Published in final edited form as:
Neuropsychopharmacology. 2009 January ; 34(1): 250–251. doi:10.1038/npp.2008.162.

Gene expression profiling in blood: new diagnostics in alcoholism and addiction?

R Dayne Mayfield[1] and **R Adron Harris**[1]

R Dayne Mayfield: dayne.mayfield@mail.utexas.edu

[1]Waggoner Center for Alcohol and Addiction Research, University of Texas at Austin, Austin, TX, USA

The successful treatment of most diseases relies heavily upon early detection. Biomarkers with diagnostic and prognostic value are critical to the addiction field. Most individuals with alcohol or drug dependence or use problems evade detection until severe medical, legal, or social consequences arise. The short half-life of alcohol in the blood after cessation of drinking eliminates the feasibility for using blood alcohol as a biomarker. Carbohydrate-deficient transferrin (CDT) is currently the most specific serum marker of chronic, heavy alcohol use (Reynaud *et al*, 2000), but the low sensitivity of the CDT test in the general population makes it an unreliable candidate for predicting either heavy alcohol use or for diagnosing alcohol abuse and/or dependence (Alte *et al*, 2004). Except for the drugs and their metabolites, there are not biomarkers for addiction.

Advances in the field of genomics offer new diagnostic and screening potential for complex genetic diseases like addiction. The ability to simultaneously measure the level of all possible transcripts (mRNAs) provides an unbiased view of potential biomarkers. The importance of understanding gene expression changes in alcohol and drug dependence can be appreciated by the impact of expression profiling in other diseases, most notably cancer, where studies have led to improved pharmacotherapies and to a molecular classification of disease. Gene expression profiling is only beginning to be applied to psychiatric illnesses and may also provide an accurate means to diagnose these conditions. Human brain gene expression studies of alcoholics and cocaine abusers suggest that specific patterns of gene expression may underlie addiction-related phenotypes and provides evidence that a molecular classification of alcoholism may be feasible in the future (Liu *et al*, 2006; Mash *et al*, 2007). However, in order for expression profiling to be useful in the clinical screening of dependence and consumption, the tissues or cells under investigation need to be readily accessible. A wide variety of screening tests are available that relies upon peripheral blood samples for assaying biological markers. For example, blood tests allow early detection, and in some cases prevention, of conditions such as prostate cancer, diabetes, thyroid dysfunction, and heart disease. Blood samples offer advantages over procedures such as tissue biopsy as they are fast, noninvasive, and can be repeated many times on the same individual. Blood biomarkers also offer the potential to predict disease before any detrimental symptoms are manifested. Genomic profiling of peripheral blood samples could be of great value in identifying biomarkers for complex diseases including addiction. This idea is supported by studies utilizing white blood cells to identify discrete patterns of expression associated with modeled complex disease states in animals (Tang *et al*, 2001). In

DISCLOSURE/CONFLICT OF INTEREST

The authors declare that, except for income received from my primary employer, no financial support or compensation has been received from any individual or corporate entity over the past 3 years for research or professional service and there are no personal financial holdings that could be perceived as constituting a potential conflict of interest.

addition, patterns of gene expression have been identified from blood samples obtained from a large number of healthy individuals, revealing surprising consistency in expression of genes associated with age, gender, and blood composition (Tang *et al*, 2001). Thus, it's feasible that nucleated blood cells of alcohol-dependent individuals could show changes in gene expression that will provide a 'signature' of the disease.

Discovery of reliable blood-based molecular markers of alcohol dependence and use would mark a milestone for addiction research and offer a great benefit for predicting the disease even without knowing the role of the markers in the disease process. Once biomarkers are discovered, the opportunity for early detection and intervention as well as personalized therapeutics should lead to new treatments for the disease.

References

Alte D, Luedemann J, Rose HJ, John U. Laboratory markers carbohydrate-deficient transferrin, gamma-glutamyltransferase, and mean corpuscular volume are not useful as screening tools for high-risk drinking in the general population: results from the Study of Health in Pomerania (SHIP). Alcohol Clin Exp Res 2004;28:931–940. [PubMed: 15201636]

Liu J, Lewohl JM, Harris RA, Iyer VR, Dodd PR, Randall PK, et al. Patterns of gene expression in the frontal cortex discriminate alcoholic from nonalcoholic individuals. Neuropsychopharmacology 2006;31:1574–1582. [PubMed: 16292326]

Mash DC, ffrench-Mullen J, Adi N, Qin Y, Buck A, Pablo J. Gene expression in human hippocampus from cocaine abusers identifies genes which regulate extracellular matrix remodeling. PLoS ONE 2007;2:e1187. [PubMed: 18000554]

Reynaud M, Schellenberg F, Loisequx-Meunier MN, Schwan R, Maradeix B, Planche F, et al. Objective diagnosis of alcohol abuse: compared values of carbohydrate-deficient transferrin (CDT), gamma-glutamyl transferase (GGT), and mean corpuscular volume (MCV). Alcohol Clin Exp Res 2000;24:1414–1419. [PubMed: 11003208]

Tang Y, Lu A, Aronow BJ, Sharp FR. Blood genomic responses differ after stroke, seizures, hypoglycemia, and hypoxia: blood genomic fingerprints of disease. Ann Neurol 2001;50:699–707. [PubMed: 11761467]