

Gene Section

Mini Review

ACVR2 (activin receptor type 2)

Sarah Boles, Eddy Chau, Barbara Jung

Division of Gastroenterology, University of California, San Diego 9500 Gilman Drive 0063 La Jolla, CA, 92093-0063, USA

Published in Atlas Database: June 2007

Online updated version: <http://AtlasGeneticsOncology.org/Genes/ACVR2ID567ch2q22.html>

DOI: 10.4267/2042/38460

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Identity

Hugo: ACVR2A

Other names: ACVR2; ACVR2A; Activin Receptor, type 2A; Activin Receptor A type 2; T ACTR2; ActR-II

Location: 2q22.3

Local order: Genes flanking ACVR2A, in centromere to telomere direction on 2q22, are:

PAPBPCP2 2q22.3 - polyadenylate binding protein, cytoplasmic, pseudogene 2.

ACVR2 2q22.3 - activin receptor type IIA.

ORC4L 2q23.1 - origin recognition complex, subunit 4.

DNA/RNA

Description

ACVR2 gene spans a region of 85,796 bp and has 11 exons. Exon lengths are 180, 208, 110, 155, 144, 144, 146, 115, 139, 131 and 3745 base pairs. Exon 10 contains a polyadenine tract that may be mutated in microsatellite unstable cells.

Transcription

The transcript is 5217 base pairs.

Protein

Description

ACVR2 is a member of the transforming growth factor beta (TGF- β) receptor family. It is a 70-75kDA protein consisting of 513 amino acids. It is a transmembrane receptor for activin, with a cysteine-rich extracellular ligand-binding domain, a single pass transmembrane domain, and an intracellular domain with constitutive serine/threonine kinase activity.

Upon binding activin, ACVR2 associates with and phosphorylates ACVR1.

ACVR1, in turn, phosphorylates Smad2 and/or Smad3. Phosphorylated Smad2 and Smad3 associate with Smad4, translocate to the nucleus, and regulate gene expression.

There may be other non-Smad pathways in activin signal transduction. These include the RhoA-ROCK-MEKK1-JNK and MEKK1-p38 pathways.

In addition to activin, other ligands such as myostatin, nodal, and bone morphogenetic protein 7 (BMP-7) may also bind to ACVR2 and affect signal transduction.

Expression

Abundant expression in multiple tissues, including skeletal muscle, stomach, heart, endometrium, testes, prostate, ovary, and neural tissues. The cell surface level of ACVR2 and ACVR2B is regulated by proteins called ARIPs (activin receptor-interacting proteins).

Localisation

Cell surface, spanning cytoplasmic membrane.

Function

Activin signaling via its receptors has roles in cell proliferation, differentiation, apoptosis, metabolism, immune response, wound repair, and endocrine function.

Mutations

Somatic

Exon 10 polyadenine tract (A8-A7).

Implicated in

Colon cancer

Note: Colon cancer with A8-A7 deletion in exon10.

Disease

Microsatellite unstable colon cancer.

Prognosis

Increased tumor size.

Abnormal Protein

No fusion protein; truncated non-functional protein.

Oncogenesis

Occurs late in adenoma to carcinoma transition.

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This article should be referenced as such:

Boles S, Chau E, Jung B. ACVR2 (activin receptor type 2). *Atlas Genet Cytogenet Oncol Haematol.*2008;12(1):1-2.
