WHITE PAPER

Navigating the Odyssey of Big Genomics in Biopharma R&D

DNAnexus®

Contents

Introduction

In Homer's Odyssey, Hermes gives Odysseus an acetylcholinesterase inhibitor derived from a plant called 'moly' to protect him from the witch-goddess Circe's intoxicating deliriants. While modern-day drug discovery lacks the drama of Greek mythology, we are still faced with the odyssey of how to deliver on the promise of genomics-based precision medicine.

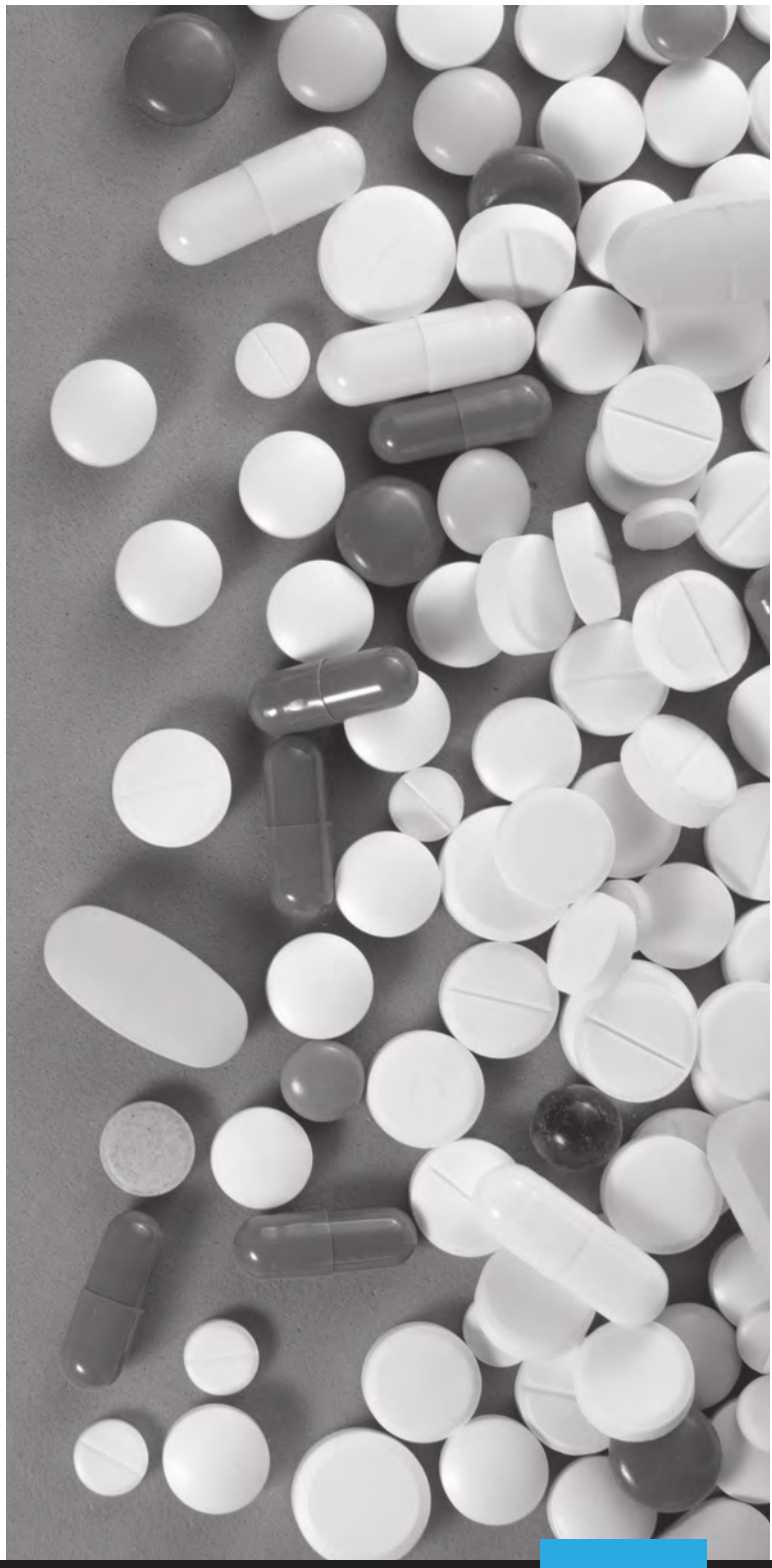
Introduction

Incorporating Genetics into the Early Stages of Drug Discovery

Many pharmaceutical companies are now adopting strategies rooted in human genetics because evidence suggests that doing so can nearly double the chance of a drug's clinical success [1]. Yet incorporating genomics data, while helpful, can also introduce new challenges.

Across the pharmaceutical industry, we've witnessed some of the clever ways that pharmaceutical companies are navigating the journey to incorporate human genetics into the early stages of drug discovery. In this white paper, we highlight three important strategies to consider: cohort studies, strategic partnerships, and building the proper ecosystem.

> ***... cohort Studies, strategic partnerships, and building the proper ecosystem.***



Epic Journeys Call for Epic Cohorts

Bridging the Gap Between Disease SNPs & Interpretation

Since the very first genome wide association study (GWAS) was conducted in 2005, which compared 96 patients with age-related macular degeneration to 50 healthy control subjects [2], GWAS studies have taken a central role in advancing our understanding of common diseases. Thus far, over 3,000 GWAS studies have identified variants that can modify an individual's predisposition to disease.

Yet GWAS tells only part of the story. Although they have contributed to the identification of greater than 100 loci associated with complex disease, because most SNPs identified are located in non-coding regions, researchers are unable to easily discern which SNPs actually predispose individuals to disease.

Functional studies offer one solution for identifying disease-associated SNPs, but they are time-consuming and challenging. Thus, there is a gap between disease SNPs and their more in-depth interpretation [4]. Fortunately, large-scale cohorts involving heavily phenotyped individuals are helping to bridge this gap.

Cohort studies help pharmaceutical companies accelerate discovery by integrating genomic and phenotypic data on a massive scale. Cohort studies associated with genetic data enable researchers to identify common variants associated with an increased or decreased disease risk, identify those rare variants that are potential drug targets, and classify patient populations for which certain treatments may be suitable [1].

GWAS tells only part of the story.

Epic Journeys Call for Epic Cohorts

Applications for Geno/Pheno Data-Dense Cohorts

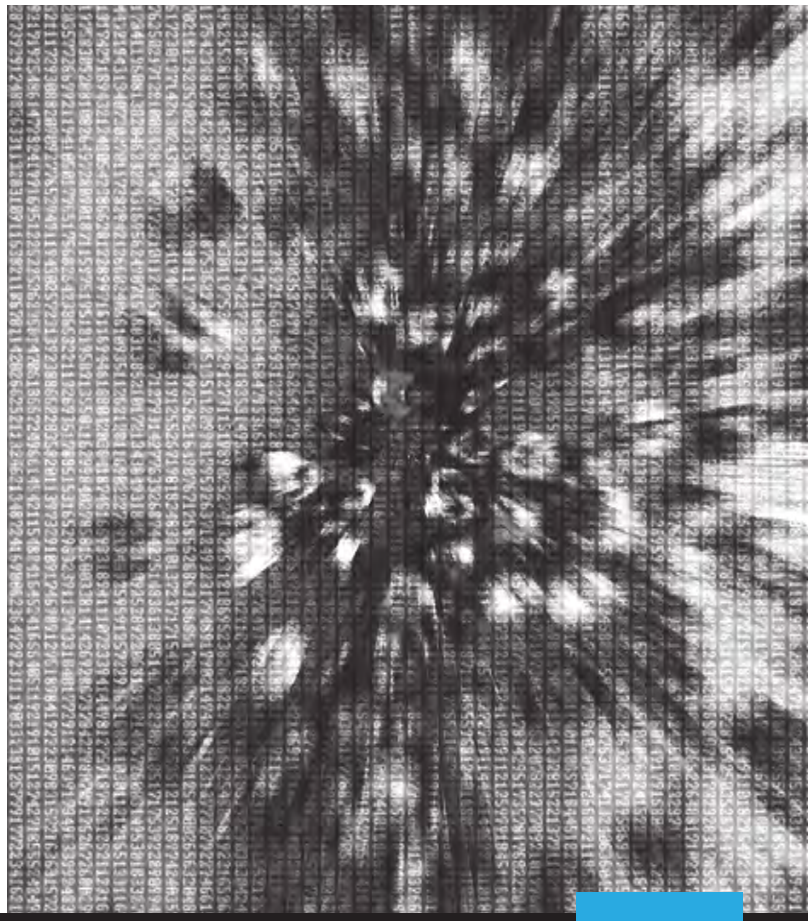
Apart from drug discovery, combining large cohorts of deeply phenotyped individuals with their genomic data is useful in a wide range of applications, including the development of companion diagnostics, patient stratification, and clinical trial recruitment.

The DiscovEHR collaboration between Regeneron Genetics Center and Geisinger Health System demonstrates how next-generation sequencing (NGS) data can be integrated with longitudinal electronic health records for the discovery of genetic variation important to understanding human disease and therapeutic response. Two large-scale studies from this collaboration were published in the journal Science and discussed the analyses of genetic and phenotypic data from more than 50,000 patients. This is one of the richest resources available for drug discovery [4], [5].

Regeneron has also embarked on a joint project with GlaxoSmithKline (GSK), UK Biobank, and a number of other pharmaceutical companies in which the genetic variants of 500,000 people will be analyzed. AstraZeneca announced a similar initiative, which will sequence more than 2 million genomes over the next 10 years to inform discovery and development.

All of these studies seek to combine data from a large number of participants, data that are longitudinal in nature, and subjects who are deeply phenotyped. Combining these datasets involves harmonizing data from multiple sources, such as electronic health records, and multiple formats. At DNAnexus, we believe that the realization of precision medicine will require the intelligent integration of genetic data with a range of additional data types. Successfully doing this requires the technology and experience that will enable the effortless collaboration around large, diverse volumes of data in a secure and compliant fashion.

One way to gain access to large volumes of data is by building partnerships with the right allies.



Find Strategic Allies on Your Journey

Leveraging Existing Datasets

Deeply phenotyped genetic data to use in cohorts doesn't exactly grow on trees. Traditionally, clinical genetic studies are time-consuming endeavors that involve recruiting patients with specific conditions. Moreover, once the patients are finally recruited, the researchers still need to collect and analyze the data on each of these subjects.

Imagine how useful it would be to leverage the knowledge that already exists in a large health system, so that after you designed a study, and decided on the characteristics of patients you wanted to include, you could identify matching patients and controls, all at the click of a button.

Imagine how useful it would be to leverage the knowledge that already exists in a large health system...

This is the situation created by the previously mentioned Regeneron Genetics Center and Geisinger Healthcare partnership. De-identified EMR data from consented Geisinger patients participating in Geisinger's MyCode Community Health Initiative is integrated with whole exome sequencing data from these same patients in an effort labeled the DiscovEHR Project, which is currently being used to drive discovery.

Find Strategic Allies on Your Journey

Symbiotic Relationships

Likewise, many other pharmaceutical companies are discovering that they can't go it alone. Instead, they are seeking out industry partners who have what they need: clinical data. Undeniably, medical centers and health systems are increasingly willing to partner with pharma because they benefit too. Since we are still in the early days of reimbursement for extensive patient NGS testing, medical centers can help finance more in-depth comprehensive genomic analysis through these partnerships with pharma.

Another perfect example is the relationship formed between Advocate Healthcare, a large integrated delivery network (IDN) out of Illinois, and multiple pharmaceutical companies. When faced with a move to its accountable care organization and a move away from fee-for-service based healthcare, Advocate needed to rethink its data collection methods and patient engagement model, which provided opportunities for pharma to conduct clinical studies that could improve the value of their care [6].

Direct-to-consumer genetic test providers also make a suitable ally for pharmaceutical companies. One such example is the relationship between 23andMe and GlaxoSmithKline. Their partnership aspires to improve selection of drug targets, identify drugs that produce less toxicities, and more quickly identify clinical trial candidates [7]. Given that roughly 65% of people consent to sharing their genetic information when they understand the purpose behind it, these relationships make a lot of sense [8].

Pharmas who engage in these partnerships have generally gotten more from the arrangement when clear governance structures are established, when they find partners who are aligned with their product pipeline in some way, and when they engage in creative contracting, so they can pursue additional projects if the opportunity arises [7].

Find Strategic Allies on Your Journey

Pharma Collaboration is Trending

A less expected trend is also beginning to emerge: that of pharmaceutical companies collaborating with each other. The Pistoia Alliance supports collaboration across pharmaceutical companies in a precompetitive space, bringing together key opinion leaders to identify causes of R&D inefficiencies and develop best practices and technology pilots to overcome obstacles. Likewise, PrecisionFDA, a cloud-based community platform launched in 2015 as part of the Precision Medicine Initiative (now All of Us), supports the development of novel analysis tools and regulatory science, and allows pharmas to collaborate with the regulators.

Pharmaceutical companies are even working to redefine the precompetitive space. The Centre for Therapeutic Target Validation (CTTV) posits that when the precompetitive space is expanded and pharmaceutical companies don't compete over identifying drug targets, there's less duplication of efforts, which can ultimately speed a therapy's time to market for a patient who needs it. The CTTV is unique in that it also brings together people from different backgrounds who are all asking different things of the data, sharing their insights with all members [1].

This transparent approach to the global sharing of data, tools, and methodologies reflects an awareness within the genomics community that only through collaboration will the industry overcome significant challenges in the modern-day drug discovery and development odyssey.

Only through collaboration will the industry overcome significant challenges...”

Get a Better Boat

A Platform to Float It All

A significant amount of time in the drug discovery odyssey is spent creating data analysis workflows that can integrate data, process them and generate insights that advance development. There are hundreds of tools that will answer specific questions but none that are a perfect fit for everyone. Researchers should find a flexible platform where they can build a collection of best-in-class workflows and deploy their own proprietary tools.

Ideally, a platform is called for, one which integrates seamlessly with other upstream and downstream system components, including lab information management systems (LIMS) and reporting software and one that is hardened for enterprise-based data management, so that researchers can facilitate consistent workflows and ensure uniform analytical treatment and reproducibility.

We are now witnessing the globalization of pharmaceutical drug discovery and development. It is no longer possible to successfully operate in a single location: data (e.g. NGS and EHR) is sourced from biobanks; researchers are distributed across many locations around the world; and clinical trials can now be conducted in locations such as China. Given the complexity and scale of these efforts, infrastructure requirements must accommodate seamless communication and integration demands inherent to cross-sector partnerships as well as the legal requirements for protection of patient privacy and regulatory oversight.

Get a Better Boat

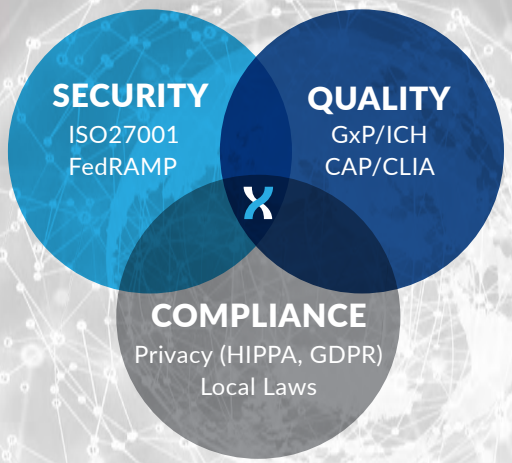
The Critical Need for Security

Above all else, security is a must when working with patient data. With genomic sequencing emerging as a central component to clinical development and the delivery of both diagnostics and therapies, compliance with regulations that apply to the handling of these data, and its subsequent integration into other medical data systems, are equally critical. As raw data are converted into more meaningful information, they become an asset as valuable and sensitive as any other personal information, currency, or intellectual property.

DNAnexus provides a platform that introduces an additional layer of security on top of commercial cloud providers.

A platform that introduces additional layers of security on top of commercial cloud providers, such as Amazon Web Services (AWS) or Microsoft Azure, can provide best-in-class security in the cloud. Platform features such as two-factor authentication, end-to-end encryption, need-based network access control, 24/7 security monitoring and updates, audit and access logging can provide comprehensive security and privacy framework.

DNAnexus® Ecosystem



Find Your Way Home

In Homer's Odyssey, Odysseus eventually did find his way home. He summoned his strength and bravery to do so, but most of all, he relied on his cleverness. There's no getting around the extensive journey that pharma must take to develop new drugs, but by embracing at-scale cohorts, building mutually beneficial partnerships, and honing the proper infrastructure, the journey can become less fraught with obstacles.

REGENERON® GENETICS CENTER

precisionFDA

M2GEN

Case Studies: Co-navigating Precision Medicine with DNAnexus

REGENERON GENETICS CENTER

Regeneron Genetics Center: Enabling one of the largest scale integrations of next-generation sequencing and patient EHR data, DNAnexus worked closely with Regeneron to bring them online, rapidly scale up, and allow the seamless and secure interactions with collaborators like Geisinger Health System.

precisionFDA

PrecisionFDA: The DNAnexus Platform is powering precisionFDA, providing the underlying cloud-based compute and data management infrastructure. In addition, DNAnexus is working with the FDA to build a community around its informatics platform to help drive standards around secondary analysis, the process of mapping, alignment, and variant calling of DNA sequence data.

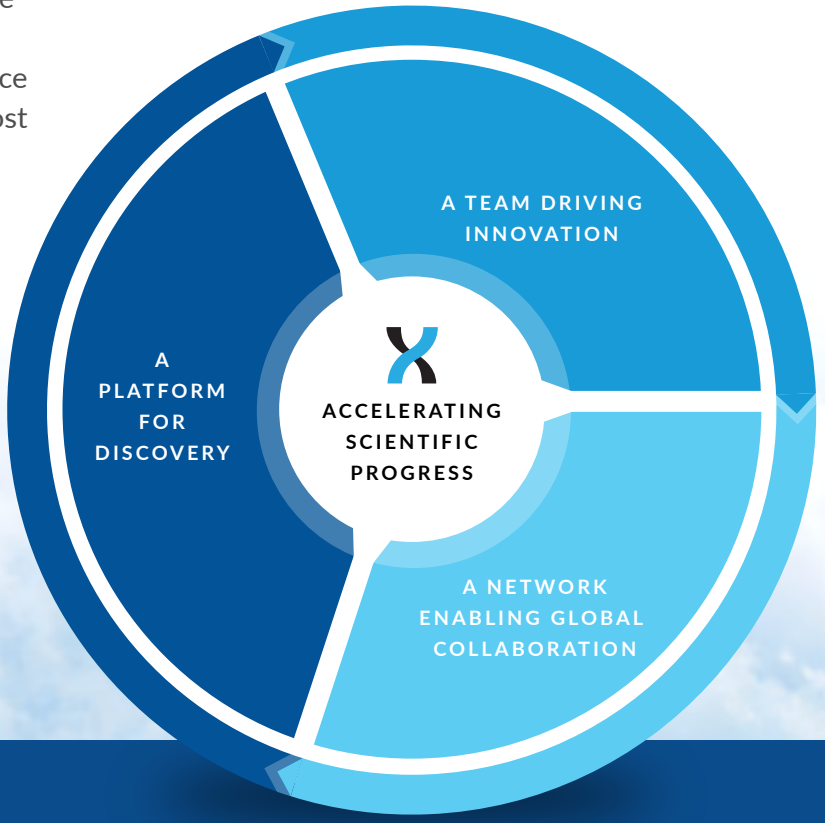
M2GEN

ORIEN Cancer Research Network: M2Gen adopted the DNAnexus Platform to support data analysis and collaboration for the Oncology Research Information Exchange Network (ORIEN) Avatar Research Program. This innovative program joins academic cancer centers and pharmaceutical companies in their efforts to study and treat cancer through the development of more precise treatments for patients.

About DNAnexus®

DNAnexus® has built the world's most secure cloud platform and global network for scientific collaboration and accelerated discovery. We embrace challenges and partnership to tackle the world's most exciting opportunities in human health.

Along with its broad network of partners, DNAnexus helps global companies navigate the modern-day genomic medicine odyssey by providing an environment where data is accessible in a secure and compliant manner, ultimately accelerating drug development and other pharmaceutical science.



Dedicated to Enabling Your Success.

Start the process with a brief scientific consultation to determine how we can help.

Contact us at: info@dnanexus.com

For more information about DNAnexus solutions, visit www.dnanexus.com