Pilot & Feasibility Awards—Year 3

In this issue we would like to highlight the work of one of our two Pilot & Feasibility awardees for Year 3 of the P30 grant.

Dr. Gabriel Mbalaviele, PhD, is a Research Associate Professor of Medicine in the Division of Bone and Mineral Diseases at Washington University Medical School.

NLRP3 is one of the most studied members of the family of intracellular NOD-like receptors (NLRs), and one of the few NLRs shown to form inflammasome. Dr. Mbalaviele’s research is focused on the role of the Leucine rich Repeat with a Pyrin domain 3 (NLRP3) inflammasome in bone. They are investigating whether and to what extent NLRP3 inflammasome mediates low grade aseptic inflammation as a component of the so-called “non-targeted bone remodeling” i.e. basal remodeling not induced by specific stimulators or damage. As unresolved inflammation can exacerbate tissue damage or disorders caused by other etiologies, they are also investigating how NLRP3 inflammasome contributes to some forms of pathological bone remodeling.

P&F funding from the Center for Musculoskeletal Research:

Since systemic inflammation occurs in NOMID mice due to the broad expression of mutant NLRP3, the bone phenotype observed in these mice might be secondary to a direct super-activation of osteoclasts or to an indirect effect via cytokine production by non-hematopoietic cells. In the latter case, cells of the osteogenic lineage represent the most likely candidate since they express NLRP3 and pro-

For more information on the Cores, please click on the links below:
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Core B—Structure and Strength Core
Core C—In Situ Molecular Analysis Core
Core D—Mouse Genetics Models Core

http://musculoskeletalcore.wustl.edu/
Mbalaviele, cont.

The huge impact of the P&F funding has been the in-depth characterization of the phenotype of NOMID mice, the execution of in vitro mechanistic studies and the ongoing acquisition of floxed mice in which NLRP3 activation is restricted to the myeloid lineage (lysozyme M driven Cre expression). This funding was instrumental in generating data which were used for an RO1 application in June 05, 2011, an abstract selected for oral presentation at the ASBMR 2011 Annual Meeting, September 16-20, 2011 at San Diego, and a manuscript in preparation.

Dr. Mbalaviele anticipates that these studies will not only unravel an important role of NLRP3 inflammasome in physiological or pathological bone development and remodeling, but also position this inflammasome as a potential new target for therapeutic intervention in bone diseases.

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