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学位論文 Abstract

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論 文 題 名

The iodide transporter *Slc26a7* impacts thyroid function more strongly than *Slc26a4* in mice

Abstract

***Background*:** SLC26A4 is a known iodide transporter, and is localized at the apical membrane of thyroid follicular cells. However, more than half of patients with Pendred syndrome, which is caused by the loss of function of SLC26A4, have normal thyroid function. This suggests the existence of other iodide transporters. We previously reported that similar to SLC26A4, SLC26A7 is involved in iodide transport at the apical membrane of thyroid follicular cells, and that *Slc26a7* is a novel causative gene for congenital hypothyroidism. However, its detailed role in vivo remains to be elucidated. In this study, we aimed to elucidate the roles of SLC26A7 and SLC26A4 in iodide transport in the thyroid glands of mice, and perform a comparative analysis of *Slc26a7* and *Slc26a4* deficiency in these animals.

Methods: Auxological, serological, and morphological aspects were analyzed in wild-type (WT), *Slc26a7*-deficient (*Slc26a7*$^{-/-}$), *Slc26a4*-deficient (*Slc26a4*$^{-/-}$), and double-deficient mice. To detect differentially expressed genes (DEGs) in each mouse, RNA-seq analysis was performed.

Results: *Slc26a7*$^{-/-}$ mice showed goitrous congenital hypothyroidism similar to that in humans, and mild growth failure on a normal diet. When pregnant mice were fed a low iodine diet and the pups were exposed to a low iodine environment, *Slc26a7*$^{-/-}$ mice showed marked growth failure; all of these animals died after weaning. On the other hand, *Slc26a4*$^{-/-}$ mice showed no growth failure in the same low iodine environment, and thyroid function remained normal. Double-deficient mice showed more severe growth failure than *Slc26a7*$^{-/-}$ mice. RNA-seq analysis revealed that the number of

DEGs in *Slc26a7*$^{-/-}$ mice was significantly higher than that in *Slc26a4*$^{-/-}$ mice. When the DEG analysis in *Slc26a7*$^{-/-}$ mice was limited to genes involved in thyroid hormone synthesis, *Slc26a4* was found to be the most upregulated gene.

Conclusions: These results indicate that SLC26A7 is much more strongly involved in iodide transport and the maintenance of thyroid function than SLC26A4 in mice.