

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/38502> holds various files of this Leiden University dissertation.

Author: Cai, Jie

Title: BMP signaling in vascular and heterotopic bone diseases

Issue Date: 2016-03-09

Propositions

1. The recurrent ALK2 mutation in FOP patients provides a specific target for drug development. *This thesis*
2. Differentiated FOP hiPSCs recapitulate aspects of the disease phenotype *in vitro*, and can be used for further elucidation of underlying mechanisms and development of therapeutic agents. *This thesis*
3. ALK2 antisense oligonucleotides can induce exon skipping in cells, which results in downregulation of ALK2 and BMP-induced osteoblast differentiation in endothelial cells. *This thesis*
4. By binding the 12-kDa FK506-binding protein FKBP12, FK506 can activate BMP signaling via a dual mechanism, as a calcineurin inhibitor and as a derepressor of BMP type I receptors. *This thesis*
5. Monomeric sEng has multiple effects on BMP9 induced signaling, and does not only function as a ligand trap. *This thesis*
6. The functions of bone morphogenetic protein (BMPs) within the body are more versatile than initially suspected and thus a name change to body morphogenetic proteins has been proposed. (*Wagner et al. Sci Signal. 2010 Feb 2;3(107):mr1.*)
7. Enhancement of BMP receptor II (BMPRII) signaling by increasing cell-surface levels of BMPRII or by endothelial-selective BMPRII agonists shows promise in preclinical models of pulmonary arterial hypertension. (*Morrell et al. Nat Rev Cardiol. 2015*)
8. FOP mutations break critical interactions that stabilize the inactive ALK2-FKBP12 complex, and the presented ALK2 structure provides a new model for structure-based lead optimization of BMP inhibitors. (*Chaikuad et al. J Biol Chem. 2012 Oct 26;287(44):36990-8*)
9. iPSCs can have clonal variations and carry different genomic mutations. Thus future models may need to use multiple iPSC lines from different individuals or gene-edited iPSCs lines as a control group. (*Sterneckert et al. Nat Rev Genet. 2014 15(9):625-39.*)
10. Every time we are saying 'yes' to something, we are saying 'no' to something else.
11. Hang on to your hat. Hang on to your hope. And wind the clock, for tomorrow is another day. (*E. B. White, Letters of E. B. White, 1973 March*)