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seminar

Friday, 3rd June, 12.00pm

Seminar Room

Host: Prof. Aitziber L. Cortajarena

Growth factor microenvironments in stem cell engineering

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The physical properties of the extracellular matrix (ECM) and the use of growth factors are powerful tools to control cell behaviour, including fundamental processes such as cell migration and (stem) cell differentiation.[1] Integrins are mechanotransductors that feel and respond towards the mechanical properties of the ECM. Growth factors are important molecules that trigger signalling cascades that control e.g., osteogenesis and vascularisation. The field has moved from soluble administration/release of growth factor from biomaterials to solid-phase presentation of growth factors, recapitulating aspects of the ECM. We have developed material systems that allow simultaneous stimulation of integrins and growth factors receptors. We have engineered polymers and 3D hydrogels that unfold and assemble proteins to allow exposure of the integrin and growth factor binding regions. For example, we show the use of BMP-2 in synergy with □5□1 integrins to promote osteogenesis and regeneration of critical-sized defects and VEGF to promote vascularisation.[2-4] Using laminin-based hydrogels we have demonstrated the combined effect with NGF to trigger neural processes.[5]
In parallel, we have also engineered dynamic systems that allow control over temporal release of adhesion molecules and growth factors. Unconventionally, we have used non-pathogenic bacteria in co-culture with stem cells that have been engineered to express a fribronectin fragment and BMP-2 in a dynamic way.[6] We present bacteria-based – living – biomaterials in which symbiotic bacteria/mammalian cell interactions occur and their use for stem cell engineering.[7] We have first genetically modified *L. lactis* to produce a fibronectin fragment (FNIII7-10) that allows integrin binding and cell adhesion to the bacteria biofilm and then stimulation of ostegenesis by inducing the expression of BMP-2 in a dose-controlled manner.

References

1. Dalby, M.J., García, A.J. & **Salmeron-Sanchez, M.** (2018) Receptor control in mesenchymal stem cell engineering. *Nature Reviews Materials* 3, 17091.

2. Llopis-Hernández, V., Cantini, M., González-García, C., Cheng, Z., Yang, J., Tsimbouri,P., García, A.J., Dalby, M.J. and Salmeron-Sanchez, M. (2016) Material-driven fibronectin assembly for high-efficiency presentation of growth factors. *Science Advances*, 2(8), e1600188.

3. Moulisová, V., Gonzalez-Garcia, C., Cantini, M., Rodrigo-Navarro, A., Weaver, J., Costell, M., Sabater i Serra, R., Dalby, M.J., García, A.J. & **Salmerón-Sánchez, M.** (2017) Engineered microenvironments for synergistic VEGF - integrin signalling during vascularization. *Biomaterials*, 126, 61-74 (2017). IF 10.3

4. Trujillo, S., Gonzalez-Garcia, C., Rico, P., Reid, A., Windmill, J., Dalby, M.J., and Salmeron-Sanchez, M. (2020). Engineered 3D hydrogels with full-length fibronectin that sequester and present growth factors. *Biomaterials*, 252, 110104.

5. Dobre, O., Oliva, M.A.G., Ciccone, G.,Trujillo, S., Rodrigo-Navarro, A., Venters, D.C., Llopis-Hernandez, V., Vassalli, M., Gonzalez-Garcia, G., Dalby, M.J. and Salmeron-Sanchez, M. (2021) A Hydrogel Platform that Incorporates Laminin Isoforms for E cient Presentation of Growth Factors – Neural Growth and Osteogenesis. *Advanced Functional Materials*, 31, 210225.

6. Hay, J., Rodrigo-Navarro, A., Petaroudi, M., Bryskin, A. V., Garcia, A.J., Barker, T.H., Dalby, M.J. and Salmeron-Sanchez, M. (2018) Bacteria-based materials for stem cell engineering. *Advanced Materials*, 30, 1804310.

7. Rodrigo-Navarro, A., Sankaran, S., Dalby, M.J., del Campo, A., and Salmeron-Sanchez, M. (2021) Engineered Living Biomaterials. *Nature Reviews Materials* 6, 1175.