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Editorial

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Research Opportunities for Metabolomics at NIH

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Metabolomics is an advanced, specialized form of analytical biochemistry. Metabolomics is the scientific study of chemical processes involving metabolites. Specifically, metabolomics is the "systematic study of the unique chemical fingerprints that specific cellular processes leave behind", the study of their small-molecule metabolite profiles [1]. Important small metabolites include e.g. organic acids, amino acids, sugars, volatile metabolites and a myriad of secondary metabolites such as alkaloids, phenolic components and also pigments such as carotenoids and anthocyanins. Metabolomics enables simultaneous identification and analysis of multiple metabolites in cells, tissues and body fluids. Metabolomics is primarily distinguished from more established technologies by the high throughput nature of the approach which also generates a complex dataset per analysis. As a consequence, the technology relies heavily on recent advances made in bioinformatics and Information Technology. Metabolomics technologies permit integration of biological pathways to understand how living organisms interact with its environment and produce a metabolic fingerprint or 'metabolome', analogous to the genome or the proteome. Major areas of research under the metabolomics sphere include characterization and identification of novel biomarkers, therapeutic targets, and disease signatures in the area of cancer metabolomics, a fast growing research domain in translational cancer study.

Metabolome refers to the complete set of small-molecule metabolites (such as metabolic intermediates, hormones and other signaling molecules, and secondary metabolites) to be found within a biological sample, such as a single organism [2]. The word was coined in analogy with transcriptomics and proteomics; like the transcriptome and the proteome, the metabolome is dynamic, changing from second to second.

The National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services, is the nation's medical research agency-making important discoveries that improve health and save lives. NIH is the largest source of funding for medical research in the world, creating hundreds of thousands of high-quality jobs by funding thousands of scientists in universities and research institutions in every state across America and around the globe. More than 80% of the NIH's budget goes to more than 300,000 research personnel at over 3,000 universities and research institutions. In addition, about 6,000 scientists work in NIH's own Intramural Research laboratories, most of which are on the NIH main campus in Bethesda, Maryland.

An increasing focus in metabolomics research is now evident in academia, industry and government, with more than 500 papers a year being published on this subject. Indeed, metabolomics is now part of the vision of the NIH road map initiative [3]. The result was a novel program aimed at providing organizations and companies with the tools to promote high risk, high reward research and enabling them to focus on emerging areas of science and creative ways to move research from laboratory to clinic more quickly. Some of the initiatives within the roadmap focus on issues such as providing better interdisciplinary training for graduate students and postdocs, awarding grants to scientists who propose innovative and high risk research, and fostering collaboration between researchers in different fields.

In comparison to proteomic and genomic research, adoption of metabolomics as a viable research area remained low. But, in the last couple of years there was a continuous increase in the number of committed dollars for metabolomics research at NIH. *The funding for metabolomics related research at NIH from 2008-2011was $25,656,838.* *In contrast, the funding for genomics and proteomic research was much larger during the same period ($210,458,301 and $90,251,168).* The number of publications in the year 2010 was 4000 for proteomics, 3000 for genomics, and only 600 for metabolomics related topics. This shows that there is tremendous scope for people associated with metabolomic related research in the coming years.

NIH has recently released five RFA in metabolomics field. These RFAs (Request for Application) has set aside $110 million dollars for the next 5 years. *NCI (National Cancer Institute) has set aside about $110 million dollars for the same period.* The RFA's include Regional Comprehensive Metabolomics Resource Cores, Mentored Research Scientist Award in Metabolomics, Development of Courses or Workshops in Metabolomics, Technology Development to Enable Large Scale Metabolomics Analyses, and Metabolomics Data Repository and Coordinating Center.

The National Institutes of Health intends to use these funds to support new researchers who plan to pursue intensive training in metabolomics under the mentorship of an established researcher. These NIH Mentored Research Scientist Development Awards are funded under NIH's Common Fund Metabolomics Program, which is aimed at increasing metabolomics research capacity in the next few years by providing support to postdoctoral fellows or to emerging scientists. The focus areas of training for newly recreated researchers include bioinformatic methods for metabolomic analysis, mass spectroscopy, nuclear magnetic resonance imaging and data management. NIH expects that funding these R&D mentorship training projects will enable researchers to gain experience in metabolomics, help launch their

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independent research careers, and make them more competitive for new research project grant. This will also motivate new undergraduates to take up metabolomic research in graduate school, resulting in constant supply of quality manpower to increase the research output.

Recently, Bictash et al. [4] published a review to increase awareness of the application of metabolic profiling strategies to large scale population studies and to provide epidemiological and basic science researchers with an idea of future advances in the emerging field of metabonomics. Metabonomics is another term used in relation to metabolic profiling, and refers specifically to metabolic measurements in organisms in response to external stimuli or genetic modifications. Bictash et al. [4] using high-throughput technologies and advanced spectroscopic methods, applied metabolic profiling to large-scale epidemiologic sample collections, including metabolome-wide association (MWA) studies for biomarker discovery and identification. The review discussed specialized algorithms to analyze data and raised the key issue of metabolite identification in studies of human populations. It also suggested the use of various bioinformatics approach to place the putative biomarkers into various pathways.

The key priorities of NIH Common Funds Metabolomics program include 1) generation of more metabolite standards through increased collaborations between scientists 2) train more scientists in the field of metabolomics 3) Increase the capacity in metabolomics by establishment of more centers 4) development of metabolomics technology.

Future growth of the metabolomics market will be driven by three key areas: biomarker discovery services, the application of bioinformatics/chemometrics and the development of technology platforms, leading to a market size of over US $2 billion by 2012. The United States is currently the single largest market for metabolomics garnering a significant share of the world market. Europe and Asia-Pacific follow the lead as the next significant markets. In terms of fastest growth potential, the Asian market is predicted to grow at about 16% through 2017.

In the post genomic era, metabolomics has risen from the shadows of transcriptomics and proteomics as a field of great significance for both translational and basic biological research. Unlike genomic and proteomic strategies for probing human disease, metabolomics may make an almost immediate clinical impact by allowing doctors to deliver personalized medicine, based on metabolic profiling of patients. So, is there a future for metabolomics? Yes! The technology is still under development but is already well established in many fields. The amount of data which can be generated, analyzed and turned into a biologically-relevant knowledge is huge and opportunities abundant for anyone interested in metabolomics.

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