

FULL TEXT LINKS

OXFORD
ACADEMIC

Eur J Endocrinol. 2022 Apr 11;186(5):573-585. doi: 10.1530/EJE-21-0879.

Vitamin D receptor hypermethylation as a biomarker for pediatric adrenocortical tumors

Ana Carolina Bueno ¹, Mônica F Stecchini ¹, Junier Marrero-Gutiérrez ¹, Candy Bellido More ¹, Leticia Ferro Leal ¹, Débora Cristiane Gomes ², Daniel Ferreira de Lima Neto ¹, Silvia Regina Brandalise ³, Izilda Aparecida Cardinalli ³, José Andres Yunes ³, Thais Junqueira ³, Carlos Alberto Scrideli ¹, Carlos Augusto Fernandes Molina ⁴, Fernando Silva Ramalho ⁵, Silvio Tucci ⁴, Fernanda Borchers Coeli-Lacchini ⁶, Ayrton Custodio Moreira ⁶, Leandra Ramalho ⁵, Ricardo Zorzetto Nicolielo Vêncio ⁷, Margaret De Castro ⁶, Sonir Roberto R Antonini ¹

Affiliations

PMID: 35290212 DOI: 10.1530/EJE-21-0879

Abstract

Objective: Pediatric adrenocortical tumors (pACT) display complex genomic backgrounds, lacking robust prognostic markers and targeted therapeutic options. Vitamin D3 receptor (VDR) promoter hypermethylation and underexpression were reported in adrenocortical carcinomas from adult patients. In this study, we aimed to investigate VDR expression levels and methylation status in pACT and their clinical and prognostic significance.

Design: Retrospective cross-sectional study enrolling pediatric patients with ACT from two tertiary referral institutions.

Methods: We evaluated clinicopathological features, VDR mRNA (qPCR) and protein (immunohistochemistry) expression, and VDR-wide methylation of ACT samples from 108 pediatric patients. Fourteen pediatric and 32 fetal and postnatal normal adrenals were used as controls.

Results: Unlike in pre- and post-natal normal adrenals, most pACT lacked nuclear VDR expression and had reduced mRNA levels, especially the carcinomas. Unsupervised analysis of VDR methylation data revealed two groups of pACT with distinct disease features and outcomes. Tumors with high VDR methylation presented lower mRNA levels, and the respective patients presented advanced disease and reduced disease-free and overall survival.

Conclusions: VDR has a role in normal adrenocortical development and homeostasis, which is impaired during tumorigenesis. VDR hypermethylation and underexpression may be both predictive and prognostic biomarkers for pACT.

Related information

[MedGen](#)

LinkOut – more resources

Full Text Sources

[Sheridan PubFactory](#)[Silverchair Information Systems](#)

Miscellaneous

[NCI CPTAC Assay Portal](#)