One of the enzymes known to regulate the cell cycle has now been shown to play a key role in mitosis

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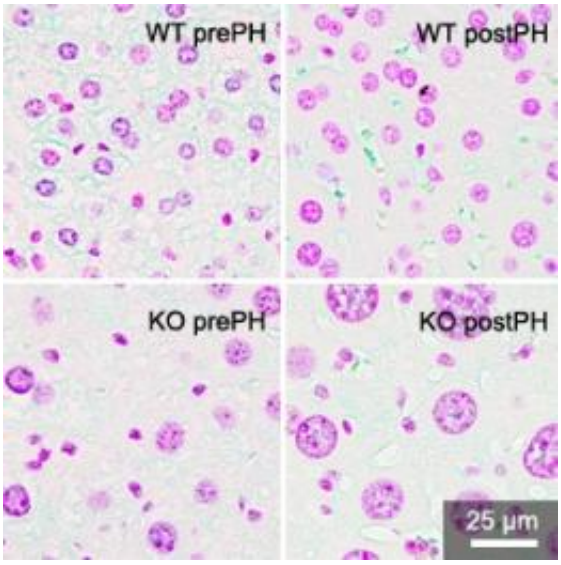

Livers from Cdk1 knockout (KO) mice (bottom row) display fewer but larger cells compared to wild type (WT) mice (top row), both before and after partial hepatectomy (PH)

Cyclin-dependent kinase 1 (Cdk1) is a member of the Cdk family of enzymes which control the cell cycle. Philipp Kaldis at the A*STAR Institute of Molecular and Cell Biology and co-workers have now shown that Cdk1 plays a critical role in cell division. Moreover, the researchers discovered that by inactivating Cdk production, they could prevent tumor formation in mice. The new finding may open up new avenues in

the development of cancer drugs and treatment.

In the mammalian genome, there exist more than 20 different Cdks that regulate different phases of the cycle of cell division, or mitosis. Previous studies have shown that mice with any one of these genes knocked out remain viable, suggesting that enzymes of the Cdk1 family have overlapping roles. Due to technical difficulties, however, no knockout mice for Cdk1 have so far been developed. Now, Kaldis and co-workers have not only generated Cdk1-knockout mice, but also developed adult mice in which active Cdk1 genes could be switched off by chemical means.

The researchers found in their experiment that mice lacking functional Cdk1 genes die within three and a half days of conception. Their embryos also display fewer but larger cells. The researchers suggest the cells in very-early-stage embryos contain remnants of the products of the mother's Cdk1 genes, which allows them to carry out limited cell division. Without Cdk1, the cells cannot divide and will instead continue to grow, suggesting that Cdk1 is critical to mitosis.

The researchers studied the role of Cdk1 in liver regeneration in adult mice. They found that of all the organs in the mammalian body, the liver could tolerate the loss of Cdk1 the most as its cells only divide in adulthood during regeneration. They made use of experimental animals whose livers were deficient in Cdk1. When they surgically removed part of the livers, the researchers found that regeneration still took place, not by producing more cells, but by increasing the size of existing cells.

The researchers also studied the impact of loss of Cdk1 activity on the generation of tumors, both in cell culture and in the livers of adult mice injected with carcinogens. They discovered that without Cdk1, tumor cells could not proliferate.

"We are now able to delete Cdk1 in any tissue or tumor type we choose at any time point," says Kaldis. "So our mouse model offers a neat method to test whether drugs targeting Cdk1 activity can be effective in treating cancers."

More information: Diril, M. K. et al. Cyclin-dependent kinase 1 (Cdk1) is essential for cell division and suppression of DNA re-replication but not for liver regeneration. Proceedings of the National Academy Sciences 109, 3826–3831 (2012).

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