

Novel peptide-based strategies to install osteointegrative properties on metallic biomaterials

Roberta Fraioli,^{1,2,3} Florian Rechenmacher,⁴ Stefanie Neubauer,⁴ José M. Manero,^{1,2,3} Horst Kessler,⁴ F. Javier Gil,^{1,2,3} and Carlos Mas-Moruno^{1,2,3*}

¹ Biomaterials, Biomechanics and Tissue Engineering Group, Department of Materials Science and Metallurgical Engineering, Technical University of Catalonia (UPC), Barcelona, Spain.

² Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Zaragoza, Spain.

³ Centre for Research in NanoEngineering (CRNE) - UPC, Barcelona, Spain.

⁴ Institute for Advanced Study and Center for Integrated Protein Science, Department Chemie, Technische Universität München, Garching, Germany

The biofunctionalization of implant materials with integrin-binding peptides and proteins derived from the extracellular matrix (ECM) has long been investigated to improve cell-material interactions. However, classical biomimetic strategies present some limitations and may prove insufficient to elicit the biological signals required in the processes of tissue regeneration [1].

In this work, two novel strategies recently developed by us to improve the osteointegrative properties of metallic materials will be presented. In the first place, a peptide-based platform with the capacity to simultaneously present two distinct bioactive motifs in a chemically controlled fashion will be introduced (Figure 1A) [2]. This molecule, which contained the RGD and PHSRN integrin-binding motifs, effectively improved osteoblast-like cells adhesion, spreading and proliferation on titanium compared to control samples. Noteworthy, it also displayed improved cell responses compared to samples coated with an equimolar mixture of the two motifs.

Moreover, a second strategy based on two RGD peptidomimetics with high activity and selectivity for integrins $\alpha v \beta 3$ or $\alpha 5 \beta 1$ will be discussed (Figure 1B) [3,4]. These molecules were grafted on titanium surfaces and significantly enhanced the attachment, spreading, proliferation, ALP production and mineralization of osteoblastic cells compared to non-coated samples, reaching values of cell adhesion comparable to those obtained with full-length ECM proteins [4].

In summary, this work introduces two innovative biofunctionalization strategies with high potential to foster bone regeneration on implant materials.

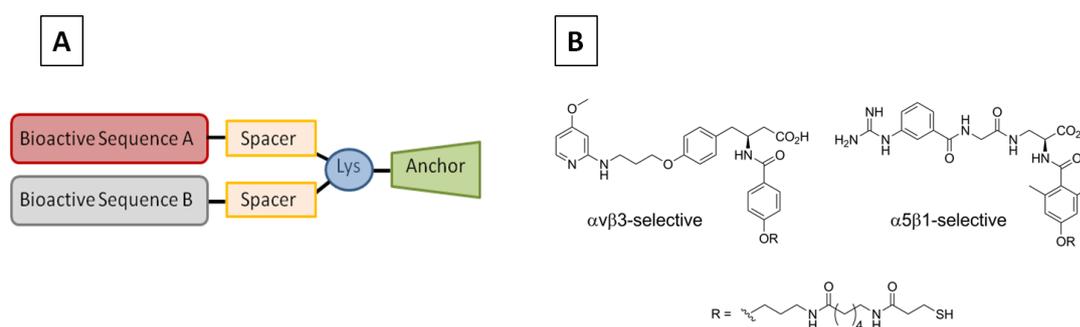


Figure 1. Biofunctional molecules for surface coating. **A)** General representation of the dimeric platform; **B)** Integrin-selective peptidomimetics.

[1] D. F. Williams. *Biomaterials* **2011**, *32*, 4195-4197.

[2] C. Mas-Moruno, et al. *ACS Appl. Mater. Interfaces* **2014**, *6*, 6525-6536.

[3] F. Rechenmacher, et al. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 1572-1575.

[4] R. Fraioli, et al. *Colloid Surf. B-Biointerfaces* **2015**, *accepted*.