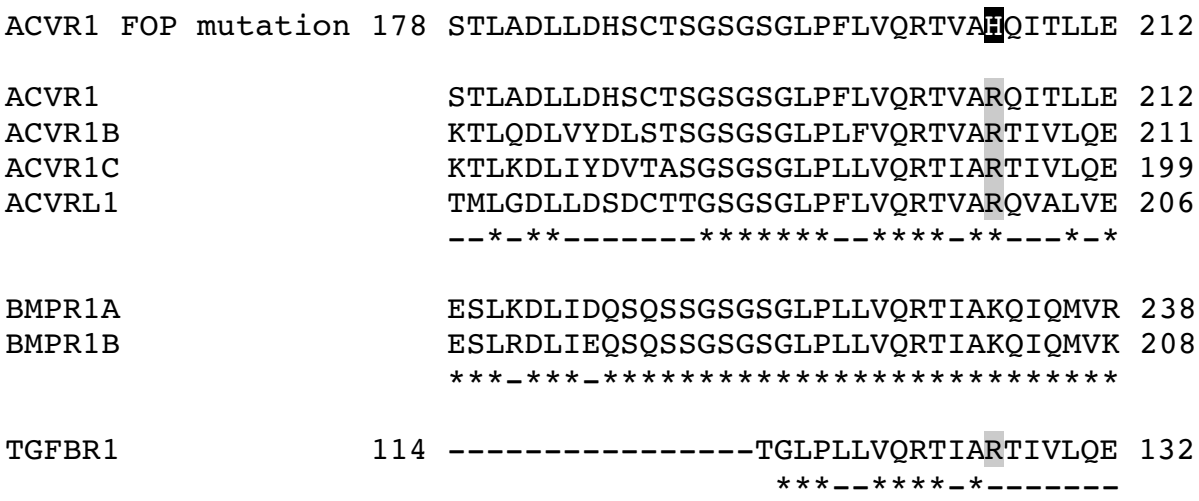

Supplementary Figure 2 Amino acid homologies among human ACVR1 family members show conservation of the GS domain in human type I BMP/Activin receptors.
Protein sequences were aligned using the Clustal W algorithm. At the position analogous to ACVR1 Arg206, there is an arginine (R) in human type I Activin receptors (ACVR1, ACVR1B, ACVR1C, ACVRL1) and TGFβR1. Of these receptors, only ACVR1 has been found to mediate BMP signaling. By contrast, two other BMP type I receptors (BMPRIA and BMPRIB) have a lysine (K) at the position analogous to ACVR1 Arg206. Like arginine, lysine is a positively charged amino acid and is expected to maintain similar function, however this amino acid difference may contribute to receptor specificity and differences in regulation of downstream signaling.

Since lysine and arginine are both positively charged amino acids, the presence of either amino acid at the ACVR1 Arg206 position indicates that both are functional, although some change in specificity and/or affinity for interacting molecules is likely, and suggests that ACVR1 function is not redundant with BMPRIA and/or BMPRIB function.

Histidine, found at position 206 in FOP patients, is also a positively charged amino acid, however its side chain ring structure suggests that its presence at ACVR1 206 could alter protein conformation due to a change in position of the positively charged side chain.

GenBank Accession numbers. Human proteins for ACVR1B (Q61271); ACVR1C (NP_660302); ACVRL1 (NP_000011); BMPRIA (NP_004320); BMPRIB (AAH47773); and TGFBR1 (AAH71181).