

## “Fishing for function”: the role of SLC41A1 in zebrafish magnesium homeostasis

### Clinical relevance

In the last decade, a lot of research has been performed in order to elucidate the molecular mechanisms involved in magnesium ( $Mg^{2+}$ ) homeostasis. However, most investigations have been carried out *in vitro* models and their results are therefore not necessarily representative for what happens in an *in vivo* setting.

In this project, we will use the zebrafish as a model to test the *in vivo* relevance of SLC41A1 in  $Mg^{2+}$  handling.

### Background

$Mg^{2+}$  can be absorbed via either a passive paracellular- or an active transcellular pathway. The transcellular pathway of  $Mg^{2+}$  absorption across epithelia has been studied for many years and the mechanisms that govern the apical entry of  $Mg^{2+}$  into the cell are very well known. However the basolateral transporter, which mediates the basolateral exit of  $Mg^{2+}$  out of the cell, is still unknown. The  $Na^+/Mg^{2+}$  transporter SLC41A1 has been proposed to be the potential basolateral extrusion mechanism for  $Mg^{2+}$ . Indeed, we have found that the zebrafish ortholog of SLC41A1 is sensitive to dietary and waterborne  $Mg^{2+}$ , indicating SLC41A1 is indeed involved in  $Mg^{2+}$  homeostasis.

In this internship, the *in vivo* relevance of SLC41A1 will be investigated in the context of  $Mg^{2+}$  homeostasis. To this end, morphological and quantitative phenotypes in zebrafish *slc41a1* morphants (zebrafish in which the SLC43A1 gene is knocked down) will be determined and the relation to  $Mg^{2+}$  homeostasis will be established.

### Goals

In this internship we want to answer the following question:

- Can we knock down SLC41A1 down using morpholino's (resembling siRNA)?
- What is the effect of knocking down SLC41A1 on zebrafish morphology?
- What is the effect of SLC41A1 on  $Mg^{2+}$  content of zebra-larvae?

### Techniques

This internship will allow you to learn and apply several techniques such as:

- Knockdown of gene expression using morpholino's
- Qualitative analyses of morphological phenotypes in morphant and control zebrafish
- Calcium/magnesium determinations in serum and tissues
- Molecular cloning techniques
- RNA isolation
- Determination of mRNA expression using realtime-techniques

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