

## **miR-122 acts as a tumor suppressor in hepatocarcinogenesis in vivo.**

Mirjam Zeisel, Sébastien Pfeffer, Thomas Baumert

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**Table 1. Phenotype of miR122 knock-out mice and effect of miR122 restoration.**

This table summarizes the characteristics of *MiR122a*<sup>-/-</sup> as well as *MiR122*-KO and *MiR122*-LKO mice [6, 7]. n. d.: not determined

	<i>MiR122</i> -KO and -LKO mice [6]	<i>MiR122a</i> <sup>-/-</sup> mice [7]
<b>Development and fertility</b>	Normal	Normal
<b>Serum lipids</b>	Reduced total cholesterol, LDL, HDL (VLDL n. d.) Normal TG	Reduced total cholesterol, HDL, VLDL (LDL n. d.) Reduced TG
<b>ALP and ALT</b>	Elevated ALP (ALT n. d.)	Elevated ALP and ALT
<b>Serum inflammation markers</b>	Elevated IL-6, TNF- $\alpha$	Elevated IL-6
<b>Liver histology</b>	Extensive lipid accumulation Reduced glycogen storage Inflammation (infiltrating inflammatory cells expressing Ccr2 and producing IL-6 and TNF- $\alpha$ ; increase of Ccl2 expression in hepatocytes) Fibrosis Proliferation of bile duct Spontaneous tumors (higher in LKO males in 12-17 months; equal penetration in KO males and females after 11-15 months but males display higher tumor weight and grades)	Extensive lipid accumulation Reduced glycogen storage Inflammation Fibrosis Portal fibrosis Spontaneous tumors (3.9-fold higher in males)
<b>Hepatic lipid metabolism</b>	Elevated TG Upregulated expression of TG biosynthesis (Acpat1, Mogat1, Acpat3, Acpat9, Ppap2a, Ppap2c and Dgat1)  Abnormal expression of genes involved in development, cellular proliferation and death, and cancer (Epcam, c-Myc, Mapre1 and Rhoa)	Elevated cholesterol and TG Reduced expression of genes involved in lipid metabolism (Acaca, Acyl, Fasn, Scd1, Cpt1a, Cpt2, Gsta2, Pklr, Slco1a, Slco1a4, Mttp, Slc27a5, Foxa1, Foxa2, Mlxipl and Nr1h2)  Increased expression of genes involved in immune response, fibrogenesis (Klf6), epithelial-mesenchymal transition, signal transduction, cell survival, cell death, and cancer

<b>Rescue of liver pathology and serum lipids</b>	n. d.	Restoration of MTTP or miR-122 expression by hydrodynamic injection
<b>Prevention of HCC</b>	Restoration of liver miR-122 expression by adenoviral delivery in 11-week-old mice	Restoration of miR-122 expression in 3-month-old mice by hydrodynamic injection