Opinion

Postgenome medicine and proteomics: the challenge of N-of-1

Summary

Discovery in molecular biology operates with the sample sizes of about n=3 up to several dozen. Validation phase prescribes the power of sampling above hundreds, while for the clinical study 1000+ samples are an essential requirement. Suppose the subject is the only "uber-client" of OMICS-based technology?. When does this anonymous subject come to be an actual person who is genuinely concerned about the n-of-1 study?

Keywords: N-of-1 trial, precision medicine, uber-client, biomarkers, proteomics, metabolomics

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Opinion

The postgenome medicine notion has been coined for the gene therapy, which amounted to targeted cure for the heritable defects of a particular person.[1,2] Today we witness the recurrence of the idea in the form of the gene editing by CRISPR/Cas9 system. That is an evolutionary leap from delayed emergency to hasty medical treatment. Situation designates the upcoming challenge of interfacing between "small data" (a particular embryo, so n=1) and "big data" (the compendium of the genome-based knowledge).

Today personal genomics provides some illustrative examples including sequencing of 1mln genomes of US citizens (precision medicine put forth by President Barack Obama).[3] As a matter of fact, OMICS-based technologies are much closer to the case of n=1, than genomics. However, given there are no useful biomarkers delivered by the omics-science, the contrary could be articulated.[4,5] If there are no biomarkers, it suggests that either proteomics is intrinsically handicapped, or it is used improperly.

Genomics influenced the modern molecular science to a great extent.[6] However, the interpretation of DNA-information suffers severely due to the "OMICS" suffix. Omics bridge a gap between the genome and other technology-oriented omics disciplines, including proteomics, metabolomics.[7–9] Being a specific case of n-of-1 science proteomics is a specific type of omics-science, indeed. Genes can be multiplied, while proteins cannot. Each protein goes its own way, being a sole creature, being n=1, without any chance to be cloned, multiplied or amplified. Due to the limited lifespan, proteins are more selfish than genes, that is why genomics provided just "small data", while proteins are the "big-data". The more selfish those proteins are, the more data should be retrieved about their behavior and habits. That is like taking selfies with a smart phone.

Conventional proteomics tries to follow the same path as Human Genome Program, but nothing works out. Just as we read each and every gene of the genome, so we expect to obtain the same observability for proteins.[10,11] As opposed to the planar genome, proteome is an object of real world with dimensions of width and breadth.[12] The width designates a variety of proteoforms (plenty of which are not observed in a proteomics exercise). The depth of the proteome is articulation of an orthogonal problem: the number of proteoforms is dependent on the sensitivity of the measurements (which is in some way a function of time.[13,14] Even though there were exhaustive information on each and every single protein with all of the peculiar modifications at a given moment, we doubt if it would be of much use. Proteomics is technology driven and therefore technology limited.[15]

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In one respect, we need to know everything about each protein, but this being so, no further significant information about health and disease will ever come up.[16] That is a typical formulation of "big-data" or "data-enabled" problem. By the right of succession the Human Genome Program it is generally thought that Big-data is fairly volume because they take a lot of storage capacities and "Winchesters" to be saved. It should be noted that in proteomics "Big Data" is not a problem of data storage; it grew to be concern of N-of-1 science.[17,18]

Postgenome medicine is being re-evaluated. It is the postgenome n-of-1 data, which have, by no means, no relevance to the genome or to the medicine. Postgenome medicine holds itself out as a specific P4 domain, matching a condition, when number of samples strive for the One, ultimately, when n=1. In such a domain the challenge of communication is clearly pronounced. For a regular molecular biologist it is hard to accept that next step of proteomics is related to molecular "sociomics" but not to the findings as to how molecules behave by themselves.[15] The clue is to use biomolecules as a matrix to study the society of citizen scientists. Oddly enough, we feel that post genome medicine serves the cause of an "uber"-client

"Uber" stands for "super" in German. In modern sense of the term "Uber" is a worldwide taxi service for a client with a smartphone. The trend of "uberization" came to medicine, the post genome medicine attempts to dissolve the role of a physician, to substituting to some extend the clinical practitioners by advanced technology, Dr. Watson.[19]

In contrast to uberization of medicine the post genome era puts forward the vision of "uber"-client, who match the simplistic formula of n=1. There are parties, which serve an uber-client: the clinician, the means for body-digitalization (from X-ray/MRI to wearable devices) and the data analyst. Inside the paradigm, efficiency of communication sets aside precision of particular measurement. The

challenge of n=1 is to deploy an uber-client and a regular scientist for them to interact with the physician and the data analyst so that valuable content could be obtained. Such an arrangement is necessary because, having previously been communicatively isolated, the n-of-1 participants lack team play. Admittedly, isolation is characteristic of n-of-1.

Over the last twenty years proteomics contributed modestly to the medical research and little or nothing to the fundamental biology. That may indicate the weakness of proteomics and other omics which are unable to regularly operate single molecules or single cells. Dating back to the 20-th century, proteomics is trying to pave its way into 21-st century.[7,20] Since the years of development of proteomics the world has taken to the communicative media. That requires making omics-based decisions, which could be communicatively interwoven into the landscape of the post genome medicine. The proteomics scientists have to opt either to intrude into the Big-data science, where n=1, or to retain within the small data, where n is in the range of 10 to 100.

Conclusively we detach the post genome medicine as a specific area of in-depth molecular interventions into human life. The area is envisaged a deficiency of back-and-forth connections between an "uber"-client and data analyst.[16] The post genome medicine is relevant as a communicative Big-data channel - not precise but quite intelligent. Proteomics, as other data-enabled omics, makes up a data-intensive domain where molecular biologist enters the area of social science for the first time.

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Conflict of interest

The author declares no conflict of interest.

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