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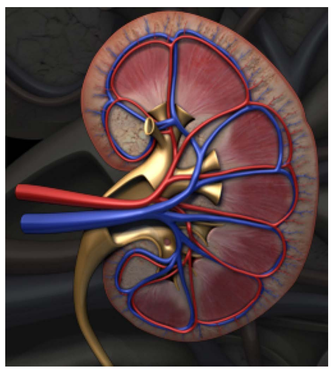

Cell Biology
Lithium-induced Nephrogenic Diabetes Insipidus

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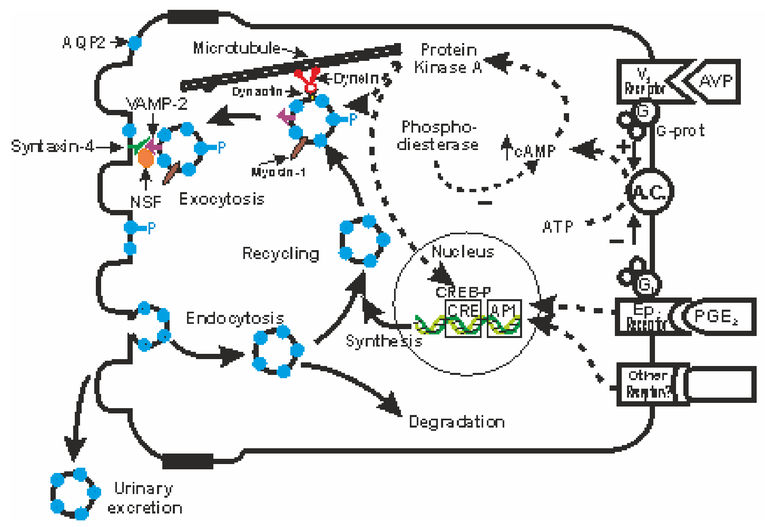
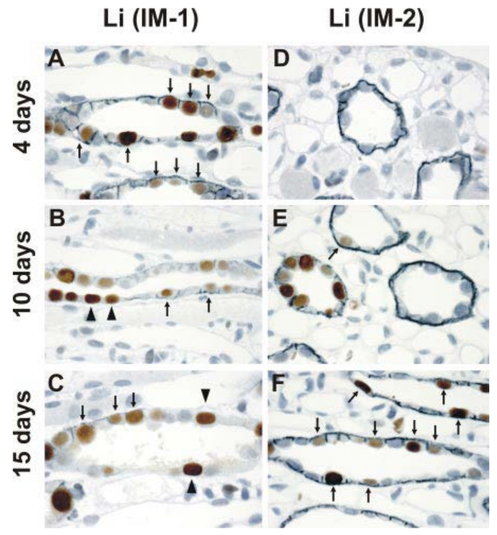
Background

Lithium (Li) salts are widely used drugs for treating patients with bipolar affective disorders. Li treatment negatively affects the ability of the kidney to concentrate urine, which is a major side-effect. As a result, patients may develop Nephrogenic Diabetes Insipidus (NDI), which results in very severe polyuria and polydipsia. At the molecular level, Li-induced NDI is associated with a marked downregulation of the water channel aquaporin-2 (AQP2), a change in the cellular composition of the kidney collecting duct and an activation of MAPK signaling pathways. Studies in mice have shown that apparently only the collecting duct and not the kidney connecting tubule respond to Li. We want to understand the molecular mechanisms behind the severe polyuria in patients, who takes Li medication and define new targets for management of the Li-NDI.





Projects

- Explore the correlation between the activation of the MAPK extracellular-regulated kinase (ERK1/2) and the down-regulation of AQP2.

- Investigate why the kidney connecting tubule is able to escape Li toxicity using a proteomic approach.

- Investigate whether the cellular changes observed in animals also apply to the human kidney.

- Investigate whether two specific statins are able to prevent the Li-induced changes in the kidney.

Techniques

- Animal experiments
- Cell culture experiments
- Biotinylation assays
- Immunohistochemistry
- Confocal microscopy
- Western blotting
- Mass spectrometry
- FACS
- Immunoprecipitation
- Bioinformatics

Relevant references:
Christensen et al, Am.J.Physiol.Renal Physiol, 291, F39-48, 2006.
Christensen et al, J Am Soc Nephrol 22: 253–261, 2011.
Trepiccione et al, Am.J.Physiol.Renal Physiol, 305(6):F919-29, 2013.
Trepiccione et al, Kidney International, 86(4): 757-67, 2014.