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Metabolomic approach for evaluating drug response

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Abstract

Metabolomics is an emerging technology which makes it possible to evaluate change of biological system in response to the physiological, environmental alterations. It has advantages in the simplicity and sensitivity to analyze metabolites since the researcher can use cutting edge instrument, such as mass spectrometry and simple sample preparation method compared to genomics or proteomics. Nowadays this technology has been tried in pharmaceutical area to investigate toxicity and efficacy of drug candidates and drugs in preclinical test. The metabolomic applications on the pharmaceuticals for early prediction on toxicity and efficacy are described in this presentation. The multivariate analysis to get metabolic fingerprinting and its relations with the physiological changes are investigated with several drugs. Feasibility of metabolomic application for pharmaceutical area would be suggested from those researches.

Key word: metabolomics, drug, efficacy, toxicity, mass spectrometry

Generals on the metabolomics and its application to evaluate responses producing by drug in biological system will be mentioned in this presentation.

Metabolomics is one of the "-omics" technology, which was ranked as one of the 10 emerging technologies by Technology Review (pressed by MIT) , a massive research effort began in the mid-1990s and culminated after 2000.

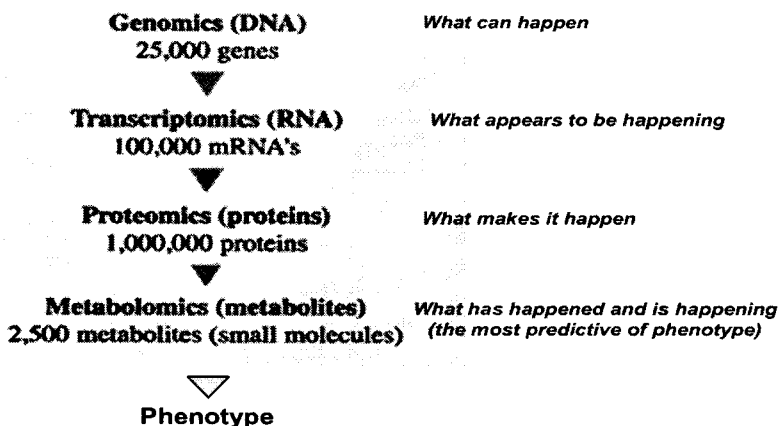


Fig.1. OMIS cascade

Metabolites are the main object for metabolomics and they are generated through metabolism-all the chemical reactions within the body that create. They have small molecular weight below than 1000 and scientists can find unique patterns, or profiles by studying the changes and concentrations of these small metabolites within all kind of biological samples. These profiles change when the body is fighting a disease, reacting to a drug, or responding to another form of stress. So metabolomics can be defined as the evaluation of tissues and body fluids, such as urine, blood, plasma, saliva, and cerebrospinal fluid, for metabolite changes that may result from bodily responses.

Nowadays metabolomics was applied on the many field of life science. The bellows are representative application of metabolomics.

- To make safer drugs by predicting the potential for adverse effects (toxicity) earlier
- To target specific groups of people most likely to benefit from a drug, while excluding its use by those who may be harmed by it
- To speed the discovery and development of drugs
- To diagnose disease or predict the risk of disease
- To determine whether a treatment is working or not
- To monitor healthy people to detect early signs of disease.

Among the field mentioned above, it is quite challengeable to use metabolomics to investigate drug response, efficacy and toxicity since metabolite is the best compound to express phenotype which is appeared by drug treatment. Metabolite could be determined invasive all kind of biological samples like urine, hair by novel instrumental analysis and it response fast and researcher can detect it with very slight change of genetic or environmental change. Moreover it is cheaper and faster than any other –OMICS technologies.

With these advantages, metabolomics has been used recently to evaluate drug efficacy and toxicity.

Rodenburg R.J.T and colleagues (1) used metabolomics approach to evaluate action mechanism of anti-inflammatory compounds with score plot of lipid pattern (Fig.2).

In this research the lipid expression patterns of zilpaterol, salbutamol and clenbuterol are clustered together in the lower left corner. This result indicates a similarity in lipid expression pattern of the three β -agonists and it was suggested that those drugs clustered together might have similar action mechanism as anti inflammatory drugs.

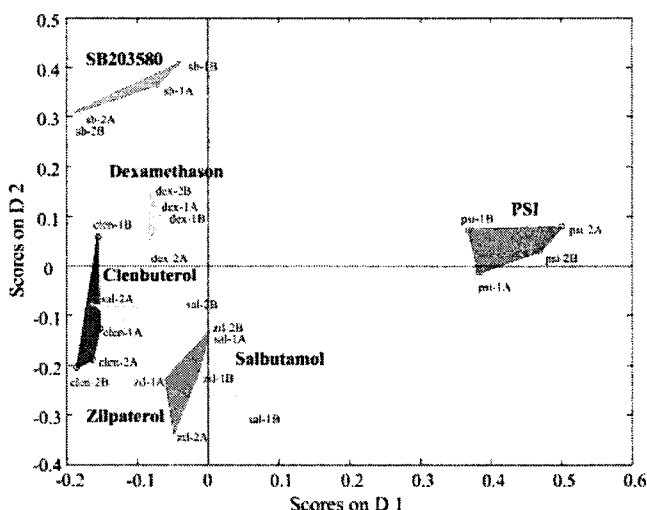


Fig.2. Score plots of the lipid patterns of zilpaterol. Clenbuterol, salbutamol, SB203580, dexamethasone and protease inhibitors. (by Rodenburg RJT et al)

In conclusion, it is thought that metabolomics approach should be a useful tool to evaluate drug efficacy and toxicity and new drug development area, and its application on the pharmaceutical area could be extended in near future.

References

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