Oncotarget. 2015 Jun 20;6(17):15628-38.

Ccdc6 knock-in mice develop thyroid hyperplasia associated to an enhanced CREB1 activity.

Leone V[1], Langella C[1], Esposito F[1], Arra C[2], Palma G[2], Rea D[2], Paciello O[3], Merolla F[1], De Biase D[3], Papparella S[3], Celetti A[1], Fusco A[1,4].

Author information

Abstract

CCDC6 was originally identified upon rearrangement with RET in human thyroid papillary carcinomas generating the RET/PTC1 oncogene. We have previously reported that CCDC6 interacts with CREB1 and represses its transcriptional activity. Since the function of at least one allele of CCDC6 is lost following RET/PTC1 rearrangements, we aimed at the generation of mice, carrying a CCDC6 mutant gene. Previous studies suggested that the coiled-coil domain of CCDC6, mainly encoded by human exon 2, is required for the protein function. Therefore, we engineered a murine Ccdc6 construct, carrying a deletion of the exon 2, that was able to exert only a mild repression on CREB1 transcriptional activity, with respect to the wild type Ccdc6. Subsequently, we generated Ccdc6-ex2 knock-in mice. These mice developed thyroid hyperplasia associated with an enhanced CREB1 activity and an increased expression of the CREB-1 regulated genes. These results strongly support a CCDC6 promoting role, ascribed to its functional impairment, in the development of thyroid papillary carcinomas harboring the RET/PTC1 oncogene.

KEYWORDS:

CREB1; Ccdc6; knock-in mice; thyroid