How do cells count?

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In the 13th January print edition of the journal *Current Biology*, Instituto Gubenkian de Ciencia researchers provide insight into an old mystery in cell biology, and offer up new clues to understanding cancer. Inês Cunha Ferreira and Mónica Bettencourt Dias, working with researchers at the universities of Cambridge, UK, and Siena, Italy, unravelled the mystery of how cells count the number of centrosomes, the structure that regulates the cell's skeleton, controls the multiplication of cells, and is often transformed in cancer.

This research addresses an ancient question: how does a cell know how many centrosomes it has? It is equally an important question, since both an excess or absence of centrosomes are associated with disease, from infertility to cancer.

Each cell has, at most, two centrosomes. Whenever a cell divides, each centrosome gives rise to a single daughter centrosome, inherited by one of the daughter cells. Thus, there is strict control on progeny! By using the fruit fly, the IGC researchers identified the molecule that is responsible for this 'birth control policy' of the cell - a molecule called Slimb. In the absence of Slimb, each mother centrosome can give rise to several daughters in one go, leading to an excess of centrosomes in the cell.

In recent years, Monica's group has produced several important findings relating to centrosome control: they identified another molecule, SAK, as the trigger for the formation of centrosomes. When SAK is absent, there are no centrosomes, whereas if SAK is overproduced, the cell has

too many centrosomes. These results were published in the prestigious journals *Current Biology* and *Science*, in 2005 and 2007. Now, the group has discovered the player in the next level up: Slimb mediates the destruction of SAK, and in so doing, ultimately controls the number of centrosomes in a cell.

Monica explains, 'We carried out these studies in the fruit fly, but we know that the same mechanism acts in mice and even in humans. Knowing that Slimb is altered in several cancers opens up new avenues of research into the mechanisms underlying the change in the number of centrosomes seen in many tumours'.

Mónica first became interested in centrosomes and in SAK when she was an Associate Researcher at Cambridge University, UK, and has pursued this interest at the IGC, where she has been group leader of the Cell Cycle Regulation laboratory since 2006. Inês Cunha Ferreira travelled with Monica from Cambridge, and is now in her second year of the in-house PhD programme. Two other PhD students in the lab also contributed to this research, Ana Rodrigues Martins and Inês Bento.

Source: Instituto Gulbenkian de Ciencia