

Researchers at the CSIC-UMH Neuroscience Institute discover molecules in unicellular organisms that are crucial for the organization of vertebrate tissues

- The Eph/ephrine signaling system, a type of cellular communication that promotes cell adhesion or repulsion, contributed to the development of the first animals.

Researchers at the Institute of Neurosciences (CSIC-UMH) in Alicante (Spain), under the supervision of **Professor Ángela Nieto**, have discovered that molecules necessary for the correct development and organization of tissues in vertebrates already existed in unicellular organisms prior to animals, contrary to what was previously believed.

These molecules are the Eph receptors and their interaction partners, the ephrins, which constitute a receptor-ligand intracellular signalling system. This signalling system influenced the evolution of cell adhesion mechanisms that made possible the transition from unicellular to multicellular organisms by promoting the segregation of different cell populations.

The transition from a world populated by microscopic individual cells to one inhabited by the first animals formed by many (multicellular) cells was an important evolutionary leap. In this transition, the union of similar cells and the separation of different cells was fundamental for the appearance and development of different tissues in animals. In this context, Eph receptors and ephrins must have had an ancestral function in cell-cell interactions that contributed to the formation of boundaries between different cell types. This research, published in the journal *Molecular Biology and Evolution*, also has the participation of David Wilkinson, expert in Ephs and Ephrines, from the Francis Crick Institute in London.

"Until now it was believed that the oldest Eph/ephrine signalling systems were in cnidarians, a group of relatively simple animals to which jellyfish or corals belong. But we have discovered that their origin is much older and that they were already present in organisms prior to the appearance of the animals," notes Angela Nieto, director of the study.

"We have identified similar molecules in coanoflagellates, unicellular organisms closely related to animals. In addition, the three-dimensional structure predicted for the Eph receptor and the ephrine of these organisms shows that they could unite as in animals and, therefore, a rudimentary Eph/ephrine signalling could already be produced in coanoflagellates", adds Aida Arcas, first signatory of this work.

The coanoflagellates are a small group of unicellular eukaryotes, sometimes colonial, that have a great phylogenetic importance, since they are considered the closest unicellular relatives of the animals themselves, or metazoans, that form the animal kingdom. This study also shows that sponges, which are the oldest animals, possess more than 70% of the genes that in humans participate in the Ephs/ephrines signalling pathways. For this reason, it is very probable that in the most primitive animals there already existed mechanisms for the separation of cellular populations similar to those found in vertebrates.

Arcas A., Wilkinson DG. and Nieto MA. *The evolutionary history of Ephs and ephrins: toward multicellular organisms*. Molecular Biology and Evolution. DOI: 10.1093 / molbev / msz222