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## **Inhibition of signaling cascades in osteoblast differentiation and fibrosis**

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1. "It is now possible to engineer BMP variants, which overcome their innate antagonist regiment through amino acid substitution which allows for development of more effective, second generation BMP proteins with potential clinical application in spinal fusion, long bone non-union fracture treatment and osteoarthritis." (*this thesis*)
2. "It will be of interest to see in the future whether the rigid coupling of for instance BMPs to BMP receptors and their common Smad effectors will not need to be replaced by superior super-signaling complexes that govern a multitude of signaling events." (*this thesis*)
3. "In order to get a clear picture on the impact of a certain signaling cascade in tissue development and maintenance one will need to not only look at signaling dynamics of the desired pathway but also always need to reflect this signaling events in the context of surrounding signaling cascades, something I would like to call a 'signaling niche.'" (*this thesis*)
4. "In any case where an innate adaptability of a signaling network is altered, either through interminable induction or continuous inhibition of trigger pulses one will have to assume that signaling drifts occur which eventually disconnects the signaling network from critical parameters that influence healthy tissue development and maintenance." (*this thesis*)
5. "Although BMPs may inhibit TGF- $\beta$  driven fibrotic responses, when discussing it as a potential therapeutic agent, one needs to take into account its strong osteo-inductive properties." (*this thesis*)
6. "I believe very strongly that the fundamental unit, the correct level of abstraction, is the cell and not the genome." (*Sydney Brenner*)
7. "BMP should no longer be an acronym for bone morphogenetic protein but for body morphogenetic protein." (*A. Hari Reddi*)

8. "Degenerative disease was chosen as the first condition to be treated with BMP because of concerns from experts in the field that BMP could possibly stimulate the growth of tumor cells or spread infection if used improperly or in the wrong patient." (*Brian Subach*)
9. "The theory of our modern technique shows that nothing is as practical as theory." (*Julius Robert Oppenheimer*)
10. "The great tragedy of science - the slaying of a beautiful hypothesis by an ugly fact." (*Thomas Huxley*)
11. "Marshall Urist literally took roomfuls of bone and distilled out the essence that enabled cells to lay down new bone." (*Michael DeMane, Medtronic*)
12. "If you think research is expensive, try disease." (*Mary Lasker*)