ORACLE®
Health Sciences

Bridging the Gap in Precision Medicine

An Informatics Solution Connecting Research, Pathology, and Clinical Care

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Executive Summary

Precision medicine continues to expand its reach in clinical care as genomics-based, translational research yields major scientific advances. Oracle Healthcare has designed a solution suite that enables collaboration between researchers, molecular pathologists, and clinicians utilizing a common foundation of shared information and communication.

Each stakeholder has an important, coordinated role to play in delivering high-quality, scientific research to the bedside to improve patient care and outcomes. This kind of patient care can also yield further basic science research and clinical trials, completing the loop of translational medicine by further advancing scientific discovery.

Understanding the interconnected needs of researchers, pathologists, and clinicians, Oracle Healthcare Precision Medicine (OHPM) enables the entire team to operate from a common informatics system. Yet, it does not sacrifice the unique workflows that drive efficiency and productivity in individual departments within the broader organization.

Oracle Healthcare incorporates internal omics, clinical, and other data while also providing access to external public and proprietary knowledge repositories to empower precision medicine teams. Taken together, these elements effectively interpret and act upon all information available to them.

Precision medicine will continue to become an integral part of medical research and care delivery, and Oracle Healthcare continues to support institutions striving to provide the best possible results from that work.

Introduction

Although precision medicine has numerous synonyms (personalized medicine, targeted therapies, individualized medicine, stratified medicine, etc.), they all share a core objective. That is, to tailor the treatment and prevention planning through more accurate diagnosis based on the molecular profile of each patient.

Precision medicine focuses therapeutic and preventive treatments on patients who will most likely benefit, while sparing expense of, and any side effects on those who will not. The realization of precision medicine's promise requires a team of professionals enabled with powerful informatics tools to push the science to the next level, while also implementing the latest discoveries in clinical practice.

Generally speaking, there are three main groups of professionals closely involved in precision medicine. Researchers (who work on biomarker discovery), molecular pathologists (who identify actionable patient biomarkers), and clinicians (who diagnose/plan, treat, and counsel patients), each group has different training and daily workflows. Though they can be further categorized into sub groups (researchers into bio-informaticians and genomic scientists, molecular pathologists into wet-lab technologists and interpretive staff, and clinicians into genetic counselors, registered nurses, ancillary support staff, and treating physicians), this paper discusses the three main groups and their interrelated workflow.

Although each of the three groups generates information through different kinds of processes, their practices are highly interrelated (Figure 1). Ideally, the researcher's discovery of a clinically actionable biomarker influences the molecular pathologist's interpretation of a single patient's molecular profile. The molecular pathologist's interpretation of a patient's molecular profile, packaged in the form of genomic report, influences the clinician's decision in treatment planning. The outcome of a treatment decision provides researchers with new research ideas. The spirit of translational medicine necessitates a tight interactive workflow among these team members from bench to bedside and back to the bench. This constant feedback loop of scientific discovery yields steadily-improving patient care.
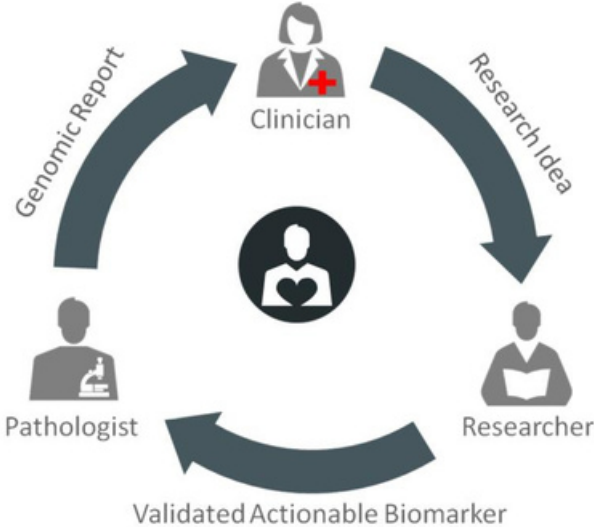

Circle of Influence in Precision Medicine

Figure 1. The three main groups -- researchers, molecular pathologists, and clinicians – participating in the circle of influence makes precision medicine a reality. This figure also illustrates the circle of influence among these three groups.

Effective study planning, however, is becoming increasingly challenging for study sponsors. Factors ranging from greater complexity of study protocols to the increasingly global nature of studies are adding pressure throughout the planning process. In addition, the growing reliance on service providers such as clinical research organizations (CROs) for planning, costing, and conducting clinical studies has reduced the planning visibility and control of study sponsors.

The incentive to be more efficient in study planning is increasing in parallel with the pressures described above. When companies can optimize their study planning, they achieve a higher return on research and development (R&D) capital and are able to compress study planning cycle times, reduce execution timelines, and reduce costs–while maintaining study feasibility.

This white paper explores the current landscape of planning trends and challenges in clinical development, and presents solutions and best practices that biopharmaceutical and medical device companies are utilizing to increase planning efficiency.

Unfortunately, in practice at many institutions, due to the diverse training backgrounds and daily workflows of these three groups, the operations required of each in contributing to a precision medicine-related effort collectively often occur independently of each other. This produces suboptimal data siloes that limit the most efficient combination and utilization of available data that could enhance the team's progress. Cohesive collaboration across these groups often breaks down, preventing the provision of the best treatment for the patient, as well as any continuous advancement in medical knowledge.

Furthermore, a vast majority of informatics platforms and applications have only been designed to address the needs of one group or sub-group of specialty users. These applications, for example, focus on biomarker discovery, clinical reporting, or clinical decision support, alone. None of them is able to bridge any of the existing gaps, or what is missing, from basic biomarker discovery through clinical decision support.

This paper – based on peer conversations with key opinion leaders, literature research, and conference attendance -– discusses what is missing and necessary in current informatics platforms and applications. These missing elements reduce the friction that exists across the circle of influence in precision medicine.

Gap One: Knowledge Exchange Methodology

Knowledge sharing is one of the biggest gaps in the implementation of a precision medicine program. Traditionally, research findings are published in journal articles, leaving the audience with the full responsibility to discover and digest the information. Peer-reviewed journal articles are an excellent means for scientists to share their findings. However, those individual studies may not be easily accessible to drive further advancement and utilization. As a result, the same studies are often repeated in multiple locations, wasting resources. [1] Furthermore, meta-analyses can take years to generate. This can slow the advancement of scientific progress related to knowledge sharing.

When molecular pathologists and clinicians have a question on a newly identified variant in a patient, they want to review the variant information and any case studies with similar patients' prognosis and treatment outcomes. Under this knowledge exchange methodology, the approach often means hours of literature search. Similarly, a clinician may present a patient case at a conference, hoping other researchers will work to validate the preliminary findings or contribute similar cases. However, in practice, this type of case reporting often stalls at the conference stage, because uncovering a matching case means hours to days of manual curation and comparison.

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1 http://www.nytimes.com/2016/01/14/health/moonshot-to-cure-cancer-to-be-led-by-biden-relies-on-outmoded-view-of-disease.html?_r=0

To address the knowledge sharing gap, both the public community and the private sector must contribute to the solution. Public community databases (such as ClinVar[2], Single Nucleotide Polymorphism Database[3] (dbSNP), and Catalogue of Somatic Mutations in Cancer (COSMIC[4])), can provide an application programming interface (API) for research scientists and clinical care teams to submit variants. Metadata information, such as the reference genome version[5], assay type, basic demographic, related diagnosis, treatment information, and outcomes should be part of the submission.

Although the public consortium is a good starting point, this kind of knowledge exchange requires additional contributions from the private sector, such as curation experts and software companies. Curation experts can further distill the submitted information along with other details reported in publications to make the information more actionable to users. Their contributions can be in the form of concise, clinically-actionable summaries on the identified variants after viewing all the clinically relevant assessments. Once the contents are in place, users need simple software applications to access the variants and the associated clinical interpretations.

OHPM makes knowledge retrieval seamless in genomic report creation. Researchers and molecular pathologists can efficiently assess and synthesize available data for rapid interpretation to share with their clinical colleagues to impact treatment planning. OHPM pulls corresponding interpretations through an API connection to multiple publicly and privately curated knowledge databases. This allows molecular pathologists to abstract the most relevant interpretation into a genomic report which is released to clinicians after an internal approval and sign-off procedure. The knowledge pulling from disparate public and private databases is automated, based on the detected sequence variants. A concise, clinically actionable summary is present at the very beginning of the report and the detailed evidences, such as supporting publications, are presented in the section details. Using this format, molecular pathologists and clinicians can understand the critical information.

Given the rapid growth of domain knowledge in precision medicine, OHPM provides a version control capability. This means that there can be complete traceability – no matter the versioning – back to the original evidence. If a clinical genomic report linking a drug and a variant had been created six months ago, and the understanding of the drug's effect had changed within those six months, there would be a way for the molecular pathologist (who signed off on the clinical genomic report), or the clinician (who decided to use the drug as treatment), to locate the original evidence that was cited in creating the report to fulfill the compliance requirements.

Gap Two: Genomic Nomenclature

Due to different training and background experiences, researchers, molecular pathologists, and clinicians have their own genomic nomenclature preferences. This leads to communication challenges across the three groups. When describing a DNA sequence variant, researchers often prefer a description of the genomic coordinate and the underlying nucleotide change. They are also interested in quality score and reference identities to other public databases (such as dbSNP, COSMIC, and Online Mendelian Inheritance in Man (OMIM[6])). However, clinicians often have a much lower description specificity of the same variant, most likely at the gene level. Some can name the exome number or the amino acid change and the associated coordinate.

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2 http://www.ncbi.nlm.nih.gov/clinvar/

3 http://www.ncbi.nlm.nih.gov/snp/

4 http://cancer.sanger.ac.uk/cosmic

5 http://www.nature.com/news/technology-the-1-000-genome-1.14901

6 http://www.omim.org

Figure 2 provides a graphic illustration of a specific scenario. There are several common variants in the Epidermal Growth Factor Receptor (EGFR) gene associated with cancer, such as c.2156G>C (G719A), c.2369C>T (T790M), c.2573T>G (L858R), and so on. While researchers often can recite the details of these variants, clinicians tend to communicate at a less specific manner, such as gene EGFR mutated or not.
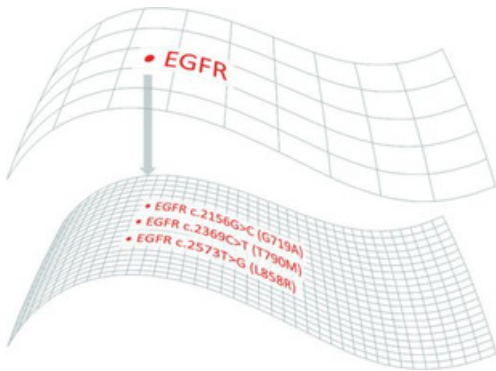

Figure 2. Different levels of specificity in genomic nomenclature between researchers and clinicians

In order to bring research and care delivery together, the nomenclature barriers must be reconciled. This does not mean that researchers and clinicians must use the same terminology. There is no common terminology that allows the three groups to work effectively, each in their own workflows. Nonetheless, they need to communicate seamlessly through terminology translation enabled by informatics technology.

To accommodate these different nomenclature preferences, an informatics solution must capture multiple levels of specificity for each of the variant as illustrated in Figure 2. At the very bottom layer, the solution should store information about the variant, with as much detail as possible, for unique identification of the variant. Reference genome version (GRCh37 vs. 38), genomic position, and nucleotide change must be captured at the bottom layer. The solution also needs to manage coarse specificity descriptions for each variant. Clinicians can retrieve variant information based on the gene and the exome region information, such as EGFR exome 19.

OHPM is designed to address the nomenclature requirements in these multiple levels of specificity. Even though researchers and clinicians have different preferences in nomenclature, OHPM can easily determine whether or not they are talking about the same variant.

Gap Three: Workflow Applications

A third gap exists between the different informatics systems in the research world and the care delivery world. In the research world, data is captured by an electronic data capture system, Microsoft Excel, or (sometimes) paper forms. In the care delivery world, clinicians use an Electronic Health Record (EHR) system to document an episode of care.[7]

Compared to the research world in which forms and data elements are designed prior to a study, the care delivery world frequently uses free text in EHRs, such as discharge summaries. Molecular pathologists commonly use a laboratory information system (LIS) for specimen tracking and report sign-off.

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7 http://project-redcap.org/

The data analytic systems used by the three user groups are also different. While researchers require flexible tools (such as the R statistical package) to analyze data based on public or proprietary algorithms, clinicians require analytic tools for clinical decision support. The majority of analytical tools used by clinicians have been "home-grown" (built by internal IT departments in collaboration with the medical informatics team). There are also several companies building care pathway software for specific therapeutic areas. No matter whether these tools are home-grown or commercial-off-the-shelf (COTS), they tend to be rigid.

Molecular pathologists might require use of several home-grown and COTS analytic applications to identify actionable biomarkers from raw data. Then, they would need to massage the data to produce a structure suitable to report the findings. Analysis reporting using these types of software systems is really quite a cumbersome, semi-manual, process today.

As mentioned in Figure 1, the workflow of the three groups is highly interrelated in precision medicine practice. In order to support the full circle of influence in precision medicine, a good software solution must connect all the disparate data and workflow analytics tools used by the three groups into a common data management infrastructure.

Oracle Healthcare solution suite (Figure 3), including OHPM and Oracle Healthcare Translational Research, links the workflow of all three user groups. One of the core capabilities in the solution suite is to aggregate and normalize the clinical and omics data collected in almost any care and research setting. The connection happens via an EHR or a molecular pathology analytic tool combining into a common repository and making data ready for researchers to discover new biomarkers. The new findings from researchers can then be incorporated into future molecular pathology reports as part of new clinical interpretations of the biomarker, thereby accelerating the "bench to bedside" process and bridging the research divide.

The solution suite also connects the final report created by the molecular pathologist relevant, longitudinal, clinical information from the EHR system via Health Level Seven (HL7) standard.[8] Then, clinicians can review the collective information in the EHR to determine the best treatment strategy for a patient.
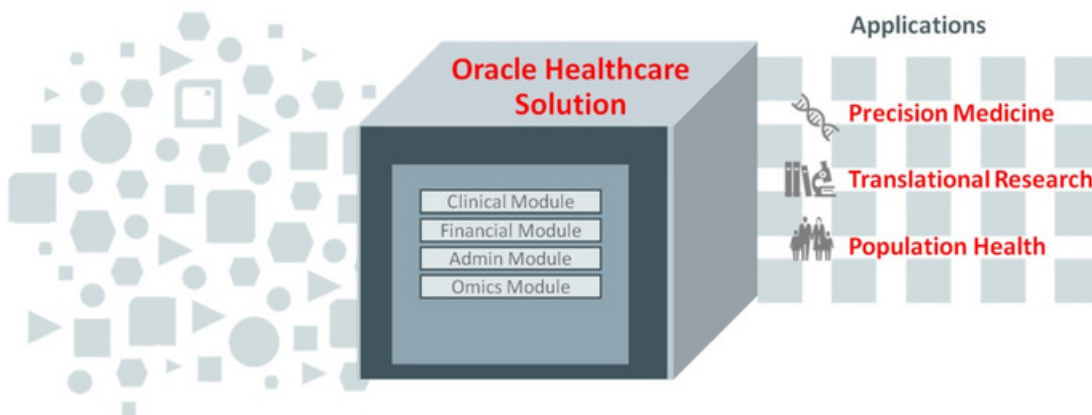

Figure 3. Oracle Healthcare solution suite aggregates and normalizes disparate data and connects workflow analytic tools to support the circle of influence.

8 http://www.hl7.org/

Conclusion

Utilizing the right informatics solution can accelerate applying better targeted therapies and prevention plans in a clinical practice. This kind of solution can also deliver the right information to foster further advancement in research discovery.

Oracle has worked with researchers for many years to aggregate and normalize these large genomic data sets in support of research to identify genetic biomarkers. It has also built cloud based tools to accelerate clinical trial design and implementation. As the science moves from the research setting to application in the clinical setting, Oracle continues to expand its technology foundation in support of precision medicine.

With Oracle Healthcare Precision Medicine, an organization can eliminate silos, streamline knowledge curation/ exchange, facilitate nomenclature communications, and optimize workflows among researchers, molecular pathologists, and clinicians. By advancing the pace of precision medicine with new informatics tools, healthcare organizations can harness the power of precision medicine to improve the quality of care on a global scale.

Oracle Corporation, World Headquarters
500 Oracle Parkway
Redwood Shores, CA 94065, USA

Worldwide Inquiries
Phone: +1.650.506.7000
Fax: +1.650.506.7200

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Author: Wanmei Ou, PhD, Director , Product Strategy, Translational and Precision Medicine
Contributing Authors: Sean Sigmon, Director, Business Development
Summerpal S. Kahlon MD, Director, Care Innovation