Application Title: Transgenic models of Fibrous dysplasia and models of intervention.

PI: Mara Riminucci
Institution: Sapienza University, Rome, Italy

The main goal of our project is to test a pharmacological treatment that could reduce the incidence of skeletal fractures and deformities in Fibrous Dysplasia of bone (FD). The treatment targets a factor (RANKL) that stimulates bone resorption. Bone resorption is a process that normally occurs in our skeleton in a tightly controlled way to allow the replacement of old and/or damaged bone. In FD, bone resorption is inappropriately activated and this leads to the replacement of normal bone with abnormal FD bone and to skeletal fragility.

Last year, thanks to MDBR funding, we started to treat one of our FD mouse models with an antibody that recognizes mouse RANKL and makes it inactive. A similar drug is available for humans, which has already been used as a therapeutic agent for different skeletal diseases. The results obtained to date in our mice, demonstrate that the treatment may prevent the appearance/evolution of FD lesions in our mouse model. The goal of future experiments will be to assess the best way to administer the antibody, and to investigate any potential undesirable side effects.

In addition, we will analyze other FD mouse models that we have recently generated. We think that these models will clarify in detail how FD lesions develop and unveil additional, novel therapeutic targets.