Deciphering new molecular mechanisms altering magnesium transport

Background

Magnesium is an essential ion for the human body since it is involved in a broad range of physiological processes. 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. 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, which will determine the maintenance of Mg^{2+} levels.

Clinical relevance

Recently, we have identified a group of patients that suffer from cardiomyopathy, nephrocalcinosis and hypomagnesemia. They present mutations in a gene that regulates the mammalian target of Rapamycin (mTOR), specifically mTOR complex 1. This protein regulates many fundamental cell functions. It is involved in energy metabolism and cell growth and it is sensitive to environmental inputs including nutrients and growth factors. In the kidney it has an essential role regulating ion transport but the specific mechanisms and factors affecting mTOR pathway remain unknown.

Aim and research question

The aim of this project is to understand the role of mTORC1 signaling in renal magnesium transport and unravel the molecular mechanisms underlying the symptoms present in these patients. Preliminary data in our group showed that the alterations on Mg^{2+} transport might be taking place in TAL. For this reason, we will use an in vitro model of mouse kidney TAL cells (MKTAL). The following research questions will be addressed:

1. How does mTORC1 overactivation regulate the paracellular transport in TAL?
2. Are the different mutations that affect mTORC1 activity affecting ion transport in the same manner, or they act on different targets?
3. Can external inputs such as glucose modulate the activity of mTORC1 in cells that carry the mutation?

Internship and techniques

Our department offers 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. You will have your own project in which you will formulate your research question and design and perform your own experiments accordingly with the guidance of your supervisor

Techniques that can be used during your internship:
- Cell culture and transfection
- RNA studies (Real-Time qPCR, gene expression analysis)
- Protein studies (Western blotting, immunohistochemistry)
- Imaging techniques (chemiluminescence, fluorescence)

Contact

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