Kidney organoids as an innovative tool to study electrolyte homeostasis

Scientific context

Plasma levels of electrolytes (i.e. Na^+, K^+, Ca^{2+}, Mg^{2+}) play a major role in the regulation of key physiological (i.e. blood pressure, cardiac function, brain development) and biochemical processes (i.e. enzymatic activity). The kidney is one of the main organs regulating electrolyte levels. This results from a complex and fine regulated balance of glomerular filtration, electrolyte reabsorption and secretion. Different ion channels and transporters, accessory proteins, intracellular kinases and transcription factors are involved in this process. Malfunction of one or more of these molecular elements constitute the bases of several diseases (i.e. hypertension, polycystic kidney disease, seizures, etc.).

Project background

In vitro and *ex vivo* models constitute a useful tool to understand the mechanisms underlying electrolyte homeostasis and its regulation. Currently, most studies rely on the use of primary culture and cell lines to model physiological and pathological phenomena taking place in the human body. However, these models bear different drawbacks such as limited growth *ex-vivo* or presence of transforming mutations, which may lead to conclusions poorly representing the *in vivo* situation. Organoids constitute self-renewing 3D cultures that retain many structural and functional properties exhibited by the organ of origin. Furthermore, human organoids constitute a promising tool in regenerative medicine. In this regard, human kidney organoids may exhibit a high potential for treatment of renal disorders such as inherited electrolyte disorders, chronic kidney disease, etc. Currently, the transport of ions in kidney organoids and its molecular regulation is poorly investigated.

Aims and Research Question

The aim of this project is to evaluate the transport of physiologically relevant electrolytes (Na^+, Ca^{2+}, Mg^{2+}) and its regulation in different types of kidney organoids (i.e. induced pluripotent stem cell (iPSC)-derived, adult stem cell-derived). The main research question to be answered is whether kidney organoids constitute an adequate model to evaluate electrolyte transport and to which extent this resembles the *in vivo* situation.

What will you do?

You will gain experience in the generation and culture of kidney organoids from different starting materials (genetically engineered iPSCs, human adult kidney, mice kidney). Characterization of the obtained organoids will be performed by qPCR, western blot and immunofluorescence with confocal microscopy. Electrolyte transport will be evaluated using radioactive tracers, stable isotopes and electrochemical methods.

Your internship will take place in the group of Ion Transport at the Department of Physiology. We are an international team with people from more than 8 different nationalities where scientific exchange takes place in a continuous basis. During your time with us, you will be supervised by a team of PhD candidates and postdocs who will be involved in the planning and execution of your experiments, data analysis and presentation.

Contact

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