

Gene Targeting of Low Density Lipoprotein(LDL) Receptor Related Protein 5(LRP5) Involved in the Wnt Signaling Pathway

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The Wnt signaling pathway plays pivotal roles in embryonic development and oncogenesis through various signaling molecules including Frizzled receptor, recently characterized LRP5/6 and Dickkopf protein. Although Wnt signaling has been characterized in both developmental and oncogenic processes, little is known about its function in the normal adult. The ability of LRP5 to bind apolipoprotein E(apoE) and the abundant expression of LRP5 transcripts in hepatocytes, raise the possibility that LRP5 plays a role in the hepatic clearance of ApoE-containing chylomicron remnants, a major plasma lipoprotein carrying diet-derived cholesterol.

To evaluate the *in vivo* roles of LRP5, we generated mice carrying a mutated LRP5 gene. An insertion-type vector was constructed to disrupt an exon encoding a ligand-binding repeat of the mouse LRP5 gene(exon 18). Three line of mice lacking LRP5 were identified by Southern blotting, and the absence of LRP5 protein was confirmed by immunoblotting liver extracts. Wild-type(LRP5^{+/+}), heterozygous (LRP5^{+/-}), and homozygous(LRP5^{-/-}) mice were born with frequencies predicted by simple Mendelian ratios. LRP5^{-/-} mice of both sexes developed and appeared normal, gaining weight at a rate equal to that of LRP5^{+/+} mice and normally fertile. The LRP5^{-/-} mice allows an efficient approach to functional analysis of the low density lipoprotein(LDL) receptor related protein 5(LRP5).

Key words) *LRP5, gene targeting, Wnt signaling*