested positive for known AmpC promoter point mutations, leading to ampC overexpression. Of great concern, was the pESI-like megaplasmid presence in all ESC-R, MDR Infantis isolates, containing genes coding for different AMR genes and markers of virulence, enhanced colonization capability and fitness.
*S.* infantis isolates (N=27) were also included in a large dataset of 382 S. Infantis to investigate the genetic relatedness of *S.* Infantis clones and pESI-like circulating in different European countries and sources (animals, meat, feed, and humans).