Commentary

The potential of Precision Medicine

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ABSTRACT

The evolving field of Precision Medicine is revolutionizing drug discovery and healthcare delivery. In this article, we take a look at how this nascent field has already impacted drug development for targeted therapy and the widespread use of genetic testing to assist clinical decision making at point-of-care. We also examine how the interaction of people and technology plays a critical role in Precision Medicine delivery. Finally, we conclude with how Precision Medicine can bring healthcare’s spiralling costs down, while improving patient outcomes.

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1. Introduction

Personalised or Precision Medicine, as it has been called more recently, is evolving and growing rapidly across the globe. Precision Medicine offers a more personalised and targeted approach to disease diagnosis, treatment and prevention, that takes into account the individual patient’s lifestyle, environment and genetic makeup. From Prime Minister Cameron pledging in August 2014 that the UK will sequence 100,000 human genomes by 2017 [1] to US President Obama announcing the Precision Medicine Initiative in January 2015 [2], governments are increasing their public spending on such initiatives. Elsewhere, the Kingdom of Saudi Arabia has already embarked on their Saudi Human Genome Project [3], Qatar launched the Qatar Genome Project [4] and according to The Australian, public and private organisations in Australia are contemplating their own 100,000 genomes project [5].

2. Some success stories of Precision Medicine

Precision Medicine employs a much more patient-centric care delivery approach, moving away from one-size-fits-all therapeutic strategies characteristic of the past. While there are many examples of the use of Precision Medicine in Oncology, its practice in other therapeutic areas is also emerging.

In an effort to provide a more targeted therapy without the life-threatening side effects of conventional cytotoxic chemotherapy, a pioneer cancer drug was Tamoxifen in the early 1970s that targeted Oestrogen Receptor (ER)-positive breast cancer cells. However, this drug was originally developed as a morning-after contraceptive pill in 1966 and was later reinvented for treating breast cancer [6]. An important discovery in the late 1990s that paved the way for the use of biomarkers in rational drug design was Imatinib (Gleevec), a tyrosine kinase inhibitor that targets the BCR-ABL protein in Chronic Myelogenous Leukaemia. The BCR-ABL protein is encoded by a fusion gene that arises from a chromosome translocation that generates the Philadelphia chromosome. This also highlights the importance of basic science in rational drug design. It took just two and a half years from new drug application to FDA approval in 2001, highlighting how strategic targeting of biomarkers can accelerate drug discovery [7]. Another example of targeted therapy based on biomarkers is Ixacaftor (Kalydeco), which targets the CTRF G551D mutation present in 5% of Cystic Fibrosis patients [8]. The table below lists more examples of FDA approved targeted drugs and their biomarkers (Table 1). These drugs demonstrate how Precision Medicine, based on a refined, deep understanding of genetic variance and patient individuality, can impact clinical trial effectiveness, time-to-market, drug efficacy and safety. Today, 42% of all drugs and 73% of oncology drugs in development have the potential to be used in Precision Medicine delivery [9].

Precision Medicine has also been applied to disease prevention and diagnosis. An example of targeted prevention of cancer is Curcumin, an anti-inflammatory drug that inhibits nuclear factor kappa B activation, which is involved in many cancers [10]. In the area of diagnostics, Oncotype DX was one of the first genomic tests
approved in 2004, able to determine the likelihood of disease recurrence in women with early-stage ER-positive breast cancer by analysing the activity of a panel of 21 genes [11]. Today, more than 2000 genetic and genomic tests are used routinely for prognostic, diagnostic and forensic purposes, including disease diagnosis and risk estimation, drug suitability and dosage (i.e. Pharmacogenomics), non-invasive prenatal testing (NIPT), paternal testing and so on. Traditionally, these genetic tests examine one gene, as in the case of monogenic diseases, (i.e. diseases caused by a mutation in a single gene such as Cystic Fibrosis), or a small number of genes, as in Oncotype DX. With the advent of new, faster and cheaper genome sequencing technologies, we now have the possibility of examining the entire exome or genome to identify multiple mutations or genetic variations that may be associated with any given disease phenotype, an ability highly relevant to complex diseases, such as cancer, heart disease and type 2 diabetes.

3. Use of technology in Precision Medicine

It is becoming increasingly evident that a large number of disciplines and technologies need to work together towards empowering personalised, point-of-care treatment. Biologists, bioinformaticians, software engineers, molecular pathologists, genetic councillors and physicians all form the core of Precision Medicine. From research and discovery to care delivery, this wide spectrum of disciplines requires the latest cutting-edge technology, including medical devices, such as next generation sequencing (NGS) platforms and enterprise software, such as electronic health records (EHR) and clinical decision support tools. Today, a number of health systems in the US, such as the Mayo Clinic and the Sloan Kettering Cancer Center, have the capability of running NGS-based genomic tests for diagnostic purposes in their own labs. In the UK, the Oxford University Hospitals NHS Trust provides 46-gene panel testing that can help predict cancer patients’ responses to treatment [12]. Additionally, a number of molecular diagnostic vendors provide NGS-based genomic tests, including Foundation Medicine, Myriad Genetics and Genomic Health. Such molecular diagnostic testing is already becoming part of a new standard of care and will be progressively adopted by hospitals across the world.

Performing NGS-based tests routinely, leads to the proliferation of data, referred to as omics data. Hospitals need the capacity to manage and indeed combine omics data with real-world clinical data collected at point-of-care. Oracle has addressed this need through its Translational Research Center (TRC), a data management platform deployed at leading medical centres globally that can store and aggregate a vast amount of clinical and omics data easily and efficiently [13]. Users can access the data securely for downstream analysis by proprietary and open source applications, such as Spotfire, tranSMART and the R statistical package. More recently, software applications, such as Oracle Healthcare Precision Medicine (OHPM) and GenoSpace FullView, provide powerful solutions able to integrate results from genomic tests, allowing users to filter and annotate genetic variants in order to facilitate clinical interpretation and genomic reporting. Such genomic reports are already integrated in clinical decision support systems and are helping physicians in their everyday care delivery workflows.

4. Can Precision Medicine tackle healthcare’s spiralling costs?

The ageing population has skyrocketed healthcare expenditure, which stands at approximately 9% of UK GDP and 17% of US GDP according to data from the World Bank [14]. Precision Medicine can play an important role in addressing this defining, global problem.

Getting the right drug to the right patient at the right dose could save significantly more in treatment costs. In the US, Intermountain Healthcare has published the results of a retrospective study where the survival time of patients with metastatic cancer of diverse subtypes receiving “precision cancer medicine” nearly doubled that of those on conventional chemotherapy. At the same time the cost for patients receiving precision cancer medicine was lower than that of control patients on standard treatment. Therefore, it was shown that additional survival is not associated with increased costs [15]. The potential of Precision Medicine to improve patient outcomes, while minimising harmful side effects and doing so in a cost-effective way, has led several governments to put Precision Medicine high on the agenda. The future of Precision Medicine is bright and this is great news for patients.

Conflicts of interest

Dimitris Kalaitzopoulos is Director of Precision Medicine Solutions at Oracle Health Sciences.

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Ethical statement

None.

References


