

PTH-independent regulation of blood Ca²⁺ concentration by the calcium sensing receptor “CaSR”

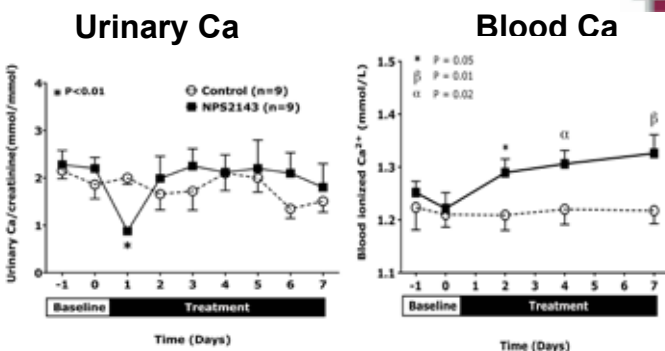
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Introduction and aims

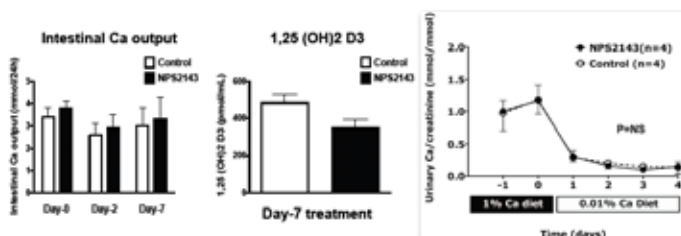
- CaSR plays a crucial role in Ca²⁺ homeostasis by inhibiting parathyroid hormone (PTH) secretion.
- In contrast, there is less understanding of the PTH-independent homeostatic importance of CaSR.
- CaSR is significantly expressed in the kidney where its role remains incompletely understood.
- **The present study aims to determine if CaSR control Ca homeostasis independently of PTH, and how CaSR acts on the renal tubule.**

Results

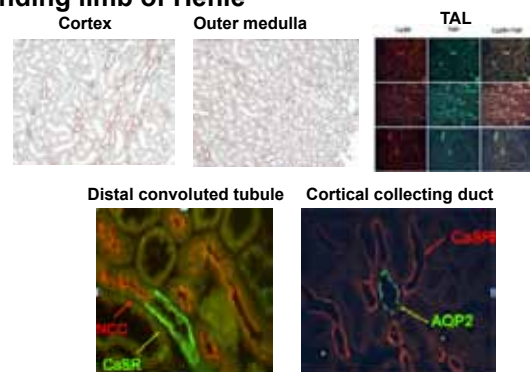
1) Changes in PTH secretion are not required for the effects of Casr on calcium metabolism: effects of the Casr inhibitor NPS2143



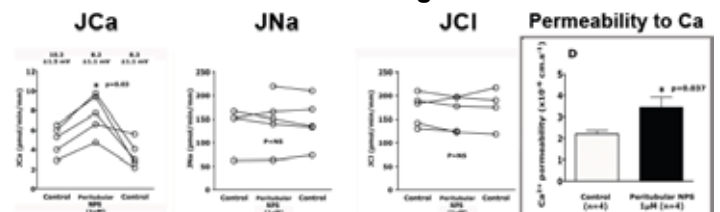
2) Chronic PTH independent CaSR blockade does not modify intestinal Ca absorption and bone Ca release



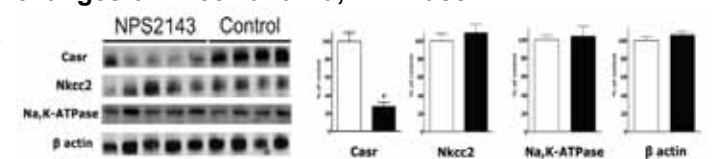
3) Renal CaSR expression is restricted to the thick ascending limb of Henle



4) CaSR controls the paracellular pathway permeability to calcium in the thick ascending limb of Henle



5) Long-term PTH-independent Casr blockade decreases the renal expression of Casr without changes of Nkcc2 and Na,K-ATPase



Conclusion - Perspectives

- Renal CaSR is a factor participating in the homeostasis of calcium independently of PTH.
- We provide here the proof of concept of potential therapeutic relevance in human hypoparathyroidism

Publications

Alexandre Loupy, Bharath Woolia, Suresh Krishna Ramakrishnan, Régine Chambrey, Renaud de la Faille, Patrick Bruneval, Chantal Mandet, Erik Ilo Christensen, Hélène Faure, Lydie Cheval, Kamel Laghmani, Corinne Collet, Dominique Eladari, Robert H Dodd, Martial Ruat, Pascal Houillier **PTH-independent regulation of blood calcium concentration by the calcium-sensing receptor – Enrevision**
 Renaud de La Faille, Alexandre Loupy, Suresh K Ramakrishnan, Barath Woolia, Pascal Houillier. **Characterization of the specific effects of renal tubular calcium-sensing receptor (CaR) – Soumis**

CONTACT :

pascal.houillier@egp.aphp.fr

