Bactericidal/permeability-increasing (BPI) - like proteins in *Giardia intestinalis*

Dimitra Peirasmaki

Giardia intestinalis is a protozoan parasite and one of the ten most important enteric parasites that affect humans worldwide.
Since *G. intestinalis* is found to be pathogenic to humans, it is consider to be an intestinal parasite of medical importance and it is also very interesting in an evolutionary aspect since it is an early diverging eukaryote.
At the same time, different kinds of bacteria threaten the health of the physical barriers of the human organism, like the skin and mucosa. LPS and lipid-binding family proteins (LBP) called bactericidal/permeability proteins (BPI) play an important role on the way the innate immune system interacts and is being activated, including the antimicrobial defense.

The purpose of this project was the study of proteins found in the genome of *Giardia intestinalis* that contain a BPI domain. After *G. intestinalis* was transfected with 7 of these BPI-like proteins, interaction experiments between *G. intestinalis* and bacteria were performed. During the project we studied the expression levels of these proteins and how they may change during the interaction of the parasite with 3 different kind of bacteria. Localization experiments were also performed in order to find where these BPI-like proteins localize in the parasite, giving us a better view of their purpose for the survival of the parasite and probably of their function in the cell. Since there is the possibility that these proteins could belong to the lipid-binding protein family, the purification of these proteins was essential in order to have a better understanding of their function.

Structural studies of these BPI-like proteins showed high similarities with human BPI and LBP proteins regardless the very low sequencing similarities that they present. What is more, it seems that the pI of the BPI-like proteins which is around 5 which is very close to the pI of the human LBP (approximately 6.3) than the pI of the human BPI protein (approximately 9.4).
The results of the experiments mentioned above showed that these BPI-like proteins create a typical ER membrane pattern in the parasite which is connected with the secretory transport system in *G. intestinallis* and membrane transportation, essential for the survival of the organism. Interaction experiments between the parasite and the bacteria showed that the presence of the parasite inhibits the growth of the bacteria, something that could indicate the action of the parasite and the BPI-like proteins against them and also an up-regulation of the expression of the BPI-like proteins. Finally, one of the seven BPI-like proteins was chosen to be purified. However, due to purification problems, possibly only a part of the protein was managed to be obtained.
The overall results show promising indications that BPI-like proteins studied above from *G. intestinalis* could belong to either the BPI or the LBP family of proteins. Although it seems that due to the highly acidic pI these BPI-like proteins could be closer to the LBP family of proteins, a series of experiments should be performed in order to have more conclusive results, including the optimization of the protein purification process and further interaction experiments between bacteria and the purified recombinant BPI-like protein. Finally, an ELISA assay for testing the LPS binding ability of the purified protein would be extremely helpful in order to prove that these BPI-like proteins bind to the LPS.