Exhaled breath carries a 'breathprint' unique to each individual, study shows

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Swiss researchers could show that exhaled human breath contains a characteristic molecular "fingerprint". The scientists want to use this finding to diagnose diseases based on the chemical analysis of patient's exhaled breath, using highly sensitive and precise instrumental methods.

Bodily fluids contain lots of information about the health status of a person. Medical doctors routinely have blood and urine analysed in order to obtain hints for infectious and metabolic diseases, to diagnose cancer and organ failure, and to check the dose of medication, based on compounds present in these body fluids. Researchers at ETH Zurich and at the University Hospital Zurich now propose to extend such analyses to breath, and in particular to take advantage of modern high-resolution analytical methods that can provide real-time information on the chemical composition of exhaled breath.

Unbiased Chemical Analysis of Breath

The scientists developed an instrument-based version of a principle that has been known for a long time in traditional Chinese medicine: TCM doctors draw conclusions about the health state of a patient based on the smell of the exhaled breath. It is also known that trained dogs and rats can distinguish the smell of the breath of people suffering from certain variants of cancer. In these cases the entire smell of the patient's exhaled breath is gauged, which can give rise to bias. The scientists, led by Renato Zenobi, professor at the Laboratory for Organic Chemistry, aim

at eliminating this bias and identifying the chemical compounds in breath. Like this, doctors should be able to use specific compounds, which are present in breath at minute concentrations, for medical diagnosis.

Using mass spectrometry, these goals can be reached, as shown in a recent study where the ETH researchers analysed the exhaled breath of eleven volunteers. They found that the chemical "fingerprint" of exhaled breath, largely based on volatile and semi-volatile metabolites, shows an individual core pattern. Each volunteer was found to have his/her own characteristic "breathprint".

Stable Pattern

Using regular measurements extending over 11 days, the researchers could furthermore show that this metabolic "breathprint" stays constant. "We did find some small variations during the day, but overall the individual pattern stays sufficiently constant to be useful for medical purposes", says Pablo Martinez-Lozano Sinues, senior scientist in Zenobi's research group. If the measurements would show too large variations, they would not be useful for medical diagnosis.

To carry out these measurements, Zenobi and his colleagues modified commercial mass spectrometers, for example by adding a breath sampling inlet line that delivers exhaled breath from a mouth piece directly into the ion source of the instrument. Mass spectra showing peaks of roughly 100 compounds in breath can be easily and rapidly obtained in this fashion. The researchers were able to identify acetone, a product of the sugar metabolism. Most of the other signals present in the "breathprints" have not been assigned yet, which is something the scientists have on their to-do-list.

Chemical fingerprints of diseases

The next step the ETH chemists plan to take is not only to elucidate the personal breathprints of individuals, but to recognize characteristic patterns of diseases with the same technology. For this endeavour, they are collaborating with medical doctors at the Division of Pulmonology of the University Hospital Zurich. "If we find a consistent pattern in patients with a given lung disease, we can develop a diagnostic tool", explains Sinues. They believe that their chances are highest to find characteristic biomarkers in the exhaled breath of patients with lung diseases, which is why they focus on these disorders. In the future, they hope to extend their methodology to other groups of diseases.

Although the potential usefulness of analysing breath for medical diagnosis has been known, it is rarely done in academic medicine. "This might be due to the fact that existing methods for breath analysis are either rather slow, or are limited to a small number of compounds that they can detect", says Sinues.

Compared to analysis of blood or urine, a significant advantage of the approach the ETH researchers have taken is that the breath fingerprint is available within seconds after delivering the breath sample. Analysing urine or blood in a specialized laboratory usually takes a lot longer. Another advantage is that exhaling into the ion source of a mass spectrometer is completely non-invasive, i.e., there is no need to poke the patient with a needle (when a blood sample is taken). "Our goal is to develop breath analysis to the point where it becomes competitive with the established analysis of blood and urine", says Malcolm Kohler, professor at the University Hospital Zurich, and one of the co-authors of the study. Regular survey of breath could, for example, be used to obtain an early warning for healthy persons with a known risk for a certain disease. It is also imaginable to monitor the progress or the side effects of an on-going medical therapy.

For this method to be accepted in the clinic, the instrumentation has to be improved. The highly sensitive and accurate mass spectrometers that are currently used for these analyses are large and expensive. Zenobi: "Small, portable mass spectrometers already exist; if their performance can be improved, they will eventually find their way into clinics and doctor's offices."

More information: Martinez-Lozano Sinues P, Kohler M, Zenobi R (2013) Human Breath Analysis May Support the Existence of Individual Metabolic Phenotypes. *PLoS ONE* 8(4): e59909. doi:10.1371/journal.pone.0059909. dx.plos.org/10.1371/journal.pone.0059909

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