Metabolomics: CSI Comes to the Bedside

Scott E Walker

I have always enjoyed suspense thrillers, in book or movie form, and enjoy them even more when they include some science fiction. About 10 years ago, the movie *Gattaca* caught my interest. The slightly futuristic world portrayed in the movie required some suspension of disbelief as one prospective mate turned in the hair of a companion at a roadside kiosk, where the companion’s entire DNA sequence was determined and the likelihood of future diseases revealed, all in a matter of minutes.

Closer to present day, but at times still requiring a large dose of suspended disbelief, is the currently popular TV series *CSI: Crime Scene Investigation*. I enjoy the show, but am sometimes a little irritated by the ease with which the analyst samples room air for the lingering trace of a unique perfume or manages to examine a sample of mixed blood spatter, easily differentiating criminal from victim, all of which culminates in a quick arrest and presumably swift and accurate justice (O J Simpson, are you paying attention?).

My own reality is more mundane. I have access to liquid chromatographic equipment and a variety of methods of detection, including mass spectrum detection—equipment that allows us to determine the concentration of several hundred drugs—but our analytical abilities pale in comparison to the speed and accuracy of the methods used by Gil Grissom and his band of merry analysts. For example, I recently participated in a project to examine metal ointment tubes containing hand-cream that had begun to swell with gas over a period of weeks. Hospital staff interested in the safety of their patients asked us to analyze the gas within the tubes, but because of the analytical and methodological limitations of our laboratory and those of a lab at the University of Toronto, we could not discriminate analytically between oxygen and nitrogen, nor could we distinguish between the air trapped within the tube and the “air” released during the degassing process.

With my staunch belief in the limitations of current routine analytical procedures, you can imagine my amazement when I attended a presentation by Dr Thomas Marrie from the University of Alberta in Edmonton. Marrie described the development of metabolomics as a diagnostic tool to identify the etiology of community-acquired pneumonia, an infection that is most commonly treated empirically with antimicrobials covering the most likely bacterial pathogens. Metabolomics involves the simultaneous measurement of a series of end-products of metabolism. Computer algorithms then analyze changes in the concentration of each compound relative to normal values, which allows accurate diagnosis. Marrie presented data from evaluations of patients with and without infections due to *Streptococcus pneumoniae*, the prototype infection that his team is investigating. Simultaneous analysis of about 40 small “fingerprint” molecules in a single urine sample from each patient showed differences between healthy controls and those with infection. The molecules they measured included citrate, lactate, amino acids, and many other small molecules representing the end-products of metabolism. These metabolites form the link between genotype and phenotype. By identifying the variations in metabolites after environmental, pathogenic, or toxicologic insult, metabolomics may revolutionize the diagnosis of disease. Nuclear magnetic resonance (NMR) spectroscopy has become one of the main tools for measuring these changes. The Human Metabolome Database is currently the most comprehensive curated collection of human metabolite and human metabolism data, containing records for more than 2180 endogenous...
metabolites. It is thought that selection of a series of appropriate markers and accurate NMR measurement of their concentration (a process called targeted profiling) could allow the development of robust computer algorithms allowing accurate diagnosis. To date, the measurement in urine of metabolites related to mitochondrial energy metabolism has been used to differentiate individuals on the basis of their sex and age, and other compounds have been identified that allow accurate differential diagnosis between pneumococcal respiratory disease, viral pneumonia, and chronic obstructive pulmonary disease.

Obviously, this is a work in progress, and research investigating the potential application of metabolomics is still in its very early phases. Full-scale applications would appear to require just a single urine sample (blood is not required), provided on presentation to a physician’s office, clinic, or emergency department, that would be quickly analyzed for a series of 40 or more metabolites. The concentration of each metabolite would be evaluated by a computer algorithm and the diagnosis made. The evolution of this research may have a significant impact on the question of how much physical assessment is required, to the point where some aspects of physical assessment may no longer be required of pharmacists or physicians.

And thus science fiction becomes reality. I have seen the future, and it is good.

References


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