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Molecular mechanisms controlling cell fate determination in *C. elegans*

POSSIBLY THE most fundamental problem of developmental biology is that of cell determination: how are cells allocated their characteristic fates during the development of an organism? I am using the nematode worm *Caenorhabditis elegans* as a model system for studying the genetic controls underlying this process. However, given the conservation of developmental control genes across metazoan phyla, studies of *C. elegans* cell fate determination should be applicable to more complicated organisms, like ourselves.

Genetic mutations which transform cells from one developmental fate into another provide a means of tackling this problem as they are likely to be affecting genes involved in the choice of a particular fate. One *C. elegans* mutant, *mab-9* (male abnormal), has gross defects in tail development because of a transformation in the

identity of two particular cells which are normally very important for correct tail development. In *mab-9* mutants these two cells take on an inappropriate fate, and so the development of the tail goes wrong. *mab-9* is therefore a key regulatory gene which dictates the distinguishing characteristics of individual cells. Understanding how genes of this type operate in molecular terms is one of the central goals of research in developmental biology. I have recently cloned the *mab-9* gene and discovered that it encodes a member of the T-Box family of transcription factors, the prototype of which, *Brachyury*, was first identified as a mutation disrupting tail development in mouse. We are beginning to discover important clues as to how this transcription factor may be acting on a molecular level to dictate the developmental fates of particular cells. Other projects include the genetic

and molecular analysis of *mab-2*, mutants of which have defects in the development of the sensory structures (rays) of the male tail which are required during mating.

Key Publications

Hayles, J., Fisher, D., Woollard, A. and Nurse, P. (1994) Temporal order of S phase and mitosis in fission yeast is determined by the state of the p34cdc2/mitotic B cyclin complex *Cell* **78**, 813–822

Chang, F., Woollard, A. and Nurse, P. (1996) Isolation and characterisation of fission yeast mutants defective in the assembly and placement of the contractile actin ring. *J. Cell. Sci.* **109**, 131–142

Woollard, A., Basi, G. and Nurse, P. (1996) A novel S phase inhibitor in fission yeast. *EMBO J.* **15**, 4603–4612

Woollard, A. and Hodgkin, J. (1999) *stu-7/air-2* is a *C. elegans* aurora homologue essential for chromosome segregation during embryonic and post-embryonic development. *Mech. Dev.* **82**, 95–108

Woollard, A. and Hodgkin, J. (2000) The *Caenorhabditis elegans* fate-determining gene *mab-9* encodes a T-box protein required to pattern the posterior hindgut. *Genes Dev.* **14**, 596–603