## Precision medicine for musculoskeletal regeneration, prosthetics and active ageing - PREMUROSA: a Marie Skłodowska-Curie Innovative Training Network

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INTRODUCTION: Musculoskeletal diseases are a major burden on individuals, healthcare and welfare systems. Treatment of musculoskeletal disorders is currently based either on prosthetic or regenerative surgical procedures, often involving medical device implantation. In both cases, individual tissue healing and regeneration, together with the appropriateness of the implanted device, markedly affect the outcome. A great improvement could be achieved by precision medicine, specifically designed on patient's individual characteristics. This implies combining the personalized clinical approach with individual 'omic' characterization and proper choice of medical device. The concept is "To take care with care". This is the meaning of the Italian word "premurosa" and the ultimate goal of the Innovative Training Network PREMUROSA project, aimed to train a new generation of scientists with an integrated vision of the whole value chain in musculoskeletal regeneration technologies and able to boost the necessary innovations to achieve precision principles in developing innovative devices and optimized clinical applications.

MATERIALS and METHODS This aim have been achieved by a "triple i" (interdisciplinary, intersectoral, international) approach of thirteen Early Scientific Researchers (ESRs), who have had benefit from an excellent scientific environment, up-date technologies, and supervision by international leaders in the field.

RESULTS AND DISCUSSION: ESRs have investigated the links between physico-chemical properties of metallic (titanium and its alloys and ceramic (bioactive glasses and glass-ceramics) materials, including chemistry (chemical composition, surface functionalization), surface morphology (topography, roughness) and hierarchical porosity (at the macro-, meso-nanoscale), and cells (pro- and eukaryotic) and tissues functionality and they studied the impact of surface chemistry, charge and topography on model protein adsorptions and conformation, stem cells fate and extracellular vesicles release and composition. They clarify the role of the extracellular matrix composition as well as the role of the vascular, nervous, and immune system on musculoskeletal tissue regeneration and they developed ad hoc technologies to test safety and efficacy of biomaterials including bioreactors, cellular and computational methods. In addition, they learnt to integrate academic and industrial aspects and they sharpen their experimental and complementary skills in a well-designed and diversified and unprecedented training program.

More than 30 open access papers have been published on high impacted journal and posted on Zenodo.org, and more than 70 conference communications have been released.

CONCLUSIONS: PREMUROSA has contributed to develop personalized tools for the rational and appropriate application of the musculoskeletal regeneration technologies and to clarify the interplay between tissues, cells, and materials in view of regeneration technologies optimization.

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