

P052 ATP-dependent chromatin remodelling factors and *Dictyostelium* chemotaxis

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Inhibition of the enzyme prolyl oligopeptidase (PO) in *Dictyostelium* leads to resistance to the effects of lithium via a mechanism that requires the enzyme multiple inositol polyphosphate phosphatase (MIPP). Our analysis demonstrates that this is due to an indirect mechanism via increased expression of a number of genes that regulate the synthesis and metabolism of inositol phosphates, including myo-inositol synthase (*ino1*) and inositol monophosphatase (IMPase). In yeast, the chromatin remodelling factors, Ino80 and Swi/SNF2 are required for expression of *ino1*, and it has been proposed that they are regulated by a higher order inositol phosphate, InsP_5 . As MIPP regulates the cellular concentration of InsP_5 , it may act to mediate the effects of PO inhibition through alteration of the InsP_5 concentration. Consistent with this we have isolated a lithium resistant mutant, *lisG*, which encodes a chromatin remodelling factor of the chromo-helical domain (CHD) protein family.

In addition to *lisG*, the *Dictyostelium* genome contains representatives of all four families of ATP-dependent chromatin remodelling factors: CHD, Swi/SNF, Isw1 and Ino80. We are currently examining the role of Ino80. This forms a multimeric complex that includes actin-related protein 8 (Arp8).

We have recently identified several chemotactic defect phenotypes in *Dictyostelium* *Arp8*- and *lisG*-null mutants and are in the process of incorporating this information into the larger picture, looking at changes in *ino1* expression.