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Human Volatilome Complex System and their Categorization

Kim Jung Seok*

Department of Public Health, Madda Walabu University, Robe, Ethiopia

Commentary

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***For Correspondence:**

Dr. Kim Jung seok,
Department of Public Health,
Madda Walabu University,
Robe, Ethiopia

E-mail: kim@031295mail.com

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DESCRITPION

The human volatilome is a complex and dynamic system in which the origins of each volatilome compound can be varied and manifold. The distribution of different classes of compounds within the human volatilome for specific bodily fluids. Overall, exhaled volatilome compounds can be categorized as endogenous, *i.e.*, com- pounds originating within the body, or exogenous, *i.e.*, foreign compounds from the environment; many compounds can have endogenous and exogenous contributions. Commensal and pathogenic microorganisms residing in the body emit volatiles that contribute to the volatilome. Endogenous compounds derive from normal metabolic processes but can also arise from an imbalance in the body in relation to disease or (organ) dysfunction; these are the compounds typically sought as biomarkers. Collectively, the latter contribute to what is referred to as the human exposome.

Clearly, the origin of any compound present in breath-or any other bodily medium, for that matter-is rarely singular, with many contributing factors. This is illustrated conceptually, which depicts the varied sources of individual VOCs. Some volatiles might have a dominant source, with only minor contributions from other routes, whereas others might derive from many minor sources. It is analytically challenging-if at all possible-to tease out the different origins of potential markers.

Exogenous compounds might also be metabolized by the human body and subsequently measured in their altered form. More recently, breath gas analyses have been used to assess occupational or environmental exposures to airborne contaminants from industry, cars, water disinfection, and commercial products *via* detection of VOCs. The differences between inhaled and exhaled VOCs have also been used to assess potential dose. In terms of endogenous compounds, exhaled acetone and isoprene measurements were the first attempts at understanding exhaled markers of metabolism and physiology. High levels of exhaled acetone were considered a marker for uncontrolled diabetes and isoprene changes from baseline were found to be indicative of exercise, sleep cycle and cholesterol metabolism. Other compounds were also explored, such as exhaled ethane and pentane, for which changes were linked to oxidative stress. The most prominent biomarker is Fractional Exhaled Nitric Oxide (FENO), which has become a major factor in assessing respiratory diseases in humans. Patterns of trace-level gas-phase aldehydes, ketones and alcohols have been used in various physiology and preclinical comparisons. Condensed-phase breath samples have yielded probative information of inflammation and pulmonary damage *via* cytokine, chemokine, and fatty acids measurements.

The hypothesis and justification for exploring breathborne biomarkers is that a disease state would induce a perturbation of a general pattern from "baseline" conditions. This could be described as observing a remarkable event in an otherwise un- remarkable profile. The "holy grail" in disease screening is, of course, to find that one very special and unique compound that announces "lung cancer!" or "kidney disease!" etc., well before any standard clinical test. Such an unambiguous flag could save lives through early medical intervention. Regrettably, finding a single unambiguous biomarker for a specific disease has largely eluded the breath research community so far and chasing this goal has led to frustration and skepticism that breath analysis has value in clinical practice. There are notable exceptions, such as the progress made with the analysis of changes in FENO as an indicator of preclinical asthma and other health states, but in general, common biomarkers are present in all samples, albeit often at different concentrations. Furthermore, it is worthy of note that variance among people is often large, which renders any individual (single) measurements ambiguous.

Among researchers, it is now widely thought that a subtle pattern shift in a group of biomarkers or perhaps even the whole exposome, is more likely to signal an overall perturbation of the human system that can be exploited for diagnostic purposes. This approach has been implemented in numerous studies using case-control epidemiology and longitudinal (time-trend) analyses, for instance, in the Hearts breath test for screening heart transplant rejection. Other pattern-based methods have been developed for cancer screening with varying degrees of success. The current state of the art is exploratory, but detecting changes in the breath exposome for cancer screening is considered a promising area of research.