Creation of structure-based RANKL mutants and analysis of their biological effect

Project description

Receptor activator of nuclear factor NF-κB ligand (RANKL) is a member of the Tumor Necrosis Factor (TNF) superfamily and plays an important role in bone extracellular matrix (ECM) regulation. RANKL can stimulate its receptor RANK, which is expressed on macrophages and activate differentiation of osteoclasts, leading to degradation of bone ECM. Osteoprotegerin (OPG) is a decoy receptor of RANKL, and can block the interaction of RANKL and RANK.

Imbalances in the RANK / RANKL / OPG pathway can lead to diseases. An example is an excessive degradation of bone, leading to osteoporosis. In addition, pulmonary fibrosis is characterized by progressive alteration of the lung structure due to the excessive production of ECM. Fibroblasts and macrophages are abundantly presented in fibrotic lung tissue and can contribute to fibrosis, as well as increased OPG levels.

As RANKL appears to be in the middle, we hypothesize that improved RANKL mutants can be created and used as a therapeutic protein to battle disease.

In this project, you will:

1. Construct RANKL mutants (PCR, digestion, ligation etc).
2. Produce and purify RANKL mutants.
3. Determine the binding of RANKL mutants to RANK-Fc and/or OPG (ELISA, SPR).
4. Assess the biological effect of the constructed RANKL mutants in cell-based assays.

Organization

The master research project will be conducted in the Department of Chemical and Pharmaceutical Biology. In our laboratory we work on the molecular (DNA) and macromolecular (protein) level. We offer a stimulating research environment for a student interested in molecular biology.

Contact

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