

Seminar
Engineering biomimetic materials to target inflammation and tune immune response

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Abstract: The rate at which nanotechnology and tissue engineering has seen innovations move from bench to bedside has been slower than expected. The demand for products with desired properties for clinical therapy (high targeting, low toxicity) and surgical applications (high biocompatibility, compliance with organ function) remains elevated. We recognized that the body has incredible healing capabilities and have worked to harness these to their fullest potential by creating biomimetic platforms able to mimic the cellular and molecular events that occur during the physiologic healing process and to elicit desired cell and tissue responses. Our approach to biomaterials for tissue engineering is focused on studying the reactions of inflammatory cells such as macrophages, dendritic, and T cells, to biomaterials. We demonstrated that all regenerative processes are dependent on a complex dialogue between multiple cell types, also involving the

chemical and physical cues provided by the surrounding microenvironment. We were among the first to characterize the cascade of inflammatory events triggered by the host's immune system in response to an implanted biomaterial. Through our studies, we showed that immune and stem cells respond to an implanted material according to its composition, structure, and surface properties. Our work in tissue engineering pioneered the synthesis of scaffolds and membranes that mimic native tissue at the nano- and micro-scale in order to bestow the function of natural tissues upon synthetic constructs. To augment implant biocompatibility and minimize immunogenic response, we developed several immune-instructive biomaterials able to tune the immune-response towards improved regeneration. Similarly, we developed a new class of biomimetic nanoparticles inspired by the ability of leukocytes to target inflammation and infiltrate inflamed tissues. By using the cell membrane proteins of leukocytes and other immune cells as building blocks, we created injectable nanoparticles able to avoid reticuloendothelial clearance, specifically target cancer vessels, cross the endothelial layer, and increase accumulation of therapeutic payloads in the cancer parenchyma. Our approach leverages on the high versatility of assembly methods typical of liposomes, which permits the formulation of a stable highly standardized product. At the same time, it allowed us to transfer to and miniaturize the functional peculiarities of the plasma membrane on synthetic nanoparticles. This approach represents the first time such a complex material as the plasma membrane is formulated into a lipid vesicle, using an established method, usually used to synthesize liposomes, to exploit the incorporation of membrane proteins into a lipid bilayer.

Bio: Dr. Ennio Tasciotti graduated in Molecular Biology at Scuola Normale Superiore in Pisa in 2000, and earned a PhD in Molecular Medicine in 2005 at the International Center for Genetic Engineering and Biotechnology.

In 2006 he accepted a Postdoctoral position at the Department of Biomedical Engineering at the University of Texas' Health Science Center. In 2008 he published his first research on 'multistage nanodelivery system', which becomes a cover story on Nature and was selected by Nature Medicine as one of the "Top 5 breakthroughs in Nanomedicine".

In 2009 he became an Assistant Professor at the first Department of Nanomedicine in an American Medical School and in 2010 he was recruited by Houston Methodist Research Institute as Chair of the Department of Nanomedicine. From 2012 he is the Director of Surgical Advanced Technology Lab of the Department of Surgery and in 2015 he founded and directs since then, the Center for Biomimetic Medicine. He is a Professor of Regenerative Medicine at the Institute of Academic Medicine and he holds affiliated and honorary positions in 6 universities in USA, Europe and China.

Between 2009 and today, he received generous funding (\$15M) by DoD and DARPA, to create bioactive nanomaterials to regenerate of muscle-skeletal tissues. He coordinates a multidisciplinary research group of 30 people, has published more than 100 research articles, 10 books and presented at 150 international conferences.

Dr. Tasciotti obtained 10 international patents on nano- and bio-materials for biomedical use and he is currently engaged in the creation of 2 startup biotech companies to develop and commercialize technologies for targeted drug delivery and musculoskeletal tissue regeneration.