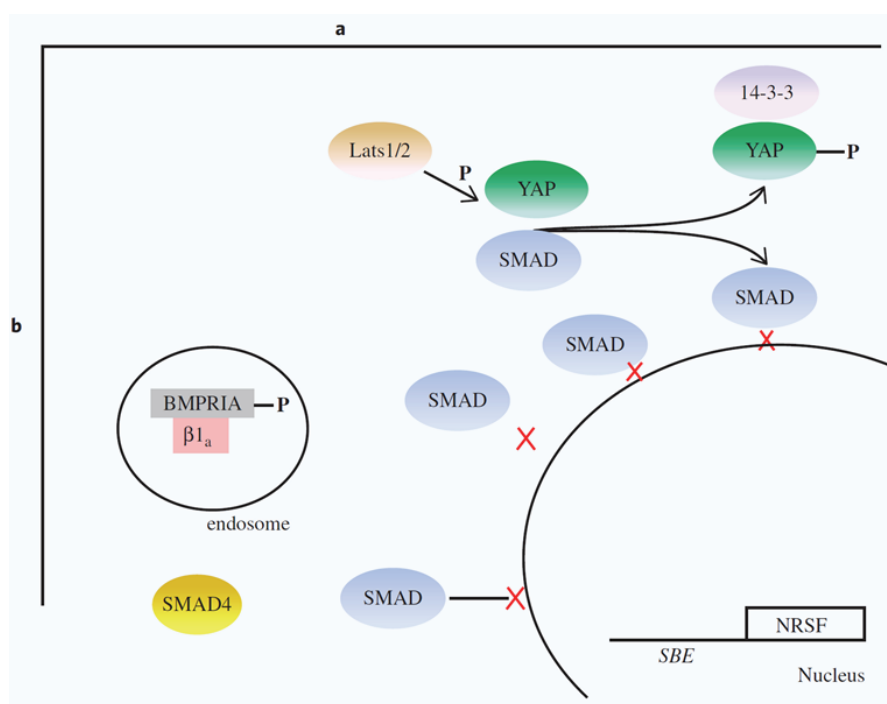


## PRESS RELEASE

### Signal transduction of the physical environment in the neural differentiation of stem cells



*Molecular mechanisms explaining the role of SMAD during induction of neural differentiation of stem cells on soft surfaces. (a) Phosphorylation of YAP by Lats 1/2 causes YAP to be bound and sequester in the cytoplasm by 14-3-3, reducing the ability of YAP to shuttle SMAD to the nucleus. (b) Soft surfaces increase BMPRIA internalization by endocytosis and reduce its ability to phosphorylate SMAD, thereby reducing the localization of SMAD on soft surfaces and its upregulation of NRSF expression.*

Tissue engineering, the integration of cells and synthetic or natural materials to support the growth and replacement of damaged tissues in pathological conditions, frequently involves precise and controlled delivery of biochemical and physicochemical factors to encourage regeneration of damaged tissue. Stem cells, in particular, hold much promise in regenerative medicine, in particular, for cell replacement therapy in the treatment of degenerative diseases including Alzheimer's, Parkinson's, ALS, etc. Advances in biomaterial research have made great strides in the development of substrates that mimic the physiological microenvironment to encourage stem cell differentiation. Scaffolds can be loaded with growth factors and extracellular matrix components (ECM) to mimic the physiological niche of the tissue to control the cell environment and promote stem cell differentiation. However, it is increasingly evident that the physical

environment also contributes to cell lineage determination, as evident by the neural markers expressed in stem cells cultured on soft (low modulus) surfaces. Therefore, understanding the signaling mechanisms that contribute to these changes could benefit stem cell-based therapies. How the cell senses and responds to the physical environment to induce or alter stem cell differentiation has remained an enigma until recently.

A review from researchers at Michigan State University in East Lansing, addresses how physical stimuli signal through RhoGTPases and the BMP-SMAD signaling pathway, pathways well known to function in neural development and recently shown to respond to physical stimuli through changes in the cytoskeleton and surface receptors. In addition, they highlight the Neuron Restrictive Silencer Factor (NRSF) transcription factor, given its function as a master regulator of the neural phenotype, and discuss how surfaces might transduce mechanical stimuli to regulate its expression. The review appears in a forthcoming 2016 issue of the journal *TECHNOLOGY*.

The lead author of the *TECHNOLOGY* review paper is Ryan Thompson of Michigan State University.

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