ACVR1

The ACVR1 protein is found in many tissues of the body including skeletal muscle and cartilage. It helps to control the growth and development of the bones and muscles, including the gradual replacement of cartilage by bone (ossification).

ACVR1 (Activin A Receptor Type 1) is a Protein Coding gene. Diseases associated with ACVR1 include Fibrodysplasia Ossificans Progressiva and BrainStem Glioma. Among its related pathways are NF-kappaB Pathway and PEDF Induced Signaling. Gene Ontology (GO) annotations related to this gene include protein homodimerization activity and protein kinase activity. An important paralog of this gene is ACVRL1.

Recurrent ACVR1 mutations in posterior fossa ependymoma [1)]

Somatic mutations in ACVR1 are found in a quarter of children with diffuse intrinsic pontine glioma (DIPG), however, there are no ACVR1 inhibitors licensed for the disease. Using an Artificial Intelligence-based platform to search for approved compounds for ACVR1-mutant DIPG, the combination of vandetanib and everolimus was identified as a possible therapeutic approach. Vandetanib, an inhibitor of VEGFR/RET/EGFR, was found to target ACVR1 (Kd=150nM) and reduce DIPG cell viability in vitro but has limited ability to cross the blood brain barrier. In addition to mTOR, everolimus inhibits ABCG2 (BCRP) and ABCB1 (P-gp) transporters and was synergistic in DIPG cells when combined with vandetanib in vitro. This combination is well-tolerated in vivo, and significantly extended survival and reduced tumor burden in an orthotopic ACVR1-mutant patient-derived DIPG xenograft model. Four patients with ACVR1-mutant DIPG were treated with vandetanib plus mTOR inhibitor, informing the dosing and toxicity profile of this combination for future clinical studies [2)].

1)
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2)
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