



Altered DNA Methylation and Gut Microbiota Mediate the Effect of Smoking on Obesity: Implications for Public Health Interventions



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BACKGROUND

Smoking and obesity are amongst the leading modifiable contributors to global mortality and disease burden. While complex epidemiological associations are observed, the causality and underlying pathways remain elusive. Epigenetic modifications (e.g., DNA methylation) and gut microbiota are hypothesized mediators. Here, we assess causalities and explore mediation roles of DNAm and gut microbiota between smoking and obesity using MR.

METHODS

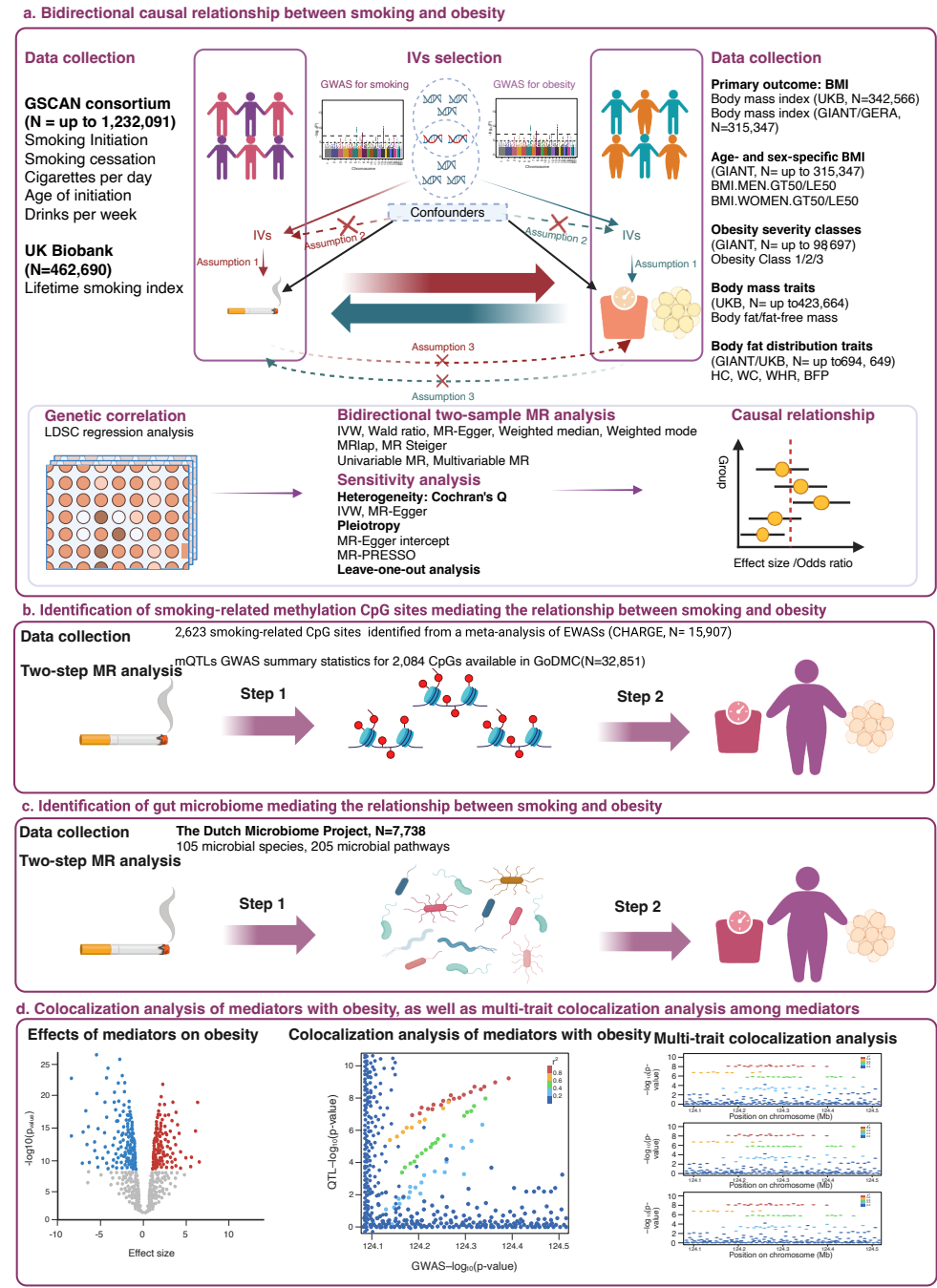


Figure 1. Mendelian Randomization study design. Step 1 assesses causal effects of smoking on potential mediators (DNAm/microbial features). Step 2 evaluates causal effects of identified mediators on obesity.

RESULTS

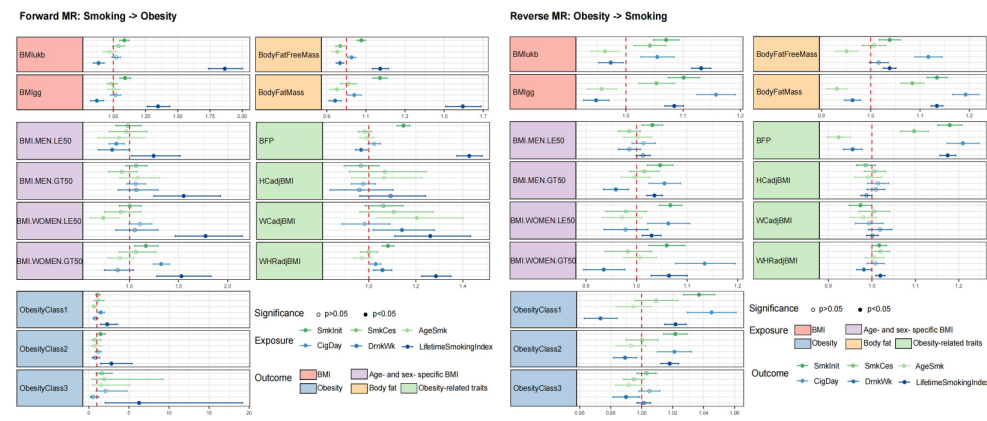


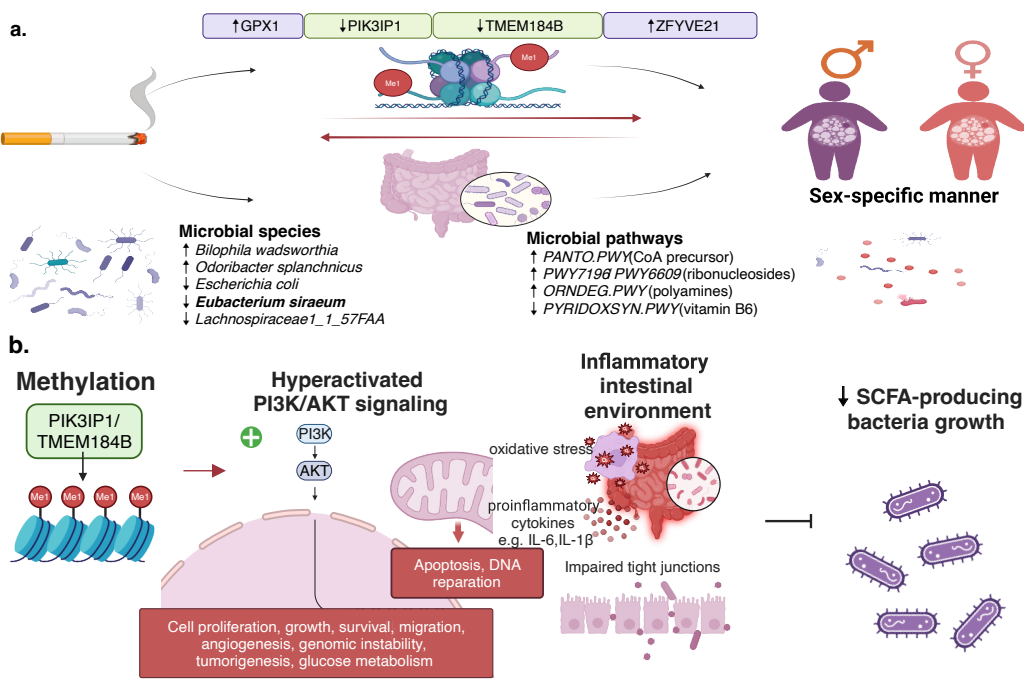
Figure 2. The bidirectional causal effects between smoking and obesity. Smoking initiation and lifetime smoking causally increase body mass index, while higher BMI elevates smoking likelihood.

RESULTS



Figure 3. Analysis of the mediation effect of identified smoking-related methylation CpG sites, microbial species and microbial pathways. Seven smoking-related CpGs (e.g., cg08548559 in PIK3IP1), five microbial species (e.g., Eubacterium siraeum), and five microbial pathways (e.g., vitamin B6 biosynthesis) mediated these effects, with cg08548559 and E. siraeum mediating 64.65% and 7.23% of obesity risk, respectively ($P < 0.05$).

SUMMARY OF FINDINGS



1. Smoking causally induce obesity, and vice versa.
2. Altered DNA methylation within GPX1, PIK3IP1, TMEM184B and ZFYVE21 loci, and gut microbiota changes mediate the effect of smoking on obesity.
2. Smoking drives obesity through epigenetic-microbial crosstalk (especially E. siraeum and epigenetic modifications on PIK3/AKT signaling).

CONCLUSION AND FUTURE DIRECTIONS

There is bidirectional, causal relationship between smoking behaviours and obesity, with DNA methylation and gut microbiota potentially mediating the effects of smoking on obesity. These findings pave the way for a deeper scientific understanding of the biological pathways linking smoking and obesity and open new avenues for integrated public health strategies. They also highlight the importance of considering these bidirectional relationships in tobacco control and weight management for improving public health.

REFERENCES & ACKNOWLEDGEMENTS

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