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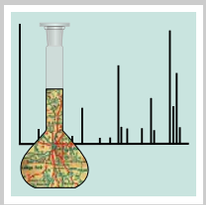

Highlights of Analytical Sciences in Switzerland

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A Close Look at the Fate of Compounds we are Exposed to

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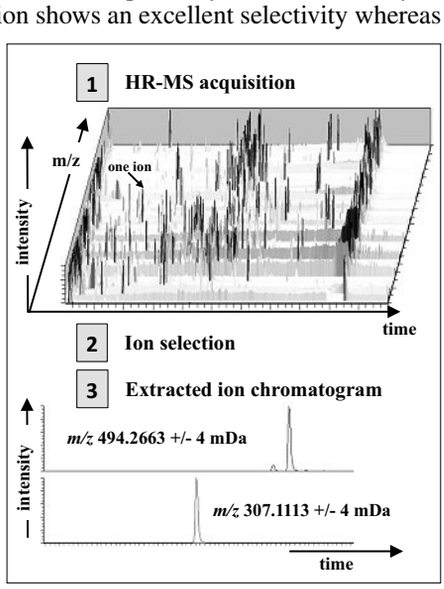
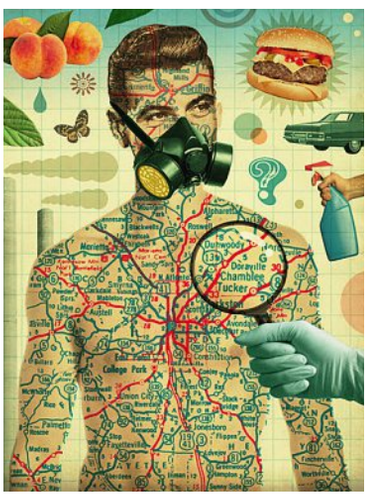
The exposome was defined by C. P. Wild as non-genetic and encompasses "every exposure to which an individual is subjected from conception to death". An exposome can be endogenous microbes, physical activity, infectious agents, stress, xenobiotics such as pollutants or drugs and so forth and is a new term rather than a new concept. The capacity of new liquid-chromatography mass-spectrometry (LC-MS) to detect, in the same analysis, a large number of molecules (100s to 1000s) at low levels has advanced our understanding of the exposome. These new detectors are LC-high-resolution mass-spectrometers (HR-MS) and are mainly composed of Orbitrap- and Time-Of-Flight-MS.

HR-MS allows for the discrimination between very close ionized molecular masses (m/z for mass-over-charge ratio). For instance, $C_{15}H_{14}O_3N$ or $C_{16}H_{16}OS$, ionized by an H^+ adduct, would easily be discriminated by their m/z values: 257.10464 and 257.09946 Da (delta = 5 mDa), respectively. LC-HRMS analysis with full scan acquisition shows an excellent selectivity whereas 1000s of ions are recorded in a LC-MS analysis. HR-MS has shown similar quantitative capabilities in comparison to traditional quantification technology, triple-quadrupole-MS.

We studied the fate of a drug, tamoxifen, taken for three months or more by women with breast cancer. We discovered over 44 tamoxifen metabolites in their blood that are the result of different biotransformation enzymes, with up to seven biotransformation steps. This underscores that, when we are exposed to one molecule chronically, the body can eventually be exposed to a lot of different derived molecules. We revealed the inter-individual differences in the levels of some tamoxifen metabolites, demonstrating that the effect of a xenobiotic and its metabolites can strongly vary from person to person.



Typical LC–high-resolution mass-spectrometry analysis. 1) A high resolution (HR) full scan is acquired from sample extracts. 2) The ionized molecules of interest are selected based on their accurate m/z ratio. 3) The extracted ion chromatograms are constructed.



Michael Waraksa's illustration shows how our environment shapes our health and underscores the concept of the exposome.

Today, using high-resolution mass-spectrometry, the fate of drugs and pollutants in humans can be studied more in-depth and with ease. From a single compound we are chronically exposed to, there are tens of metabolites produced that could have adverse reactions. Although our body is armed to cope with most exposures, a more in-depth analysis allows to relate toxic events, *e.g.* in a sub-population, and xenobiotic and its various metabolites.

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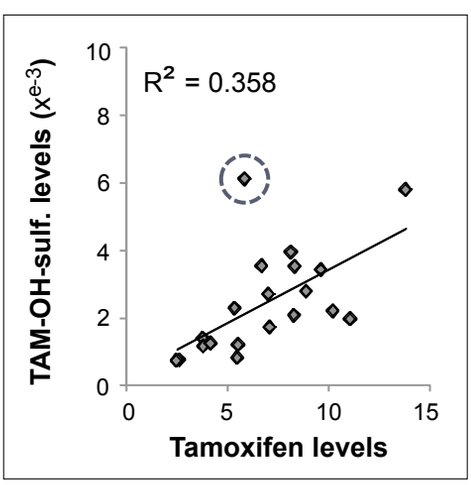

Determination coefficient (R^2) between relative levels of tamoxifen metabolites and tamoxifen) in 20 patients treated with tamoxifen (TAM). TAM-OH-sulf.: Tamoxifen-hydroxy-sulfate. Data reveal high inter-individual variability of tamoxifen metabolite levels with potential outliers (dashed circle).

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