Embryonic epithelial Pten deletion through Nkx2.1-cre leads to thyroid tumorigenesis in a strain dependent manner.

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Public Summary:
Even though the role of the tyrosine phosphatase Pten as a tumor suppressor gene has been well established in thyroid cancer, its role during thyroid development is still elusive. We therefore targeted Pten deletion in the thyroid epithelium by crossing Pten(flox/flox) with a newly developed Nkx2.1-cre driver line in the BALB/c and C57BL/6 genetic backgrounds. C57BL/6 homozygous Pten mutant mice died around 2 weeks of age due to tracheal and esophageal compression by a hyperplasic thyroid. By contrast, BALB/c homozygous Pten mutant mice survived up to 2 years, but with a slightly increased thyroid volume. Characterization of the thyroid glands from C57BL/6 homozygous Pten mutant mice at postnatal day 14 (PN14) showed abnormally enlarged tissue with areas of cellular hyperplasia, disruption of the normal architecture, and follicular degeneration. In addition, differing degrees of hypothyroidism, thyroxine (T(4)) decrease, and thyroid-stimulating hormone elevation between the strains in the mutants and the heterozygous mutant were detected at PN14. Finally, C57BL/6 heterozygous Pten mutant mice developed thyroid tumors after 2 years of age. Our results indicate that Pten has a pivotal role in thyroid development and its deletion results in thyroid tumor formation, with the timing and severity of the tumor depending on the particular genetic background.

Scientific Abstract:
Even though the role of the tyrosine phosphatase PTEN as a tumor suppressor gene has been well established in thyroid cancer, its role during thyroid development is still elusive. We therefore targeted Pten deletion in the thyroid epithelium by crossing Ptenflox/flox with a newly developed Nkx2.1-cre driver line in the BALB/c and C57BL/6 genetic backgrounds. C57BL/6 homozygous Pten mutant mice died around two weeks of age due to tracheal and esophageal compression by an hyperplasic thyroid. By contrast, BALB/c homozygous Pten mutant mice survived up to two years but with a slightly increased thyroid volume. Characterization of the thyroid glands from C57BL/6 homozygous Pten mutant mice at postnatal day 14 (PN14) showed abnormally enlarged tissue with areas of cellular hyperplasia, disruption of the normal architecture and follicular degeneration. In addition, differing degrees of hypothyroidism, T4 decrease and TSH elevation between the strains in the mutants and the heterozygous were detected at PN14. Finally, C57BL/6 heterozygous Pten mutant mice developed thyroid tumors after 2 years of age. Our results indicate that Pten has a pivotal role in thyroid development and its deletion results in thyroid tumor formation with the timing and severity of the tumor depending upon the particular genetic background.