Genome Engineering and Functional Discovery Platform

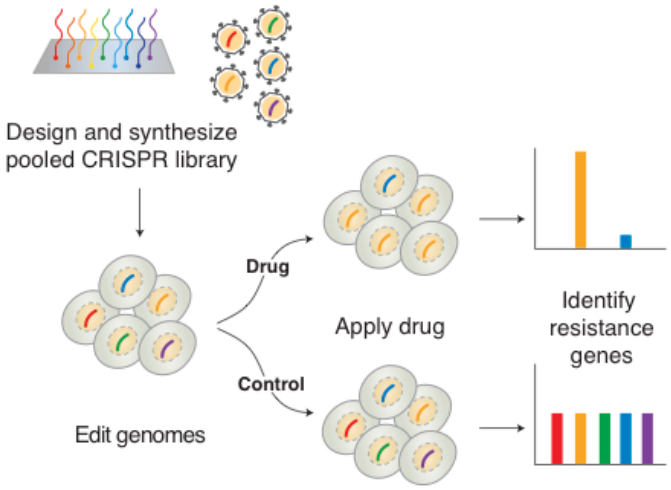
Applying High-Throughput CRISPR Gene Editing for Functional Genomic Screening and Target Identification at the New York Genome Center (NYGC)

The Genome Engineering and Functional Discovery Platform (GEFDP) at NYGC works collaboratively with partners to establish and carry out high-throughput genome editing screens to functionally query emerging disease systems. These functional genomics methods include genome-wide loss-of-function and gain-of-function screens *in vitro* and *in vivo*, as well as scanning mutagenesis to identify functional elements in the noncoding genome. In addition to developing and optimizing new gene editing technologies and pooled screening assays, GEFDP scientists have built the computational tools necessary to analyze genome-wide datasets for functional discoveries. The GEFDP scientific team engages with academic and industry collaborators from experimental design through project execution to optimize the biological system and depth of discovery.

Enabling Genome-wide Screens

GEFDP scientists support collaborators to design and implement high-throughput screens to investigate the effect of genetic alterations on biologic phenotypes of interest, including:

- Pooled CRISPR library design, synthesis, and production
- Cell culture library screening
- Sequencing and data analysis
- Array screen to validate primary screen hits



Value for Collaborative Partners

The expertise of the GEFDP scientists enables collaborators to have access to high-throughput screening technology to:

- Understand resistance mechanisms to a drug of interest
- Identify disease-relevant genetic variants
- Discover new clinically actionable pathways
- Investigate noncoding and regulatory elements

Representative Screen Projects: *Which mutations drive resistance to targeted chemotherapies? What genes are essential to tumor growth and proliferation? Which regions of the genome enable lymphocytes to kill target cells? What are novel druggable targets for metabolic disorders? Where are thereapeutic gene editing targets within genetic association study hits?*

CRISPR Screening Methodology

To create thousands of mutations in the genome, these studies harness a gene editing technique called CRISPR, Clustered Regularly Interspaced Short Palindromic Repeats. This revolutionary technology enables scientists to quickly engineer thousands of CRISPR guide sequences to target many different parts of the genome. It is precise, programmable engineering, and allows parallel editing of, for example, each individual gene in a genome, noncoding regions around a single gene of interest, or a subset of particular genes. Each cell receives a targeted mutation from within the library, and the resulting pool of engineered cells can be tested for virtually any biological phenotype to enable functional discoveries.

New York Genome Center Overview

NYGC is an independent nonprofit focused on advanced genomic research and clinical molecular diagnostic tests to improve diagnosis and treatment of serious diseases. NYGC's next-generation research and CLIA (CLEP) certified clinical sequencing facilities include 16 Illumina HiSeq X machines, yielding 20,000 whole human genomes per year, and 12 Illumina HiSeq 2500 machines for high throughput and rapid turnaround time. High-performance computing infrastructure enables efficient and highly parallelized analysis of large-scale datasets. NYGC's bioinformatics scientists combine streamlined pipelines and diverse technical methods to solve biological problems, including custom application-specific analyses. NYGC creates synergies through collaboration. We have partnered with 600 researchers and clinicians from academia and industry around the world on over 2200 projects. Connect with us to learn more about ways NYGC can help facilitate your genomics research needs.

For more information, please contact:

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The GEFDP is led by Neville Sanjana, PhD. Dr. Sanjana is a Core Member and Assistant Investigator at NYGC and holds a joint appointment as Assistant Professor in the Department of Biology and Center for Genomics and Systems Biology at New York University. He is listed on a number of foundational patents related to CRISPR-Cas systems and functional genomics, and performed the first genome-wide CRISPR screens *in vitro* (*Science* 2014) and *in vivo* (*Cell* 2015) and the first noncoding CRISPR screen (*Nature* 2015).

Review Articles: CRISPR screens (http://bit.ly/NYGC-GenEng1) and applications (http://bit.ly/NYGC-GenEng2)