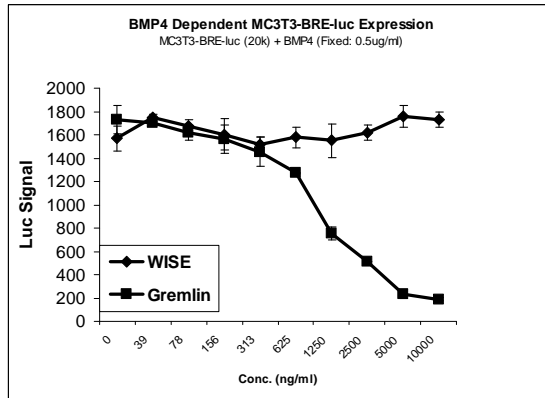


S1. In vitro activity of WISE on BMP signaling



The effect of purified recombinant Wnt-modulator In Surface Ectoderm (WISE) protein on modulating BMP signaling was tested in MC3T3-E1 cells. BMP signaling was evaluated by establishing stable BMP Response Element-driven luciferase construct in MC3T3-E1 cells and followed by incubating with 0.5 ng/ml BMP4 with or without various concentrations of WISE proteins or a positive control BMP antagonist, Gremlin (10 ug/ml with 2 fold serial dilution) for 24 hours. The luciferase activity was measured using dual luciferase assay kit (Promega) and the signal was captured using Luminometer (LMAX, Molecular Device) according to manufacture's instruction. Similar results was also obtained with other BMP proteins such as BMP2, BMP6 and BMP7.