

P007 ARL1 and ARF6 have essential roles in *Trypanosoma brucei*
H.P. Price, D. Goulding* and D.F. Smith
Department of Biology, University of York, UK
**CMMI, Imperial College London. UK*

Myristoyl-CoA: protein *N*-myristoyltransferase (NMT) catalyses the *N*-myristoylation of target proteins and is essential for viability in the protozoan parasites, *Leishmania major* and *Trypanosoma brucei*. In our investigations to define the essential downstream targets of NMT, we have focused on the ADP-ribosylation factor (ARF) family of proteins, as growth arrest in *Saccharomyces cerevisiae* mutants with reduced NMT activity correlates with decreased *N*-myristoylation of Arf1p. We have identified 9 ARF/ARLs in the *T. brucei* and *T. cruzi* genomes and 10 in *L. major*. The *T. brucei* ARL1 homologue is localized to the Golgi apparatus and is differentially expressed only in the mammalian bloodstream form of the parasite. RNA interference was used to demonstrate that ARL1 is essential for viability in these cells. Prior to cell death, depletion of ARL1 protein results in disintegration of the Golgi structure and a delay in exocytosis of the GPI-anchored variant surface glycoprotein (VSG) to the parasite surface. In contrast, RNAi of a putative ARF6 homologue results in a gross enlargement of the flagellar pocket, appearance of intracellular flagella and severe inhibition of endocytosis. As all endocytosis in *T. brucei* is clathrin-dependent, this may represent evolutionary convergence of the clathrin and ARF6-associated endocytic pathways in this ancient eukaryotic organism.