

## MEETING ABSTRACTS

# HETEROLOGOUS EXPRESSION OF SDR ENZYMES FROM *H. CONTORTUS*

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The aim of this project is heterologous expression of chosen carbonyl-reducing enzymes from *Haemonchus contortus*, a gastrointestinal nematode of small ruminants. Carbonyl-reducing enzymes (such as SDR and AKR) catalyze the first phase of xenobiotics biotransformation and thus participate in drug metabolism. Increased elimination leads to decreased toxicity and reduced efficacy of drugs in Barber's pole worm. One of the proven mechanisms of deactivation of anthelmintics (e.g., flubendazole) is the reduction of the carbonyl group by these enzymes.

In addition, the previous metabolism analysis has demonstrated a higher ability of resistant strain of *H. contortus* to reduce flubendazole more effectively than the sensitive strain. The genome of *H. contortus* contains approximately 70 SDR genes and 24 AKR genes; however, information about expression and function is not yet known. Furthermore, previous quantitative analysis of gene expression in *H. contortus*, have shown that the most highly expressed genes were SDR1, SDR3, SDR12 and SDR18. Also, expression of SDR12 was significantly higher in all life stages of the resistant strain.

These genes have been selected for heterologous expression, including cloning and expression in two systems: in *E. coli* typical expression system for soluble enzymes, and in eucaryotic cell lines, an expression system enabling a higher level of posttranslational modifications. Expression of selected SDR or AKR, in a suitable system will allow us to characterize them, determine their enzyme activity, even test new potential inhibitors in the future.

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