Research Project Proposal
Academic year 2018-2019

Project Nº 4

Title: *Mechanism of fracture nonunion*

Department/ Laboratory: Experimental Orthopaedics Laboratory (Edif. Los Castaños, UNAV). Cell Therapy Area/Department of Orthopaedic Surgery and Traumatology (CUN).

Director 1 Froilán Granero Moltó
Contact: *fgranero@unav.es*
Codirector:
Contact:

Summary

In high energy fractures as well as in surgical reconstructions affecting oncologic patients, in patients affected of endocrinology and/or vascular conditions, the remarkable 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 fully determined. We have demonstrated (PI13/01633) that a mechanism that determines fracture nonunion impairs BMP2 expression through an imbalance in hypoxia-derived reactive oxygen species (ROS) scavenging in periosteum-derived mesenchymal progenitors (PMSCs). The use of PMSCs 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) Empowering PMSCs-based therapies through increased resistance to hypoxia and oxidative stress. 2) Optimization of mimetic autografts through designed implants that favor vascularization and osteogenic coupling of the PMSCs. 3) To develop a model of fracture nonunion by silencing the molecular pathway that control reactive oxygen species homeostasis.

yes	**X**
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?