**Signal mingle: Micropatterns of BMP-2 and fibronectin on soft biopolymeric films regulate myoblast shape and SMAD signaling**

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In vivo, bone morphogenetic protein 2 (BMP-2) exists both in solution and bound to the extracellular matrix (ECM). While these two modes of presentation are known to influence cell behavior distinctly, their role in the niche microenvironment and their functional relevance in the genesis of a biological response has sparsely been investigated at a cellular level. Here we used the natural affinity of BMP-2 for fibronectin (FN) to engineer cell-sized micropatterns of BMP-2. This technique allowed the simultaneous control of the spatial presentation of fibronectin-bound BMP-2 and cell spreading. These micropatterns induced a specific actin and adhesion organization around the nucleus, and triggered the phosphorylation and nuclear translocation of SMAD1/5/8 in C2C12 myoblasts and mesenchymal stem cells, an early indicator of their osteoblastic trans-differentiation. We found that cell spreading itself potentiated a BMP-2-dependent phosphorylation of SMAD1/5/8. Finally, we demonstrated that FN/BMP-2-mediated early SMAD signaling depended on LIM kinase 2 and ROCK, rather than myosin II activation. Altogether, our results show that FN/BMP-2 micropatterns are a useful tool to study the mechanisms underlying BMP-2-mediated mechanotransduction. More broadly, our approach could be adapted to other combinations of ECM proteins and growth factors, opening an exciting avenue to recreate tissue-specific niches in vitro.