Gauging the forces between cells

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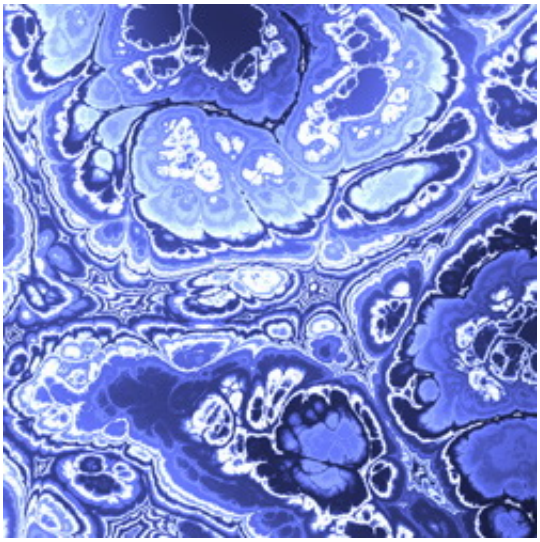

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Cell-cell junctions are important for communication, transport, signalling, waste evacuation and water homeostasis. An European project has investigated how biophysical forces can influence the fulfilment of this vast range of functions.

Communication and signalling between cells in almost all tissues is achieved by gap junctions or intercellular channels. Gap junctions are pairs of half-channels or connexons each having an assembly of six proteins (connexins) that come together. Although the functions and chemical components of gap junctions are well documented, little is known about the forces and energies these structures can support.

The 'Biophysical determinants of the adhesion strength of gap junctions' (Gapjunction Strength) project aimed to use advanced nanotools and atomic force microscopy (AFM) to measure the kinetics and binding strength between the cell-cell junctions. Project scientists used purified connexin proteins in reconstructed lipid membranes to obtain biophysical data on the intercellular bonds.

The Gapjunction Strength scientists applied force to the interacting protein molecules and measured the dissociation characteristics. A rapid dissociation rate is indicative of a dynamic bond while a slow association rate reflected reduced flexibility and small size of the specially constructed structures mimicking extracellular loops. Adhesion strength was found to be significant, suggesting that the bond can support important forces prior to dissociation.

Results of the project have been published in journals. *The* Journal of Molecular Biology has presented the group's results on the nature of the bond. Another paper is currently under review on a novel AFM imaging mode that is capable of mapping mechanical properties of membrane proteins at submolecular resolution.

Characterization of the protein-protein bonds from a biophysical angle at gap junctions promises to hold the key to an understanding of the nature of intercellular channels. Crucial to the structural and biochemical integrity of multicellular organization, gap junction function will guide the direction of future molecular therapies for associated diseases.

Provided by CORDIS

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