

Highly Prolific Booroola Sheep Have a Mutation in the Intracellular Kinase Domain of Bone Morphogenetic Protein IB Receptor (ALK-6) That Is Expressed in Both Oocytes and Granulosa Cells¹

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ABSTRACT

The Booroola fecundity gene (*FecB*) increases ovulation rate and litter size in sheep and is inherited as a single autosomal locus. The effect of *FecB* is additive for ovulation rate (increasing by about 1.6 corpora lutea/cycle for each copy) and has been mapped to sheep chromosome 6q23-31, which is syntenic to human chromosome 4q21-25. Bone morphogenetic protein 1B (BMP-IB) receptor (also known as ALK-6), which binds members of the transforming growth factor- β (TGF- β) superfamily, is located in the region containing the *FecB* locus. Booroola sheep have a mutation (Q249R) in the highly conserved intracellular kinase signalling domain of the BMP-IB receptor. The mutation segregated with the *FecB* phenotype in the Booroola backcross and half-sib flocks of sheep with no recombinants. The mutation was not found in individuals from a number of sheep breeds not derived from the Booroola strain. The BMP-IB was expressed in the ovary and *in situ* hybridization revealed its specific location to the oocyte and the granulosa cell. Expression of mRNA encoding the BMP type II receptor was widespread throughout the ovary. The mutation in BMP-IB found in Booroola sheep is the second reported gene from the TGF- β pathway affecting fertility in sheep following the recent discovery of mutations in the growth factor BMP15.