



## Scientists identify how epilepsy drug functions (图)

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08-May-2007, Valproic acid is a commonly used treatment for epilepsy, migraine and bipolar disorder (manic depression). It is also currently in clinical trials for Alzheimer's disease, cancer and HIV treatment, but exactly how it works remains unknown. Research by Dr Robin Williams, published in the scientific journal 'Eukaryotic Cell' and reviewed in the 'Encyclopaedia of Life Sciences', shows how we can better understand the function of this psychiatric drug.

Valproic acid has been shown to inhibit a number of enzymes in the animal brain. Dr Williams, a molecular cell biologist in the School of Biological Sciences at Royal Holloway, University of London, has shown that many of these enzymes are also inhibited by Valproic acid in the social amoeba Dictyostelium.

Dictyostelium exists as single cells consuming micro-organisms and dividing until it starts to starve, then cells migrate together to form a multi-cellular 'fruiting body'. This organism provides an excellent biomedical model for understanding what the targets of drugs are, since it is haploid (having only one copy of every gene), and it is therefore easy to knockout every gene in the organism and examine the role of each gene in drug resistance. The ability to screen banks of mutants for drug resistance provides an advantage over multi-cellular animal models such as worms, fruit fly, zebra fish, and frogs. The fully sequenced genome of Dictyostelium also contains many genes that are absent in other more simple models like yeast and fungi.

Dr Williams' research involves identifying genes, proteins and signalling pathways affected by Valproic acid in Dictyostelium. By isolating mutants that are resistant to Valproic acid, and then identifying the gene that has been blocked in each mutant, it is possible to identify proteins that potentially control the action of the drug. These proteins can then be characterised in both Dictyostelium and mammalian cells to better understand their potential role in medicine.

Commenting on these latest developments, Dr Williams said: "Using this simple amoeba, we have for the first time identified an effect of valproic acid in changing cell signalling processes that, in humans, are associated with epilepsy. This is an exciting step forward in understanding how the drug works."

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