INTRINSIC

21st Scientific Symposium of the Austrian Pharmacological Society: Joint Meeting with the British Pharmacological Society and the Pharmacological Societies of Croatia, Serbia and Slovenia Graz, 16–18 September 2015

MEETING ABSTRACT

A3.3

Transmembrane proteins of *Fasciola hepatica:* identification and characterization of new putative drug targets Bulut HAMALI^{1,2}, Sandra PICHLER¹, Katrin JANTSCH¹, Nina HOFER²,

Elisabeth WISCHNITZKI², Maria BERENYI², Joachim LIPP¹, Oliver KUDLACEK^{1,*} and Silvia FLUCH²

¹Institute of Pharmacology, Center for Physiology and Pharmacology, Medical University of Vienna, Austria; ²Health & Environment Department, AIT Austrian Institute of Technology GmbH, Tulln, Austria

Background: *Fasciola hepatica*, a parasitic flatworm (phylum Platyhelminthes, class trematode, subclass Digenea, family Fasciolidae), is the cause of one of the most important diseases affecting animal health all over the world: liver fluke disease (fascioliasis). Triclabendazole (TCBZ) is the drug of choice for more than 25 years because of its high activity against both adult and juvenile flukes. However, there are an increasing number of reports on drug resistance against TCBZ in *F. hepatica*.

Methods: We performed next-generation sequencing (NGS) to identify new ABC transporters of *F. hepatica* and mutations in these transporters that could confer resistance to TCBZ. For this approach, TCBZ-resistant and susceptible adult flukes from Northern Ireland and Lower Austria were used. In parallel, we also generated antibodies against putative ABC transporters of *F. hepatica*. Additionally, cells were transfected with ABC transporters to perform cell viability assays (CVA).

Results: Next generation sequencing data provided us about 60 ABC transporters in *F. hepatica*. We found *F. hepatica* multidrug resistance transporter (MDR) involved in TCBZ efflux by CVA. As seen by CVA, *F. hepatica* MDR might be a candidate to elicit drug resistance. **Discussion:** The results from both the bioinformatics part and the functional analysis will probably shed light on how flukes became resistant.

Acknowledgements: Supported by AIT (1.G8.00016.0.0).

^{*}Corresponding author e-mail: *oliver.kudlacek@meduniwien.ac.at*