ABOUT THE REGENERON GENETICS CENTER AND GEISINGER HEALTH SYSTEM COLLABORATION

The RGC is a large-scale, fully integrated genomics program that builds on Regeneron's long-standing strength in genetics and related technologies.

The RGC uses state-of-the-art automation and cloud-based informatics to sequence and analyze at a rate of 100,000 exomes per year.

With Regeneron’s integrated discovery-to-commercialization capabilities, RGC findings are being used to identify and validate drug targets and pharmacogenetic markers, and to obtain biologic insights into disease and disease mechanisms. This information feeds back into the ongoing work of many functional groups at Regeneron.

Geisinger is one of the largest integrated health systems in the U.S. and a pioneer in the use of electronic health records (EHRs).

It serves more than three million PA residents, throughout 48 counties in central, south-central and northeast Pennsylvania, making it the largest rural health services organization in the country.

Geisinger plans to enroll more than 250,000 fully-consented patient volunteers to share DNA samples along with their corresponding de-identified EHRs.

Geisinger is a leader in utilizing Precision Medicine in practice, and if results of the collaboration are validated by Geisinger in a CLIA-certified lab, clinicians can provide patient participants with such results from sequencing that show understood genetic risks for disease.

THE COLLABORATION

Together, the RGC and Geisinger teams plan to create one of the world’s most comprehensive databases of paired exome sequences (genotypic) and real-world health records (phenotypic) information.

A genotype is a person's unique set of genetic material. The exome is the 1-2 percent of the genome that encodes for proteins. Most disease-causing or disease-protective mutations have been found here, so sequencing the exome is often considered a higher yield and more efficient strategy for gene discovery.

The expression of genes into physical characteristics is called the phenotype. Variations in genes will result in differences in traits such as height, eye color and susceptibility to certain diseases.

By analyzing this data and making associations between genes and disease, the goal of the collaboration is to make discoveries that inform and speed the drug development process and, ultimately, improve patient healthcare outcomes through the development of new therapeutics.
PROTECTING PATIENT PRIVACY

- Patient privacy and consent are extremely important to both the RGC and Geisinger.
- All participants have fully consented to providing their genetic information, and Geisinger de-identifies all health records.

WHAT ARE WE FINDING?

To date, the RGC has sequenced over 50,000 exomes from Geisinger patient volunteers. From this data and data from other collaborators, we are exploring:

<table>
<thead>
<tr>
<th>New gene targets or biomarkers associated with disease</th>
<th>20 novel candidate gene targets found thus far</th>
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<td>Loss of function (LoF) variants that offer insights on a certain gene’s role in health and disease.</td>
<td>Predicted LoF variants have been identified for virtually all of Regeneron’s target genes</td>
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Ongoing use of human genetic findings to identify new targets and validate existing targets from Regeneron R&D and clinical program.

This collaboration also allows for the potential to do “call-back” studies, where the RGC and Geisinger can pursue clinical research on genes of interest and their impact on patient health and disease.

*The relationship with Geisinger is a cornerstone of the effort the Regeneron Genetics Center is building, which we believe can advance the goals of human genetics research and personalized medicine.*

George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer, Regeneron Pharmaceuticals and President, Regeneron Laboratories

*For Geisinger, this relationship is about the potential to improve individualized patient care….we expect that many of our patients and their family members will directly benefit from their participation in this research.*

David H. Ledbetter, Ph.D., Executive Vice President and Chief Scientific Officer, Geisinger Health System

*Electronic medical records let doctors and researchers across the country collaborate more closely than ever before. More powerful computers help us analyze data faster than ever before. If we combine all these emerging technologies, if we focus them and make sure that the connections are made, then the possibility of discovering new cures, the possibility of applying medicines more efficiently and more effectively so that the success rates are higher, so that there’s less waste in the system, which then means more resources to help more people — the possibilities are boundless. So the time is right to unleash a new wave of advances in this area, in precision medicine, just like we did with genetics 25 years ago.*

President Barack Obama