

# Deep insights into proteins through Deep Mutational Scanning

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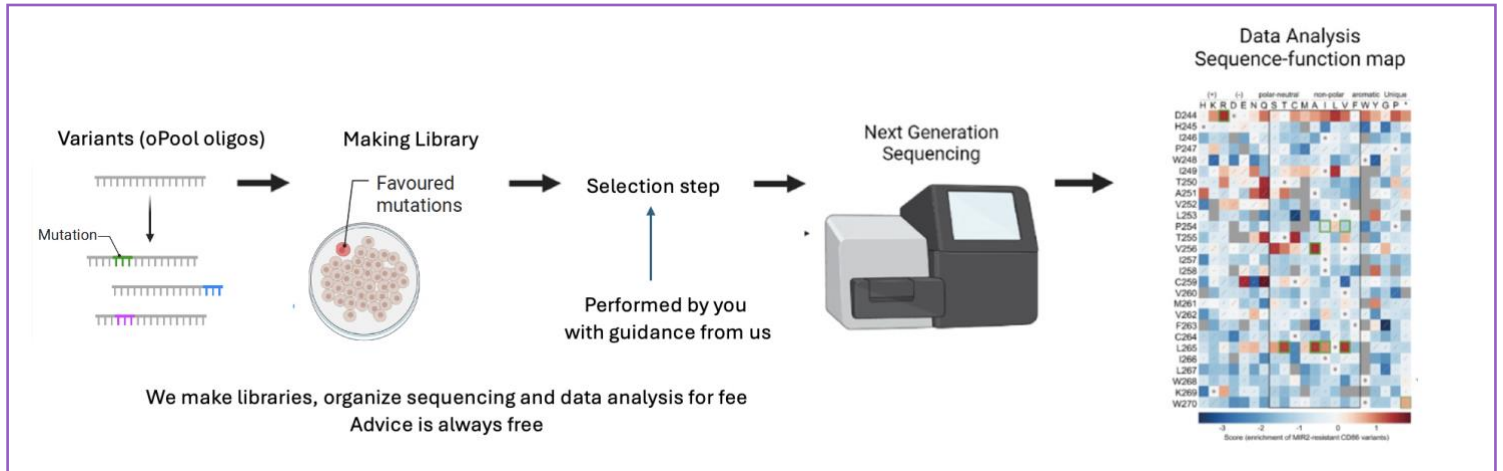
DISCOVERIES FOR HUMANITY

## Introduction to Deep Mutational Scanning

Deep Mutational Scanning is an experimental approach that enables the simultaneous measurement of the activity of  $10^5$  or more unique protein variants using next-generation sequencing technology.

- The depth of data coverage enables the study of protein interactions, protein function, prediction of the severity of the diseases, antibody-antigen binding, and drug escape pathway during its development.
- Now there is a cost and time effective way to measure the outcome of every possible single mutation in your protein of interest.

## DMS workflow



## Variants and making Library

- Codon by codon using oPool oligos with choice of mixed bases, NNN (A,T,G,C) or NNK (G,T) or NNS (G,C) at the position(s) of interest.
- Help with ordering and cloning Twist Libraries by Decode Science for precision libraries.
- Comfortably target regions ranging from 1 to more than 500 codons in phage display or retroviral expression vectors.
- Constructing DNA libraries using diverse cloning techniques (HiFi Assembly, Ligation or Gateway cloning) in electrocompetent cells achieving libraries of up to 1M colonies in one transformation.

## Selections

Any assay where genetic material can be enriched and depleted based on protein function:

Eg Phage Display, Cell-based survival assays, Flow-cytometry based assays, ribosome display, antibody-antigen binding, in vivo selections.

### Next Generation Sequencing step

- Direct sequencing of the target region less than 300bp- Illumina
- Barcoded variants-Nanopore to make barcode-variant lookup table and Illumina for barcode sequencing.

### Data Analysis

- Data is presented in the form of Sequence-function map with enrichment, unchanged and depletion of certain amino acids.
- Bioinformatics data can be easily analysed by the client.
- Analysis programs can be customised.

### Contacts

To discuss collaboration, please contact:  
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**Talk: Mutational profiling of SARS-CoV-2 PLpro exposes inhibitor escape routes (27/03/26)**

## Published Papers

- *Shared and distinct sequence-function signatures define different modes of human TpoR activation*, Xinyu Wu et al. bioRxiv 2025
- *Divergent resistance pathways amongst SARS-CoV-2 PLpro inhibitors highlight the need for scaffold diversity*, Xinyu Wu et al. PLoS Pathog 2025
- *Mutational profiling of SAR-CoV-2 papain-like protease reveals requirements for function, structure, and drug escape*, Xinyu Wu et al. Nature comm 2024
- *Deep mutational scanning reveals transmembrane features governing antibody-antigen surface expression of the B-cell antigen receptor*, Samyuktha Ramesh et al. Front.Immunol 2024
- *Human EGFRvIII chimeric antigen receptor T cells demonstrate favorable safety profile and curative responses in orthotopic glioblastoma*, Rebecca C Abbott et al. Clinical & Translational Immunology 2023
- *Human and viral membrane associated E3 ubiquitin ligases MARCH1 and MIR2 recognize different features of CD86 to downregulate surface expression*, Raphael Trenker et al. J Biol Chem 2021
- *Novel drivers and modifiers of MPL-dependent oncogenic transformation identified by deep mutational scanning*, Jessica L Bridgford et al. Blood 2020