BERT and ERNI proteins control brain development

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Scientists at University College London have discovered how two proteins called BERT and ERNI interact in embryos to control when different organ systems in the body start to form, deepening our understanding of the development of the brain and nervous system and expanding our knowledge of stem cell behavior.

The new research published this week in the open-access journal *PLoS Biology* solves the puzzle of how vertebrates prioritize the order in which they begin to develop different sets of structures. During development, only a few signals instruct cells to form thousands of cell types, so the timing of how cells interpret these signals is critical. An international research team led by Professor Claudio Stern of the UCL Department of Anatomy & Developmental Biology has shown that the first stage of development of the brain and nervous system is, paradoxically, a block on its progression.

The scientists describe a sequence of reactions that take place when vertebrate embryos are only a few hours old that together act as a timing mechanism, temporarily preventing the development of neural cells (cells that go on to form the brain and nervous system). This gives a head start to other cells in the embryo that will go on to create the body's internal organs and skin, and prevents the nervous system from developing prematurely.

Dr. Costis Papanayotou of the Stern laboratory discovered a new protein, BERT, which then binds with the protein ERNI (also discovered by

Professor Stern's team) and other proteins to unblock a gene called Sox2, which gives the green light to cells to start forming the brain and nervous system.

Professor Stern said, "Scientists have been looking for a long time for the switches that determine when cells in the embryo take on specific roles. Our work shows that the proteins BERT and ERNI have an antagonistic relationship: BERT is stronger and overrides ERNI's suppression of the Sox2 gene, which has a crucial function in setting up the nervous system. As the Sox2 gene is also needed for stem cells to retain their ability to take on a variety of roles in the body and to renew themselves, this research also advances our knowledge of stem cell behavior in adults, which could have implications for this growing area of medical research."

Citation: Papanayotou C, Mey A, Birot AM, Saka Y, Boast S, et al. (2008) A mechanism regulating the onset of Sox2 expression in the embryonic neural plate. PLoS Biol 6(1): e2.doi:10.1371/journal.pbio.0060002

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