# Sandwiches to better understand cells

The human body is formed by complex organ systems. These organ systems are moreover composed by cells of different types that have to co-operate in order to make the body work properly. This is the reason why scientists have studied cells in the laboratory, aiming to understand how these different types of cells behave in the body to make it work.

To do so scientist used to take the cells from the body and place them in a plastic container filled with liquid, which is commonly called a “cell culture”. In this container, cells attach to the bottom and live thanks to the nutrients dissolved in the liquid. This method allowed scientist to study different cellular processes such as cell-cell interaction, cell migration or cell proliferation, which are important processes for diseases like cancer.

However, in the body, cells usually live confined in a 3D environment much more complex than these flat plastic containers. This fact concerned several researchers who then showed that cells tend to adapt to this unnatural 2D environment resulting in unreliable behaviours. This explains why cells cultured in the plastic container in the laboratory do not always behave as in our body. For example, it is a common fact that drugs showing good efficiency in the laboratory do not work when administered to a patient.

In order to avoid this problem many research groups are developing cultures that mimic the different organs (i.e. liver, lungs or muscles). However, working with 3D systems is not easy because:

– 3D systems are usually more complex than the 2D culture and thus are more difficult to handle.

– The experimental techniques and equipment have been developed based on (and for) the 2D cultures and cannot be easily established for 3D cultures. Particularly relevant are the difficulties to extract proteins & nucleic acids or imaging a whole 3D system.

Our research group wondered whether we could develop a simple culture system that could overcome some of these disadvantages while still mimicking physiological environments in order to obtain reliable results. To do so we studied the physiological conditions of the cells and realized that the 3D interaction with the environment is key for the cell to receive and send information. This is not preserved in the 2D cultures where cells only interact with the bottom of the container via the ventral receptors. We therefore thought that sandwiching the cells between two 2D substrates could be a simple and easy way to mimic the 3D interaction of the cell with the environment since ventral and dorsal receptors are stimulated (Fig. 1).

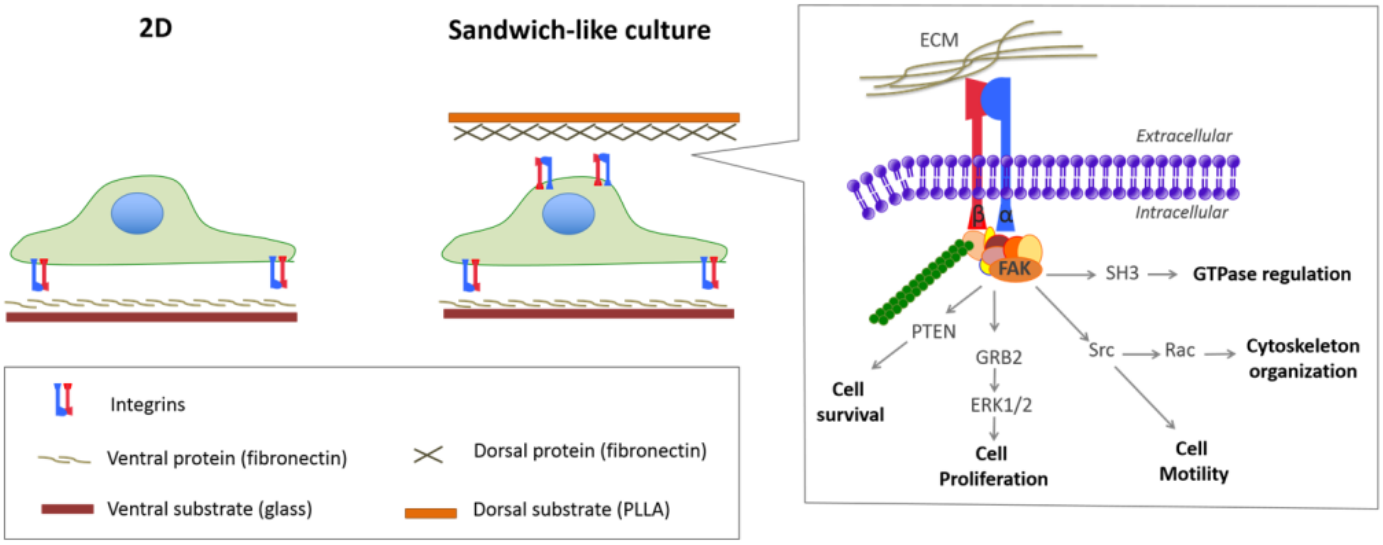


Fig. 1. Sketch of the standard 2D culture and the proposed sandwich-like culture. The extra stimulation of the dorsal receptors within the sandwich-like culture triggers additional signaling that modulates important cellular processes. Adapted from Ballester-Beltrán, et al., Cell/MaterialInteractions, 2015

During 4 years of research we have studied different cellular processes such as cell proliferation, cell differentiation, cell migration and cell shape; comparing the standard 2D culture with our sandwich-like culture. We have shown that our system triggers important changes with respect to 2D cultures, which results in cells behaving more similar to the in vivo condition. Additionally we have shown that the sandwich-like culture is very versatile, allowing the possibility of mimicking different environments just by changing the culture conditions such as using different proteins to mimic different environments. Other parameters such as the stiffness of the substrate can be tuned to mimic different environments such as bone (stiff), muscle and brain (softer). To sum up, the sandwich-like culture is a simple system that offers the possibility to investigate cell behaviour under different environments.

## Publication

Sandwich-like Microenvironments to Harness Cell/Material Interactions.
Ballester-Beltrán J, Lebourg M, Salmerón-Sánchez M
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