FURTHER EVIDENCE THAT BOREALIN/CDCA8 IS INVOLVED IN THYROID MORPHOGENESIS AND AGING

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INTRODUCTION

We found BOREALIN/CDCA8 mutations in patients with Congenital Hypothyroidism and Thyroid Dysgenesis, varying from asymmetric lobes to athyreosis1. Borealin is a major component of the Chromosomal Passenger Complex, an essential regulator of mitosis. We demonstrated a new feature of BOREALIN involvement in the adhesion and the migration of the thyrocites.

METHOD

Borealin+/− mice were studied during development, at the adult stage and during old age. Borealin+/− mice were not available because they die at E5.5.

We documented thyroid morphology, performed immunohistochemistry with thyroid markers (Nkx2-1, Thyroglobulin, T4) and we analyzed the thyroid function. Thyroid surface area were normalized for weight of each embryo. We used a well-established model with antithyroid drug induced hypothyroidism which was applied to the Borealin+/− and wild-type mice. All data were statistically evaluated (*P<0.05, ** P<0.01).

RESULTS

Figure 1: Thyroid Development: Early stage: 9.5

Figure 2: Adult stage: 4 months

Figure 3: Adult stage: 18 months

Figure 4: Borealin+/- mice had no hypothyroidism at the adult stage (4-month-old). They were significantly more sensitive to a more profound hypothyroidism than wild-type when treated with antithyroid drugs (at DO: a: T4: 41% less for Borealin+/- vs wild-type, P<0.01; b: TSH: 214% more Borealin+/- vs wild-type and more 51% at D3 for TSH). A4 months, male mice were treated during 3 weeks with methimazole 0.02% and sodium perchlorate 0.05% to induce hypothyroidism. Serum T4 and TSH levels were determined three weeks after treatment (DO) and three days (D3) after withdrawal the treatment.

Thyroids of Borealin+/− mice were significantly hyperplastic (c) with larger follicles surfaces in comparison with wild-type (P<0.05) (d). Follicles were divided into size categories (lumen area, 1000---3000 μm2, and >3000 μm2). At 4 months, the Borealin+/- mice remain euthyroid because they developed a goiter with large follicles.

CONCLUSIONS

Summary: Thyroid development is altered in Borealin+/− mice. Goiter do develop in adult Borealin+/− mice and they are more prone to hypothyroidism when treated with anti-thyroid drugs.

Conclusion: Borealin is involved during crucial steps of the thyroid lifetime cycle. These data demonstrated the involvement of Borealin in the structural organization of the thyroid gland. The role of Borealin in thyroid development and function was strengthened here and supports its involvement in thyroid dysgenesis of patients with congenital hypothyroidism.

REFERENCES


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