BDi CH3 Behavioral Diagnostics, LLC

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XXXXX XXXXX MD PhD, Director

Patient Name
John G. Smith
Patient ID: XX22092
Sample ID: XX22092A

Test Information
Order ID
Order Date: 11/12/23
Specimen Type: Blood
Date Received: 11/12/23
Date of Report:11/14/23

Ordering Clinician
Dr. James Kildare
Blair General Clinic
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Smoke Signature©

Results

Smoke Signature© Methylation Score	XX%
Estimated average cigarette consumption per day*	Y

Guide to Interpretation

Almost all lifetime non-Smokers have methylation scores > 80%.

*Estimated average cigarette consumption per day assumes regular current smoking. The average methylation in lifetime smokers is 86.6% ± 2.9. Methylation status in those who have quit smoking slowly reverts to the value found in non-smokers. Subjects who have quit smoking are often highly de-methylated at this locus for substantial periods of time. In cases where smoking cessation has taken place, we recommend repeat testing to monitor this reversion process.

About this test

The Smoke Signature© test is designed to determine smoking status and for those who are currently smoking cigarettes, to predict current cigarette consumption.

Interpretation of Results

The smoking of tobacco (i.e. smoking) is the leading preventable cause of death in the United States. [1] The combustion of tobacco and certain other products results in the generation of a large number of toxic substances, in particular, polyaromatic hydrocarbons (PAH) and dioxins, which when inhaled, are metabolized through the xenobiotic pathway. [2] Chronic inhalation of these toxins results in the dose-dependent demethylation of cytosine phosphor guanine (CpG) residues, such as cg05575921, that control the transcription of the aryl hydrocarbon receptor repressor, a key regulator of the xenobiotic pathway. [3,4] Conversely, cessation of smoking is associated with the gradual re-methylation of this locus. [5,6] This test uses the methylation status of cg05575921 to assess smoking status and in those who are current daily smokers, the intensity of current consumption as expressed in cigarettes per day.

Interpretation of Results

The use classification and smoking intensity algorithm was produced using data from 421 daily adult smokers and 423 biochemically confirmed adult non-smokers. [3] The test is not meant as a comprehensive epigenetic assessment and may be affected by rare genetic variation. Exposure to other sources of PAH and dioxins, such as chronic cannabis smoking, may also alter DNA methylation, and are not considered in these results. The performance characteristics of this test have been described [3] and are available upon request upon request at info@bdmethylation.com. There is the rare possibility that laboratory errors may occur and their occurrence cannot be completely excluded. Possible sources of error include, but are not limited to, contamination, sample mix-up and assay-based errors. For example, errors in methylation can occur as a result of degraded DNA, contamination or rare genetic variation.

Disclaimers:

This test should be interpreted by the patient's healthcare provider(s) within the appropriate clinical context and with consideration of all other clinical information. This risk assessment for smoking is not intended to prevent, diagnose, cure, mitigate, treat smoking or any other smoking related disease. There is no guarantee of benefit to the patient. Behavioral Diagnostics makes no promises or guarantees with respect to reimbursement of testing costs from insurers or other third parties. This risk assessment does not replace a comprehensive clinical assessment of smoking and tobacco use disorders. This test was developed and its performance characteristics determined by Behavioral Diagnostics. It has not been cleared nor approved by the Food and Drug Administration (FDA). This test should be used for clinical purposes and should not be considered investigational or for research purposes only. Behavioral Diagnostic's lab is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high-complexity clinical laboratory testing.

References

1. US Department of Health and Human Services. Smoking Cessation: A Report of the Surgeon General. (2020).
2. Esser, C. Biology and function of the aryl hydrocarbon receptor: report of an international and interdisciplinary conference. Archives of Toxicology 86, 1323-1329 (2012).
3. Dawes, K., et al. The relationship of smoking to cg05575921 methylation in blood and saliva DNA samples from several studies. Scientific Reports 11, 21627 (2021).
4. Gao, X., Jia, M., Zhang, Y., Breitling, L.P. & Brenner, H. DNA methylation changes of whole blood cells in response to active smoking exposure in adults: a systematic review of DNA methylation studies. Clinical Epigenetics 7, 113 (2015).
5. Philibert, R., et al. The Reversion of cg05575921 Methylation in Smoking Cessation: A Potential Tool for Incentivizing Healthy Aging. Genes 11, 1415 (2020).
6. Philibert, R., et al. Using Cg05575921 methylation to predict lung cancer risk: a

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potentially bias-free precision epigenetics approach. Epigenetics, 1-13 (2022).