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Prescriptomics: the next frontier in medicine

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Analysis of proteins has been an integral part of clinical chemistry for decades. However, recent technology advances have opened new opportunities for the large-scale analysis of proteins for clinical diagnostic purposes and personalized medicine [1]. First, the development of mass spectrometers with significantly higher resolution and larger dynamic range has allowed generating high-quality quantitative data from complex sample matrices such as serum, plasma, urine, cerebrospinal fluid, and tissue biopsies without the need for isotopic labellings [2, 3]. Instruments like TOF, Orbitrap, FT-ICR and the most recent timsTOF [4, 5] were a stepping-stone towards proteomic-based personalized medicine by facilitating the detection of patient-specific protein signatures that reorganize over time due to genetic, environmental, and treatment constraints.

Second, the development of high-throughput robust sample preparation methods has allowed the processing of many clinical specimens in an efficient and reproducible manner [6]. Parallel to such achievements, the exciting advances experienced by bioinformatics have been a cornerstone in translating quantitative proteomics data into actionable clinical information [7]. Thus, the development of new and powerful algorithms, artificial intelligence, and information theoretics, combined with large datasets available in data repositories such as TCGA [8] or Proteome exchange [9] are moving biology and medicine where no other sciences have gone before [10]. Nowadays, the proteomics community is addressing a critical question: is it possible to obtain helpful information from these datasets to determine which combination of FDA or EMA-approved

drugs is best suited to treat each patient? [11]. Exciting discoveries are expected from re-analyzing these already available datasets.

The concept of genomics soon evolved into the concept of phenome [12], the latter referring to the actual expression of an individual's genes. As phenomics evolves and matures, it is becoming clear that pre-defined categories where diseases were classified and grouped, contradict the vast heterogeneity of phenotypes. Thus, the treatment of phenotype-dependent complex diseases with extensive heterogeneity, like cancer, is likely to overlook unique patients that must be treated individually. We are what we express. And what we express can be now quantified with unprecedented precision and accuracy. By quantifying the proteome expressed by a patient, any disease can be diagnosed, prognosed and followed either using a tissue or in a liquid biopsy (urine, serum, plasma). However, a challenge remains. Can the information provided by proteomics and phenomics be translated to prescriptomics? This is, based on patient-specific alterations in protein-protein networks will prescription be personalized? Yes, proteomics will be a good bridge between diagnostics and therapeutics. This is our best answer based on our current knowledge on disease, genomics, proteomics, and phenomics [11–16].

So far, this is how we visualized the revolution in medicine ahead of our time. Within the next five to ten years, the ultrafast analysis of proteomes of liquid and solid biopsies via high-resolution mass spectrometry will be done in minutes. Currently, mass spectrometry technologies allow

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for the absolute quantification of hundreds of proteins in just 15 min. [16, 17]. Next, the bioinformatic analysis of the sampled proteome(s) will deliver information about the altered biological pathways in each patient, for instance, to uncover whether specific signalling pathways or the inflammatory and immune response pathways are dysregulated [18, 19]. Also, it will collect information about single and well-characterized biomarkers to complement the information taken from the interpretation of the proteome.

Altogether, each unique phenotype will lead to a personalized prescription based on a diagnosis done at a protein-pathway interaction level. This is what we call prescriptomics. Further, linking this technology with communication via electronic interface and drone delivery will make physician and patient interaction faster. Within the next ten years, technological tools will be implemented, allowing proteomic analysis to be done at home just using saliva or urine, not to mention blood. These tools are currently used in hospitals, but interfaces making them ready to use at home are soon expected. By accomplishing the tool to the computer or the mobile phone, the information will be delivered to the physician via a software interface addressing a potential prescription. In case of need, specific tools or sample collecting devices will be provided to the patient and picked up by drones, then transporting again the sample to the laboratory of analysis. Such an approach brings several advantages. For instance, a lower number of patients attending the hospital face to face, thus avoiding the risk of becoming infected or vectors spreading diseases. Also, a most effective medical decision making is expected. Furthermore, the following up of the patient's proteome during and after medical care will thus be made easier and will allow the implementation of dynamic therapy as the standard method to treat disease providing a unique system to alert for relapses.

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