

Using Saliva to Understand Exposures and Monitor Health

Collecting saliva may be a practical alternative to blood for characterizing a person’s exposures, according to new research from the Superfund Research Program (SRP) Center at the University of California (UC), Berkeley. The researchers found that saliva contains a rich set of molecular information that can be used to construct individual exposure histories and discover risk factors for chronic diseases.

The technique could be used to study the exposome, or the totality of human exposures over the lifespan, to link complex exposures throughout life to chronic diseases that occur later. Through studies known as exposome-wide association studies (EWAS), scientists typically investigate associations between small molecules measured in blood or urine and health outcomes.

Because saliva contains small molecules that have been shown to correlate with concentrations of the same compounds in blood, researchers investigated saliva as a viable and simple alternative to blood for EWAS studies. In the new study, Stephen Rappaport, Ph.D., from the UC Berkeley SRP Center, along with colleagues from the University of Waterloo and Silent Spring Institute, documented for the first time that metabolites in saliva are linked to at least 14 important metabolic pathways. These pathways include amino acid metabolism and gluconeogenesis, among others, and underlie many human chronic diseases.

Mapping the Saliva Exposome to Metabolic Pathways

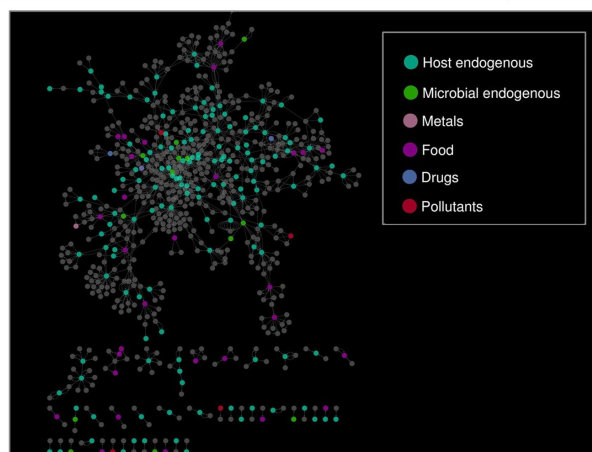
In the study, Rappaport, Vincent Bessonneau, Ph.D., and Janusz Pawliszyn, Ph.D., used the open-source [saliva metabolome database](#) to compile information on the concentrations of 1,233 chemicals in saliva. They then used PubMed Medical Subject Heading (MeSH) terms to link the chemicals in saliva with human metabolic pathways. After performing pathway enrichment and topology analyses, they were able to determine which metabolic pathways in the saliva exposome were most important.

Using the [Metscape database tool](#), which integrates metabolomics and gene expression data, the authors mapped 196 of the chemicals measured in saliva to 49 metabolic pathways. They then connected salivary metabolites with chronic human diseases.

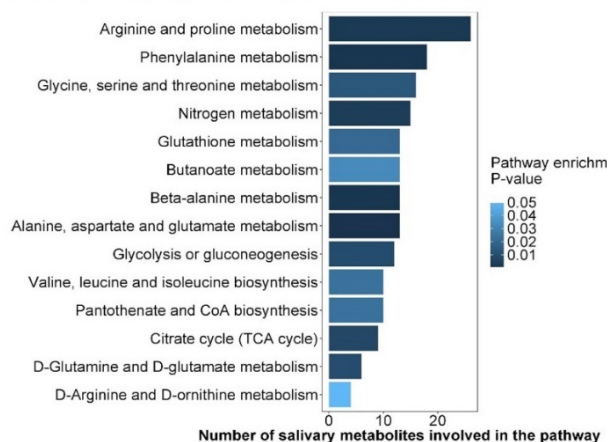
Linking the Saliva Metabolome to Human Disease

Using a text-mining application called MetDisease, the authors evaluated associations between metabolites of chemicals in saliva, called the saliva metabolome, and MeSH terms. This tool

Network of biochemical reactions reconstructed from salivary metabolites



Metabolic pathways represented by the saliva metabolome



Top: Reconstructed network of metabolic pathways from all 1,233 metabolites in human saliva from the saliva metabolome database. Gray circles represent metabolites that had not been detected in saliva previously but that have direct neighbors in known metabolic pathways. Bottom: Metabolic pathways represented by the saliva metabolome that were determined to be the most important (statistically significant, $p < 0.05$) during the pathway enrichment analysis.

enabled them to make a network illustrating how salivary metabolites were associated with many human diseases, such as cardiovascular disease, neoplasms, and respiratory diseases.

For example, of 14 salivary metabolites known to originate from microbes, 12 were associated with congenital, hereditary, and neonatal disease. Eleven were associated with nervous system diseases, ten with nutritional metabolic diseases, eight with digestive system diseases, and seven each associated with neoplasms, urogenital complications, and pregnancy complications.

Linking saliva metabolites to human disease may be a first step in developing targeted studies to understand exposure sources and biological mechanisms underlying disease.

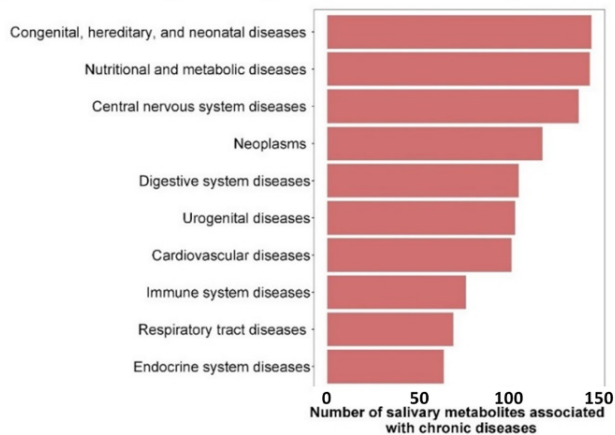
Why Saliva is Well Suited for EWAS

Rappaport and colleagues demonstrated that saliva contains a great deal of useful molecular information that can be examined using EWAS. Though the concentrations of small molecules are often lower in saliva than in blood and may be difficult to detect, scientific advancements are overcoming this challenge.

Collecting saliva is much less invasive than collecting blood samples, and commercial saliva collection kits can be used by study participants to collect samples themselves that are then sent to a lab. The ease of collection that comes with saliva, along with the increased willingness of subjects to participate, also would allow researchers to make multiple exposure measurements and reduce measurement errors.

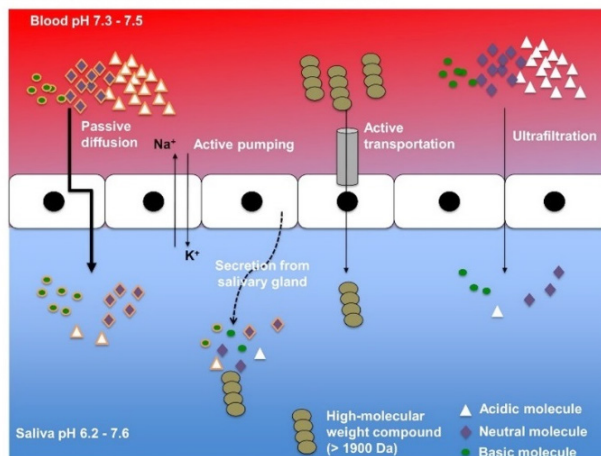
Using saliva can improve health monitoring by characterizing a person's exposome and can increase the power of analyses to link complex exposures to diseases through repeated measurements over the human lifespan.

PubMed Medical Subject Heading terms associated with salivary metabolites



Summary of PubMed Medical Subject Heading terms, representing important human chronic diseases, associated with 196 metabolites in saliva from the saliva metabolome database.

Transfer of small molecules from blood to saliva



Small molecules can transfer from blood to saliva, making it a useful alternative to collecting blood samples. The transfer process involves passive diffusion of lipophilic compounds, active transport of high molecular weight compounds, and ultrafiltration of low molecular weight hydrophilic compounds.

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To learn more about this research, please refer to the following source:

Bessonneau V, Pawliszyn J, Rappaport SM. 2017. The saliva exposome for monitoring of individuals' health trajectories. *Environ Health Perspect* 125(7):077014 PMID: [28743678](https://pubmed.ncbi.nlm.nih.gov/28743678/) doi: [10.1289/EHP1011](https://doi.org/10.1289/EHP1011)

