

PR Abstract “Factors of metronidazole resistance in *Trichomonas vaginalis*”

Trichomonas vaginalis is a worldwide occurring single cell parasite which infects the urogenital tract of humans, mainly in women. Those affected often develop vaginitis and cervicitis, symptoms usually referred to as trichomoniasis. In pregnant women, *T. vaginalis* infections can lead to preterm deliveries or even the death of the foetus. In addition, trichomoniasis does also predispose for HIV infection making it a considerable health problem in Southern Africa where both pathogens are highly prevalent.

Since there is no vaccine available against *T. vaginalis*, management of the disease exclusively rests on chemotherapy. Of the chemotherapeutics available, the 5-nitroimidazole drug metronidazole is by far the most frequently used. Metronidazole was developed more than 60 years ago and is still widely effective. However, in some parts of the world, treatment failures with metronidazole occur with up to 20% of the people treated. At least in a proportion of these cases treatment failure is caused by metronidazole resistance in the trichomonads. The mechanisms behind metronidazole resistance are still badly understood, mainly due to insufficient data. Based on previous results it is assumed that enzymes involved in the antioxidant defence have a role in metronidazole resistance. Furthermore, it is known that metronidazole resistance only becomes manifest in the presence of oxygen. It is important to note that *T. vaginalis* is an anaerobe, i.e. a microorganism which is harmed by oxygen and therefore quickly removes it, a process termed oxygen scavenging. An impaired capacity to scavenge intracellular oxygen had been described before in metronidazole-resistant *T. vaginalis*.

It is the main goal of this project to considerably deepen our understanding of metronidazole resistance. To this end, candidate enzymes, possibly involved in resistance, will be expressed and characterized. Moreover, their expression levels will be measured in resistant and susceptible strains and compared, mainly by application of methods that identify and quantify the total protein content in cells (proteomics). It is hypothesized that resistant and susceptible cells display discrete and relevant differences with regard to their protein expression profiles.

We expect that after completion of this project the understanding of molecular mechanisms causing metronidazole resistance in *T. vaginalis* will have improved greatly.