Evidence for cross-talk between the aquaglyceroporins in *Trypanosoma brucei*

Aquaglyceroporins (AQPs) are ubiquitous transporters responsible for the uptake of water, glycerol and other small molecules. *Trypanosoma brucei* and *Leishmania* each possess several AQPs, some of which mediate drug uptake. LmAQP1 transports the reduced form of sodium stibogluconate (SSG), while TbAQP2 contributes to the uptake of pentamidine and melarsoprol. Functional loss of these proteins leads to clinical drug resistance. Following selection of our genome-scale RNAi library, we previously showed that TbAQP3 can mediate the uptake of SSG by bloodstream-form (BSF) *T. brucei*. However, this screen did not identify TbAQP1, even though it has the same selectivity filter as TbAQP3 and LmAQP1, suggesting that other regulatory processes may influence TbAQP1 activity and substrate selectivity. I will present my latest data revealing that TbAQP1 can indeed mediate SSG uptake by BSF *T. brucei* but only in the absence of TbAQP2 and TbAQP3; the loss of these proteins increases TbAQP1 levels. Expression of TbAQP2 or TbAQP3 suppresses TbAQP1 expression. Furthermore, while overexpression of TbAQP1 has no effect on wildtype BSF *T. brucei*, overexpression in parasites lacking the *TbAQP2-TbAQP3* locus is toxic. I am currently exploring the nature of this toxicity and seeking to identify the *trans*-acting factors and *cis*-acting elements underlying this apparent inter-AQP cross-talk in *T. brucei*.