

Functional aspects of SNPs in the succinate receptor: links to renal damage and diabetes?

Clinical relevance

The succinate receptor SUCNR1 (also called GPR91) is a G protein coupled receptor that acts as a local sensor of disturbed metabolism. This receptor recently emerged as a key player in sensing oxidative stress and hyperglycemia and mediating tissue adaptive responses in e.g. diabetes mellitus. As such, we believe SUCNR1 and its ligand succinate is a major intermediate in the development of diabetes and its associated renal damage/end stage renal disease.

Background

Currently, >20 missense SNPs have been identified in the coding sequence of the SUCNR1 gene, which may affect receptor function through altered receptor localization, receptor signaling or binding of its ligand succinate. As a first step to identify whether these SNPs may result in a phenotype in patients, a cell-biological analysis of these SNPs needs to be performed.

Goals

SNPs will be introduced into the SUCNR1 cDNA and subsequently stably transfected into polarized renal cells. Cells will be analyzed for relevant signaling pathways using western blotting for signaling intermediates and calcium mobilization assays, while receptor localization will be determined using immunocytochemistry and confocal laser scanning microscopy. Identification of SNPs that induce constitutive activity of the SUCNR1 may identify this gene as a risk factor for diabetes and its resulting renal damage/end stage renal disease.

Techniques

This internship will allow you to learn and apply several techniques such as:

- Molecular cloning
- Cell culture
- Westernblotting
- Calcium mobilization assays
- Immunocytochemistry
- Confocal laser scanning microscopy

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