

GPR40 differentially impacts osteoblast behavior depending on differentiation stage and environment.

Claire Philippe_{1,2,3}, Fabien Wauquier_{1,2,3}, Véronique Coxam_{1,2,3} and Yohann Wittrant_{1,2,3*}

1. INRA, UMR 1019, UNH, CRNH Auvergne, F-63009 CLERMONT-FERRAND, FRANCE
2. Clermont Université, Université d'Auvergne, Unité de Nutrition Humaine, BP 10448, F-63000 CLERMONT-FERRAND, FRANCE
3. Equipe Alimentation, Squelette et Métabolismes

GPR40 is a free fatty acid receptor that has been recently shown to be involved in bone remodeling. In fact, this receptor protects skeleton by inhibiting differentiation of resorbing cells, osteoclasts. In this study, due to its expression on osteoblast, we hypothesized that GPR40 could also modulate the activity of bone forming cells. GW9508, a synthetic agonist was used to characterize GPR40 influence on osteoblast differentiation, including alkaline phosphatase activity, mineralized nodule formation in MC3T3-E1 osteoblastic cells and bone marrow cultures isolated from wild-type and GPR40 knock-out mice. Both models showed a dual role of GPR40 on osteoblast behavior. Indeed, receptor stimulation induces early stimulation of differentiation marker expression while inhibiting mineralization process. Finally, in vivo data obtained from ovariectomized mice given GPR40 agonist indicated that osteoblasts were weakly impacted and barely contributed to the preventive effect of GPR40 on bone loss.