Research Project Proposal
Academic year 2019-2020

Project Nº 50 ASIGNADO

Title: Intestinal absorption of transition metals

Department/ Laboratory: Department for BioMedical Research (DBMR)/ Nephrology and Hypertension /Group Hediger

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Summary: Transition metal ions take part of a myriad of biochemical processes that are vital for life. Due to their unique redox properties, they are key components of numerous enzymes and electron transport proteins as well as the oxygen transporting protein hemoglobin. Remarkably, they also form the DNA-binding domains for many transcription factors and serve as co-substrates of enzymes involved in DNA replication and repair. Therefore, the homeostasis of transition metal ions is tightly regulated in living organisms. As part of the cellular mechanisms maintaining transition metal homeostasis, our laboratory focusses on their cellular uptake, which is mediated by specific membrane transporters, known as solute carriers (SLCs).

In humans, absorption of transition metal ions occurs mainly in the brush border membrane of the small intestine, where the solute carrier family member SLC11A2, also known as DMT1, has been postulated as the main absorptive pathway. DMT1 has been largely studied due to its key role in iron (Fe) homeostasis. However, it can also transport other essential metals, such as zinc (Zn) or manganese (Mn), and even the toxic pollutants as cadmium (Cd) or lead (Pb). Consequently, studies describing its functional mechanism, pharmacology and expression patterns were and still are highly relevant for understanding the absorption of the transition metals in health and disease (i.e. anemia, hemochromatosis, Parkinson's disease, restless leg syndrome or heavy metal poisoning). Interestingly, it has been recently reported that other metal transporters are expressed along the small intestine. However, their precise contribution to the transition metal absorption is not yet known. In particular, in the Hediger group, we are interested in the SLC39 family members 8 and 14, also known as ZIP8 and 14, as they are able to transport similar transition metal ions as DMT1. Therefore, the aim of this project is to understand their contribution to the intestinal metal absorption by 1) studying their transport mechanisms, 2) developing tool compounds able to specifically inhibit their functional activity, and 3) defining their expression pattern along the small intestine.

yes	
no	**X**

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?