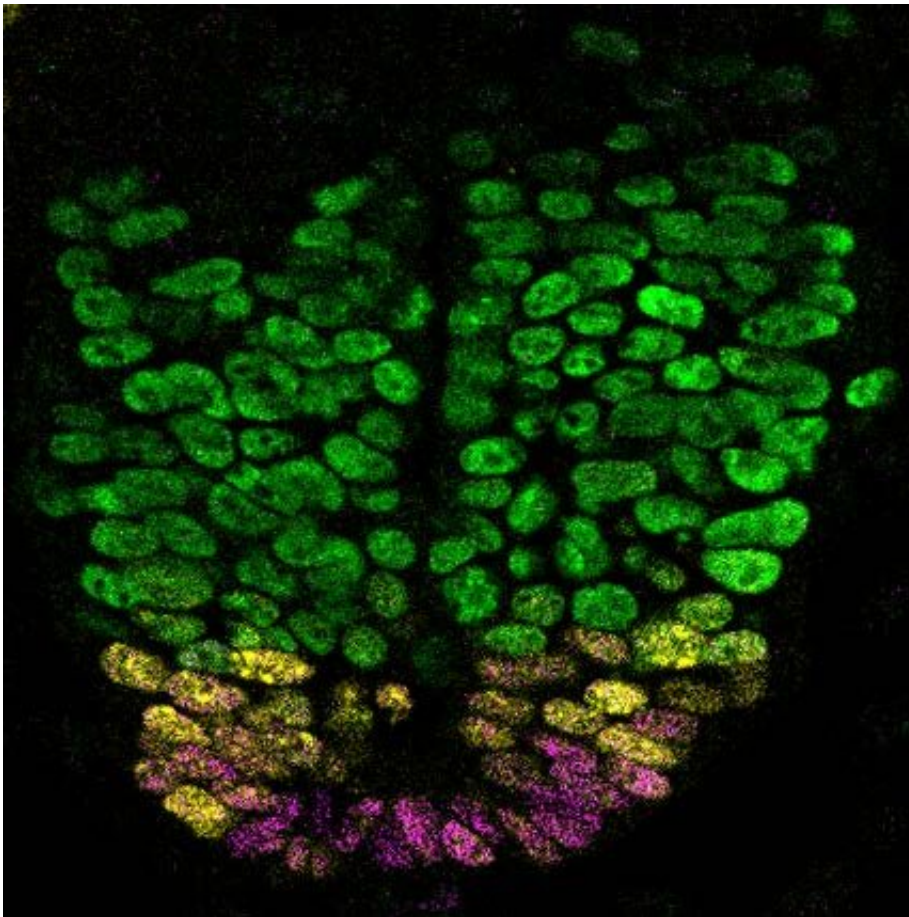


Cannabis causes birth defects in susceptible mice

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A developing mouse neural tube. Hedgehog signalling is required to produce different types of neuronal progenitor cells, indicated by the different colours. THC inhibits Hedgehog signalling in genetically susceptible mice, leading to developmental defects, including in the neural tube. Credit: Lo, H.-F., Hong, M., Szutorisz, H., Hurd, Y.L., Krauss, R.S. (2021). Δ 9-Tetrahydrocannabinol inhibits Hedgehog-dependent patterning during development. *Development*, 148, dev199585. doi:10.1242/dev.199585

A chemical found in cannabis, a common recreational drug, has now been shown to cause birth defects in mice. Scientists from the Icahn School of Medicine at Mount Sinai show that the psychoactive component of cannabis (THC) can induce face and nervous system defects in genetically susceptible mouse embryos. This study, published in *Development*, has important implications for cannabis use during pregnancy.

Cannabis, also known as weed or marijuana, is used by hundreds of millions of people worldwide. Although restricted in most countries, the increasing legalization of [cannabis](#) for recreational and medicinal consumption means that cannabis use is rising. Cannabis is also the most common illicit drug used by [pregnant women](#), but the effects of cannabis on embryonic development are not well understood. It is also important to understand the effects of cannabis on individuals with a genetic predisposition, which means they carry [genetic mutations](#) that increase the risk of environmental conditions triggering a defect or disease.

A new study from scientists at the Icahn School of Medicine at Mount Sinai, USA, has now revealed that THC, the chemical in cannabis that causes the sensation of feeling 'high', can cause birth defects in genetically predisposed mice. In this case, the researchers investigated whether THC could exacerbate a mutation that affects a mechanism that cells use to communicate with each other, called Hedgehog signaling. "Several years ago, it was reported that THC could inhibit Hedgehog signaling in cells grown in a dish," said the study's lead author Robert Krauss, Ph.D., Professor of Cell, Developmental and Regenerative Biology at the Icahn School of Medicine at Mount Sinai. "We reasoned that THC might be an environmental risk factor for [birth defects](#), but that it would require additional risk factors, such as specific mutations in the genes required for Hedgehog signaling, to induce these defects in

mice."

To address this hypothesis, Dr. Krauss and colleagues administered a single dose of THC, equivalent to exposures achieved when humans smoke cannabis, to pregnant mice about a week after conception. They then studied the embryonic development of their pups, some of which carried a mutation that meant Hedgehog signaling was not functioning at full efficiency. The scientists found that pups without the mutation developed normally, even when exposed to THC, as did pups that carried the mutation but were not exposed to the drug. However, pups that were exposed to THC *and* carried the mutation developed a brain and face defect called holoprosencephaly, a common birth defect seen in 1 in 250 human conceptions that includes the failure of the forebrain to divide into two distinct segments.

The researchers showed that the [defect](#) occurs because THC can interfere with Hedgehog signaling in the embryo. THC alone is not sufficient to disrupt Hedgehog signaling and cause defects but, in animals where Hedgehog signaling is already weakened through genetic mutation, it has significant effects. "THC directly inhibits Hedgehog signaling in mice, but it is not a very powerful inhibitor; this is presumably why a [genetic predisposition](#) is required for it to cause holoprosencephaly in mice," explained Dr. Krauss.

These first studies in mice have important implications for human health, highlighting the need for more research into the effects of [cannabis use](#) during pregnancy in humans. "The THC concentration in cannabis is now very high, so it is important to perform epidemiology studies looking at whether cannabis consumption is associated with developmental defects. Women are already advised not to consume cannabis while pregnant, but our results show that embryos are sensitive at a very early period, before many women know they are pregnant. Cannabis consumption may therefore be inadvisable even when women

are trying to get pregnant," Dr. Krauss warned.

Although this study focussed on one chemical in cannabis and one genetic mutation, further research could reveal other combinations that cause similar effects. "Many of the [mutations](#) found in human holoprosencephaly patients could conceivably synergise with THC," said Dr. Krauss. "We would also like to test the related chemical CBD in genetically predisposed [mice](#). Like THC, CBD inhibits Hedgehog signaling in cells grown in a dish, but CBD appears to work differently. As CBD is widely available and often viewed as beneficial—or at least innocuous—it would be worth investigating this as well," he added.

More information: Δ 9-Tetrahydrocannabinol inhibits Hedgehog-dependent patterning during development, *Development* (2021). [DOI: 10.1242/dev.199585](#)

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