Tailored sequencing solutions from the Sequencing and Bioinformatics Consortium

UBC Symposium: CRISPR demystified Dec. 5, 2017
Corey Nislow, Ph.D., CRC Tier 1 Chair in Translational Genomics

THE UNIVERSITY OF BRITISH COLUMBIA

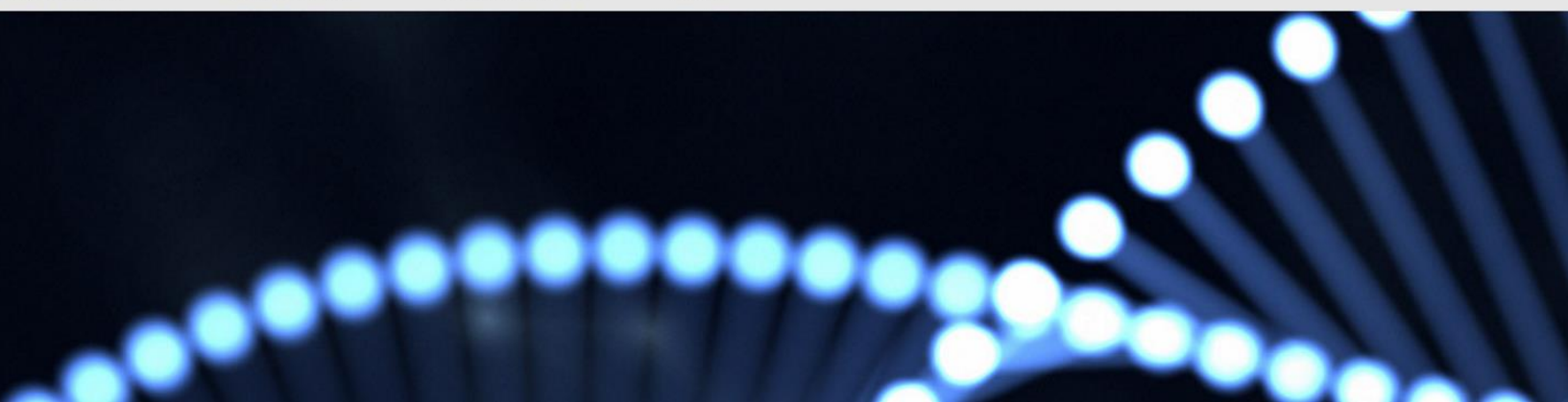Sequencing + Bioinformatics Consortium

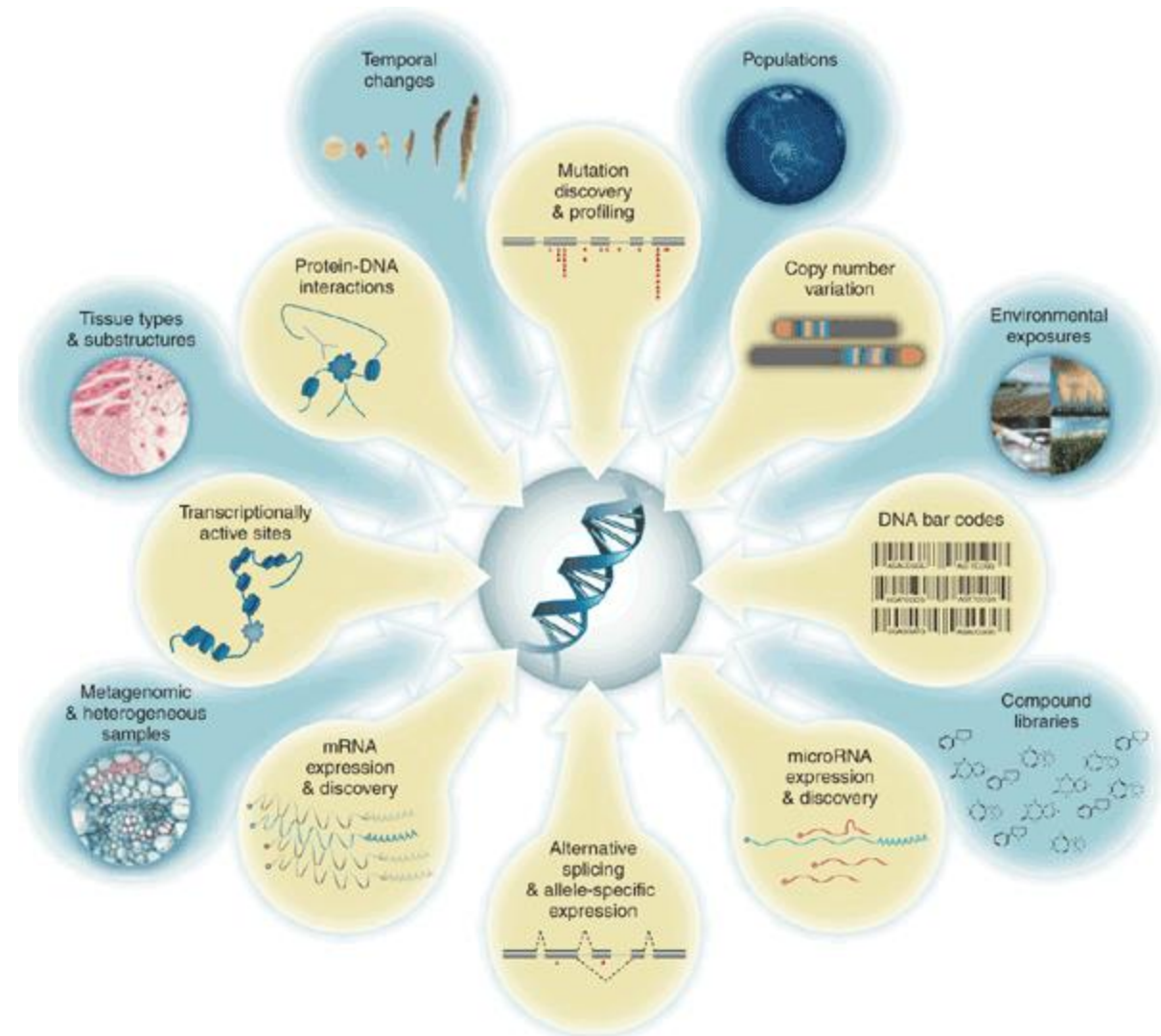Home | About the Consortium | Our Services + Equipment | How to Work with Us | Quick Links
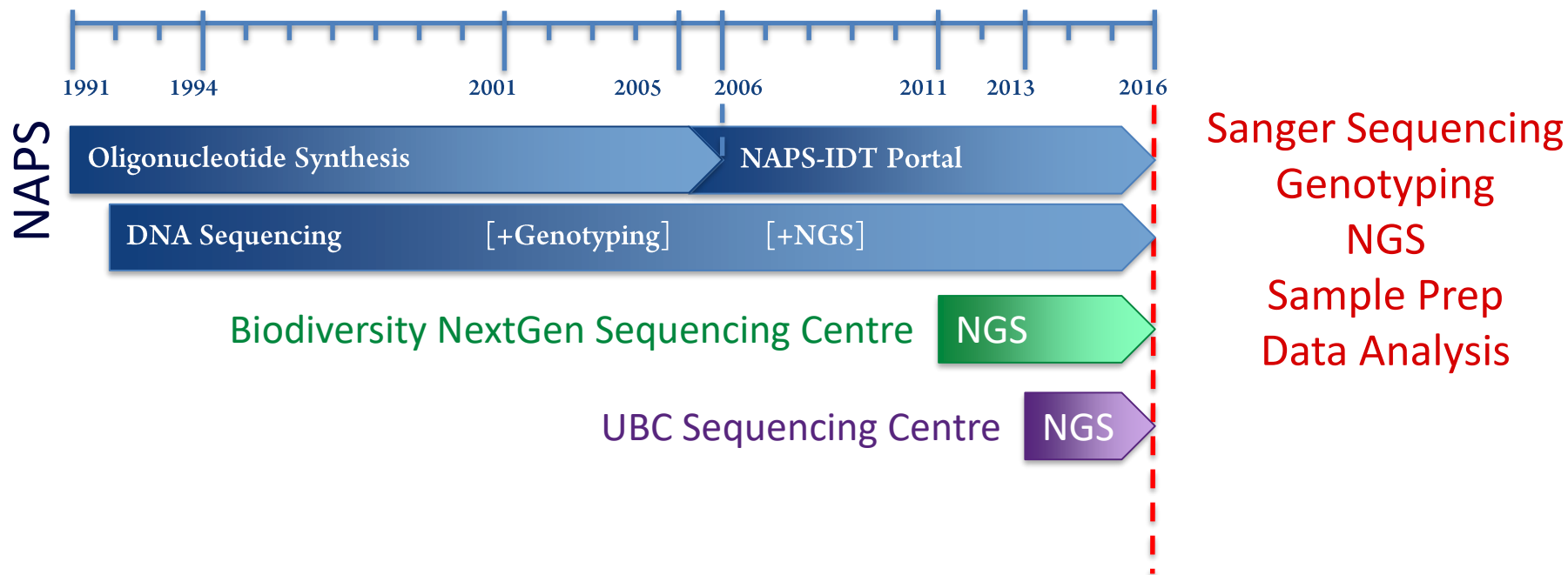
What would you do if you could sequence everything?

Avak Kahvejian[1], John Quackenbush[2] & John F Thompson[1]

Evolution of the UBC Sequencing and Bioinformatics Consortium

NAPS

| 1991 | 1994 | | 2001 | 2005 | 2006 | | 2011 | 2013 | 2016 |

Oligonucleotide Synthesis — NAPS-IDT Portal

DNA Sequencing [+Genotyping] [+NGS]

Biodiversity NextGen Sequencing Centre — NGS

UBC Sequencing Centre — NGS

Sanger Sequencing
Genotyping
NGS
Sample Prep
Data Analysis

NGS at the SBC: bespoke sequencing service from project inception to delivered data

QC QC QC QC

Project planning → Nucleic acid extraction → Library preparation → Sequencing → Data analysis → Interpretation of results → Invoicing

Cells
Tissue
Plant
Saliva
Blood
CSF
FFPE

gDNA
Amplicons
Panels
RNA
miRNA/cfDNA
ChIP

MiSeq
HiSeq
NextSeq

File conversion
Mapping
Variant calls
Security
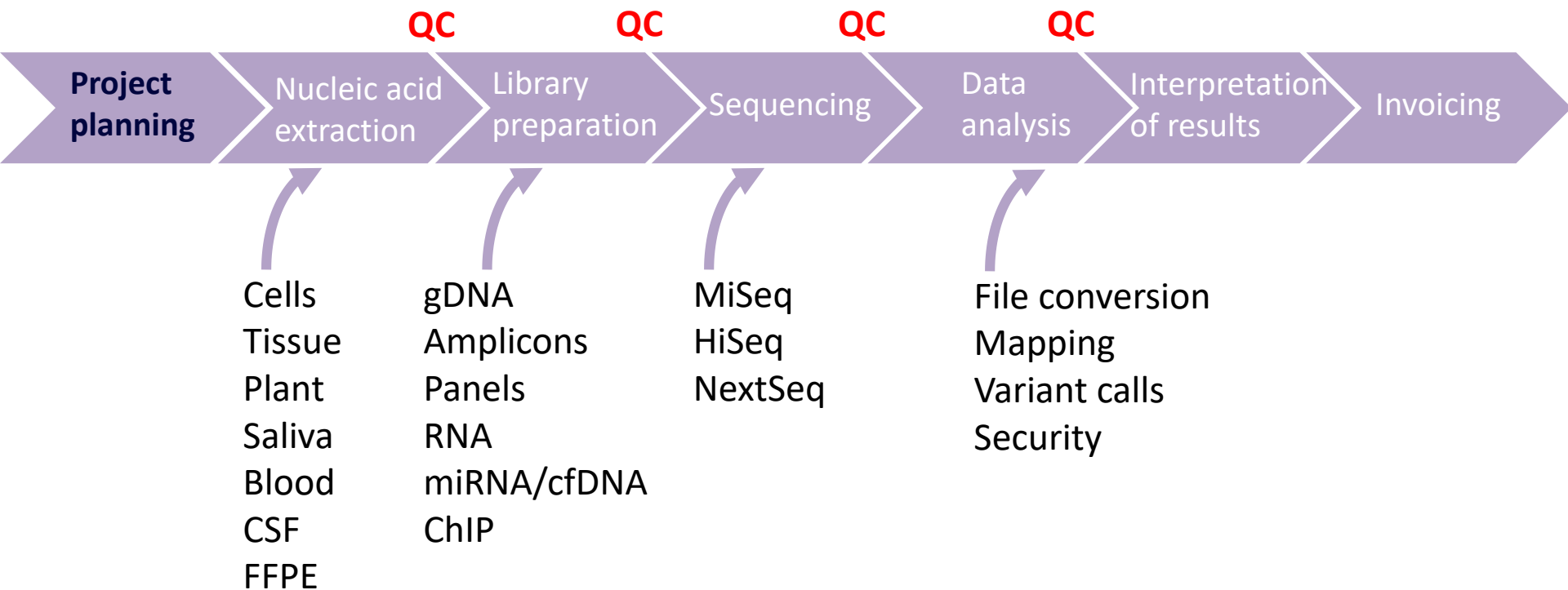
NGS at the SBC

From project inception to delivered data to Start-up

Success stories:
1. Cell Metabolism, Cell Reports: Diabesity
2. CF Lung Microbiome
3. Microbiome Insights
4. Exomes: Neurocode, RxOME, GenXys
5. Biomarkers of TBI, SCI, Anesthesia
6. Your project here

Project planning
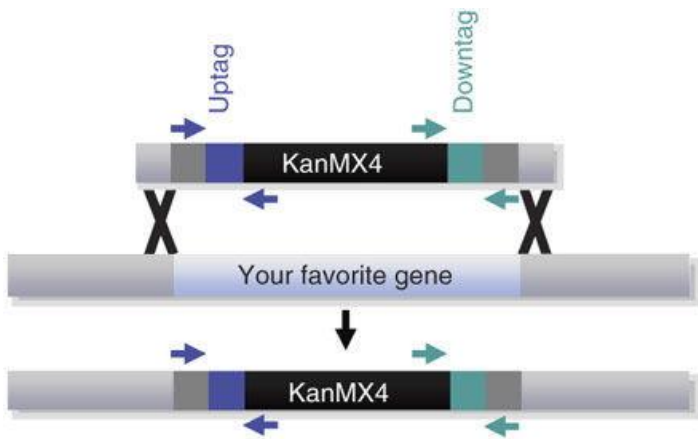
ng

Blood   miRNA/cfDNA
CSF   ChIP
FFPE

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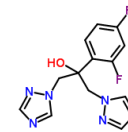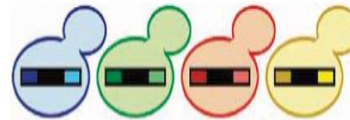
Sequencing and Bioinformatics Consortium

https://sequencing.ubc.ca

Bakers yeast: a genomic test-bed
Genome-wide assay: count Barcodes
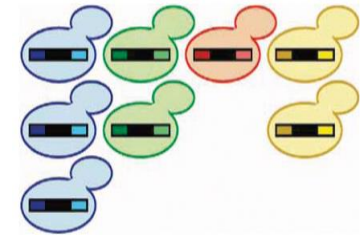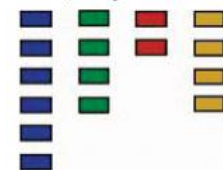
Example:
Novel compound/target pair: *SEC14* inhibitor

Heterozygous

Homozygous deletion strain
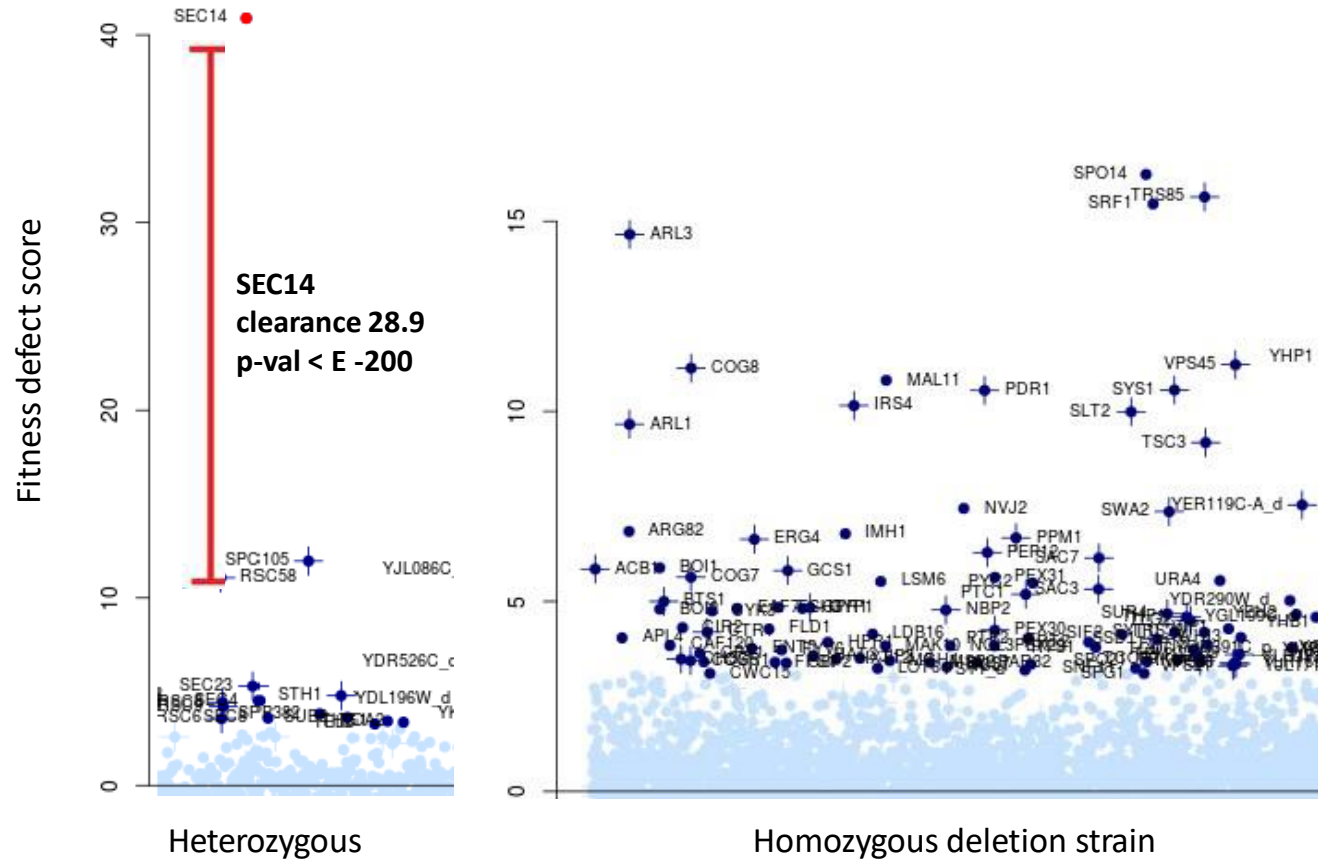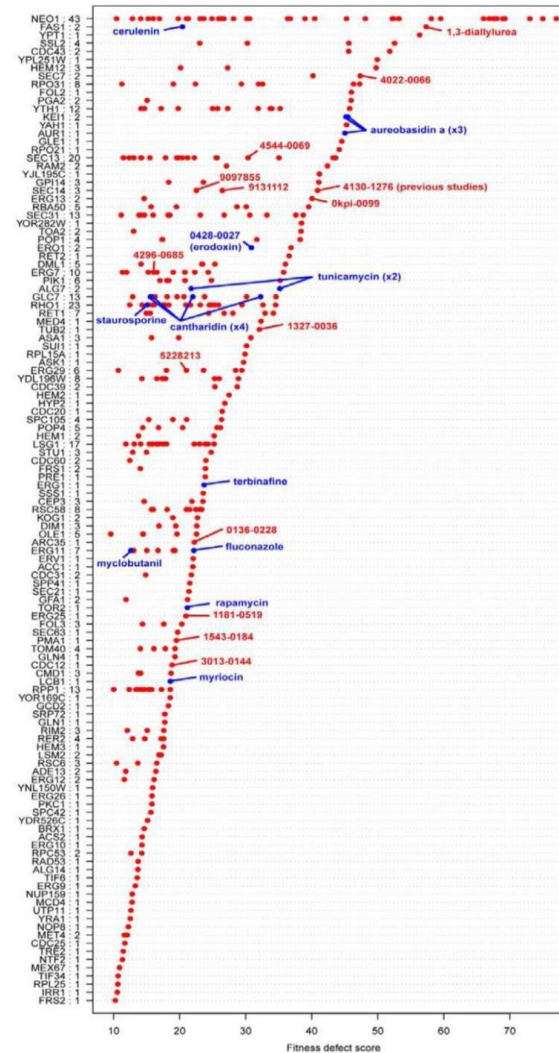
3,250 small molecule
HIPHOP profiles

317 compounds that
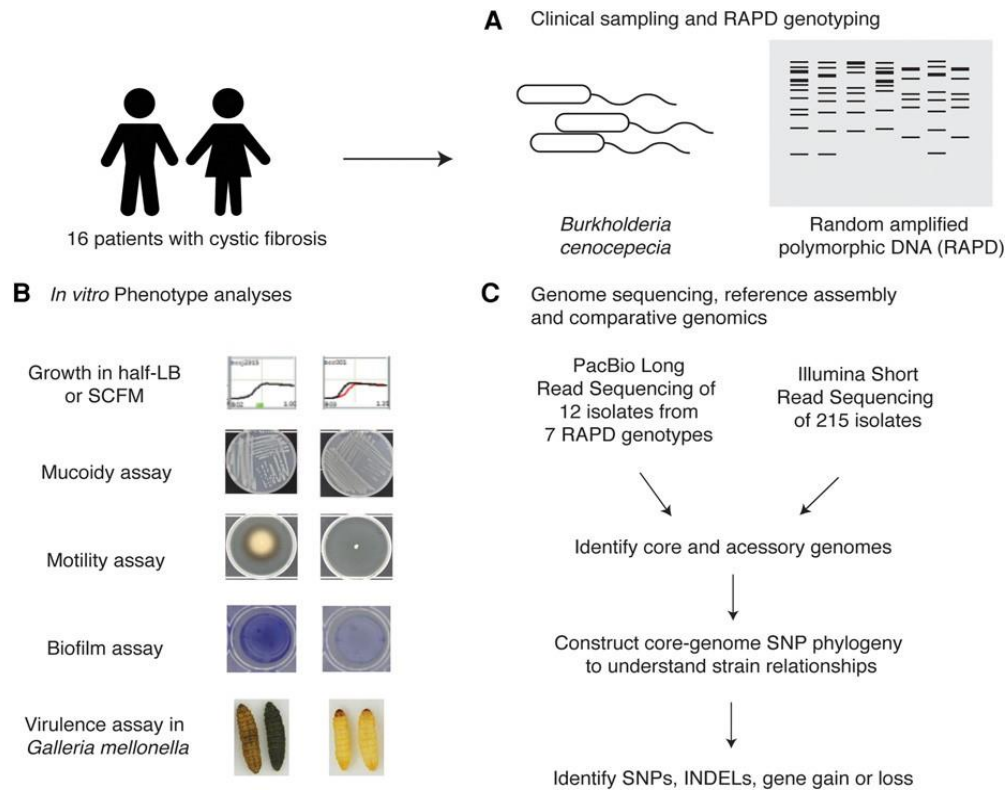perturb 121 unique genes

In 1 environment!
*Bar-seq allows
Expansion into
Diverse conditions*

Phenotypic diversity and genotypic flexibility of *Burkholderia cenocepacia* during long-term chronic infection of cystic fibrosis lungs

Amy Huei-Yi Lee,[1,2] Stephane Flibotte,[2,3] Sunita Sinha,[2] Adrianna Paiero,[2]
Rachel L. Ehrlich,[4,5,6] Sergey Balashov,[4,5,6] Garth D. Ehrlich,[4,5,6] James E.A. Zlosnik,[7] Joshua Chang Mell,[4,5,6] and Corey Nislow[2]

A Clinical sampling and RAPD genotyping

16 patients with cystic fibrosis

Burkholderia cenocepecia

Random amplified polymorphic DNA (RAPD)

B *In vitro* Phenotype analyses

Growth in half-LB or SCFM

Mucoidy assay

Motility assay

Biofilm assay

Virulence assay in *Galleria mellonella*

C Genome sequencing, reference assembly and comparative genomics

PacBio Long Read Sequencing of 12 isolates from 7 RAPD genotypes

Illumina Short Read Sequencing of 215 isolates

Identify core and acessory genomes

Construct core-genome SNP phylogeny to understand strain relationships

Identify SNPs, INDELs, gene gain or loss

1. A genotype phenotype resource of 11 reference genomes, 204 drafts (10X increase)

2. Distinct core genomes, Recurrent gene gain and loss

3. Trends of decreasing a) motility, b) biofilm formation, and c) virulence Candidate genes (dnaK, papC, gcvA and qseC)

Global Analysis of the Fungal Microbiome in Cystic Fibrosis Patients Reveals Loss of Function of the Transcriptional Repressor Nrg1 as a Mechanism of Pathogen Adaptation

Sang Hu Kim[1], Shawn T. Clark[2], Anuradha Surendra[3], Julia K. Copeland[3], Pauline W. Wang[3,4], Ron Ammar[5], Cathy Collins[1], D. Elizabeth Tullis[6], Corey Nislow[7], David M. Hwang[2], David S. Guttman[3,4], Leah E. Cowen[1]*
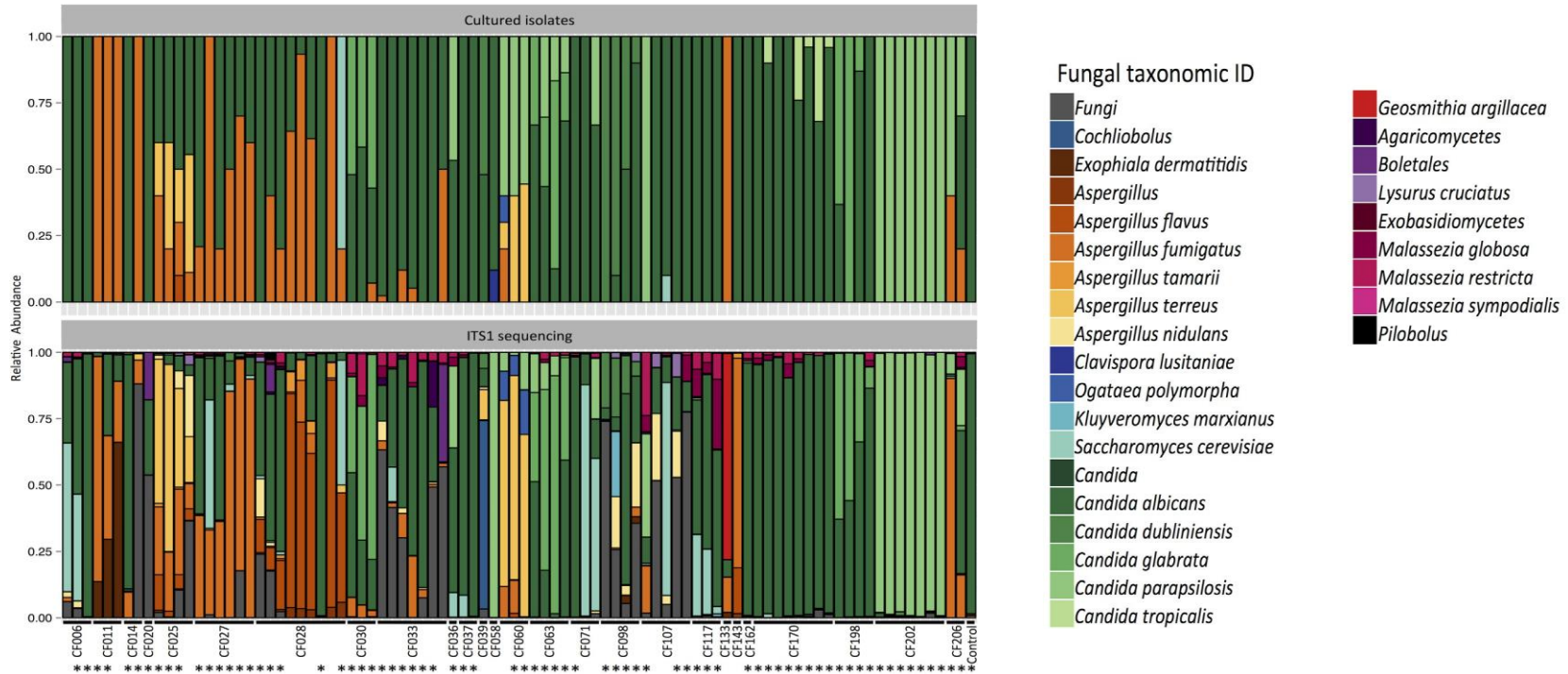
Serum MicroRNAs Reflect Injury Severity in a Large Animal Model of Thoracic Spinal Cord Injury

Seth Tigchelaar[1], Femke Streijger[1], Sunita Sinha[2], Stephane Flibotte[2], Neda Manouchehri[1], Kitty So[1], Katelyn Shortt[1], Elena Okon[1], Michael A. Rizzuto [1], Ivana Malenica[3], Amanda Courtright-Lim[3], Andrew Eisen[4], Kendall Van Keuren-Jensen[3], Corey Nislow [2] & Brian K. Kwon[1,5]
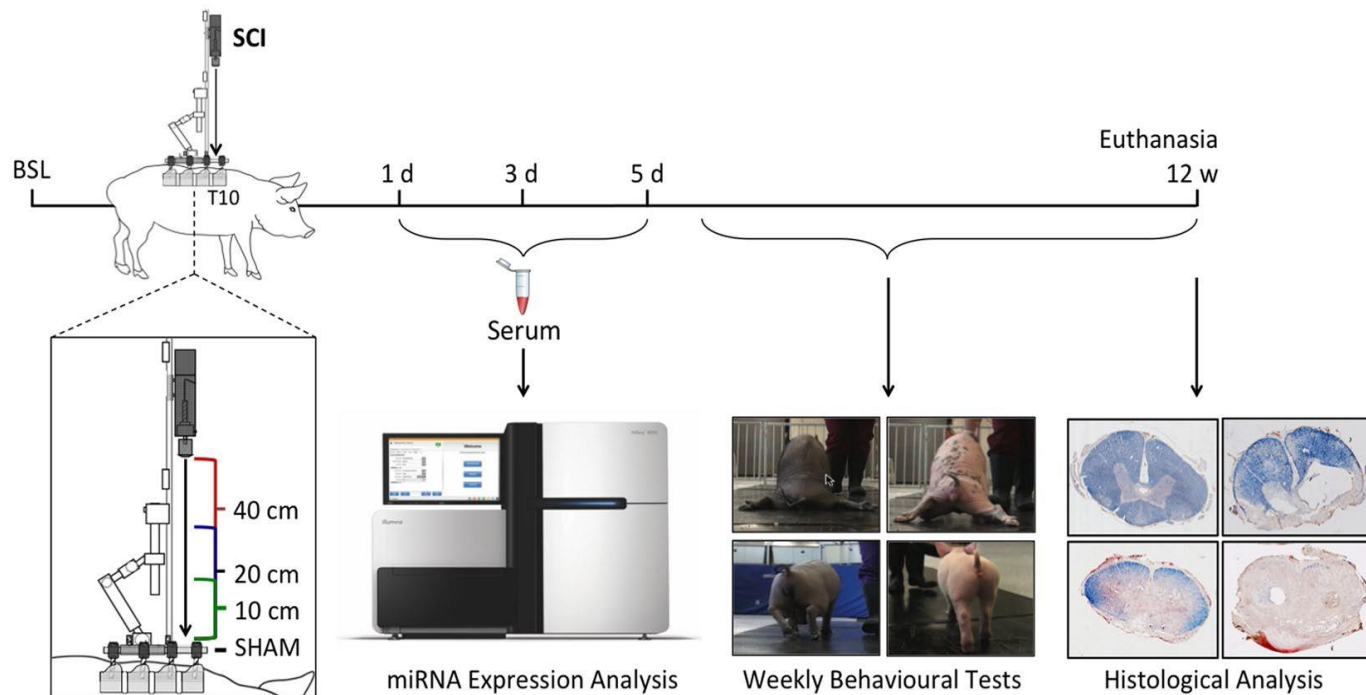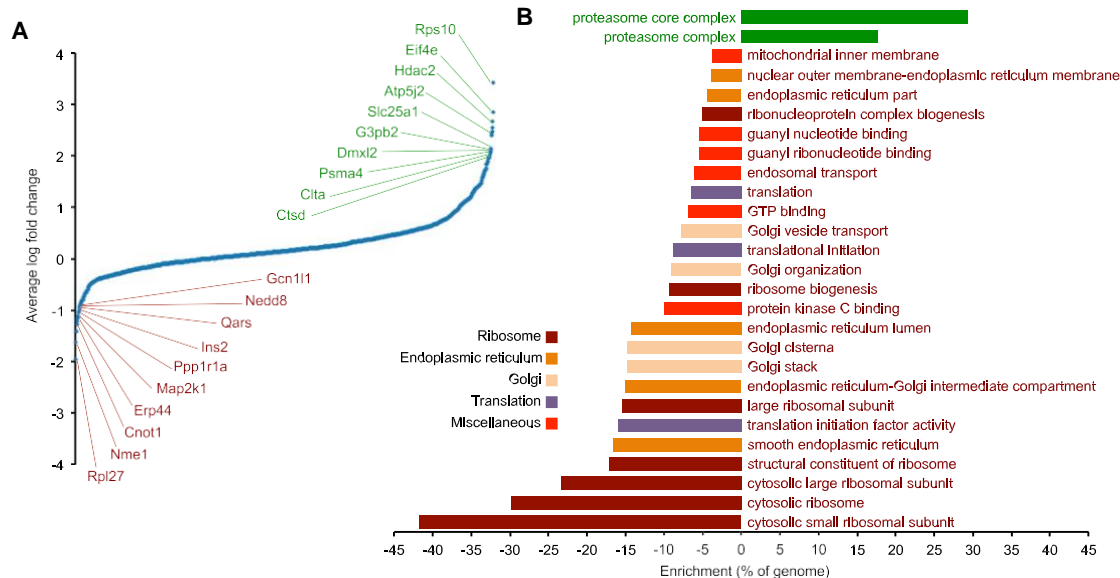
Reduced Insulin Production Relieves Endoplasmic Reticulum Stress and Induces b Cell Proliferation

Authors

Marta Szabat, Melissa M. Page, Evgeniy Panzhinskiy, ..., Corey Nislow, Timothy J. Kieffer, James D. Johnson

Highlights

Acute reduction of insulin production reverses baseline ER stress

Loss of insulin production reduces Trib3 and hyper-activates Akt

Reduced insulin production increases **b** cell proliferation cell autonomously

Insulin knockout induces glucagon mis-expression via hyperglycemia

Back to CRISPR- how can we help?

# Check your clones by NGS

Cell-based methods
1. IDLV: integrase-defective lentiviral vector capture
2. GUIDE-seq: Genome-wide unbiased ID of DSBs by sequencing
3. HTGTS: high-throughput genome-wide translocation sequencing
4. BLESS: enrichment on streptavidin and NGS
in vitro
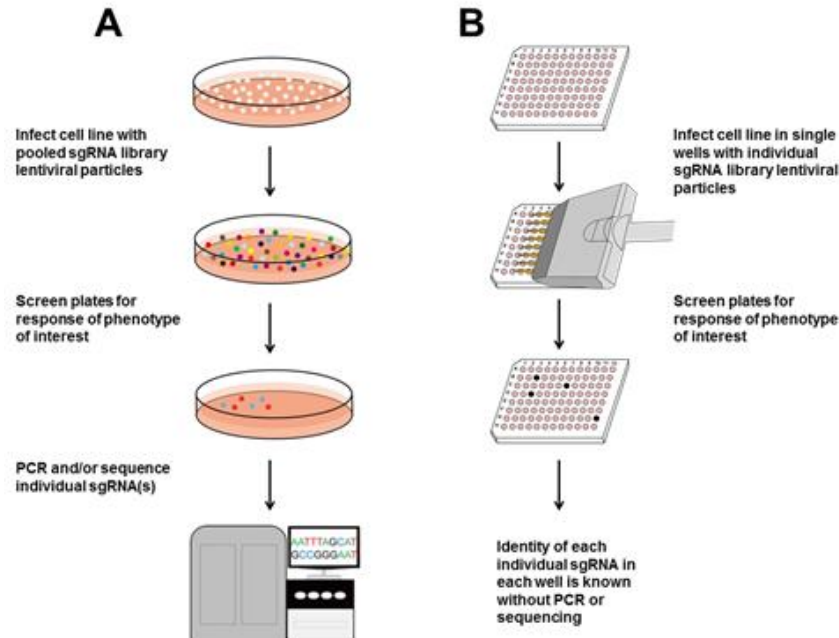5. Digenome-seq: digested genome sequencing
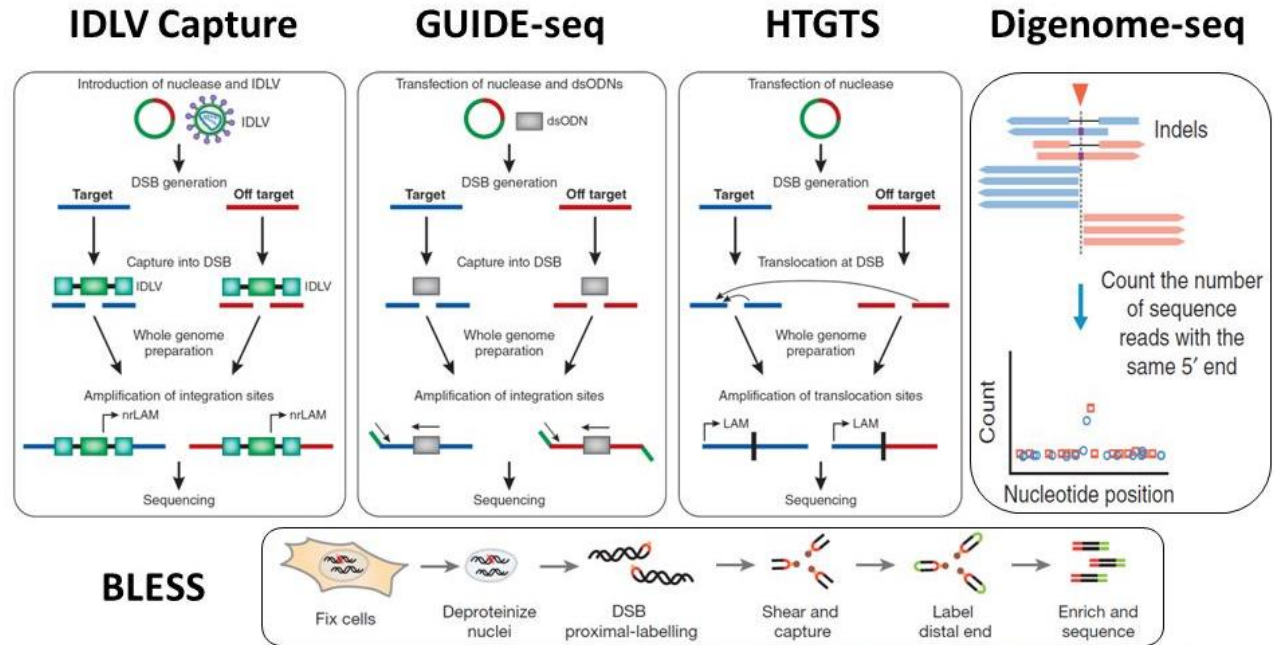
Which technique? Depends...
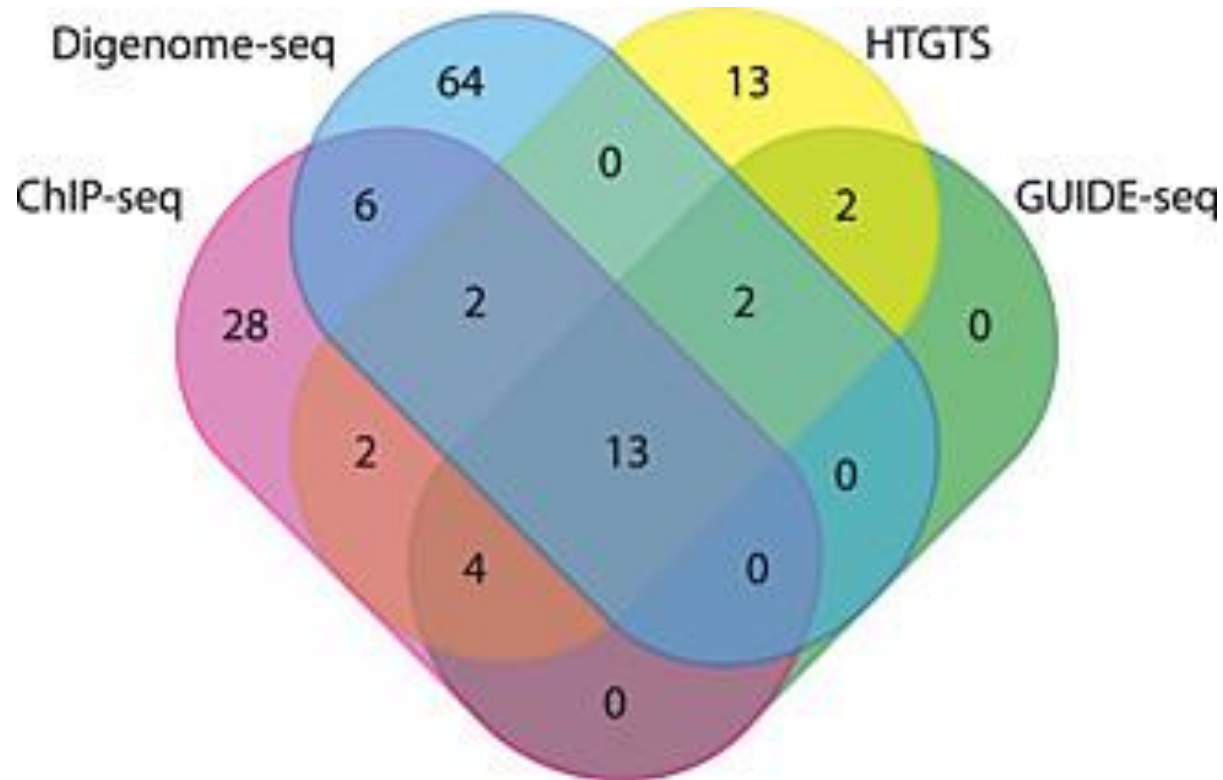
Screen your clones: by NGS
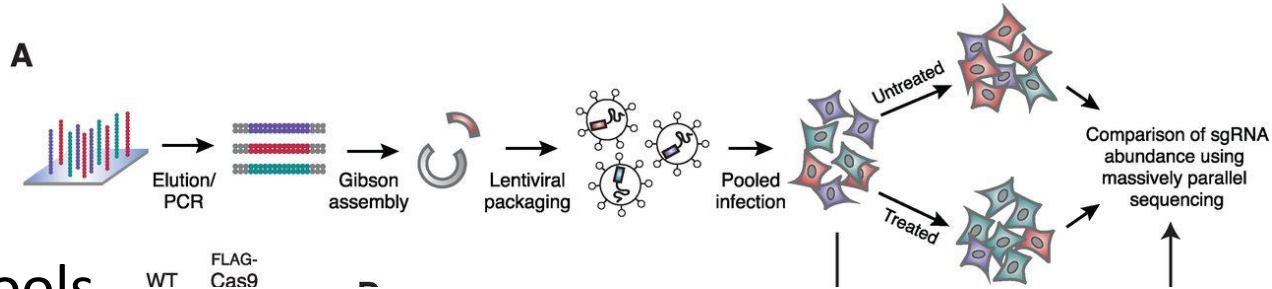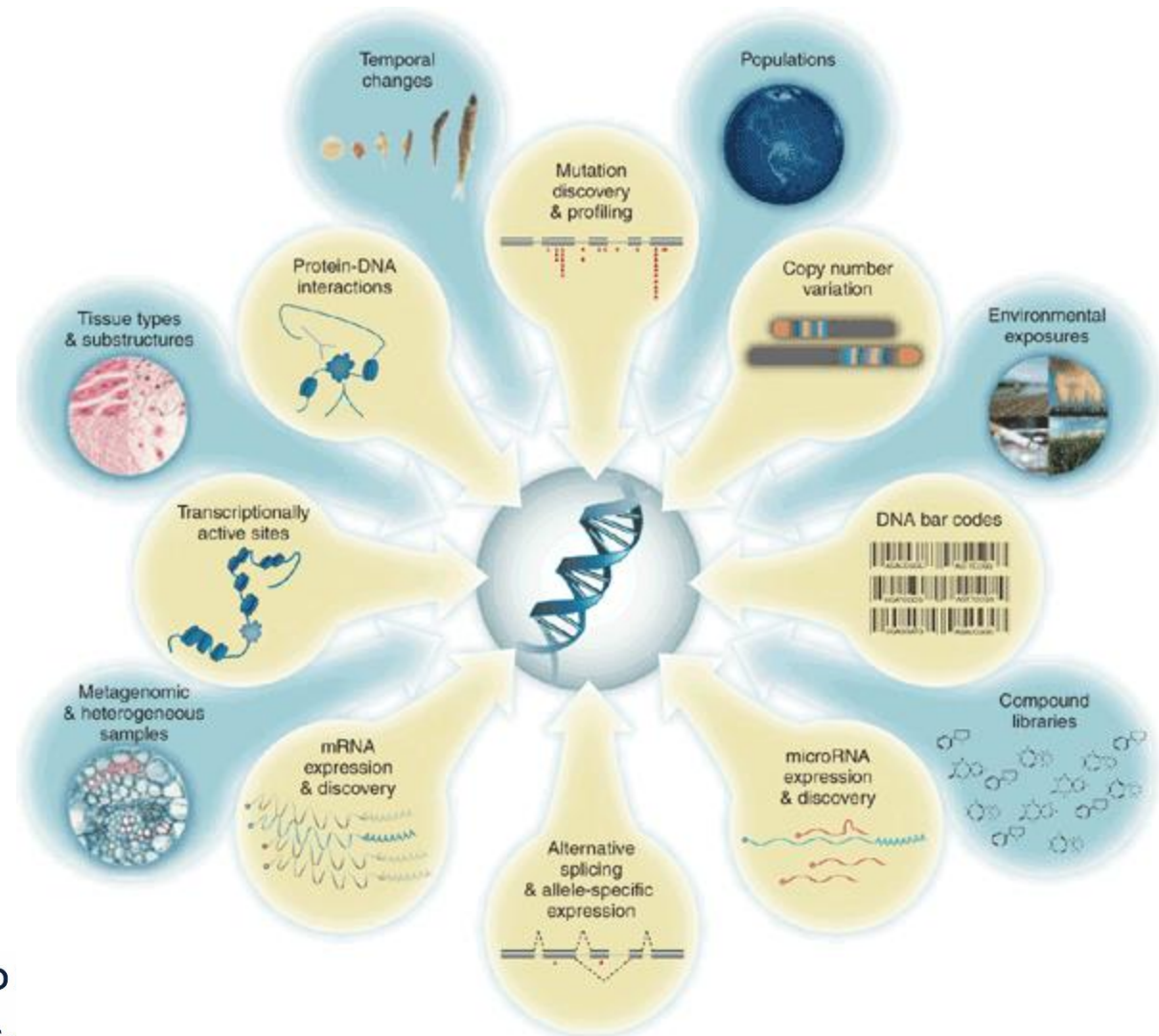
1. In pools

2. independent clones

What would you do if you could sequence ▲ and edit everything?

Avak Kahvejian[1], John Quackenbush[2] & John F Thompson[1]

Thanks!

https://sequencing.ubc.ca