**Antimicrobial resistance: Population and cell responses in *Escherichia coli* to treatment with antimicrobials**

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Antimicrobial resistance is a world health and economic problem, causing reduced treatment efficacy and increased cost of treatment and prevention of infectious diseases. Use of antimicrobials in livestock has direct effect on resistance levels seen in human medicine, and attempts should be made to reduce use of these drugs in livestock production. This presentation will first detail the regulatory tools and surveillance systems used to control antimicrobials in livestock in Denmark, and then it will present research carried out to understand how flock treatment with tetracycline affects the level of tetracycline resistant bacteria in the intestine of treated pigs, as well as a detailed characterization of the regulatory responses in cephalosporin resistant *E. coli*, when treated with a 3rd generation cephalosporin to which it is resistant.

A large multi-herd (n=5) study was carried out to investigate whether the commonly used practice of flock treatment in livestock adds significantly to the level of resistance. Nursery pig (n=1167) suffering from diarrhoea in the post weaning period were randomly allocated to flock, penwise and individual treatments with oxytetracycline for 5 days. Surprisingly, the number of tetracycline resistant coliform bacteria and the number of tetracycline resistance genes in the intestine of treated pigs did not differ significantly between the three treatments, mainly because pigs responded with high variation to the same treatment. Also, dose during flock treatment (normal, half and double dose) did not affect resistance levels significantly.

RNA-seq analysis was applied to understand regulatory responses to treatment in cephalosporin resistant *E. coli* grown with and without the 3rd generation cephalosporin, cefotaxime. A high number of genes (n=804) were significantly regulated between the two growth conditions. Blocking of selected, highly regulated genes abolished resistance to cefotaxime, and such genes may be targets for novel drugs that can re-sensitize resistant bacteria to antimicrobials. Surprisingly, transfer-genes on the conjugative IncI1-plasmid, encoding the cephalosporin resistance gene *bla*CtxM1 were highly up-regulated. The up-regulation was dependent on the presence of the resistance gene, either co-located on the plasmid or encoded from the chromosome. Treatment with cefotaxime was not only shown to increase expression of transfer-genes, but also to increase transfer efficacy of the resistance plasmid, suggesting that treatment may promote spread of the plasmid-borne resistances.