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## Hypocholesterolemic mice: total PCSK9 knockout

Reference: VAL-526-IRCM

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### Background

PCSK9 plays a critical role in the regulation of lipid metabolism and cholesterol homeostasis by binding to low density lipoprotein receptors (LDLRs) and causing their degradation. By modulating the level of LDLR, PCSK9 affects plasma LDL-cholesterol levels.

Human mutations affecting the level of PCSK9 and/or its activity towards the LDLR result in either hypercholesterolemia or hypocholesterolemia. Accordingly, PCSK9 knockout in mice leads to hypocholesterolemia. Administration of inhibitors known as “statins” results in a further reduction of circulating LDL levels in PCSK9 deficient mice, paving the way to new pharmacological drugs that combine the effects of statins with PCSK9 inhibitors.

### Technology

This technology developed by Dr. Seidah from the *Institut de recherches cliniques de Montréal* (IRCM) offers mice completely lacking PCSK9 expression.

### Results

Mice lacking PCSK9 in all tissues were generated. The knockout results in the deletion of the PCSK9 promoter and exon 1 in all cells of the organism.

- PCSK9 knockout (PCSK9 tKO)

These PCSK9 tKO mice exhibit a reduction of 80% in circulating LDL-cholesterol.

### Applications

This total PCSK9 KO animal model can provide a standard for complete PCSK9 inhibition.

It can allow the evaluation of non-specific effects of a drug.

And it can be used to complement data sets obtained with both liver-specific PCSK9 knockout mice and transgenic mice (these mice are also available for licensing).

### Competitive Advantages

This mouse model (PCSK9 tKO) is fully characterized both genetically and phenotypically.

Thanks to their unique pure C57BL/6 background, these animal models will generate highly reproducible data using only small groups of mice.

Because of promoter deletion, no residual PCSK9 expression is observed in these mice.

### Business Opportunity

Univalor is seeking a commercial partner for licensing/distribution opportunity.

These murine models can also be made available through MTA.

### Contact

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