Eppendorf Award for Young European Investigators

Assembling complex biological structures

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Introduction by Mónica Bettencourt-Dias

My work on the centrosome, which is the primary microtubule-organizing centre in animal cells, started when I was a post-doctoral researcher in the David Glover laboratory at the Cambridge University Department of Genetics. Subsequently, I started my laboratory at the Instituto Gulbenkian de Ciencia (IGC) in Oeiras, close to Lisbon, Portugal, in 2006 (http://sites.igc.gulbenkian.pt/ccr). Our research focuses on the regulation of cell-cycle progression in normal development and cancer. We are particularly interested in the roles of centrosomes and cilia, as little is known about their biogenesis or how it might go awry in human disease. In our research, we use an integrated approach, combining studies in the fruit fly (*Drosophila melanogaster*), and normal and cancerous human cells, along with bioinformatics and mathematical modelling. We predict that an understanding of the formation and function of centrosomes and cilia will generate new markers in cancer and ciliary diseases, and will provide novel therapeutic targets. I was very happy when I heard that I had received the Eppendorf Award for Young European Investigators, as it recognized our work and gave visibility to our science. This is crucial when starting a group in a small country, such as Portugal, where investment and productivity in science have come about relatively recently. The IGC is a recently renovated international research institute with excellent facilities, where truly multidisciplinary work is promoted. Perhaps the Eppendorf Award will motivate people throughout the world to consider Portugal, in particular the IGC, for their studies. In the following article, we describe some of our research in the context of developments in the field.

Of centrioles, basal bodies and centrosomes

What is the common thread linking the movement of spermatozoa, the sensing of light by our eyes and the cell-division apparatus of most of our cells? As implausible as it might seem, the structures that permit movement, light sensing and cell division are all made of microtubules, and are organized by the same organelle: the centriole or basal body (Fig. 1a). The presence of this nine-fold symmetrical structure in all branches of the eukaryotic 'tree of life' led to the suggestion of its existence in the last common eukaryotic ancestor. The basal body/centriole sets up the foundations for the axoneme, which forms the skeleton of cilia and flagella; it also participates in the formation of the centrosome[1] (Fig. 1a).

Although the details of these structures were revealed only recently with the advent of electron microscopy, their presence did not remain unnoticed by earlier cell biologists. Édouard Van Beneden and Theodor Boveri first described centrioles and centrosomes at the end of the nineteenth century using nematode eggs[2]. They suggested that these structures were important in setting up the cell-division apparatus (Fig. 1b, step 1(M)) and proposed that they were autonomous. Later, Boveri proposed that abnormal centrosome duplication would lead to an aberrant cell-division apparatus, which could result in cancer[3]. Since then, abnormalities of microtubule-organizing structures have indeed been observed in cancer and in a range of other human diseases, including cystic kidneys and retinal degeneration[1].

As centrioles and basal bodies are so important, their biogenesis should be highly regulated. Indeed, they duplicate only once every cell cycle (Fig. 1b, step 1), with one centriole (the 'daughter') forming close to an already existing centriole (the 'mother'; Fig. 1b, step 1(S)). However, numerous questions remain unanswered. How is centriole number controlled, what kick-starts their formation, how is their nine-fold symmetry defined, and how are their size and fate decided? What is their function? Because of their importance in cancer and other human diseases, there is an expectation that an understanding of the pathways involved in the regulation of the microtubule-organizing centre will help to generate new diagnostic and prognostic markers, and provide novel therapeutic targets.

SAK/polo-like kinase 4 (PLK4) is necessary for centriole biogenesis

In order to identify novel mechanisms involved in

Mónica Bettencourt-Dias is the thirteenth recipient of the Eppendorf Award for Young European Investigators, which recognizes talented young individuals working in the field of biomedical research in Europe. This is the first time that the Eppendorf Award has been presented to a researcher from the Iberian Peninsula. Mónica Bettencourt-Dias was born in Portugal in 1973. She entered the prestigious Gulbenkian Graduate Programme at the Instituto Gulbenkian de Ciência (IGC), Portugal, and did her Ph.D. at University College London in the UK under the supervision of Professor Jeremy Brockes. She then moved to the University of Cambridge in the UK, where she undertook postdoctoral research on cell-cycle regulation and centrosome function with Professor David Glover. Since 2006, Mónica Bettencourt-Dias has led an active research group at the IGC. The members of her laboratory use an integrated approach to study centrosome biogenesis and function in *Drosophila* and human cells. Here, Mónica Bettencourt-Dias describes, for a wider audience, the work that led to her receiving the Eppendorf Award, which she places into context within the broader research field.

The Eppendorf Award is presented in partnership with *Nature*. An independent jury of scientists under the Chairmanship of Kai Simons (Max Planck Institute for Molecular Cell Biology and Genetics, Dresden, Germany) selects the Eppendorf Award winner, and *Nature* and Eppendorf have no influence on the decision (http://www.eppendorf.com/awards).