

Magnesium regulates parathyroid function in normal rat glands *in vitro*

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INTRODUCTION

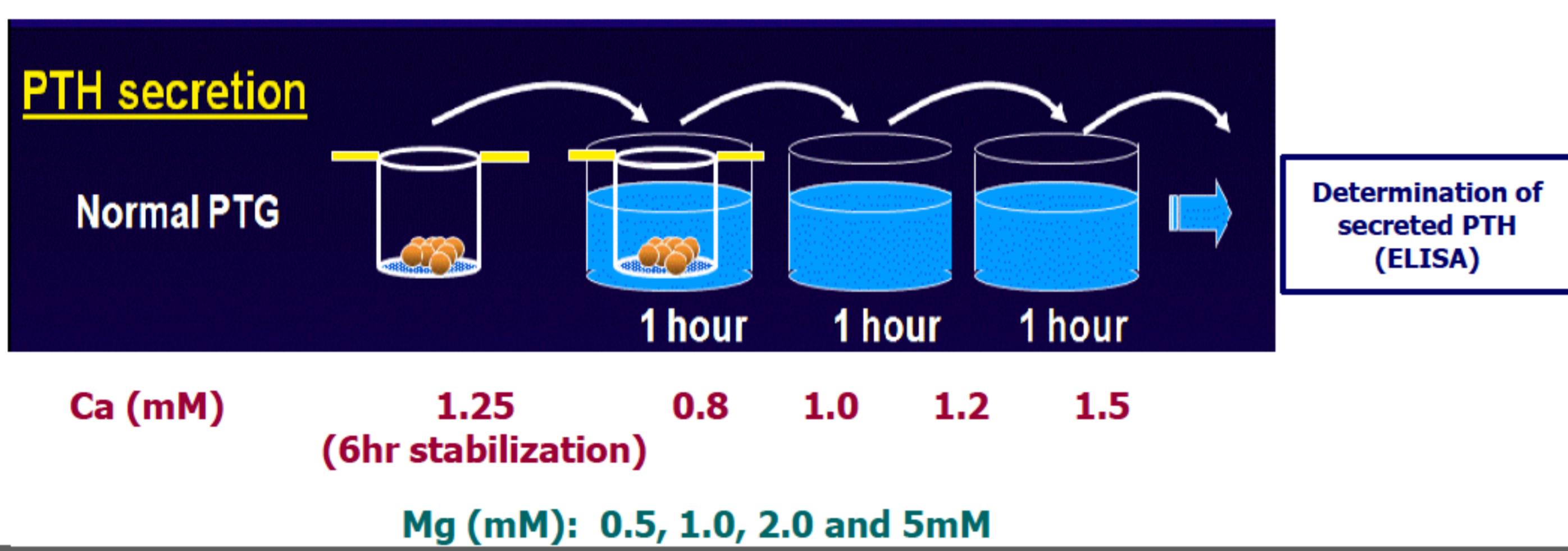
Parathyroid hormone (PTH) is essential for calcium (Ca) homeostasis. Levels of extracellular Ca are detected by calcium-sensing receptor (CaSR). These plasma membrane receptors are located on the surface of parathyroid cells, which enable an adequate secretory response. Besides Ca, other divalent cations such as magnesium (Mg) may act as orthosteric modulators of CaSR. In fact, there has been described an inverse relationship between extracellular Mg levels and PTH both *in vitro*^{1,2,3} and in uremic patients^{4,5}.

Several studies have shown the effectiveness of Mg salts as phosphate binders. Its use is growing because of the deleterious effects associated with calcium-based binders⁶. However, it is unknown whether Mg may induce a oversuppression of PTH levels.

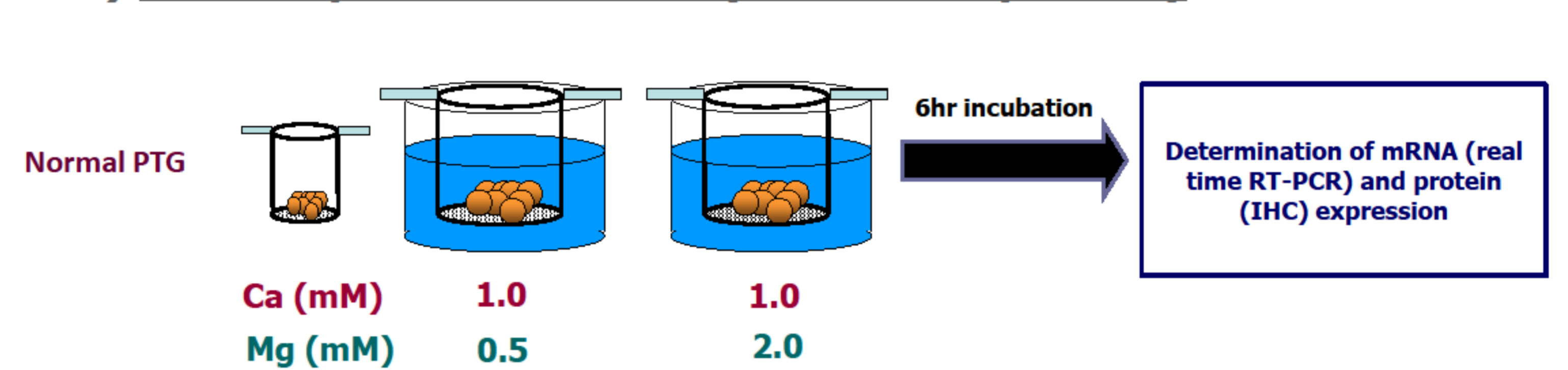
The aim of our study was to determine the influence of Mg on PTH secretion in the presence of different Ca levels. Further, we investigated the effect of Mg on the expression of the parathyroid receptors CaSR, vitamin D receptor (VDR), fibroblast growth factor receptor 1 (FGFR1) and Klotho.

METHODS

A) Secretion studies:

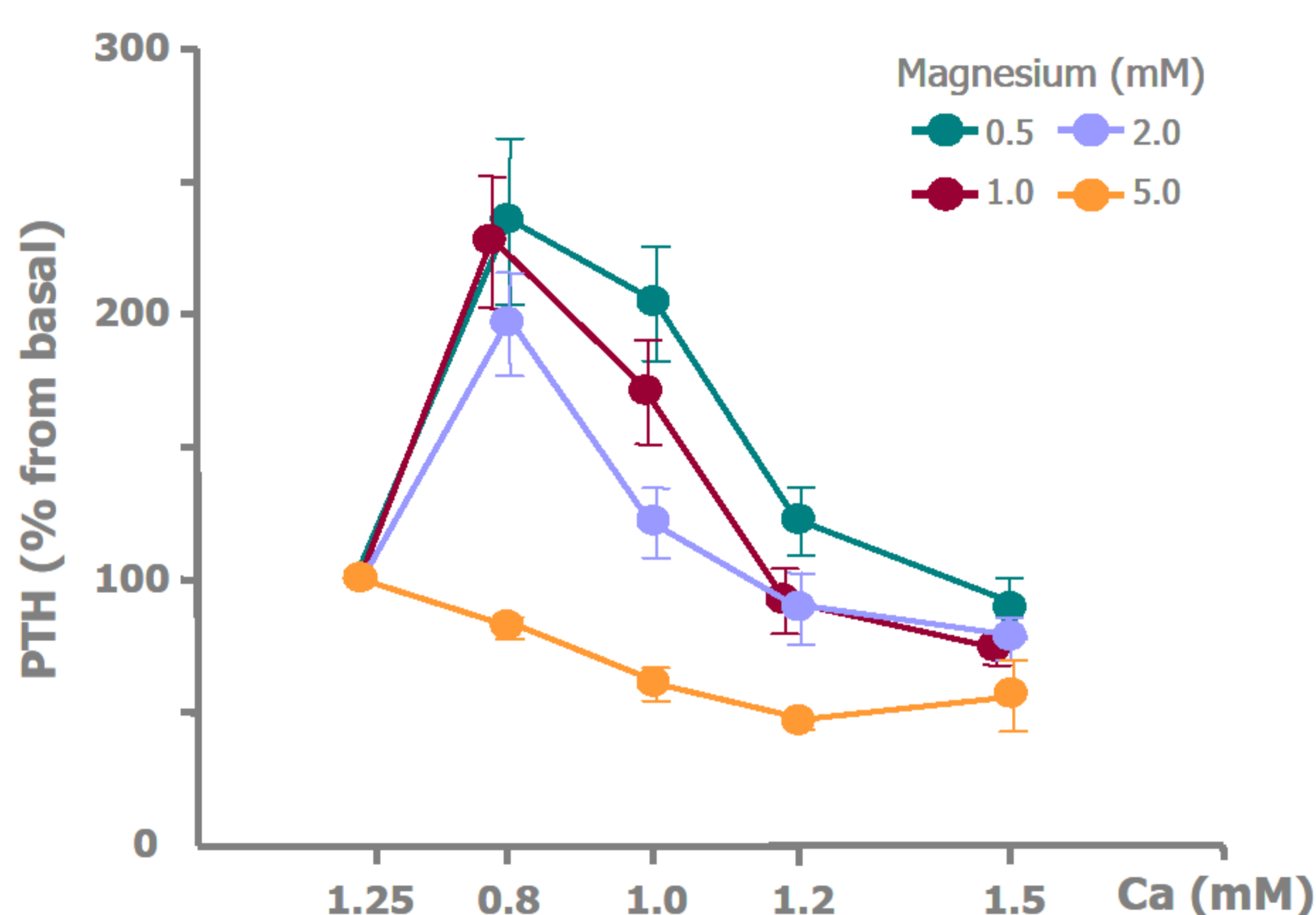


B) Gene expression studies (mRNA and protein):

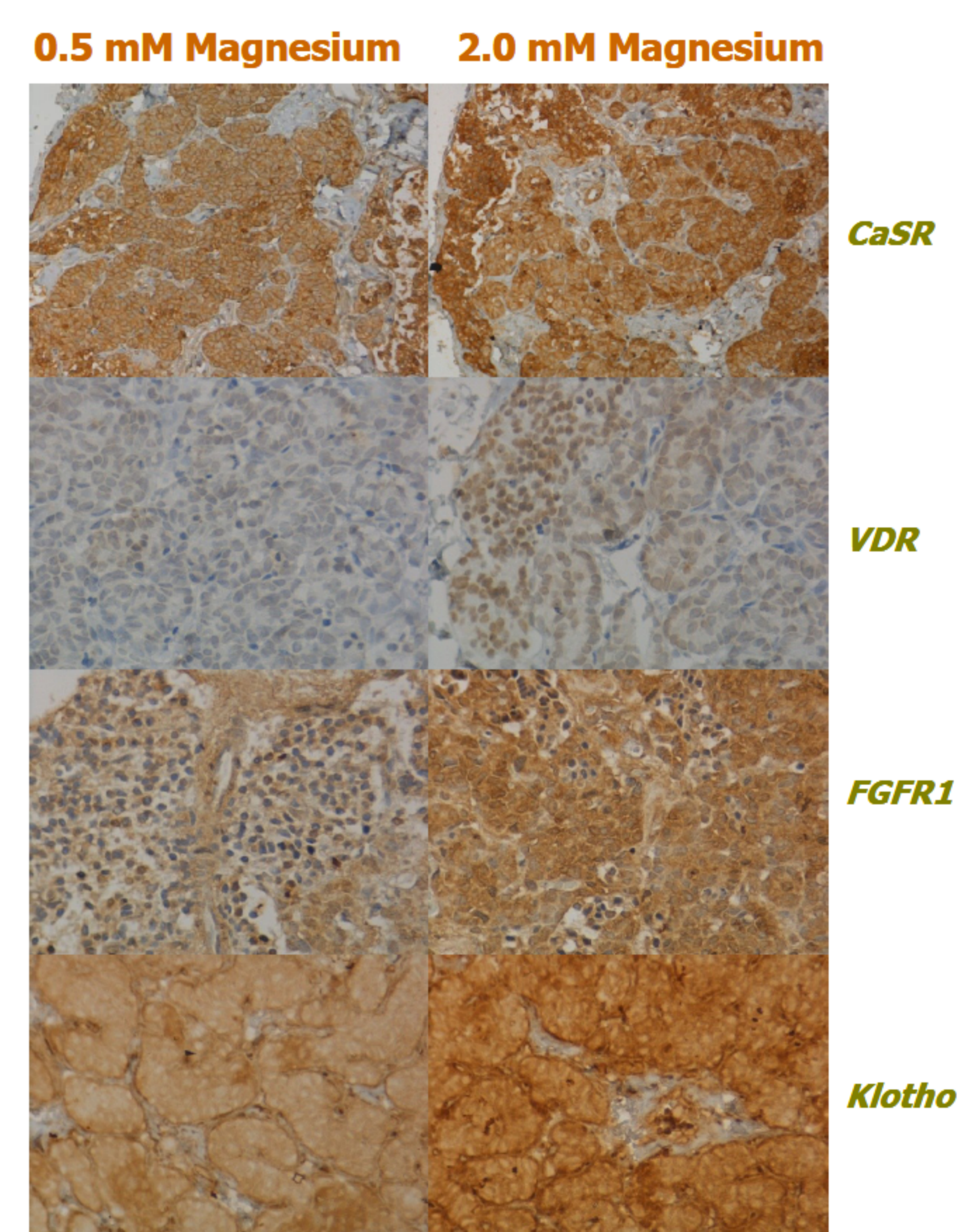


RESULTS

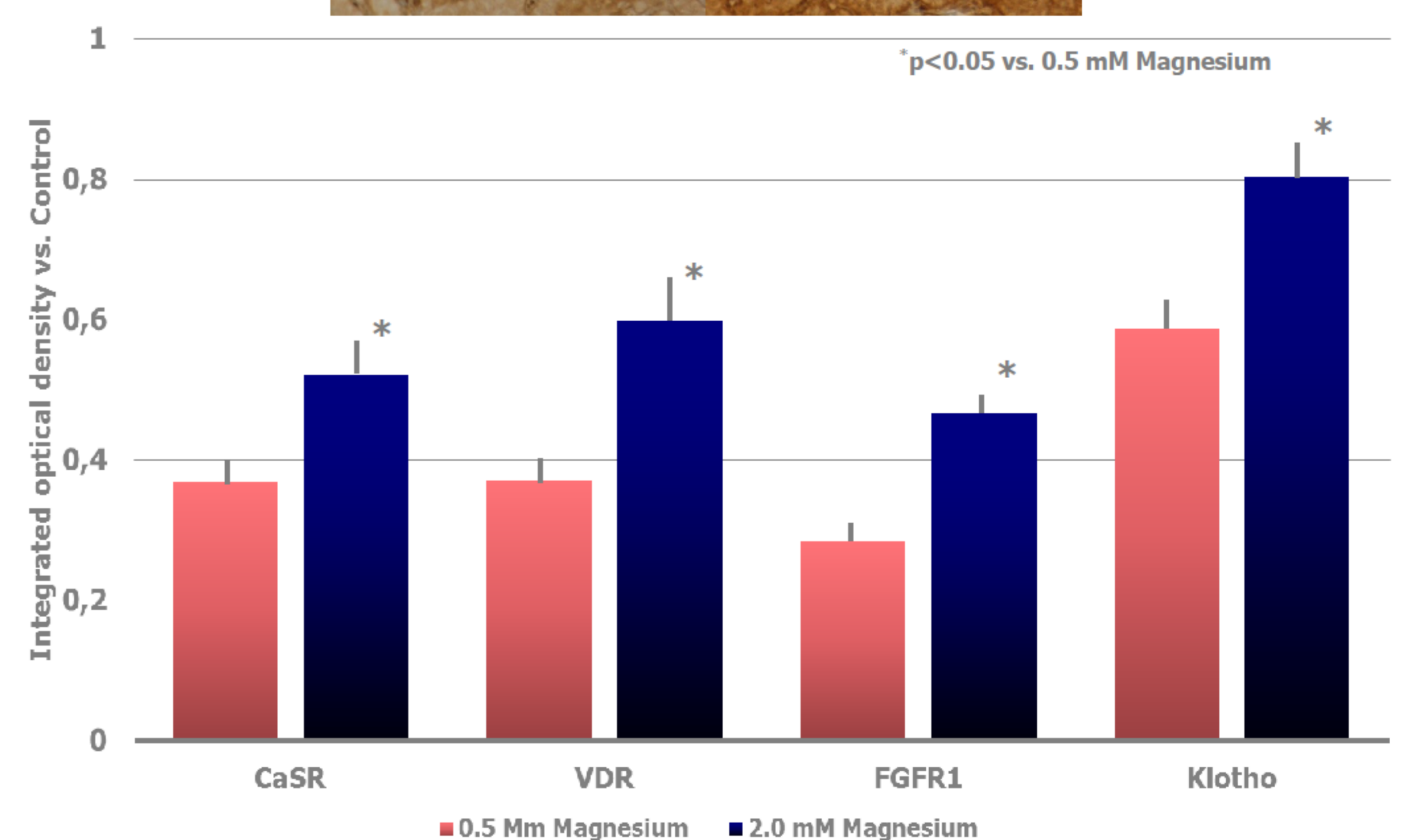
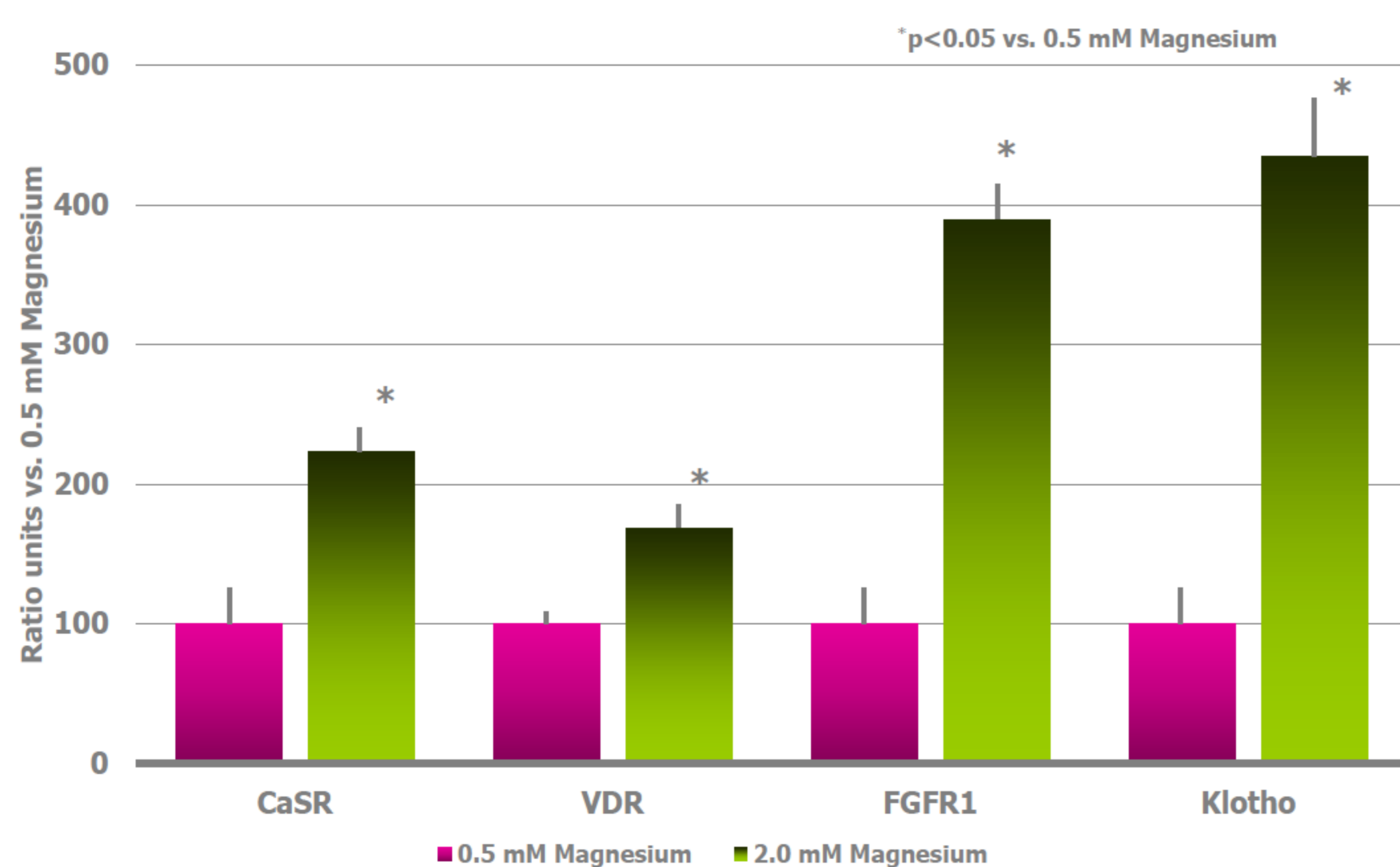
1. Effect of Magnesium on PTH Secretion:



3. Effect of Magnesium on protein levels of parathyroid receptors:



2. Effect of Magnesium on mRNA levels of parathyroid receptors:



CONCLUSIONS

1. Magnesium inhibits PTH secretion mainly when extracellular calcium is low.
2. Magnesium modulates the function of parathyroid gland through up-regulation of its key receptors.

REFERENCES:

1. Haberner JF et al. Relative effectiveness of calcium and magnesium in the secretion and biosynthesis of parathyroid hormone *in vitro*. *Endocrinology* 98:197-202, 1976.
2. Brown EM et al. Extracellular calcium potentiates the inhibitory effects of magnesium on parathyroid function in dispersed bovine parathyroid cells. *Metabolism* 33:171-176, 1984.
3. Shoback DM et al. Interaction of extracellular calcium and magnesium in the regulation of cytosolic calcium and PTH release in dispersed bovine parathyroid cells. *Mol Cell Endocrinol* 38:179-186, 1984.
4. Navarro JF et al. Relationship between serum magnesium and parathyroid hormone levels in hemodialysis patients. *Am J Kidney Dis* 34:43-48, 1999.
5. Navarro JF et al. Serum magnesium concentration is an independent predictor of parathyroid hormone levels in peritoneal dialysis patients. *Perit Dial Int* 19:455-461, 1999.
6. De Francisco AL et al. Evaluation of calcium acetate/magnesium carbonate as a phosphate binder compared with sevelamer hydrochloride in haemodialysis patients: a controlled randomized study (CALMAG Study) assessing efficacy and tolerability. *Nephrol Dial Transplant* 25:3707-3717, 2010.

