

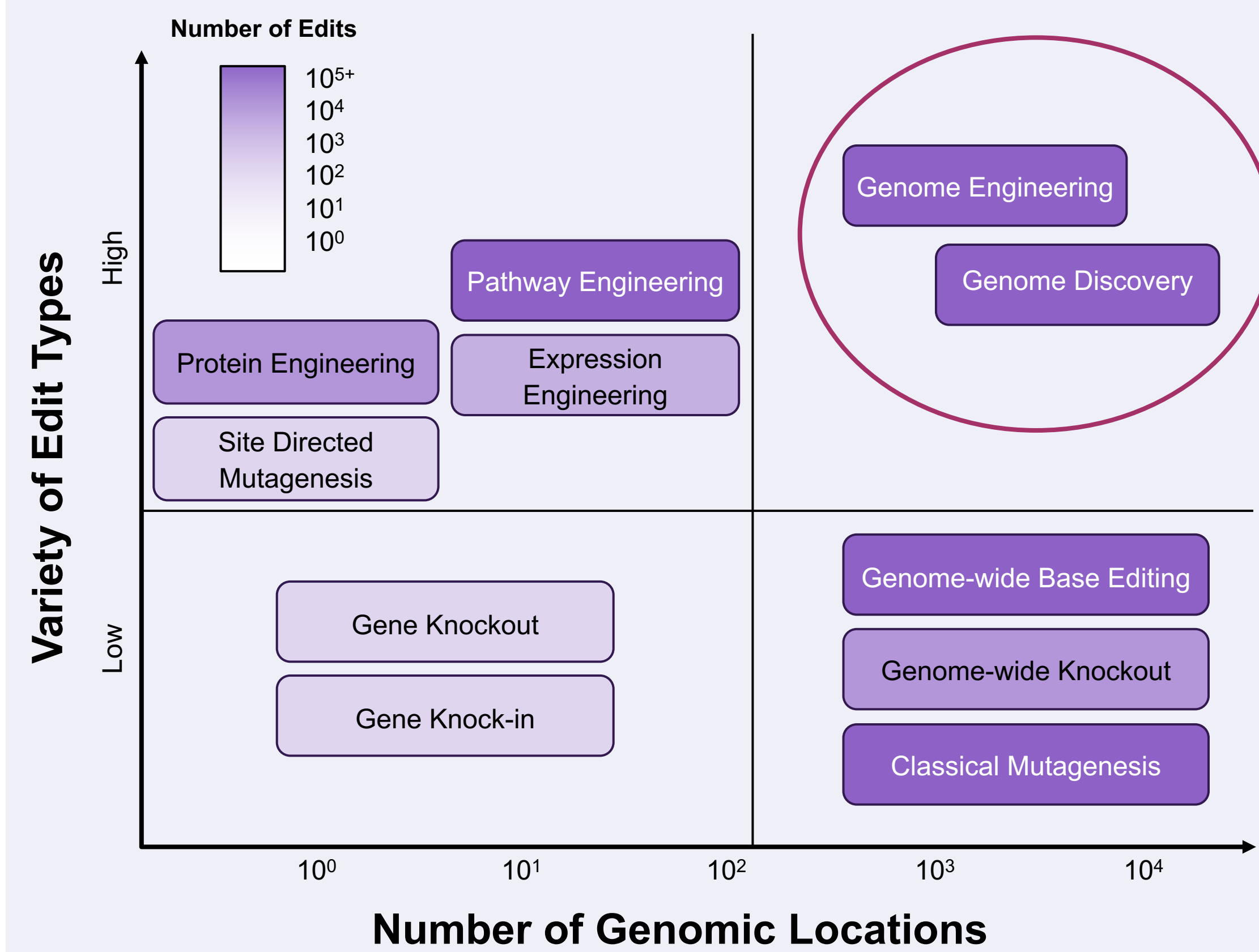
Digital Genome Engineering - Unlocking the Unlimited Potential of Biology

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ABSTRACT

To fuel the pace of discovery through CRISPR editing, the research community requires tools to efficiently deliver precise edits at the gene, pathway, and whole-genome level. Unfortunately, current editing techniques suffer from limitations in scalability, efficiency, diversity of edit types, and accessibility. The Onyx platform developed by Inscripta Inc., dramatically increases the scale of Digital Genome Engineering and simplifies the complex editing workflow for biologists. The platform offers an end-to-end solution from design to diversity generation – including software, reagents, benchtop instrument and analytics. Using the Onyx platform, we have performed high-throughput diversity generation with up to 200,000 edits across the genome in both coding and non-coding regions to improve lysine production in *E. coli* and 130,000 edits in yeast to improve tyrosine production. Inscripta's technology has also fueled large-scale discovery of genotype-phenotype relationships in antibiotic resistance and abiotic stress responses. This should have far-reaching benefits for agricultural and bio-industrial science, healthcare, and alternative energy.

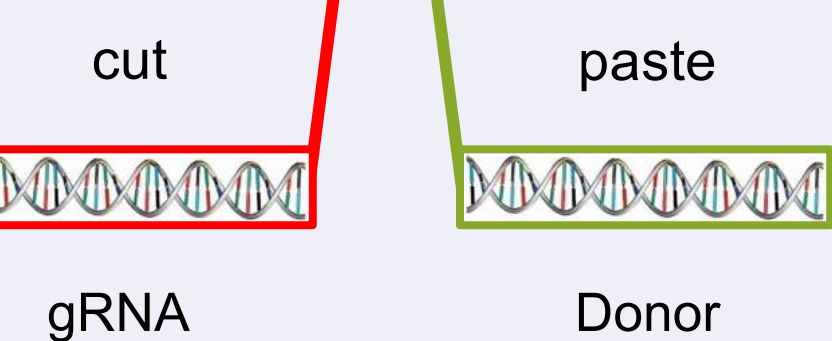
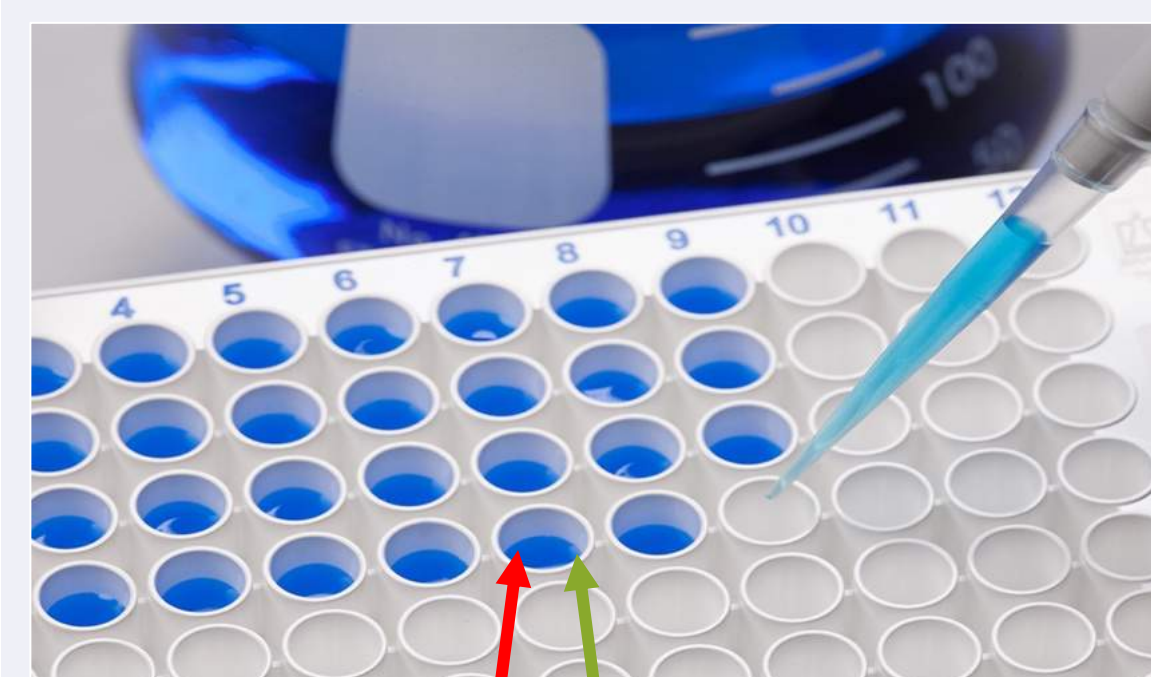
Genome engineering and discovery require greater scale and broader varieties of edit types



Inscripta offers an elegant solution for genome engineering at unprecedented scale

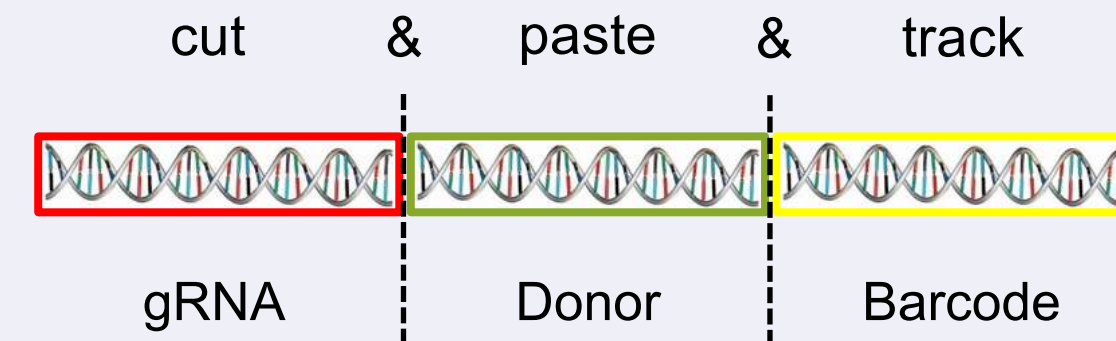
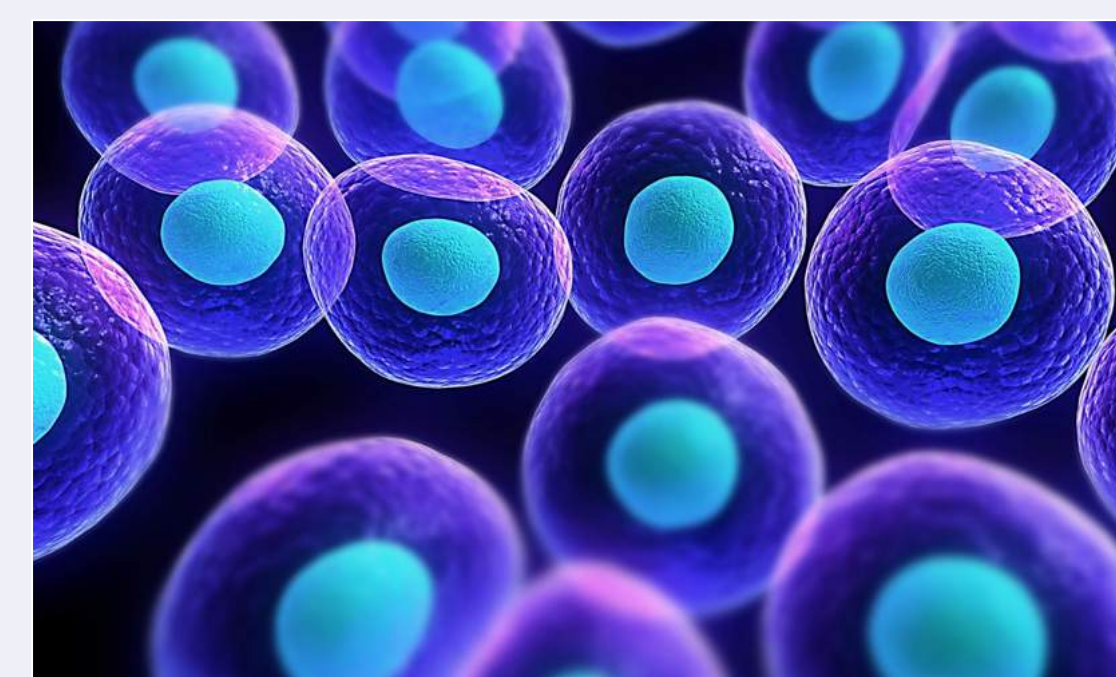
Microtiter Plate

96 partitions
(well-based)

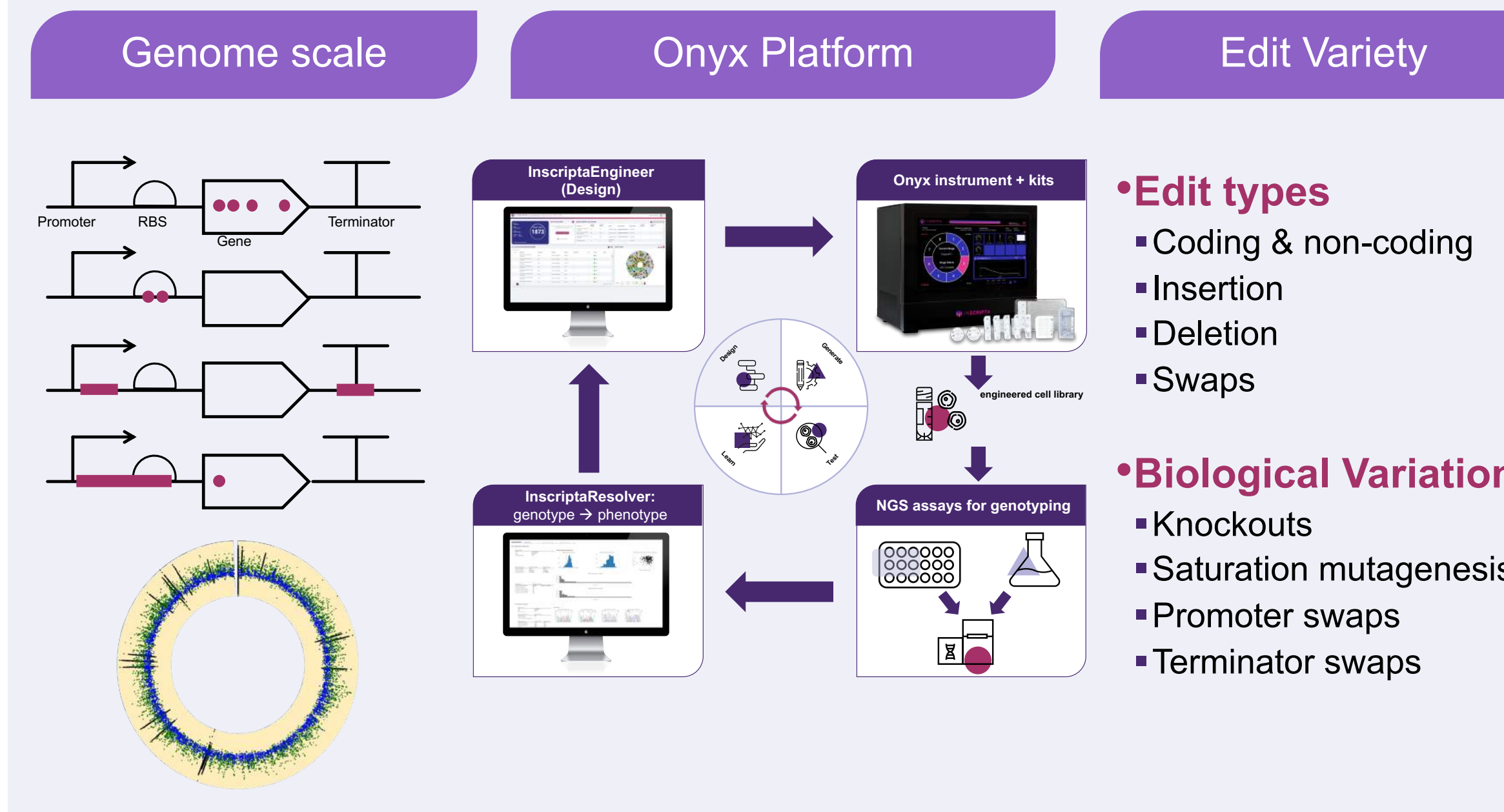


Cells

100,000+ partitions
(cell-based)



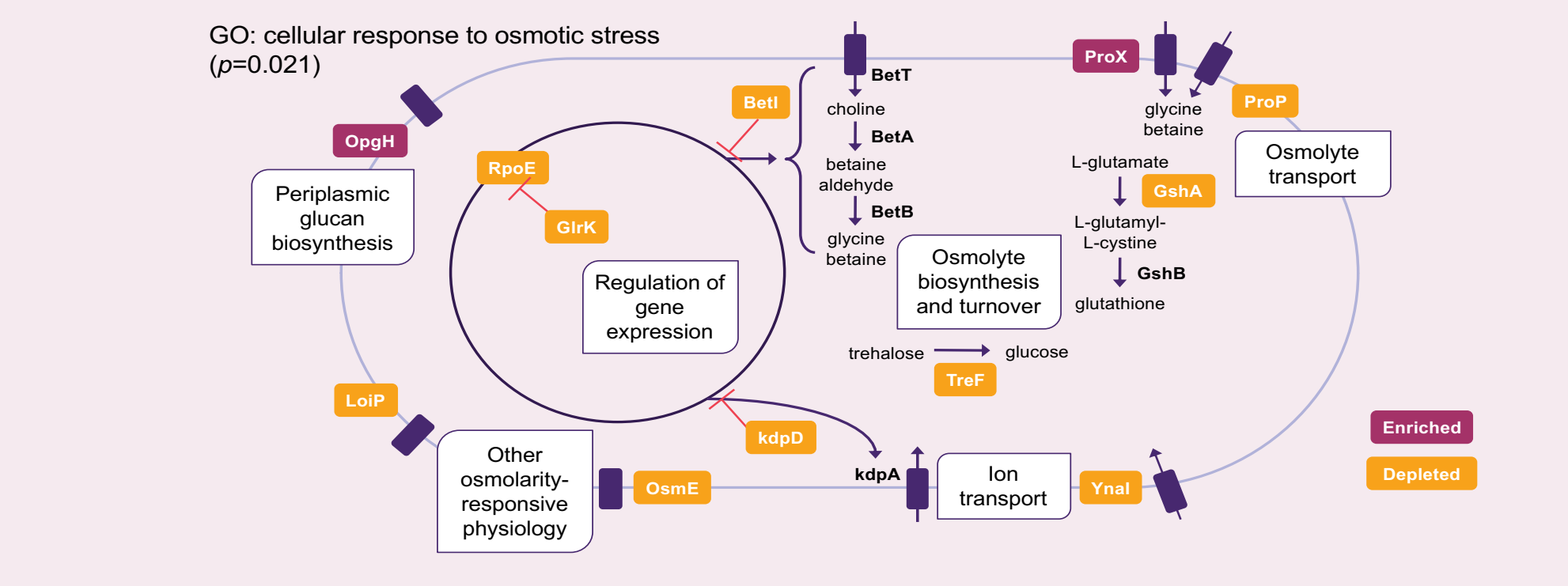
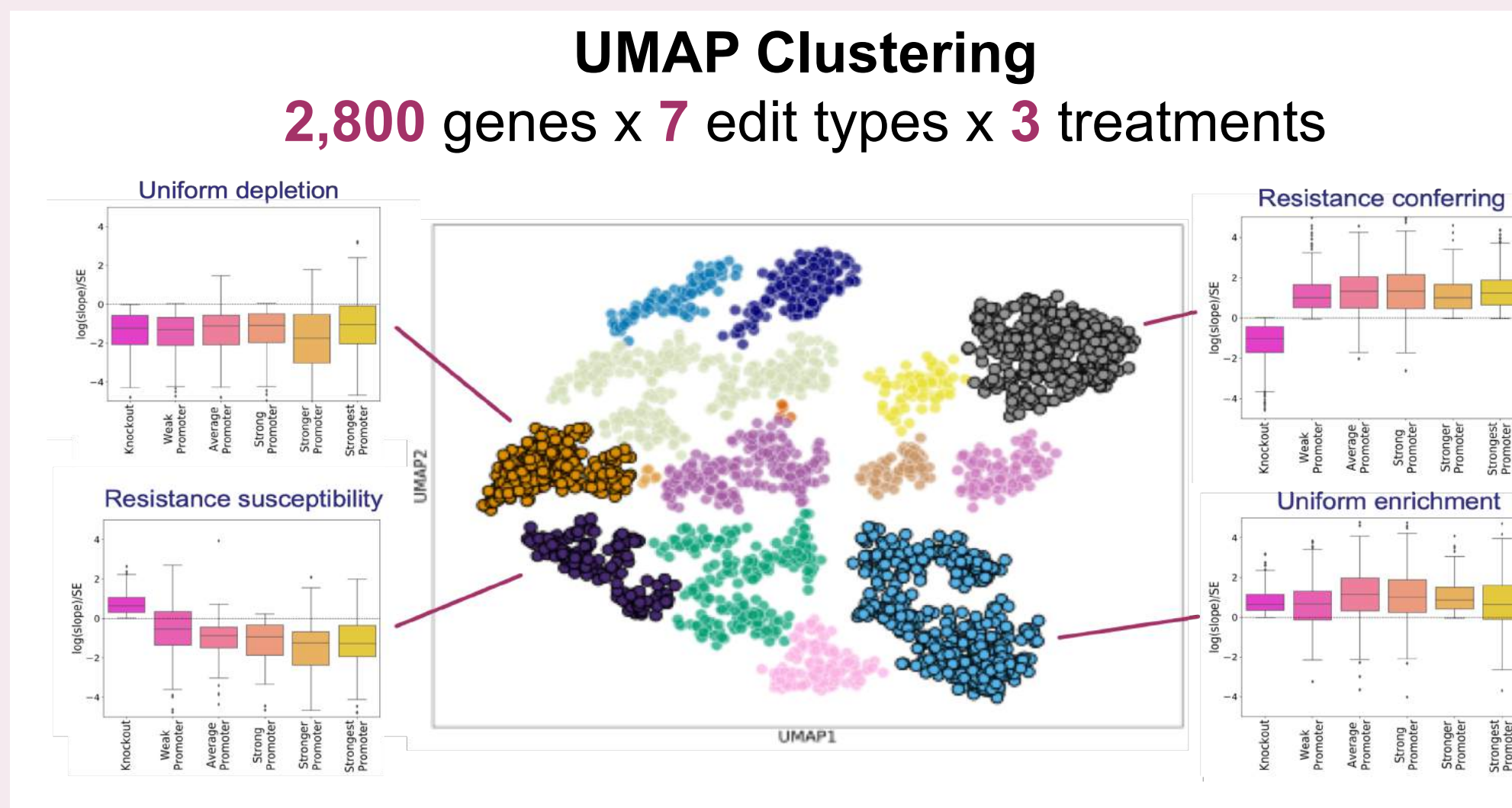
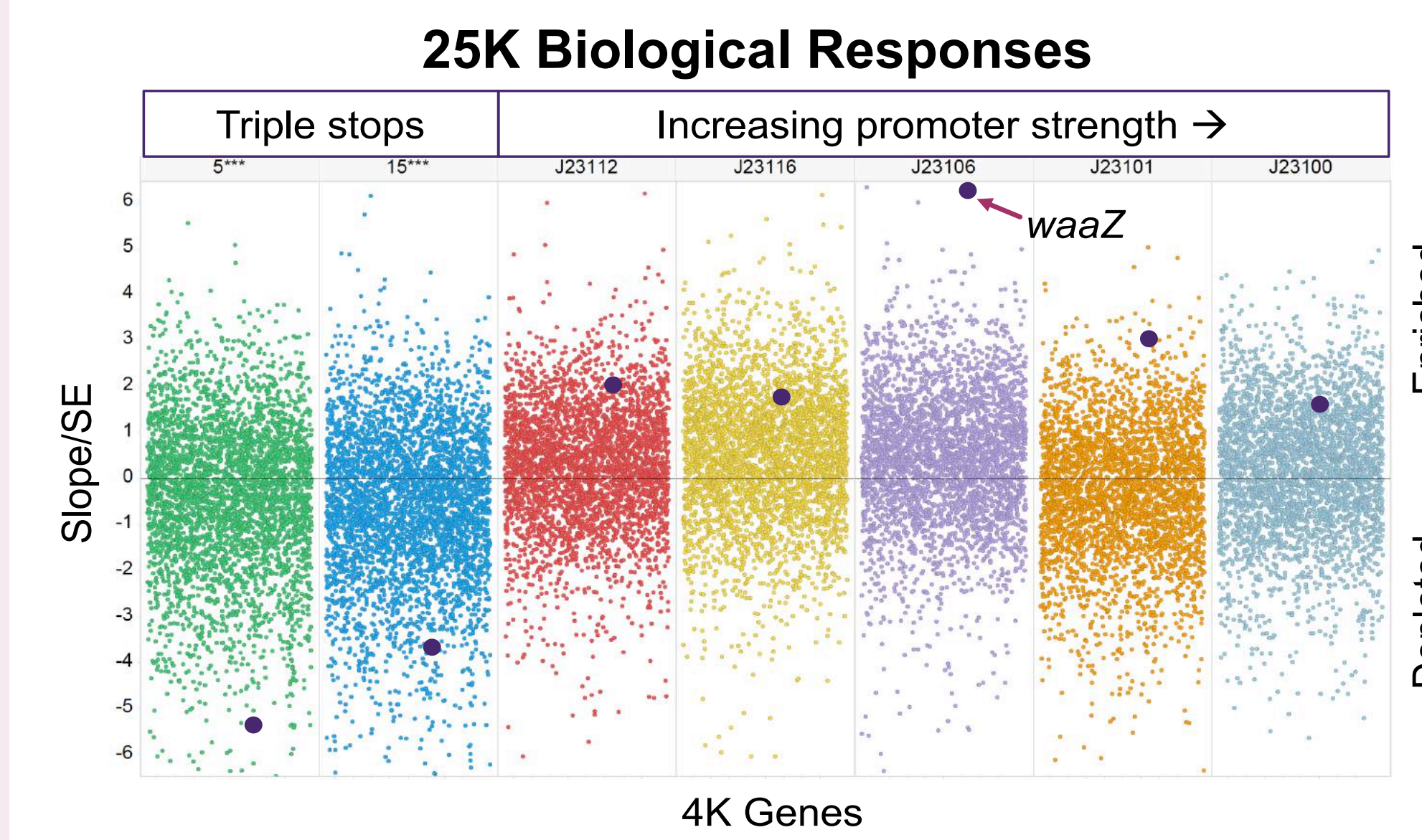
Onyx™ Digital Genome Engineering Platform delivers scale, precision and variety



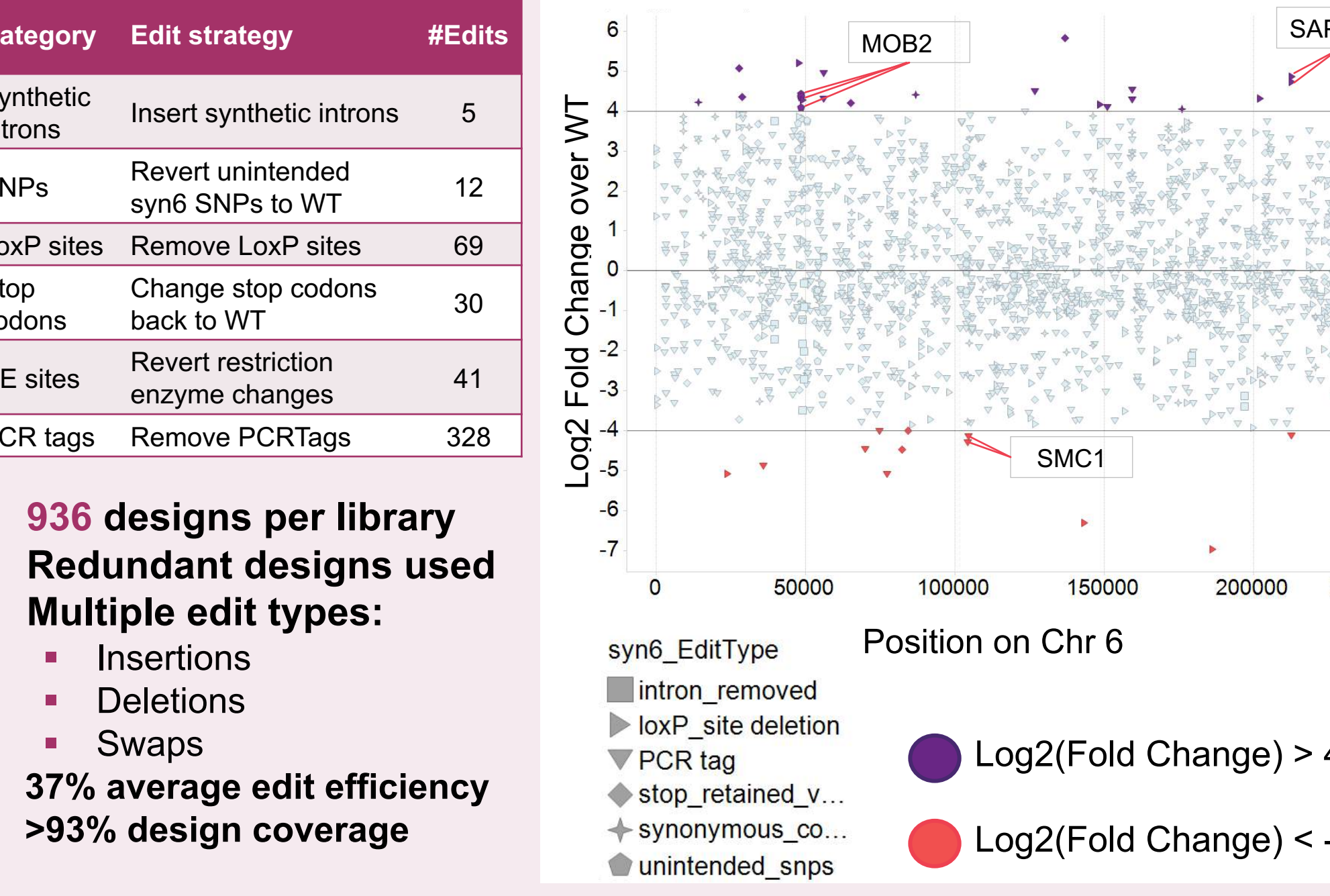
Osmotic Stress: Biological responses observed across genome-wide KO and promoter libraries

Edit variety x Genome-wide x Stress Panel

- 4191 Genome-wide targets: all *E. coli* genes
- 5 promoter ladder of varying strengths
- Genome-wide Knock-outs
- 25,000 Total designed edits; 7 libraries
- No treatment
- 0.02M NaCl
- 0.06M NaCl
- 0.2M NaCl



Synthetic chromosome 6: Rapid engineering to identify edits correcting growth defect



Metabolic Engineering: Onyx™ platform rapidly discovers novel targets for high-value amino acids

- 200,000+ designs in *E. coli*
- 130,000+ designs in yeast
- Diverse Edit Variety
 - Genome-wide KO
 - Genome-wide promoter/terminator ladders
 - Genome-wide TFBS
 - Targeted saturation mutagenesis
- High-throughput screening with Mass Spec
- Shallow sampling yielded new discoveries
- 17 Novel genome-wide targets in *E. coli*
- 25 Novel genome-wide targets in yeast

