

# Sox9 is expressed in thyroid follicular cells and regulates the expression of thyroid differentiation genes.

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## INTRODUCTION

Sox9 is a transcription factor of the HMG box DNA binding family essential for chondrocyte differentiation, sexual determination and the maintenance of the stem/progenitor cells in several tissues. Furthermore, Sox9 is involved in the development of endoderm-derived-organs. Due to the endodermic origin of the thyroid, we planned to study the expression of Sox9 in thyroid follicular cells and its regulation by TSH, TGFβ1 and by thyroid transcription factors. Furthermore, we studied its role in the regulation of the expression of thyroid differentiation genes.

## MATERIALS AND METHODS

**-Cell systems:** Rat thyroid follicular cells PCCI3 maintained in Coon's medium 6H (5% Donor serum, +TSH, +IGF-1), Coon's 4H (0.2% Donor serum, -TSH, -IGF1). Hela cells grown in DMEM medium supplemented with Fetal Bovine Serum at 10%. TSH, IGF1, Forskolin and TGFβ were added to the medium. H89, the PKA specific inhibitor, was added 1.5 hours before stimulus.

**-DNA binding Activity:** Electrophoretic Mobility Shift Assay

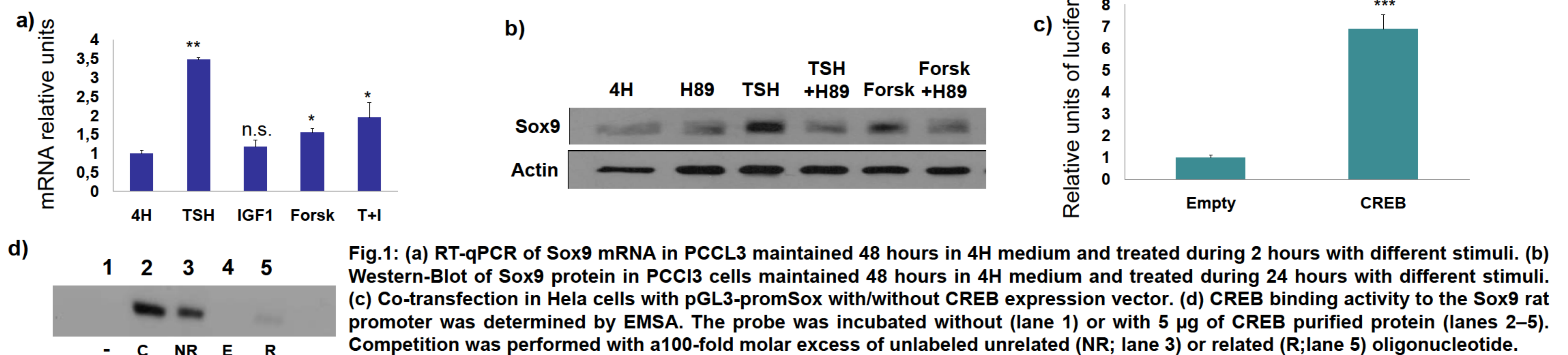
**-Protein Detection:** Western-Blot

**-mRNA detection:** RT-qPCR

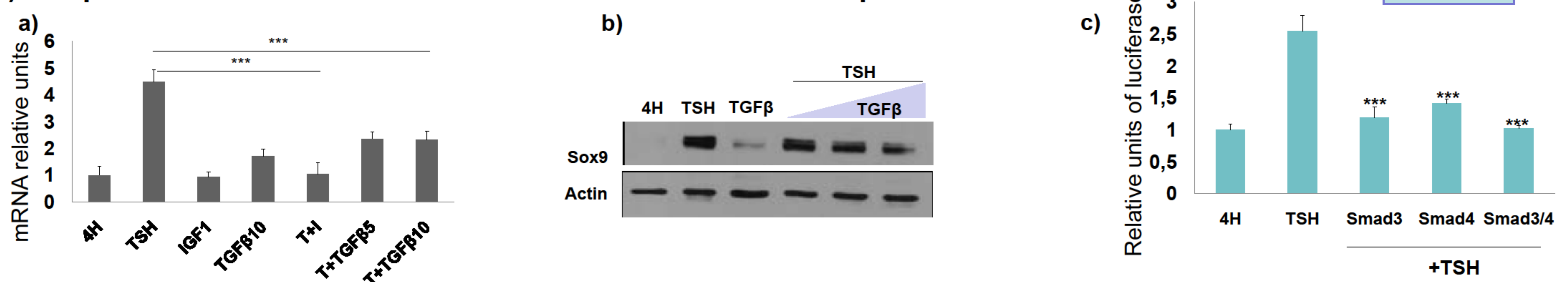
**-Transfection assays:** Determination of the luciferase activity of the construction pGL3-promRatSox9 transfected in PCCI3. Co-transfections assays were performed with different promoter constructions and expression vector of CREB, Pax8, Nkx2-1, FoxE1, Smads and Sox9.

## RESULTS

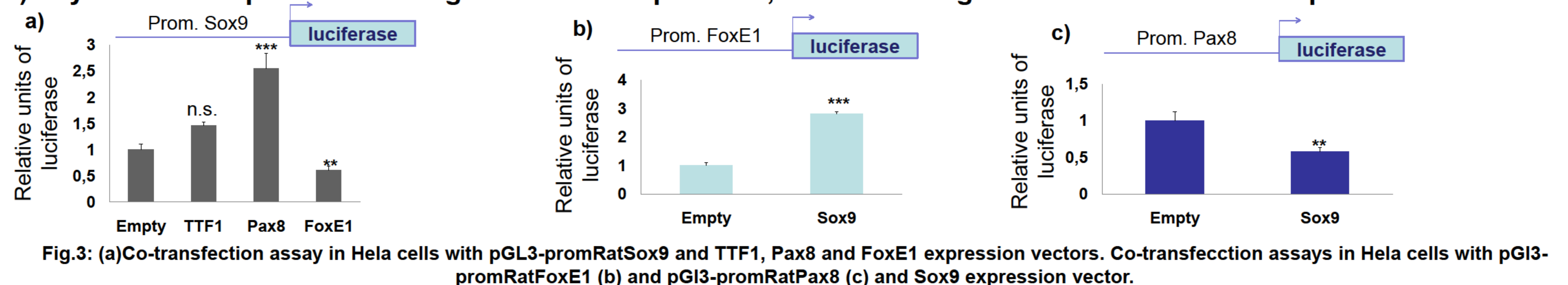
### 1) TSH induces Sox9 expression through cAMP/CREB signalling pathway



### 2) TGFβ1 and IGF1 inhibit the inductive effect of TSH in Sox9 expression



### 3) Thyroid transcription factors regulates Sox9 expression, which also regulates FoxE1 and Pax8 expression



## CONCLUSIONS

1. TSH induces Sox9 expression through cAMP/PKA signalling pathway in PCCI3 cells.
2. TGFβ and IGF1 represses the inductive effect of TSH.
3. Sox9 is involved in the expression control of thyroid transcription factors, which also regulates its expression.

## DISCUSSION

These results demonstrate the involvement of Sox9 in the pathophysiology of the thyroid, something hitherto unknown, and open a new field of study in the development and differentiation of the thyroid gland.