

## - Sugar substitutes

## News

## Health

# Sweeteners may blunt cancer therapy

Sucralose could alter the gut microbiome in a way that impairs the immune system

Grace Wade

PEOPLE who consume the artificial sweetener sucralose are less likely to respond to immunotherapy.

Immunotherapy helps the immune system detect and destroy cancer cells, making it a crucial treatment for numerous cancers. However, it doesn't work for all patients, "and in many cancer types, it only works for the minority of patients", says Abigail Overacre-Delgoffe at the University of Pittsburgh in Pennsylvania.

It isn't clear why that is, though numerous studies indicate the gut microbiome plays a role, as it helps regulate immune responses. Research has also shown that artificial sweeteners can change the composition of gut microbes in humans.

So Overacre-Delgoffe and her colleagues assessed the potential impact of artificial sweeteners on immunotherapy. They tracked treatment outcomes in 157 people

who underwent immunotherapy for at least three months. Of the participants, 91 had advanced melanoma, 41 had advanced non-small cell lung cancer and 25 had melanoma that was

**"Research has shown artificial sweeteners can change the composition of gut microbes in humans"**

surgically removed but had a high likelihood of returning.

Before starting treatment, participants completed a questionnaire that assessed their diet over the previous month, which the researchers used to estimate sucralose consumption.

Consuming more than 0.16 milligrams of sucralose per kilogram of bodyweight a day was associated with worse treatment outcomes. Participants with advanced melanoma who

consumed less sucralose lived a median of five months longer without their cancer progressing, compared with those who consumed more (*Cancer Discovery*, doi.org/g9vs9r).

For participants with non-small cell lung cancer, the difference was 11 months. In participants at high risk of melanoma returning, those who consumed less sucralose remained cancer-free for a median of six months longer than those who consumed more.

Similar differences were seen among participants who consumed more than 0.1 milligrams of another artificial sweetener, acesulfame K, per kilogram of bodyweight a day.

Further experiments in mice with tumours from common types of cancer – adenocarcinoma or melanoma – showed that adding sucralose to their water during immunotherapy

increased tumour growth and reduced survival.

Genetic analysis revealed that T-cells – immune cells leveraged by immunotherapy to kill cancer – were impaired in the mice receiving sucralose. Faecal samples also showed significant changes in the rodents' gut microbiomes, with increased activity in pathways that break down arginine, an amino acid that T-cells rely on to function.

Further experiments showed that arginine supplements improved survival in mice receiving sucralose until their survival odds were about the same as those that weren't consuming the sweetener.

However, it is unclear whether sucralose has the same effect on the gut microbiome and T-cell function in humans, says Jotham Suez at Johns Hopkins University in Maryland. ■