Abstract

Trichomonas vaginalis is a human pathogen causing trichomoniasis, one of the most common non-viral sexually transmitted diseases in both men and women. Trichomoniasis is currently treated with metronidazole, but the pathogen is known to develop resistance against this drug. However as the pathogen is eukaryotic, the targets for the pathogen elimination without seriously affecting the host are limited. Throughout the evolution *Trichomonas vaginalis* adapted to anaerobic environments by developing an alternative metabolism resulting in a reduced form of mitochondria named hydrogenosome. Hydrogenosomes lack genetic information, therefore all its proteins are nucleus-encoded and need to be transported inside the hydrogenosome using a targeting N-terminal presequence. The peptidase recognizing and cleaving those presequences at the entrance of the organelle, the hydrogenosomal processing peptidase (HPP), is unique for hydrogenosomes and therefore represents a potential drug target against the pathogen.

In this work the HPP's substrate specificity towards the targeting presequences was investigated. To do so a proteomic analysis of the proteome of *Trichomonas vaginalis* hydrogenosomes was performed using a novel optimized protocol for N-terminal peptide sequencing. N-terminal peptides were captured using a negative selection approach and their N-terminal sequencing was achieved using a bottum-up tandem mass spectrometry analysis. Based on the identified N-terminal peptide sequences the proteins present in the original hydrogenosomal sample were identified. The relevancy of the proteins obtained was evaluated and further improvements were suggested.