DNA Methylation at cg05575921 is a Highly Sensitive and Quantitative Measure of Reduction of Harm for Smoking Cessation

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Disclosures

The use of DNA methylation to assess smoking status is covered by US Patent 8,637,652, 9,273,358 and 9,994,904. Several other pending intellectual property claims involve the use of DNA methylation in the assessment of other forms of substance use and cardiovascular disorders. Dr. Philibert is part owner and royalty holder for those applications.

Smoke Signature® is trademarked by Behavioral Diagnostics. Dr. Philibert is a stockholder and Chief Executive Officer of Behavioral Diagnostics and Chief Medical Officer Cardio Diagnostics.
Epigenetics

“the study of changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself”

Beach and Philibert 2015
Epigenetics

The figure illustrates nucleosome models and major posttranslational modifications which play essential roles in gene expression regulation and disease processes.

Yim, 2004
DNA Methylation

Adapted from Taylor 2006
Rapid Publication

MAOA Methylation is Associated With Nicotine and Alcohol Dependence in Women

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Coordinated Changes in AHRR Methylation in Lymphoblasts and Pulmonary Macrophages From Smokers

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Received 14 July 2011; Accepted 21 December 2011
AHRR is a Negative Feedback Modulator of AHR in the Xenobiotic Pathway

Philibert et al., 2014
Smoking Methylation

Dose Response and Prediction Characteristics of a Methylation Sensitive Digital PCR Assay for Cigarette Consumption in Adults

Robert Philibert 1, Meesha Dogan 2-3, Amanda Noel 1, Shelly Miller 1, Brianna Krukow 1, Emma Papworth 1, Joseph Cowley 4, Jeffrey D. Long 1, Steven R. H. Beach 5 and Donald W. Black 2

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Reliable
✓ ROC AUC >0.99
✓ Replicated >50x
Quantitative-
✓ ▲Methylation ~ ▲cigs/day

Philibert et al., 2018
AHRR Methylation is Powerful Predictor of Smoking Status in both Saliva and Blood DNA

Robert Philibert MD PhD  Meeshanthini Dogan PhD,  James A Mills MS and Jeffrey D. Long PhD

In Submission

AUC in blood and saliva DNA is 0.995 and 0.981, respectively
Reversion of AHRR Demethylation Is a Quantitative Biomarker of Smoking Cessation

Robert Philibert¹,²*, Nancy Hollenbeck¹, Eleanor Andersen², Shyheme McElroy¹, Scott Wilson³, Kyra Vercande¹, Steven R. H. Beach⁴, Terry Osborn², Meg Gerrard⁵, Frederick X. Gibbons⁵ and Kai Wang⁶

Frontiers 2016
Incentive Based Approach for Smoking Cessation

• Pioneered by Kevin Volpp and Colleagues at University of Pennsylvania

• Uses financial incentives to encourage smoking cessation.
  • Can be used with any pharmacologic/psychotherapeutic approach
  • Incentives given at key time points.

• Our implementation with Dr. Eric Hoffman of the U of Iowa
  • Total pilot will have 80 subjects
  • > 50 years old getting LDCT screening
  • Subjects cannot use NRT; they are biosampled at each time point
  • $400 reward for cessation at 30, 60 and 90 days
  • 11 of the first 33 have quit as indicated by negative cotinine
  • Measure methylation at all time points
Abstinence Induced Change in cg05575921 Methylation

Absolute Change in cg05575921 Methylation

- Heavy Smokers N=5
- Medium Smokers N=2
- Light Smokers N=4

30 Day 60 Day 90 Day
Cigarette and Alcohol Consumption can be epigenetically quantified.

- Fast and compatible with blood or saliva
- Initial assessments are very useful
  - Initial methylation levels not only predict daily use but risk for lung cancer and mortality.
  - Subsequent methylation levels provide objective measurement of smoking cessation and the quantitative reduction of harm.
- Results cannot not be obfuscated by any known method
  - Completely compatible with nicotine replacement
  - Allows differentiation of smoking from vaping.
- Empowers prosocial measures to reward those who “Quit the Habit”- because when smokers quit, everybody wins!
Thanks!

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