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# Host-parasite interactions at the hormonal level in Fasciolosis

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***Abstract***

Fasciolosis is an important disease in ruminants caused by liver flukes of the genus *Fasciola*. For the development of new drugs and vaccines it is important to understand the host/parasite interactions at the molecular level. Vertebrates release a variety of hormones by which they trigger responses in distant tissues. We investigated whether *Fasciola* is sensitive to host hormones and shows specific responses. More specifically, we were interested in peptide hormones and their receptors which belong to the type II G-protein coupled receptor family. Structure, function, and pathology of this receptor family have been extensively studied in vertebrates, especially human and porcine. In contrast, data for host/trematode interactions at the hormone level are very limited. The latest study dated back 20 years and focused on changes in muscle contractions of the parasite. Proteomic and nucleic acid analysis techniques developed in the last decades will allow us to study the effects of hormones at the molecular level and to identify putative parasite hormone receptors. In the present study a cDNA encoding a putative type II G-protein coupled receptor of *Fasciola* was isolated as a partial product by cDNA library screening and completed by a rapid amplification of cDNA 5'-end (5'-RACE) method. The deduced amino acid sequence was compared to the sequences of other members in the type II G-protein couple receptor family and showed conserved key features of this family. In further studies, the protein will be localized in the parasite tissue with specific polyclonal antibodies and we would like to determine which ligand will bind to it and what its biological role is.

***Keywords:*** *Fasciola gigantica*, type II G-protein coupled receptor, peptide hormones, and rapid amplification of cDNA ends (RACE)

## Introduction

Fasciolosis, caused by the trematode species *Fasciola gigantica and F. hepatica*, is an important, worldwide disease in ruminants and leads to severe pathology in the infected animals. For the development of new drugs and vaccines it is essential to understand the host/parasite interaction at the molecular level. Few attempts were made to analyze to which extent host hormones influence the behavior of *Fasciola* in the mammalian host. The latest of these studies dates back 20 years and focused on changes in the muscle contractions of the parasite. Modern proteomic and nucleic acid analysis techniques will allow us to study the effects of hormones at the molecular level and to identify putative parasite hormone receptors.

The aim of this study is to identify a parasite hormone receptor, to determine its ligand, and to establish its biological role. The obtained primary data should be of use for further investigation of the receptor as a drug target.

## Methods

In the already performed experiments, a hormone receptor encoding cDNA was isolated using cDNA library screening and rapid amplification of cDNA ends (RACE) methods. DNA sequencing and analysis were used to confirm that a sought cDNA had been isolated. In ongoing experiments, the temporal and spatial expression patterns of the receptor

will be analyzed using polyclonal antiserum raised against a N-terminal peptide of the receptor. Mammalian peptide hormones will be studied for their interaction with the receptor and knock-out experiments will be performed to identify its biological function. Depending on promising results the use of the receptor as a drug target will be studied by structure modeling to identify putative disruptive ligands.

**Results**

A full-length cDNA encoding a type II G-protein coupled receptor of *Fasciola gigantica* was molecular cloned by cDNA library screening using a DIG-labeled specific DNA probe and the rapid amplification of cDNA ends (RACE) method. The deduced amino acid sequence was compared with members of the human type II G-protein coupled receptor family and clearly shows conserved features of this family. For the present, the protein has been named FgSCTR because of a somewhat higher similarity to the secretin receptor, this is preliminary and may change depending on its true ligand.

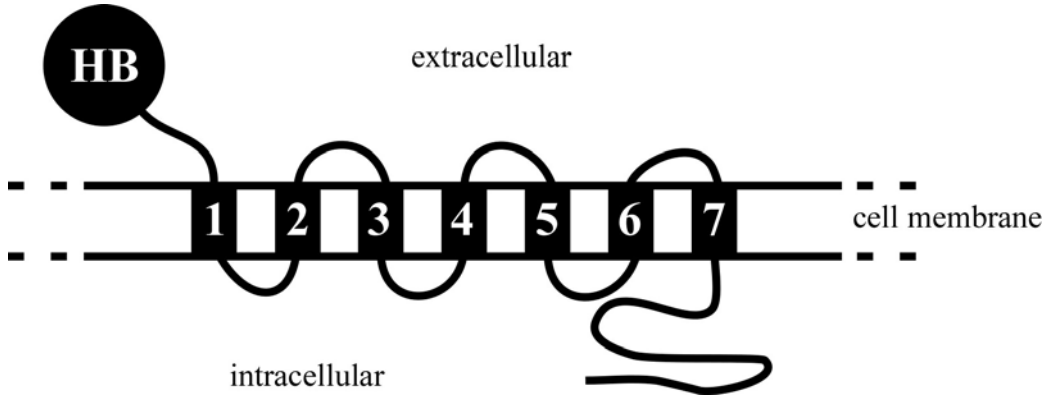


**Figure 1:** Schematic drawing of FgSCTR with the putative extracellular hormone binding (HB) domain at the N-terminus, seven transmembrane regions and a C-terminal end which might interact with an unidentified G-protein.

**Discussion**

For many years already, the knowledge about host/parasite interaction in *Fasciola* has been limited with a focus on only a small number of identified antigens. We considered the even smaller number of studies concerning host hormone/parasite interaction as insufficient and began to investigate the possibility of a molecular analysis. Starting point was a partial cDNA (EST) spanning two transmembrane regions of a predicted type II G-protein coupled receptor in *Fasciola*. So far, type II G-protein coupled receptors have not been described from trematodes. They are of interest as several of their known ligands are gastrointestinal hormones in mammals and potentially affect the parasite. Using the partial EST as a probe we isolated a full length cDNA by the described methods. As the alignment demonstrates the deduced amino acid sequence has all characteristics of a II G-protein coupled receptor and it will be important to identify first, its distribution in the parasite tissue and, secondly, the ligand in the next analyses.

**Conclusion**

We have molecular cloned the first full length cDNA of a type II G-protein coupled receptor in trematodes. In the following studies, we would like to determine its ligand and its biological role which might be important for its use as a drug target.

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