Stem cell screening to identify novel drug targets in the human parasite *Schistosoma mansoni*

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Human schistosomiasis affects approximately 250 million people in 78 developing countries and 0.8 billion people are at risk of infection. There is no approved vaccine for this disease and treatment relies solely upon one drug, praziquantel, raising concern about potential drug resistance. Schistosomes have a complex life cycle, involving several life stages in molluscan intermediate and mammalian definitive hosts. During schistosome development in the mammalian host, rapid growth and physiological change occurs, particularly during the early- to late-liver stage, where the schistosomula (somules) become packed full of proliferating somatic stem cells. These stem cells are vital for the survival and development of the parasite. This research aims to develop a better understanding of the pre-adult intra-mammalian life stages of *Schistosoma mansoni*, particularly the early and late liver stages, with a specific focus on their stem cell biology and to discover novel therapeutic targets. Early and late liver stage somules were chased using EdU in cell proliferation assays and somules co-stained with anti-phospho-kinase and anti-phospho-(kinase) substrate antibodies, revealing that multiple protein kinase pathways including protein kinase C, protein kinase A and AKT are activated and localise to the proliferating stem cells. Next a commercial stem cell library, containing 280 compounds aimed at human stem cell processes, was screened against the liver somules, using a developed pipeline employing confocal microscopy to assess the effects of each compound on stem cell proliferation in the parasite. Numerous 'hit' compounds have been identified within the library and their effects on somule viability, growth, and development are currently being explored. Ultimately, the 'hit' compounds might prove suitable as novel drugs against schistosomes or might help us identify other drugs that target specific mechanisms to interfere with schistosome growth and development.