MicroRNA-188 regulates age-related switch between osteoblast and adipocyte differentiation

Granted by the National Science Foundation for Distinguished Young Scholars of China, Prof. Luo Xianghang's team from the Institute of Endocrinology and Metabolism, Second Xiangya Hospital, Central South University, reported that microRNA-188 regulates age-related switch between osteoblast and adipocyte differentiation. Their work has been published in *J Clin Invest* (2015, 125(4): 1509—22).

BMSCs exhibit an age-dependent reduction in osteogenesis that is accompanied by an increased propensity toward adipocyte differentiation. This switch increases adipocyte numbers and decreases the number of osteoblasts, contributing to age-related bone loss. Prof. Luo found that the level of microRNA-188 (miR-188) is markedly higher in BMSCs from aged compared with young mice and humans. Compared with the control mice, the animals lacking miR-188 showed a substantial reduction of age-associated bone loss and fat accumulation in bone marrow. Conversely, the mice with transgenic overexpression of miR-188 in osterix+ osteoprogenitors had greater age-associated bone loss and fat accumulation in bone marrow relative to WT mice. Moreover, by using an aptamer delivery system, it was shown that BMSC-specific overexpression of miR-188 in mice reduced bone formation and increased bone marrow fat accumulation. The researchers identified histone deacetylase 9 (HDAC9) and RPTOR-independent companion of MTOR complex 2 (RICTOR) as the direct targets of miR-188. Notably, BMSC-specific inhibition of miR-188 by intrabone marrow injection of aptamer-antagomiR-188 increased bone formation and decreased bone marrow fat accumulation in aged mice. Together, the results indicate that miR-188 is a key regulator of the age-related switch between osteogenesis and adipogenesis of BMSCs and may represent a potential therapeutic target for age-related bone loss.

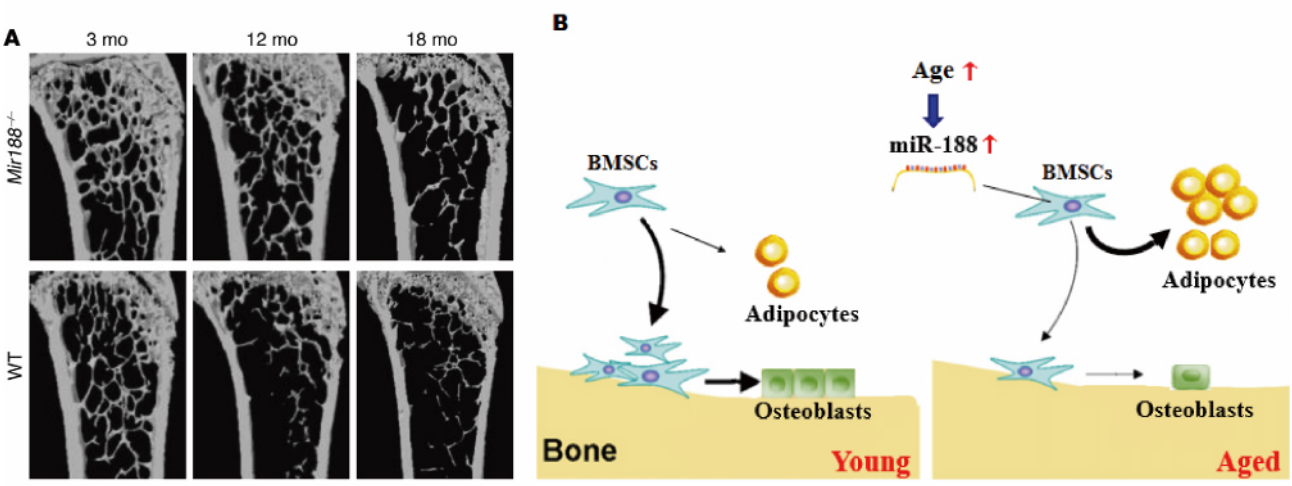

Figure MiR-188 contributes to age-related bone loss. A. The trabecular bone volume was higher and the trabecular separation was lower in the femora of aged (12 or 18 months old) Mir188-/-mice relative to their WT littermates. **B.** MiR-188 regulates the switch between osteogenesis and adipgenesis of BMSCs.