

**Osteoprotegerin-Ligand as a Key Regulator of Mammary Gland Development
a Expression of β -casein**

Hyun-Ju Kim,* Josef M. Penninger, and Young-Yun Kong***

**Division of Molecular and Life Sciences, Pohang University of Technology and Science*

***Amgen Institute, University of Toronto, Canada*

The morphogenesis and remodelling of bone requires the synthesis of bone matrix by osteoblasts and its coordinated resorption by osteoclasts. The TNF family molecule Osteoprotegerin-ligand (OPGL; also known as ODF, TRANCE, and RANKL) is a key factor stimulating the differentiation and activation of osteoclasts, and is therefore essential for bone remodelling and calcium mobilization from the bones.

In mammals, calcium transport from the mother to the fetus and neonates is a vital process to preserve the species. Mothers meet the increased requirements for calcium during pregnancy and lactation by doubling their intestinal calcium absorption and demineralizing their skeletons via activation of bone-resorbing osteoclasts. Recently we demonstrated that OPGL and RANK, the master regulators of skeletal calcium release, are essential for the formation of the lactating mammary gland, the organ required for transmission of maternal calcium to neonates in mammalian species. Moreover, we found that pregnancy hormones induce OPGL expression in mammary epithelial cells and milk protein genes, b-casein and whey acidic protein, are induced by OPGL through C/EBP β transcriptional factor, thus a mechanism independent of STAT5.