

# CRT Licensing Opportunity



## Mouse Model for the Study of Steatosis

- Model to study the role of liver steatosis in metabolic diseases such as diabetes
- Hepatospecific cytochrome b5 knockout mouse model
- A model that phenocopies genesis and progression of non-alcoholic liver steatosis
- Tool to identify agents for the prevention and treatment of steatosis

ENABLING TECHNOLOGY

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### Inventors

Professor Roland Wolf and Dr. Colin Henderson at the University of Dundee.

### The Mouse Models

Steatosis is the process describing the retention of lipids within the cells due to the abnormal synthesis and breakdown of triglyceride fat. The liver is the major organ of lipid metabolism and is the main organ affected by steatosis. The risk factors associated with steatosis include diabetes mellitus, obesity, hypertension, protein malnutrition and anoxia. Hepatic steatosis is also associated with chronic hepatitis C, caused by Hepatitis C Virus (HCV).

Cytochrome  $b_5$  is a ubiquitous electron transport hemoprotein involved in a number of oxidative reactions (1). It is implicated in lipid biosynthesis, passing electron to several fatty acid desaturases. It also participates in the metabolism of xenobiotics and compounds of endogenous metabolism and plays an important role in P450 associated metabolism.

The inventors have developed a mouse model in which cytochrome  $b_5$  has been deleted in the liver (Hepatic cytochrome  $b_5$  Null (HBN) mouse). The loss of hepatic cytochrome  $b_5$  results in a reduction in metabolism and in the development of non-alcoholic hepatic steatosis (unpublished data). The mouse model presents an age related increase in hepatic lipid and this accumulation of hepatic microvesicular steatosis reached significance at 6 months. Additionally, while the overall hepatic and plasma lipid content is unchanged

between the transgenic and the wild type mice, the fatty acid profiles are different, especially for the polyunsaturated fatty acids (n-6).

### Application

The mouse model is a valuable *in vivo* tool to study the causes of non-alcoholic liver steatosis. The model would be useful for *in vivo* preclinical studies of new therapeutics to prevent or treat steatosis. Finally, the model may also be used to study the role of liver steatosis in metabolic diseases, such as diabetes mellitus, as well as in chronic hepatitis C disease.

### Commercial Opportunity

The Hepatic cytochrome  $b_5$  Null mouse and the associated patent application are available for non-exclusive licensing.

### Intellectual Property

CRT has filed a WO 2009/106882 patent application to protect the mouse model.

### References

1. John B. Schenkman and Ingela Jansson. The many roles of cytochrome  $b_5$ . *Pharmacol Ther.*, 2003, **97**(2):139-152..

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