

## **RANKL – Bones, sex, and mammalian evolution**

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The Receptor activator of nuclear factor kappa-B ligand (RANKL, also known as ODF, TRANCE, OPGL and TNFSF11) and its receptor RANK (also known as TRANCE-R, ODF-R, and TNFRSF11A) are essential for the development and activation of osteoclasts and thus are crucial players in bone remodeling. The RANK/RANKL system also controls lymph node organogenesis, development of thymic medullary epithelial cells, central thermoregulation, and, in pregnancy, the formation of a lactating mammary gland as well as rewiring of the thymic epithelium. Expression of RANKL is strongly induced by inflammatory cytokines and hormones involved in reproduction, such as prolactin and progesterone. RANK/RANKL is also required for the differentiation of Microfold cells (M cells) in Peyer's Patches, contributing to microbial sampling and promoting IgA production in the intestine. Besides M cells, I will present new data on the role of RANK/RANKL as regulators of intestinal stem cells and intestinal epithelial expansion in pregnancy and lactation.