Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2016-2017

Project Nº 30
Title: Molecular mechanism for fracture nonunion and its treatment through the optimization of mimetic autografts
Department/ Laboratory Cell Therapy Area/Experimental Orthopedics Laboratory/Edf Los Castaños/CUN/CIMA.
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Summary In high energy fractures as well as in surgical reconstructions affecting oncologic patients, in patients affected of endocrinology and/or vascular conditions, the outstanding regeneration capacity of bone tissue can be impaired resulting in increased delayed fracture healing and in the worst case scenario fracture nonunion. The reasons why bone regeneration process is impaired are not yet determined. We have demonstrated that a mechanism that determines fracture nonunion impairs BMP2 expression through an imbalance in hypoxia-derived reactive oxygen species (ROS) scavenging in mesenchymal progenitors (MSCs). The use of MSCs in combination with osteoconductive materials (mimetic autografts) shows an important therapeutic potential. Although, in animal models of fracture nonunion such implants, despite showing increased osteogenesis, presented low efficiency in healing, hampering further progression up to preclinical animal models. Here, we hypothesize that the hypoxic environment and the imbalance in ROS homeostasis are the main cause of the fracture nonunion appearance as well as the low efficiency of the mimetic autografts therapies. To validate our hypothesis our specific aims are: 1) To determine the role of factors that control reactive oxygen species during bone tissue repair. 2) Empower MSCs-based therapies through increased resistance to hypoxia and oxidative stress. Mouse genetics (conditional silencing) and ectopic implantation of human periosteal progenitor cells transduced with genes conferring resistance to hypoxia and oxidative stress will be used to accomplish our objectives.

POSSIBILITY OF PhD

Indicate if the project could be continued with a PhD (doctoral thesis)

YES*

* (PhD grant required)