Influence of Ca^{2+} binding to titania on Platelet Activation Profiles

Swati Gupta,[1,2] and Ilya Reviakine[1,2]
[1] CIC biomaGUNE, Paseo Miramon 182, San Sebastian, 20009, Spain
[2] Department of Biochemistry and Molecular Biology, University of the Basque Country, 48940 Leiola, Spain.

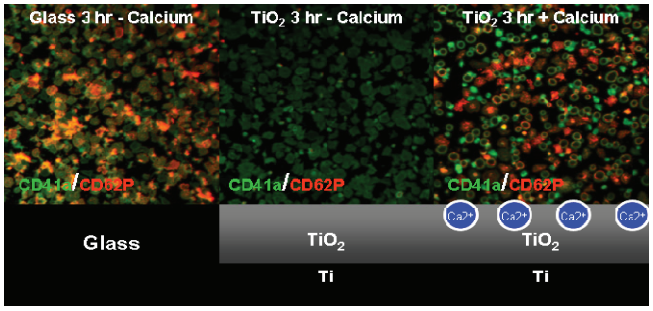

Figure 1: Platelets adhering on glass express the α-granule marker CD62P both in the presence and in the absence of Ca^{2+}. Platelets adhering on TiO_2 do not express this marker in the absence of Ca^{2+} but do express it in its presence. In both cases, they express other activation markers, such as the dense granule marker CD63 (not shown).

Surface properties of implant materials are known to influence biological responses they elicit However, complex processes operating at the interface remain poorly understood. To get an insight into these processes, we investigated the role played by surface ion equilibrium in defining interactions between an implant material (TiO_2) and components of blood (in this case, platelets), because blood is the first tissue that foreign materials come into contact with when inserted into the body and because platelet response is crucial in defining the implant's fate.

Titanium is a widely used biomaterial. Its success is in part due the favorable biocompatibility properties conferred its oxide, TiO_2. We have previously shown that Ca^{2+}-TiO_2 interactions affect the distribution of phospholipid phosphatidyl serine (PS) in model lipid membranes prepared on TiO_2. This allowed us to hypothesize that platelet activation will be affected by these interactions as well.

Platelets are anuclear cell fragments circulating in blood. Activated at wound sites, they aggregate and provide a catalytic surface for the formation of a fibrin-based clot that stops the bleeding. Recently, platelets have been recognized to participate in inflammation, wound healing, tissue regeneration, and immune responses. Activation of platelets by foreign surfaces is detrimental to blood-contacting implants but beneficial for osteoimplants. Upon activation, platelets expose on their surface and secrete a number of markers. These include PS, activated form of GPIIb-IIIa, and proteins CD62P and CD63 that are found in the membranes of the intracellular α- and dense granules of quiescent platelets. To assess the state of platelet activation on TiO_2, we assayed for the expression of these markers. In order to isolate a clear cause-and-effect relationship between Ca^{2+}-TiO_2 interactions and platelet activation, we focused on purified platelets.

Our main finding is that the platelet activation profile on TiO_2 depends on the presence of Ca^{2+}. Furthermore, in the absence of Ca^{2+}, titania differentially regulates α- and dense granule secretion. The differential granule secretion by platelets, as regulated by the surface properties, can be applied towards controlled release of molecules from platelets by nanoparticles or implants in drug delivery applications.