

Super-GDF9 to improve the oocyte quality in female

▶ Asset Overview

Product Type	Protein
Indication	female infertility
Current Stage	Lead optimization
Target(MoA)	Promotion of oocyte maturation (Activation of SMAD2/3 pathway)
Brief Description	Oocyte quality is the key rate limiting factor in female fertility. An important practical reason to improve our understanding of the determinants of oocyte quality is to enhance the clinical implementation of oocyte in vitro maturation (IVM). An engineered form of the human oocyte-derived growth factor GDF9, which potently stimulates granulosa cell signaling and function. Our 'Super-GDF9' has great potential to promote oocyte maturation and advance the clinical implementation of the assisted reproductive technique, IVM.
Organization	Monash University

▶ Differentiation

□ The success rate of IVM is lower than conventional ovarian stimulation

- In vitro maturation (IVM): The overall maturation rate after IVM of oocytes recovered from ovariectomy specimens in laboratory was 30-60%, considering the age of patient and duration of IVM
- The low pregnancy rate resulting from in vitro maturation of human oocytes represents a major obstacle for its clinical application as an adjunct to, or replacement for, costly IVF practices

□ Improved 'Super-GDF9' growth factor: ease of production, yield and activity

- The Monash team led by Prof. Craig Harrison, have modelled the cumulin and BMP15 residues that contribute to high affinity, and introduced them into GDF9 with 1000-fold greater potency than wild-type GDF9 and 4-fold greater potency than cumulin
- (Experimentally validated mechanism of action) Super-GDF9 potently activates the SMAD2/3 pathway, which is critical for granulosa cell growth and differentiation, and subsequent oocyte maturation. [SMAD - functionally related proteins, such as bone morphogenetic proteins (BMPs) and growth differentiation factors (GDFs)]
- It improves the oocyte quality and the reduce costs of assisted reproductive technologies. [GDF9/BMP15 (cumulin) heterodimers are difficult to produce and purify, limiting their potential uptake in IVM.]

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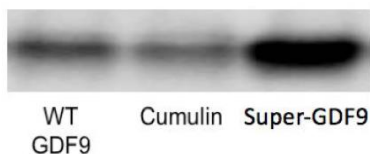
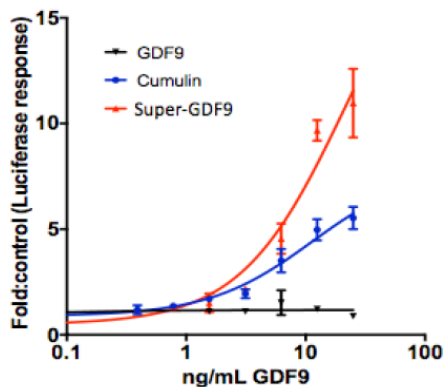
► Key Data

Type I receptor binding sites in cumulin, identified the BMP15 residues that contribute to high affinity receptor binding, and introduced these residues into human GDF9



Based on the molecular model of cumulin (GDF9/BMP15 heterodimer), BMP15 residues were introduced into human GDF9 (green stars), creating two high affinity type I receptor binding sites.

The efficacy of modified Super-GDF9



In a SMAD2/3-responsive luciferase reporter assay in COV434 granulosa cells, wild-type hGDF9 is inactive, cumulin displays moderate activity, while our modified Super-GDF9 is extremely potent.

The expression levels of the modified Super-GDF9 in HEK293 cells are 2-4-fold higher than those obtained for wild type GDF9 or cumulin.

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► Intellectual Property

Patent No.	
Application Date	
Status	
Country	

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