

# Waterpipe and cigarette epigenome analysis reveals markers implicated in addiction and smoking type inference

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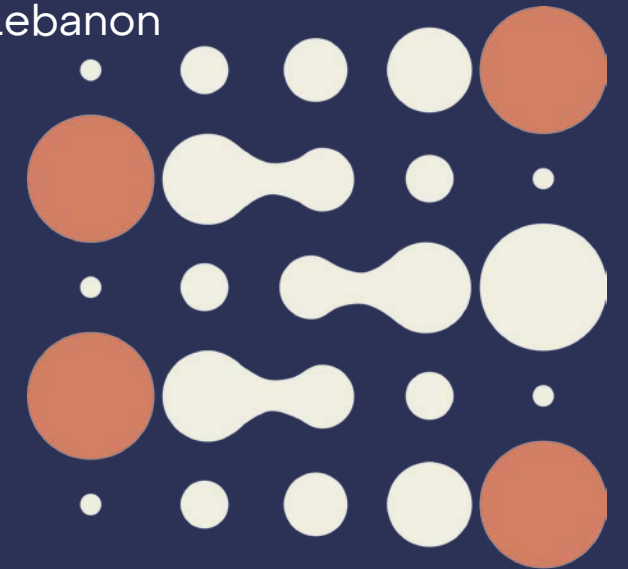
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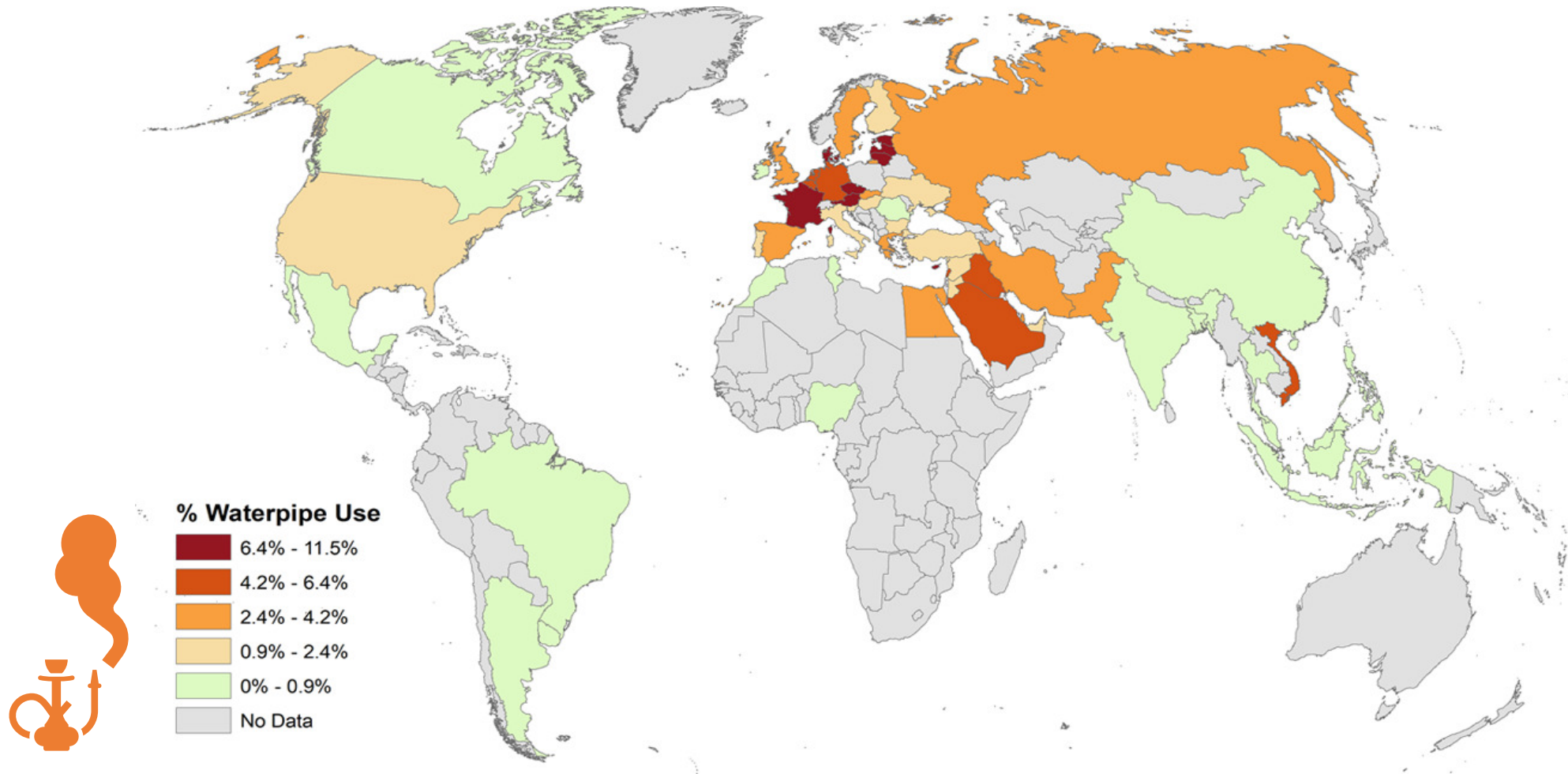
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for Research on Cancer



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Bhatnagar A et al. Circulation. 2019. © 2019 American Heart Association, Inc

# Waterpipe Smoking: Prevalence in the World





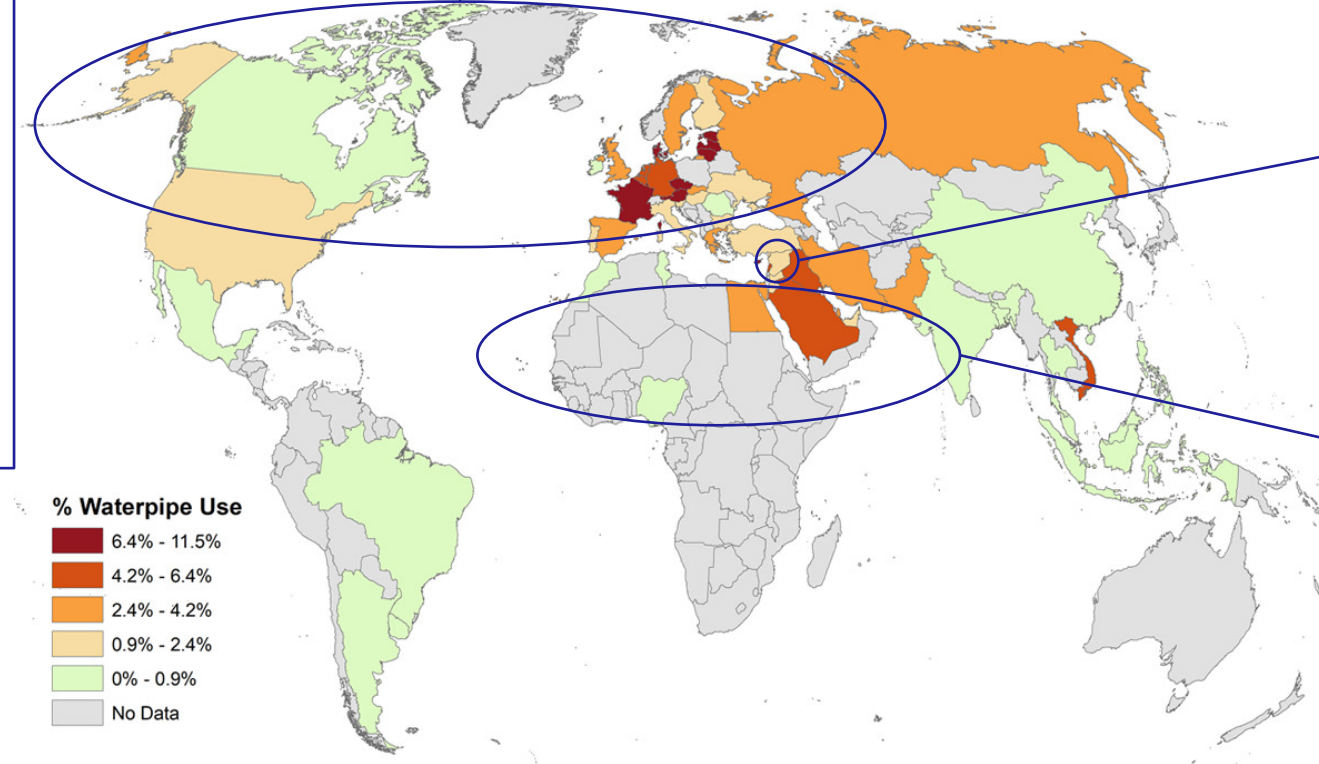
This global spread is catalyzed by the strong social appeal of waterpipe, its disguised fruit flavors and the misconception that the water in the jug detoxifies tobacco.

# Epidemiologic, mechanistic, and molecular data on waterpipe smoking are very limited

North America/Europe:  
waterpipe prevalence  
on the rise but mostly  
among young people  
(i.e. long-term follow-  
up is yet needed) +  
users tend to use other  
tobacco products.

Logical place to start with is Lebanon: high  
waterpipe prevalence + long-term nature + solid  
research infrastructure, etc.

North Africa: high waterpipe  
prevalence since many years  
+ many are waterpipe-only  
users. But epidemiologic  
infrastructure is limited.





**Knowing that the epigenome functions as a molecular imprint of nature & nurture with a central player in cancer,**

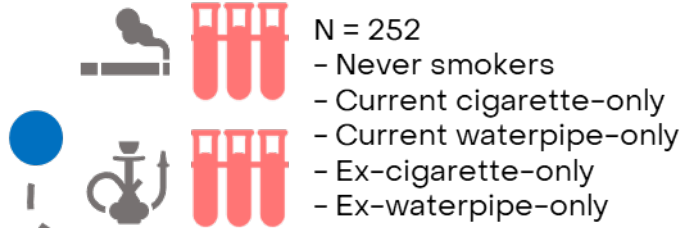


**Aims:**

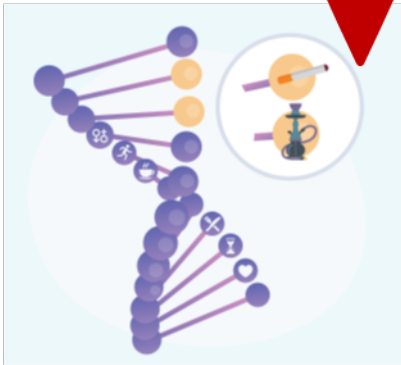
- **Does waterpipe smoking leave an epigenetic mark on our DNA?**
- **If so, how comparable is this mark to that of cigarette?**
- **What are the biological implications?**

# Discovery

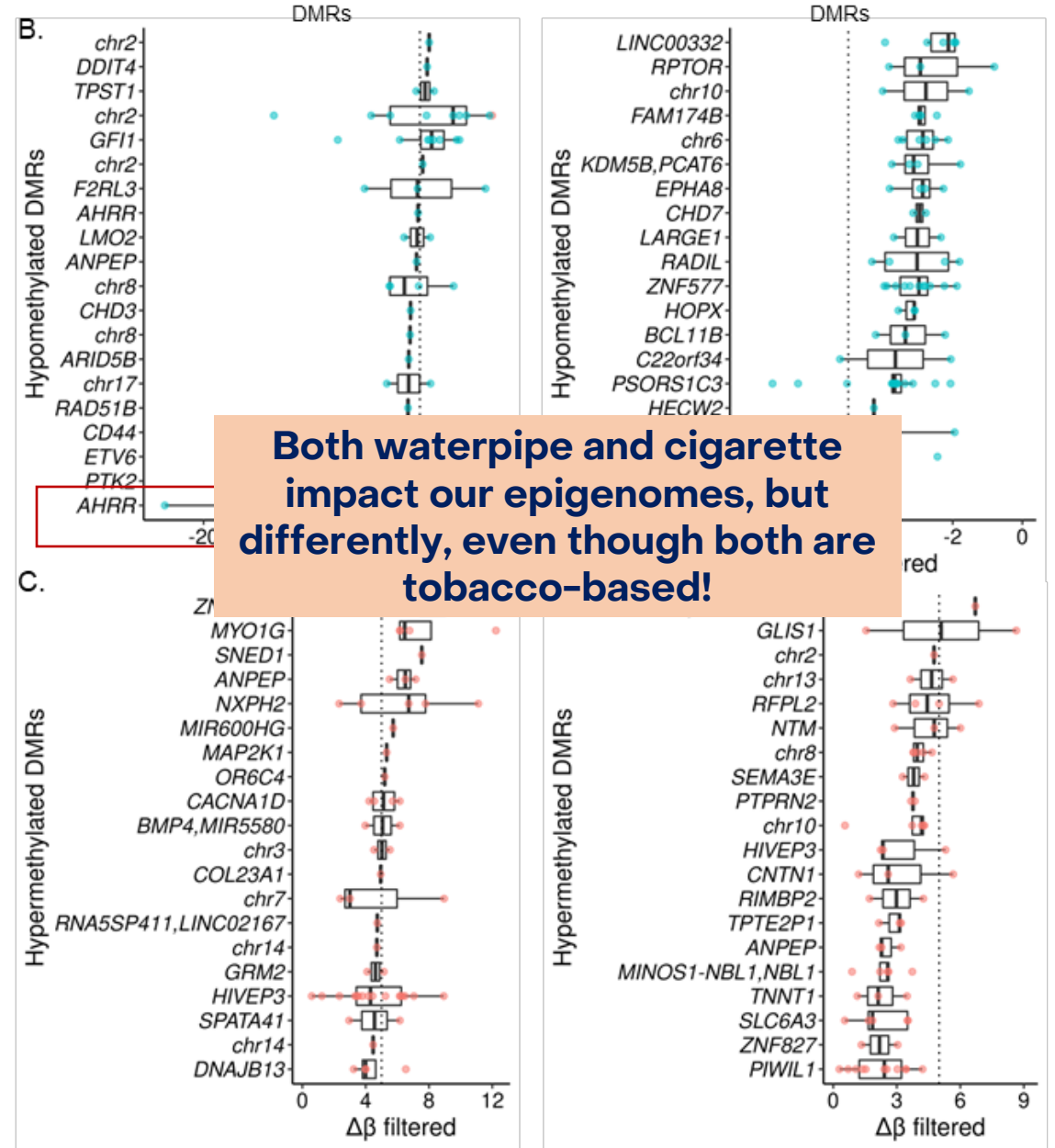
## Greater Beirut cohort



Genome-wide DNA methylation (epigenetic) markers



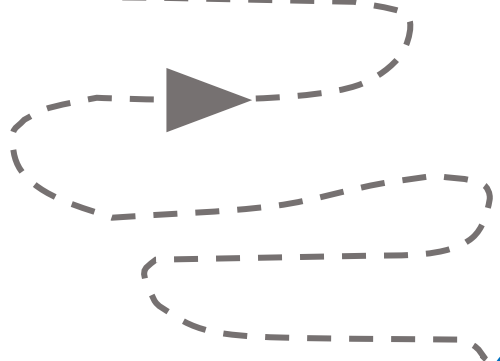
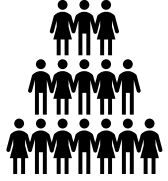
Awada, et al. *Env Int*, Dec 2023



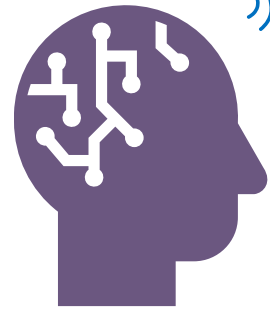
# Validation & Reverse Inference

## Replication

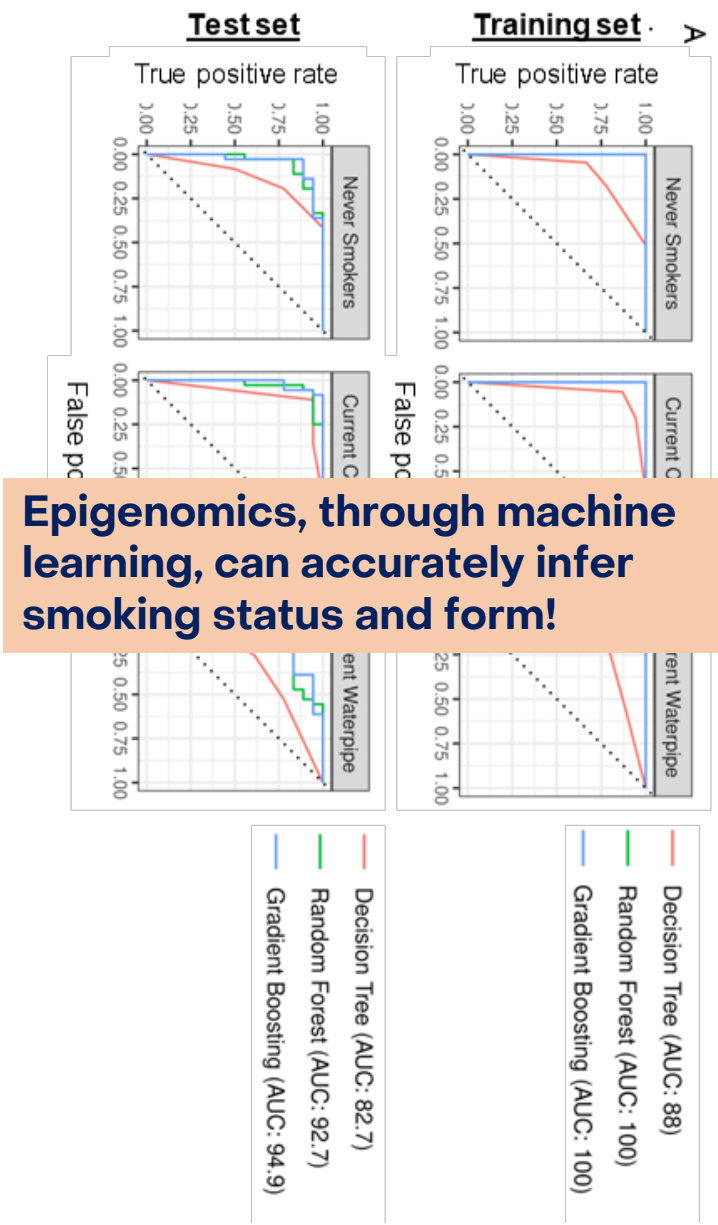
- Using independent technologies
- In additional samples
- Sensitivity analysis



Machine learning inferring smoking status



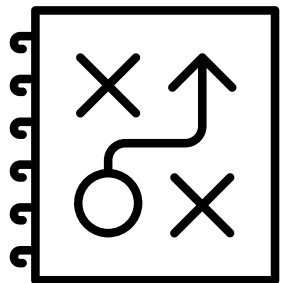
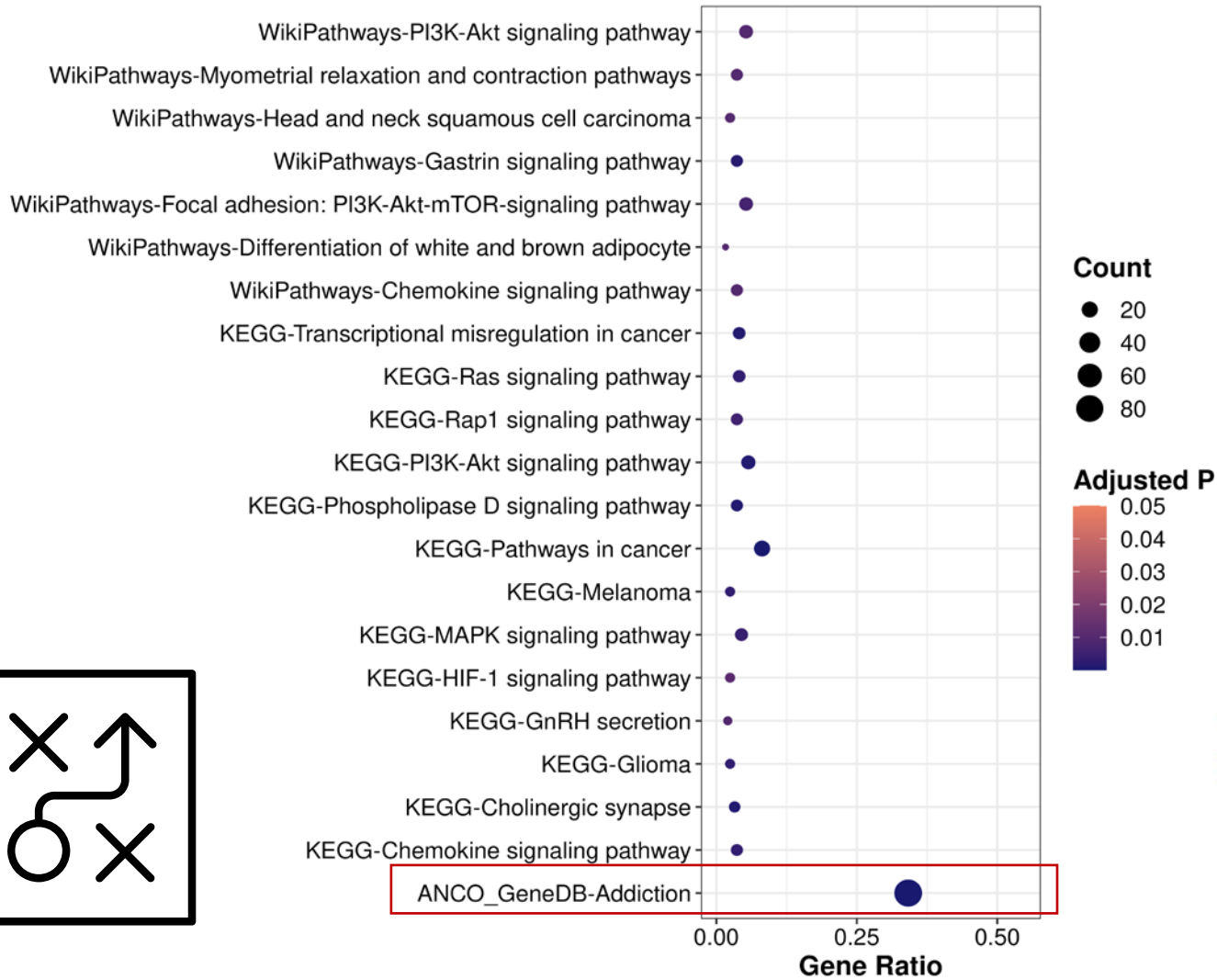
Could we trace the results using machine learning and use the subjects' epigenome to determine whether or not they are smokers? And if so, determine the type of smoking used by smokers?



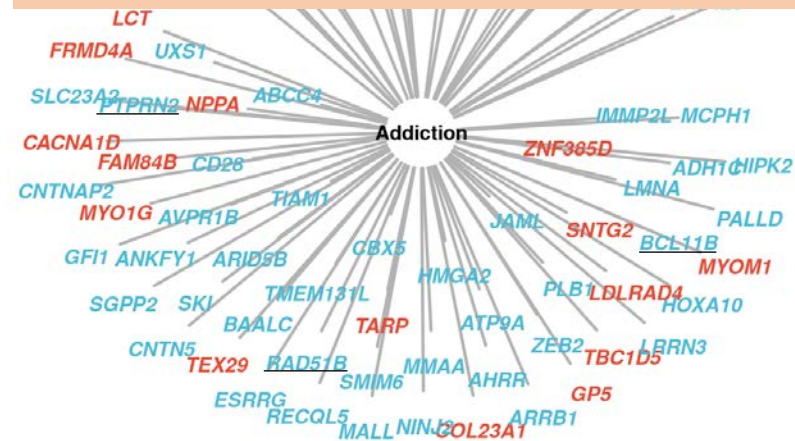
**Epigenomics, through machine learning, can accurately infer smoking status and form!**

# Biological Mapping

Current cigarette-only vs. never smokers



**The epigenetically altered genes were not associated with genetic etiology of tobacco use, and the methylation levels of addiction genes, in particular, were more likely to reverse after smoking cessation, hence, offering promising targets for prevention and therapy!**





## Impact

- These robust biomarkers of tobacco smoking can offer actionable targets to reverse the epigenetic memory of addiction as a central player in cancer prevention strategies.



## Ongoing work:





- Enrichment of these markers in cancers and association with clinical readouts (pan-cancer epigenome analysis).
- Bio-engineered smoking robots for experimental carcinogenesis models.



## Acknowledgements

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# Key take-home messages

- ✓  Waterpipe/Hookah is not just another form of tobacco as cigarette. It impacts our DNA differently.
- ✓  Many are getting hooked by hookah, especially the young, and this is spreading globally. The water does not “detoxify” smoke–this is a misconception!
- ✓  Tobacco smoking leaves an epigenetic memory on the DNA, and this affects the mechanisms of addiction, as a central player in cancer prevention strategies.
- ✓  But the epigenetic memory of addiction can be reversed, for better prevention and therapy!

✓  And our 3min video: <https://youtu.be/BV-cH89hJCA>

