ACH-1.14 Brg1 positively regulates liver regeneration after partial hepatectomy in mice

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BACKGROUND & AIMS:
Brahma-related gene-1 (Brg1), a catalytic subunit of the switch/sucrose nonfermentable chromatin-remodeling complex (SWI/SNF), is known to be involved in proliferative cell processes. Liver regeneration is a highly organized process that requires a strong proliferation rate. Up to now, the role of BRG1 in liver regeneration has not been fully elucidated. The aim of the study was to investigate the role of Brg1 in liver regeneration in vivo following partial liver resection in mice.

METHODS:
We used a hepatocyte-specific Brg1 gene knockout mouse model and performed a 70% partial hepatectomy (PH) to analyze the role of Brg1 in liver regeneration. Liver regeneration was analyzed by liver/body weight ratio and cell proliferation, and functional experiments were performed to elucidate underlying mechanisms.

RESULTS:
We found that the expression of Brg1 was markedly upregulated after PH in wildtype mice. Instead, Brg1 inactivation dramatically impaired liver regeneration and blocked proliferating hepatocytes. Liver/body ratio was significantly decreased in Brg1 liver-specific knockout mice 48h post operation. A strong proliferation was observed in hepatocytes of wildtype mice post PH while it was significantly decreased in Brg1 liver-specific knockout mice. Cyclin D1 expression was lower in Brg1 liver-specific knockout mice 40h post PH compared to the wildtype mice.

CONCLUSIONS:
These results underline the role of Brg1 in hepatic regeneration by promoting proliferation after liver injury. In addition, our findings improve the understanding of the underlying molecular mechanisms and provide a potential therapeutic target for treating chronic liver diseases.