Immunohistochemical Analysis Suggests a Role for Tmem131 in Thymic Epithelial Cell Differentiation

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Down syndrome (DS) is the most common genetic disorder in humans. It is known that trisomy of chromosome 21 causes DS, but how this chromosomal gain produces the complex DS phenotype, including immune system defects, is not well understood. Recently, altered DNA methylation, a biological process by which methyl groups are added to the DNA molecule, of a specific group of genes, including Tmem131 (transmembrane protein 131), was shown in DS individuals. To investigate biological roles of the Tmem131 gene, a mouse model of DS that lacked expression of this gene was developed. In this project, I sought to examine potential differences in prenatal thymus development between Tmem131 knockout (KO) mice and their normal (wildtype; WT) littermates. I performed immunohistochemical (IHC) and immunofluorescent (IF) staining of thymic epithelial cells of late-gestation embryos from these mice. Antibodies to cytokeratin 5 (CK5) and cytokeratin 8 (CK8) were used to label medullary and cortical thymic epithelial cells (mTECs and cTECs), respectively. I then performed quantitative analysis of the TEC populations using ImageJ, CaseViewer, and MATLAB softwares. IHC analysis showed that the KO thymus had a 2.4-fold increase in CK5+ cells (mTECs), compared to WT, without a significant change in the number of CK8+ cells (cTECs). Overall, the ratio of CK5+ to CK8+ cells was increased 2.5-fold in KO thymus glands. Merged images of CK5 and CK8 staining from two-color IF experiments confirmed the IHC results. These abnormalities in TEC differentiation in Tmem131 KO mice suggest that the Tmem131 gene is necessary for normal development of the thymus and that altered methylation in this gene may contribute to the deficient immune system in DS individuals.

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