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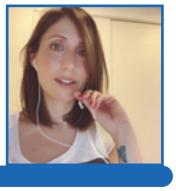

Cell-adhesive nanopatterning shows tissue organization and intercellular communication network architecture are dynamically regulated by the underlying substrate information in mesenchymal condensation

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Abstract

Intercellular communication guarantees a continuous and efficient flow of biological information between cells and their surrounding environment, which is essential to sustain homeostasis and function in living organisms.

Extracellular matrix (ECM) interactions are shown to regulate many biological processes such as cell shape, proliferation, migration, differentiation and programmed cell death. Communication networks are known to be established during morphogenesis with a determining contribution of the interactions with the ECM. Although some descriptive models on how cell membrane mechanochemical information propagates from an initial random scenario to complex tissue patterning are available, a predictable model for ECM information propagation and the establishment of a concurrent intercellular communication network is still lacking.

Hereby, we used substrates of tunable local surface adhesiveness to systematically control integrin-based cell-surface interactions during mesenchymal condensation, a prevalent morphogenetic transition, for the study of ECM information propagation within tissue. Using chondrogenic condensation as a model, we have conducted a systematic study on the influence of cell-matrix interactions in the establishment of an intercellular communication network. We used previously developed dendrimer-based nanopatterns to control local cell-surface adhesiveness at the nanoscale. We show that tuning of local adhesiveness enables control over the pre-cartilaginous condensation phase of mesenchymal cells. Cell condensates of greater cohesiveness and stability are obtained on substrates where basal cells strongly interact with the surface, in accordance with an integrin-based cohesion mechanism. More stable condensates also present increased connexin 43 (Cx43) expression and improved gap junction intercellular communication (GJIC). Through a cell condensate transplantation assay, we show that both tissue organization and intercellular communication architecture are dynamically regulated by the underlying substrate information that propagates in a continuous feedback mode. The effect of substrate induces a rearrangement and adaptation of the cytoskeleton network of the basal cell layer, which propagates through the condensate regulating membrane trafficking and the establishment of GJIC network.

These results capture the dynamics of ECM information propagation and the establishment of intercellular communication networks during morphogenesis. They also provide a predictable model for the study of mechanochemical regulation of intercellular communication during tissue formation, which can be further extended to disease-related active ECM remodeling.

Biography

Anna Lagunas is senior researcher from the networking biomedical research centre of bioengineering, biomaterials and nanomedicine (CIBER-BBN) at the institute for bioengineering of catalonia (IBEC). She holds a bachelor's degree in chemistry by the autonomous university of barcelona (UAB) and a PhD in organic chemistry by the university of barcelona (UB). Anna has pursued her research at different research institutes including the Institute for Research in biomedicine (IRB) and the institute of chemical research of catalonia (ICIQ). She works on the nanoscale behavior of cell membrane proteins and their effects in cell response. In her research she combines materials chemistry, nanopatterning and scanning probe microscopy techniques (AFM, STM) to unveil single molecule contributions to cellular mechanisms. In 2018, she organized the workshop "scanning tiny biology" and led the project "Nanoconductance of electron transfer proteins of the respiratory chain. Direct measurement at the single molecular level and therapeutic regulation in cancer stem cells" granted by the spanish ministry of science, Innovation and Universities. The results of her research have been published in leading scientific journals including nature, nano Letters, nano Research, small and chemistry of materials and in an international patent.

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