
EDITORIAL

Prioritizing personalized medicine

When Dr Michael Hayden, President of Global R&D and Chief Scientific Officer of Teva Pharmaceuticals, was asked what he thought was the largest challenge to moving personalized medicine into the clinic, he gave one clear pointer: reverting health care from treatment to prevention. Currently the medical arena is focused on reimbursing and treating diseases though our entire concept, says Hayden, should be changed. Now that reading a patients' genetic information is cheaper and easier than an MRI test we should approach this avenue more often. The most prominent field that is taking the first steps in personalized medicine is cancer, where therapeutics depends on the genomes of the cancer and the patient.

For those who are new to the field, next-generation sequencing (NGS) or deep sequencing is a game changing disruptive technology. This second-generation sequencing machine possesses the ability to read the entire DNA content of an individual in a matter of days. This opens avenues for gaining unprecedented amounts of genetic information, which after careful and challenging analysis might hint to a potential therapeutic approach.

Dr Hayden clarifies that there is still a long road ahead until health care providers embrace this idea; they need to deeply understand that genetic information is as important, or an integrative part of, medical treatment. It should even start earlier, Hayden clarifies; medical schools, geneticists and physicians should understand and believe that this can influence management of many diseases if we learn as early as possible about the susceptibility to particular diseases. This would proceed only with the professional interpretation of the data, and the involvement of primary care users, bioinformaticians and genetic counselors and geneticists.

Dr Hayden identified the first mutations underlying lipoprotein lipase (LPL) deficiency and developed gene therapy approaches to treat this condition. This was the first approved gene therapy product in the world marketed since 2012. Effectively, this means that *LPL* gene mutations are scanned in order to determine the functional activity of the enzyme, which is interpreted to the level of the patients' immunogenicity. The outcome is an operative decision of

whether a single annual injection can be the effective treatment.

Dr Michael Hayden is the recipient of numerous prestigious honors and awards. Only recently he was awarded the Diamond Jubilee Medal, on behalf of HRH Queen Elizabeth II, in recognition of his significant contributions and achievements. In June 2014, Dr Michael Hayden received the Personalized Medicine World Conference Luminary Award in honor of his leadership and significant contribution to the advance of personalized medicine.

TEVA Pharmaceuticals is taking key steps in the personalized medicine revolution. They are recruiting teams to head this field, establishing new opportunities for research and leading clinical trials in this arena. Specifically, TEVA invests in stratifying patients' genetic information in order to gain a better understanding of their gene function. These commence with genetic analysis, are based on pharmacogenomic databases, involve care systems, and eventually, one day, will lead to tailored therapeutics.

Earlier this month in a Clinical Genomic Analysis Workshop conducted in IBM-Haifa (Israel), co-organized by IBM and the Edmond J. Safra Center for Bioinformatics at Tel-Aviv University, four key figures in the field were asked to describe their perspective of personalized medicine.

Professor David Sidransky of John Hopkins Medical University and Hospital stressed that there should be another quantum change to make the next leap of understating in personalized medicine. The pharmaceutical industry needs to acquire more response data to oncology drugs and dig deeper in order to better understand the large amount of data already collected. It is not only about genetics, Sidransky says, but also about epigenetics and cellular microenvironment in primary tumor models collected from patients and implanted in mice creating patient avatars for the industry. Once we understand all of these factors and test these avatar models extensively our track to personalized medicine will be clearer. Regarding the challenges ahead, Sidransky clarifies that gathering the relevant molecular data together with clinical data is pivotal to success.

Dr Ajay Royyuru, the Director of the IBM's Computational Biology Center at the Thomas J. Watson Research Center in New York gives the example of 42 comprehensive cancer centers in the USA that, surprisingly, more than half of have a molecular tumor board, which discuss genetic changes and their effect on therapeutics. This means that the clinical decisions in these centers are based, at least partially, on genomic information. Specifically, IBM is employing their "Watson" cognitive computer system to the task. He adds that we need to invest efforts in longitudinal studies, which will aid in finding the early indicators of disease.

Dr Iris Grossman, Global Head of Personalized Medicine and Pharmacogenomics at TEVA Pharmaceuticals indicates that more than 10% of drugs have genomic information on their labels (these are mostly CYP gene family related). A total of 19 companion diagnostics were developed for drugs; and a large number of DNA-based prognostic and diagnostic tests are FDA cleared; some of which are also used to inform treatment decisions (such as for cystic fibrosis management), including sequencing-based assays. Approximately 30% of undiagnosed genetic diseases can be solved by using NGS of the patients' and some family members' DNA. Of these, a small proportion would be found to be treatable using existing drugs.

Isaac Kohane, Professor of Pediatrics and Health Sciences and Technology at Harvard Medical School, calls not to underestimate rare genetic mutations, which aggregate to 4% of the patients worldwide. The NIH supports the 'Undiagnosed Disease Program/Network' initiative, involving eight national centers in the USA. Out of around 1000 patients sequenced by the initiative there is a 30% success rate in identifying the causative mutation. Kohane, who is also the principal investigator for the coordinating center, hopes that after all the genetic and clinical data is collected, following its parsing and analysis, the interpreted information can be made understandable for physicians.

Overall, the advent of new genetic technologies places researchers and physicians in a prime position to take advantage of the plethora of data in order to interpret the information for clinical use. Dr Michael Hayden of TEVA is a magnificent example of how personalized medicine is prioritized and embraced by the pharmaceutical industry.

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