

## Cells in the early embryo battle each other to death for becoming part of the organism

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Left; An early mouse embryo has been generated in a genetic mosaic of two cell populations, green and blue. Center, three days later, the green cells, in which Myc protein increased, have won the battle and removed the blue. Right, This shows more Myc cell (green) engulfing its neighbor. Credit: CNIC

Spanish researchers at the Centro Nacional de Investigaciones Cardiovasculares (CNIC) have found that during the early stages of mammalian development, embryonic cells embark on a battle for survival. Through this battle, the less active of these cells are eliminated by their stronger sisters. The work is published today in the prestigious journal *Nature*.

This phenomenon, termed cell competition, occurs in a defined <u>time</u> <u>window</u>, between days 3 and 7 of mouse development. During this



period all <u>embryonic cells</u> compete with each other, as explained by Dr. Cristina Claveria, first author of the study, and Dr. Miguel Torres, director of this work and Head of the Department of Cardiovascular Development and Repair at CNIC.

"Thanks to cell competition the developing organism optimizes itself by selecting the cells theoretically more capable of supporting vital functions throughout the life of the new individual," says Dr. Claveria. According to the authors, this would be particularly important in long-lived organisms, like humans, where the functionality of their tissues must be maintained throughout a long life.

Dr. Miguel Torres also explains that when cell competition is prevented, cells that normally would have lost the battle now become able to contribute to the new organism: "We think, however, that this organism will probably be less capable than the one which would have been formed under normal circumstances. In what sense will it be less adequate is a matter of great interest that we will address in the coming years".

Indeed, the researchers are able to determine in advance which cells will win this battle: those with higher levels of the Myc protein, an important controller of cell metabolic capacity. Moreover, using a new technique that they have developed for the production of genetic <u>mosaics</u>, they are able to manipulate the levels of Myc protein in cells, thus changing the outcome of the fight.

According to Claveria and Torres, the study shows that the early embryo is a mosaic of cells with very different levels of Myc ,in which cells with higher levels of Myc eliminate those with lower levels. However, it is important to understand that those who die are viable cells. "Their removal occurs only because the embryo has more suitable cells able to replace them, and therefore this is an optimization mechanism, not a



repair one," the researchers point out.

A fascinating aspect of the work is the illustration that this battle does not waste cellular resources; dying loser cells are engulfed and digested by their winning neighbours, who then recycle and use all the nutrients for the benefit of the embryo. This research provides answers to some of the questions raised nearly forty years ago by Spanish scientists Ginés Morata and Pedro Ripoll, who in 1975 discovered cell competition in the fruit fly. On that occasion, by experimental manipulation, they described the phenomenon in the fly's wing. Since then cell competition has been suggested to be involved in multiple processes, including tumour progression and <u>tissue</u> regeneration; but never, until this study, had a natural function been described.

**More information:** Myc-driven endogenous cell competition in the early mammalian embryo, <u>DOI: 10.1038/nature12389</u>

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