

More than ten years ago, gas chromatography/mass spectrometry (GC-MS) of human clinical samples already suggested a "potential for diagnosis and studies of metabolism *in situ*" [1]. A study published in 2001 demonstrated that the level of several urinary metabolites can be affected by differences in the metabolic capability of the intestinal microflora [2]. Much more recently, in May 2005, an article published in *Nature Rev of Microbiol* has suggested to use "the metabolite signature that is found in host fluids such as urine" to improve "the understanding of dysbiosis and gut micro-organism related diseases processes" [3].

According to the same author (JK Nicholson), "several papers have detailed the identification of dynamic changes in the urinary levels of microbiotal products (...) after antibiotic administration" [3], even as mild as the ingestion of chamomile infusion during ten days [4]. In this study published in 2005, the metabolite signature was also obtained from the volunteers' urine [4].

It is therefore possible to spot several fungal metabolites, such as *arabinose* and *arabinitol*, in the urine of patients suspected to suffer from intestinal fungal overgrowths. *D-arabinitol* is a metabolite of most pathogenic *Candida* species [5]. Its identification in the urine provides a clue both for the existence of a candidiasis and for its severity, giving qualitative and quantitative data.

Multiple markers can be obtained from the presence and from the overgrowth of a typical putrefactive bacterial genus, *Clostridium* which metabolizes aromatic amino acids (phenylalanine, tyrosine and tryptophan) into phenolic and indolic compounds [6, 7]. We might even be able, in the future, to spot which species of *Clostridium* corresponds to a specific profile of urinary metabolites [6].

On the practical side, sophisticated data bases and experienced chromatography teams are needed because more than 250 urinary organic metabolites "are either typically present or may be encountered in [human] urine" [8]. Happily for the patients, "a random specimen, preferably the first morning voiding, is an acceptable alternative" to 24-hours urine collection [8]. Besides, on the short term, variations in the ranges of excretion "mainly depend on individual metabolic variations rather than on dietary factors" [9].

So, dysbiotic patients can benefit from an easy to collect urine assessment capable of identifying fungal or putrefactive bacterial overgrowths, providing an insight into the existence and the severity of fermentative or putrefactive imbalances of the microflora. Above all, the urinary metabolite signature studies the micro-organisms *in situ* and prevents the unacceptable flaws coming from false positive and especially false negative results linked to stool cultures. Because the lab is so different from the gut!

- 1. Larsson, L., Determination of microbial chemical markers by gas chromatography-mass spectrometry-potential for diagnosis and studies on metabolism in situ. Review article. Applies, 1994. **102**(3): p. 161-9.
- 2. Williams, R.E., et al., *Effect of intestinal microflora on the urinary metabolic profile of rats: a (1)H-nuclear magnetic resonance spectroscopy study.* Xenobiotica, 2002. **32**(9): p. 783-94.
- 3. Nicholson, J.K., E. Holmes, and I.D. Wilson, *Gut microorganisms, mammalian metabolism and personalized health care.* Nat Rev Microbiol, 2005. **3**(5): p. 431-8.
- 4. Wang, Y., et al., *A metabonomic strategy for the detection of the metabolic effects of chamomile (Matricaria recutita L.) ingestion.* J Agric Food Chem, 2005. **53**(2): p. 191-6.
- 5. Sigmundsdottir, G., et al., *Urine D-arabinitol/L-arabinitol ratio in diagnosis of invasive candidiasis in newborn infants.* J Clin Microbiol, 2000. **38**(8): p. 3039-42.
- 6. Elsden, S.R., M.G. Hilton, and J.M. Waller, *The end products of the metabolism of aromatic amino acids by Clostridia.* Arch Microbiol, 1976. **107**(3): p. 283-8.
- 7. Smith, E.A. and G.T. Macfarlane, *Formation of Phenolic and Indolic Compounds by Anaerobic Bacteria in the Human Large Intestine*. Microb Ecol, 1997. **33**(3): p. 180-8.
- 8. Kumps, A., P. Duez, and Y. Mardens, *Metabolic, nutritional, iatrogenic, and artifactual sources of urinary organic acids: a comprehensive table.* Clin Chem, 2002. **48**(5): p. 708-17.
- 9. Chalmers, R.A., et al., *Urinary organic acids in man. II. Effects of individual variation and diet on the urinary excretion of acidic metabolites.* Clin Chem, 1976. **22**(8): p. 1288-91.