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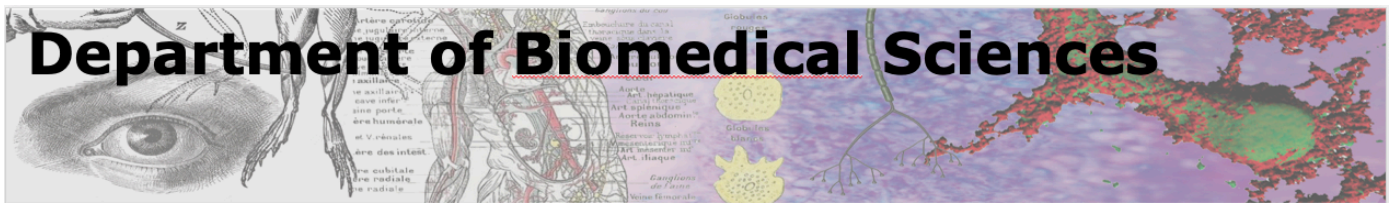


# DSB SEMINAR

**Friday, January 31th, 2020 – 12h15**
Department of Biomedical Sciences
Seminar room Lipari

## "Defective bicarbonate reabsorption in Kir4.2 potassium channel deficient mice impairs acid-base balance and ammonia excretion"

**Yohan Bignon, PhD**
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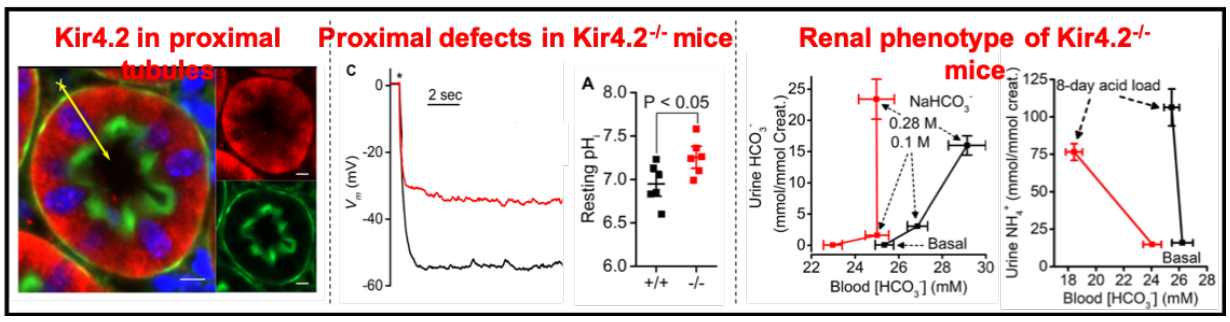
**Host**: Dr Dmitri Firsov




The kidneys excrete the daily acid load mainly by generating and excreting ammonia but the underlying molecular mechanisms are not fully understood. This study evaluated the role of the inwardly rectifying potassium channel subunit Kir4.2 (*Kcnj15*) in this process.

In mice, Kir4.2 was present exclusively at the basolateral membrane of proximal tubular cells and the invalidation of *Kcnj15* caused a hyperchloremic metabolic acidosis associated with a reduced threshold for $HCO_3^-$ in the absence of a generalized proximal dysfunction. Urinary $NH_4^+$ excretion rates in *Kcnj15*-deleted mice were inappropriate to acidosis under basal and acid-loading conditions, and not related to a failure to acidify urine or a reduced expression of ammonia transporters in the collecting duct. In contrast, the expression of key proteins involved in ammonia metabolism and secretion by proximal cells was inappropriate in *Kcnj15*-deleted mice. In addition, *Kcnj15* deletion depolarized the proximal cell membrane by decreasing the barium-sensitive component of the potassium conductance and caused an intracellular alkalinization.

We conclude that the Kir4.2 potassium channel subunit is a new regulator of proximal ammonia metabolism and the renal consequences of its loss of function in mice support the proposal for KCNJ15 as a molecular basis for human isolated proximal renal tubular acidosis.

***Reference***
*Bignon et al., Kidney International, in press.*

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