Modulating Weight Gain and Loss by Understanding the Mechanism of Smoking Related Weight Changes

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Overview

Of the approximately 30 million adult smokers in the U.S, more than half report attempting to quit smoking every year. However, smoking cessation-associated weight gain (SCWG) constitutes a major obstacle to smoking withdrawal. The molecular mechanism that drives SCWG remains elusive, and there is a great need for effective methods to prevent SCWG. Prof. Elinav and his team revealed a microbiome-dependent contribution to SCWG and identified specific metabolites that modulate weight gain during smoking cessation. Importantly, these compounds may also affect weight gain in non-smokers.

Background and Unmet Need

Nearly 13 of every 100 U.S. adults (12.5%) were reported to smoked cigarettes in 2020, resulting in approximately 30.8 million smokers. As the hazardous nature of smoking is widely known, more than half of adult cigarette smokers reported attempting to quit smoking in the past year. Smoking cessation reduces the risk of major chronic diseases, increases life expectancy, and improves the quality of life. However, it is often accompanied by smoking cessation-associated weight gain (SCWG), presenting a major obstacle to smoking withdrawal. Several mechanisms have been proposed to explain SCWG. However, the molecular mechanism remains elusive and effective methods to prevent SCWG and weight gain are highly sought after.

The Solution

Prof. Elinav and his team decoded a microbiome-dependent contribution to SCWG and identified metabolites that induce or reverse weight gain during smoking cessation. Importantly, a weight modulating effect of these compounds is also noted in non-smoking settings[1].

Technology Essence

Prof. Elinav and his team utilized a mouse model for SCWG whereby mice were placed in a smoking chamber to expose them to chronic cigarette smoke, resulting in a significant weight reduction. Mice that were no longer exposed to smoke had SCWG comparable to the weight levels of mice not exposed to smoke. The team showed that smoking alters the gut microbiome and that microbiome depletion by antibiotics prevented SCWG. Moreover, they showed that microbiome transplantation from ex-smoking mice into HFD-fed, non-smoking germ-free mice induced excessive weight gain, demonstrating the causal involvement of the gut microbiome in SCWG. The team analyzed and identified microbiome-modulated metabolites in SCWG. Specifically, they found that metabolic shunting of dietary choline into dimethylglycine (DMG) drives SCWG by enhancing gut energy harvest, coupled with the depletion of the weight-lowering, microbiome-regulated AcetylGlycine (ACG) (Figure 1a). Importantly, DMG and ACG exert their weight-modulating activities also in obese not-smoking mice (Figuer 1b). Preliminary

observations in a small cross-sectional human cohort support these findings. These results highlight dietary, host, and microbial targets for preventing SCWG and potentially modulating weight even in non-smoking settings.

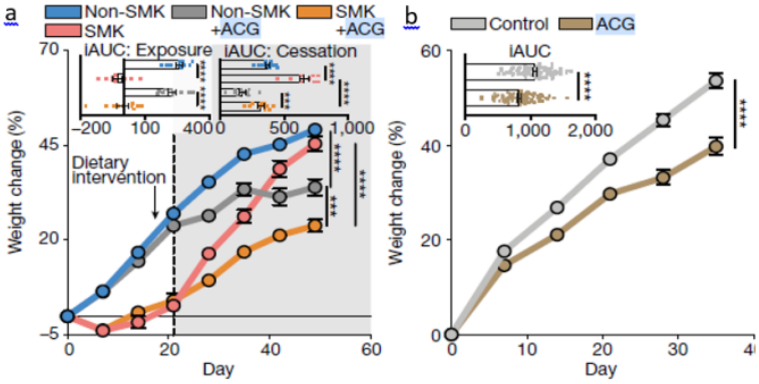

Figure 1 – (a) In the SCWG model, ACG supplementation to HFD-fed mice exposed to smoke ameliorated SCWG. (b) HFD-fed mice supplemented with ACG for 35 days (and not exposed to smoke) had a significantly lower weight gain rate compared with HFD-fed control mice.

Applications and Advantages

- Metabolites preventing weight gain during smoking cessation
- Weight modulating agents in non-smokers
- Novel dietary supplements for weight reduction

Development Status

Prof. Elinav and his team identified specific metabolites that induce or reverse weight gain during smoking cessation. Preliminary results were obtained from a small human cohort. The results were published in the prestigious Nature journal.

References

Fluhr L, Mor U, Kolodziejczyk AA, et al. Gut microbiota modulates weight gain in mice after discontinued smoke exposure. Nature. 2021;600(7890):713-719. doi:10.1038/s41586-021-04194-8

Patent Status

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