

## Dictyostelium as a model for human disease

Editorial - Ricardo Escalante

Does it make sense to use a simple organism to study human disease? I am sure that all those scientists using non-mammalian models in biomedical research have faced this question many times, perhaps informally in front of the family and friends or in more critical situations under the scrutiny of grant agencies or evaluation committees. There are obvious arguments supported by the history of science telling us the usefulness of learning from simple models and how this has become essential to understand certain pathologies. In addition to the well-known conservation of genes and molecular pathways among distant species there are practical reasons, such as their simplicity and tractability compared with the complexity and the experimental inaccessibility of the human body. An added value from the studies of simple models is that, not infrequently, they open radically new perspectives in the study of a given pathology. This is often the result of applying unbiased genetic analysis and the opportunity in a model organism to address the function of a given gene in the organism as a whole. As a consequence, this research might not be translated immediately to human disease but serve as a ground for more applied approaches. As Louis Pasteur stated "There does not exist a category of science to which one can give the name applied science. There are sciences and the applications of science, bound together as the fruit of the tree which bears it". This series of reviews exemplifies beautifully how the social amoeba *Dictyostelium* fulfills all the requirements for a useful experimental model in understanding the basic principles of human disease.

The *Dictyostelium* life style provides excellent opportunities to address disease-related processes in a meaningful way. This soil amoeba predates bacteria in its natural environment. As a result of this selective pressure, bacteria developed strategies to survive which later were used and adapted to infect other organisms including humans. The reviews by Michael Steinert and Wanessa Lima et al. describe the use of *Dictyostelium* as a model to study the interaction with several pathogens of immense importance in human health such as *Legionella*, *Mycobacterium* and *Pseudomonas*.

Social amoebae use motility and chemotaxis both to hunt bacteria and to aggregate collectively to form a multicellular organism. The underlying mechanisms driving these phenomena are essentially similar to those of mammalian cells, and thus *Dictyostelium* has become a prominent model in this field. Michael Carnell and Robert Insall review how research in *Dictyostelium* has contributed to our understanding of cell motility-related pathologies which includes deficiencies in the immune and neurological systems. One of these deficiencies is Lissencephaly, a severe brain disease caused by mutations in highly conserved genes present in *Dictyostelium*, *LIS1* and *DCX*. The molecular roles of these proteins and others involved in this pathology are now beginning to be understood thanks in part to *Dictyostelium*. Irene Meyer et al. review our current knowledge of the molecular clues underlying Lissencephaly and describe invaluable new findings on the function of the *Dictyostelium* *DCX* protein.

Dictyostelium has also proved its usefulness in pharmacogenomics helping to unveil the mechanism of action of certain drugs and at the same time to reduce the use of animals in research. Two wonderful topics have been reviewed in this issue. Stephen and Hannah Alexander explain how the isolation of a Dictyostelium mutant resistant to the cancer chemotherapeutic drug cisplatin prompted further studies in human cells on the role of sphingolipids and ceramide in regulating the response to this drug. Likewise, the review by Marthe Ludtmann et al. highlights our current knowledge of the mechanism of action of two commonly used bipolar disorder treatments (valproic acid and lithium).

Human diseases associated with the endocytic and secretory pathway, such as Chediak Higashi Syndrome, Ceroid Lipofuscinosis and Niemann Pick Disease, originate severe symptoms affecting multiple organs and compromising the lifespan of affected patients. Markus Maniak here reviews current research in Dictyostelium related to the molecular basis of these complex diseases. Finally, Lisa Francione et al. address the complexity of the mitochondrial diseases and how the simplicity of Dictyostelium can help to uncover certain aspects of the cytopathological pathways involved.

I hope this series of reviews will excite your curiosity and serve as a ground for further research using Dictyostelium as a model of human disease. It would also be gratifying if they help to convince those not working with simple models that this kind of research does indeed make sense.