Deciphering the function of a novel protein involved in magnesium balance

Scientific context

The kidneys are the principal organ of the urinary system. They excrete waste products, regulate body fluid and electrolytes (Na^+, Cl^-, Mg^{2+}, Ca^{2+}, K^+), control blood pressure, regulate hormones and support red blood cell formation. Alterations in kidney functions can lead to kidney disease and also affect other organs.

Background

Magnesium is an essential ion for the human body since it is involved in a broad range of physiological processes. The kidney is the key organ regulating Mg^{2+} reabsorption from the pro-urine. It is composed by nephrons, functional units divided into specialized segments involved in the reabsorption and secretion of water, electrolytes and organic molecules. Approximately 50-70% of the filtered Mg^{2+} is reabsorbed in the thick ascending limb (TAL) through paracellular mechanisms. Lastly, in the distal convoluted tube (DCT) the fine tuning of Mg2+ reabsorption occurs (5-10%) via active transcellular transport, which will determine the maintenance of Mg^{2+} levels.

Clinical relevance

Disturbances in magnesium homeostasis occur mainly in the form of magnesium deficiency which is reflected by a reduction on Mg^{2+} serum levels, known as hypomagnesemia. Symptoms of hypomagnesemia include weakness, heart arrhythmias, tetany, etc. To date, many cases of Mg^{2+} disturbances (e.g. seen in metabolic disease) cannot be explained with the current knowledge, meaning that there is a clinical need to further elucidate the mechanisms underlying hypomagnesemia to find an effective treatment. This project will provide new functional insights on renal Mg^{2+} handling and contribute to the discovery of potential therapeutic targets and biomarkers of electrolyte-related kidney disease.

Aim and research questions

The aim of this project is to decipher the function of a novel protein involved in Mg^{2+} homeostasis and unravel the molecular mechanisms by which it regulates Mg^{2+} handling in the kidney. The following research questions will be addressed:

1. Which is the (patho)physiological role of this new protein Mg^{2+} homeostasis?
2. In which part of the nephron exerts its effects?
3. By which mechanisms modulates Mg^{2+} transport in the kidney?

What will you do?

This project is based in the Department of Physiology and The Jackson Laboratory (USA), arrangements to go abroad can be discussed. Both locations offer an environment to perform high-quality research that includes both basic and translational aspects of biomedical science. You will be part of a professional and diverse group consisting of PhD students, post-doctoral researchers and other students. Techniques that can be used during your internship: Cell culture, Animal handling, Mass spectrometry, RNA studies (Real-Time qPCR, RNAseq), Protein studies (Western blotting, immunohistochemistry), Imaging techniques (chemiluminescence, fluorescence).

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