Involvement of PLEKHM1 in osteoclastic vesicular transport and osteopetrosis in incisors absent rats and humans, Van Wesenbeeck L, Odgren PR, Coxon FP, Frattini A, Moens P, Perdu B, MacKay CA, Van Hul A, Timmermans JP, Vanhoenacker F, Jacobs R, Peruzzi B, Teti A, Helfrich MH, Rogers MJ, Villa A, Van Hul W, *J. Clin. Invest.* (2007) 117:919-930'

This study illustrates that Plekhm1 is an essential protein for bone resorption as loss of function mutations underlie the osteopetrotic phenotype of the *incisors absent* rat as well as an intermediate type of human osteopetrosis. Electron and confocal microscopic analysis demonstrated that monocytes from the patient, homozygous for the mutation, differentiated into osteoclasts normally but when cultured on dentine discs the osteoclasts failed to form ruffled borders and showed little evidence of bone resorption. The presence of both RUN and Pleckstrin Homology domains suggests that Plekhm1 may be linked to small GTPase signaling. We found that Plekhm1 colocalizes with Rab7 to late endosomal/lysosomal vesicles in HEK293 and osteoclast-like cells, an effect that was dependent on the prenylation of Rab7. In conclusion, *PLEKHM1* is a novel gene implicated in the development of osteopetrosis, with a putative critical function in vesicular transport in the osteoclast.