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Editorial

Role of Metabolomics in Cardiovascular Epidemiology

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Editorial

Metabolomics is the study of comprehensive and simultaneous assessment of breakdown products formed in a living organism as a result of metabolism. In contrast to genome, metabolome is a dynamic set of metabolites that are in constant flux. Metabolome is tightly controlled by genome however; it differs and reacts directly with the environment giving a better insight into a particular phenotype. Since the first few studies in early 2000s, this field has rapidly grown to involve cardiovascular medicine.

The usual samples collected for a metabolomic study are plasma, serum, urine, cell culture or cell pellet. Serum and urine are the most commonly used samples in throughput technology; it has become possible to assess thousands of metabolites at a time. There are 4 basic steps epidemiology. These samples are then subjected to a chromatographic procedure. The main aim of chromatography is to elegantly separate various metabolites so that they can be detected without interference. The most common forms of chromatography used are gas chromatography and liquid chromatography. A special form of liquid chromatography called ultra-performance liquid chromatography (UPLC) is being increasingly used in untargeted epidemiological studies. The decision to employ a particular type of liquid chromatography depends upon the types of metabolites that are of interest to the researcher.

Once metabolites are separated, these metabolites are fed into either a mass spectrometer (MS) or a nuclear magnetic resonance spectroscope. Mass spectroscopy is an analytical technique that ionizes chemical compounds in sample and then passing it through an electromagnetic field separating compounds based on their mass by charge ratio. This forms a spectrum that provides information about the chemical nature as well as mass of the particular compound. Nuclear magnetic resonance (NMR) spectroscopy uses a strong magnet to produce resonance of particular atoms such as ^{1}H or ^{13}C, present in the compounds. These atoms resonate at different frequencies which depend upon electrons around them. For example, the number of electrons around a methyl group (-CH3) is different from that of methylene (-CH2) group and each ^{1}H will resonate at a different frequency within these groups. This resonant frequency provides structural information but also provides quantitative information.

Data quality monitoring and control is an important aspect of metabolomics. Once data has passed through various quality monitoring processes, it is evaluated by advanced multivariate methods. Unsupervised and supervised statistical methods have been provided in literature. Particular metabolites that show significance and increase in amount can be evaluated. Associations with various phenotypes can then be tested. Also, untargeted evaluation by NMR or MS can provide new biomarkers that can be used either as diagnostic or therapeutic targets.

Data interpretation is the most important aspect of this field. Since the advent of –omics fields, huge amounts of data are being available to humans, however interpreting that data in order to utilize it for benefit of mankind remains difficult. An advantage of metabolomics is that it characterizes a large number of metabolites at the same time, on the other hand this poses difficulties not just in data analysis but also interpretation.

Due to high throughput, a large number of samples can be used and metabolic profiles may be obtained now. There are several applications of this field. The field is mainly focused on biomarker discovery and understanding the natural history of risk factors at the moment.

Biomarker discovery and validation involves several steps and metabolomics can provide valuable help at all the levels of this journey. First, untargeted metabolomics can help discovering newer orthogonal biomarkers and then help in validating them in a group of individuals with and without particular phenotype of interest (for example a disease). After this a threshold of biomarker can be established in a retrospective case control study. Again, metabolomics can provide the quantitative values of these biomarkers. Then a screening study can assess these biomarkers in a large cohort study. Finally, these metabolic biomarkers can be evaluated in a randomized controlled clinical trial reporting their efficacy in improving disease related outcomes.

Metabolomics can also provide important insights into the patterns of metabolic perturbations. For example, nitric oxide is considered an important player in acute coronary syndrome. Metabolites of nitric oxide have provided prognostic information about asymmetric dimethylarginine (ADMA) which is an inhibitor of nitric oxide. ADMA has been found to be associated with mortality [1]. Similarly, acylcarnitines involved in fatty acid oxidation were found to be increased in type 2 diabetes mellitus [2,3] This finding led to discovery of increased inflammation caused by these acylcarnitines in diabetics [4-6]. This effect was mediated through increased transcription of NF-κß which also blunts the response of skeletal muscle to free fatty acids [7].

In conclusion, metabolomics will prove to be not just a sophisticated diagnostic tool but also a method for monitoring individual's response to therapy.

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