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IN BRIEF

STEM CELLS

IGF and FGF cooperatively establish the regulatory stem cell niche of pluripotent human cells *in vitro*.

Bendall, S. C. *et al. Nature* 11 July 2007 (doi:10.1038/nature06027)

It is thought that stem cells are directly influenced by their microenvironment, or niche. But the situation in human embryonic stem (ES) cells might be more complicated. Bendall *et al*. showed that human ES cells produce their own niche cells *in vitro* in the form of human ES-cell-derived fibroblast-like cells (hdFs). hdFs express fibroblast growth factor (FGF) receptor-1 (FGFR1) and produce supportive niche factors, such as insulin growth factor-II (IGF-II) and others, in response to FGF induction. However, the IGF1 receptor (IGF1R) is only expressed on human ES cells, and the IGF-II–IGF1R pathway is crucial for sustaining the self-renewal and pluripotency of ES cells. According to the authors' proposed model of paracrine regulation, human ES cells spontaneously and continuously differentiate into hdFs, providing a continuous source of supportive niche factors that sustain the defining properties of human ES cells.

SIGNAL TRANSDUCTION

Plasma membrane nanoswitches generate high-fidelity Ras signal transduction.

Tian, T. *et al. Nature Cell Biol.* 8 July 2007 (doi:10.1038/ncb1615)

The mitogen-activated protein kinase (MAPK) signalling pathway is controlled by the GTPase Ras, which is tethered to the inner plasma membrane in small dynamic nanoclusters. *In vivo* studies now show that the spatial organization of Ras is essential for signal transduction, but the question is why? Computational modelling of MAPK activation demonstrates that Ras nanoclusters function as sensitive nanoswitches that convert graded ligand inputs into digital signalling output. By generating a variable number of sensitive nanoswitches that are in direct proportion to the ligand input, cells convert the digital (or switch-like) pulses into a final analogue output. This analogue–digital–analogue circuit turns out to be essential for high-fidelity signal transduction for both low-strength and high-strength signals.

ENDOCYTOSIS

SNX9 couples actin assembly to phosphoinositide signals and is required for membrane remodeling during endocytosis.

Yarar, D. *et al. Dev. Cell* **13**, 43–56 (2007)

Endocytosis requires filamentous (F)-actin-dependent remodelling of the plasma membrane, but how F-actin assembly and endocytic processes are coordinated has been unclear. The authors previously showed that the sorting nexin SNX9 is required for clathrin-dependent endocytosis. They now demonstrate that SNX9 also participates in clathrin-independent, F-actin-dependent fluid-phase endocytosis. In addition, SNX9 stimulates N-WASP-mediated activation of the actin-related protein-2/3 (ARP2/3) complex and promotes F-actin branching. SNX9-stimulated actin polymerization is further enhanced by phosphatidylinositol-4,5-bisphosphate-induced oligomerization of SNX9, which is more active than the dimeric form. Together, these findings indicate a role for SNX9 in coupling F-actin nucleation to plasma-membrane remodelling during various modes of endocytosis.