Week 6: Result

GWAS, Microarrays, & NGS

Quick (Secret) Poll

- ❏ Understand FASTQ, BAM, and VCF files
- ❏ Have Successfully tested/used BWA, GATK or PLINK2
- ❏ Processed a VCF using PLINK2
- ❏ Run PCA in PLINK2 (or outside of PLINK2)
- ❏ Have looked at PCA output
- ❏ (Prefer scheduled 10min times or group office hours this week?)

Next week: 10min check-in

Discussion Questions I

GWAS (Vox)

- What is GWAS?
- How did the Human Genome Project make GWASs possible?
- What do GWASs provide? (What is the result of a GWAS?)
- What are three (3) limitations of GWAS?
- What is a polygenic risk score?

Week 5 Discussion Question:

- Why do geneticists care about population (sub)structure?

(*GWAS*) Student Question

How would we account for the fact that a major limitation to most GWAS is that they're <u>only done on white Europeans</u> in our project where we're trying to create genetic clusters of the entire world? Also, the Vox article says that scientists must <u>repeat their studies in more diverse populations</u> if we truly want to make GWAS an equitable and useful tool to predict disease risk. Are there any current studies that <u>scientists are working on to do GWAS studies on more diverse populations</u>?

Discussion Questions II

<u>Nature Reviews</u>

- How are sequencing and microarray technologies similar? How do they differ?
- What is next generation sequencing? (NGS)?
- Generate a diagram/cartoon and label it with text to explain how one NGS technology explained in the reading works.
- What is whole genome sequencing? How does that differ from exome sequencing?
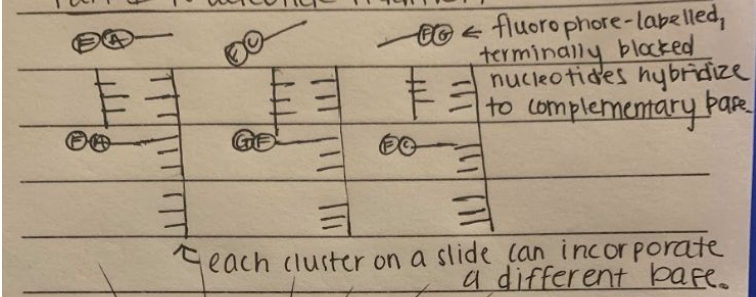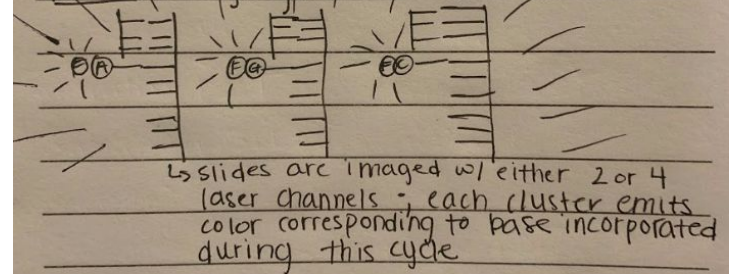
Microarrays:

⇐ DNA

⇐ we "paint" them

⇐ map for analysis

DNA microarray technology.
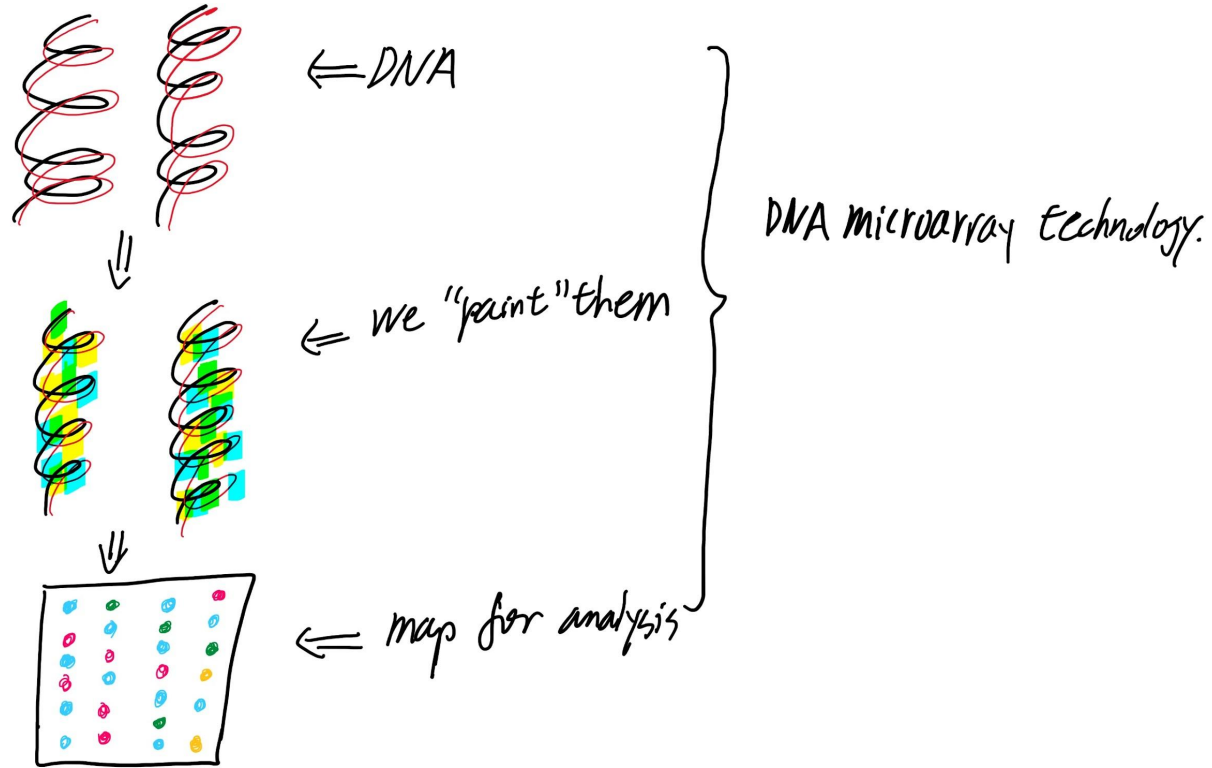
Artist: Fernie

DNA Sequencing Illumina (NGS)

Illumina Technology Explained

Part 1 Nucleotide Addition

← fluorophore-labelled, terminally blocked nucleotides hybridize to complementary base

← each cluster on a slide can incorporate a different base.

Part 2: Imaging

⤷ slides are imaged w/ either 2 or 4 laser channels; each cluster emits color corresponding to base incorporated during this cycle

Part 3: Cleavage

fluorophores → are cleaved & washed from flow cells & 3'-OH group is regenerated

⤷ new cycle begins w/ addition of new nucleotides

Artist: Samantha

DNA Sequencing
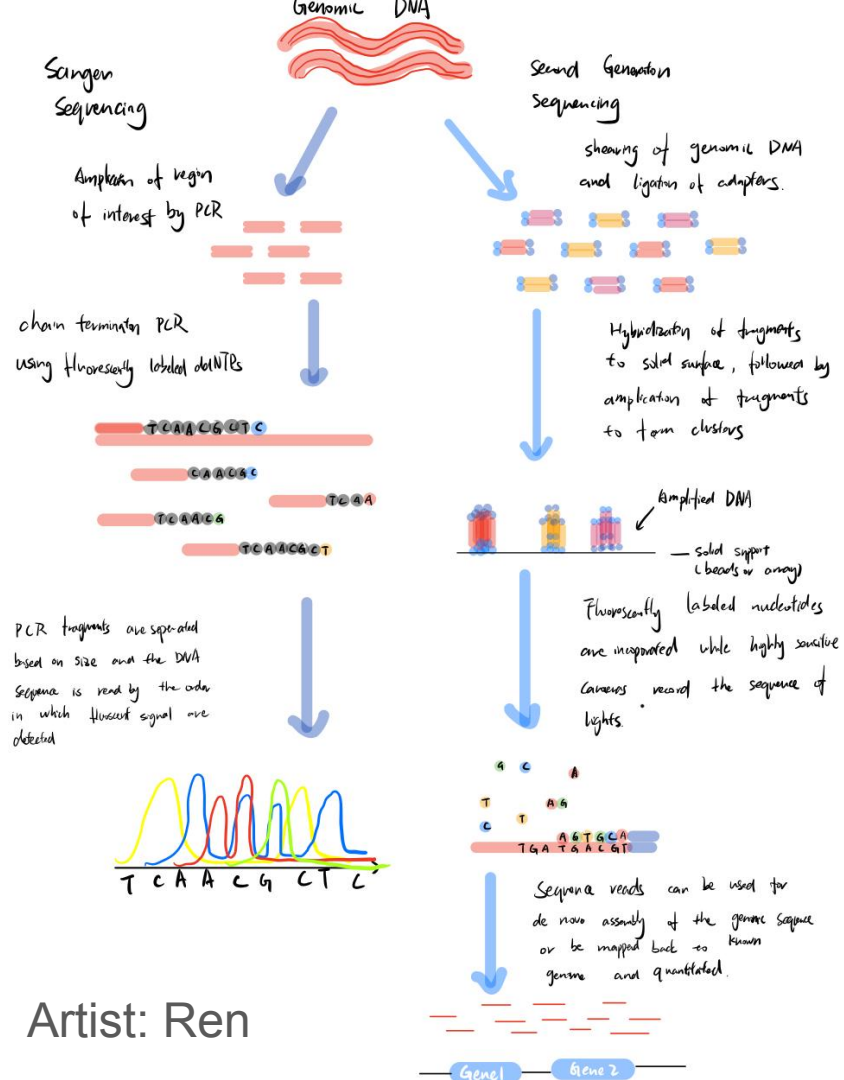
Artist: Ren

DNA Sequencing (NGS)

SBS

clusters

C

T

↑ step 1
← step 2
← step 3

have many clusters of identical strands & add one color-coded complement at a time

every time you add a complement, take a picture of color.

This is sequencing each cluster of identical strands

image 1

image 2

we saw C, then added next complement, T.

This happens simultaneously across clusters.
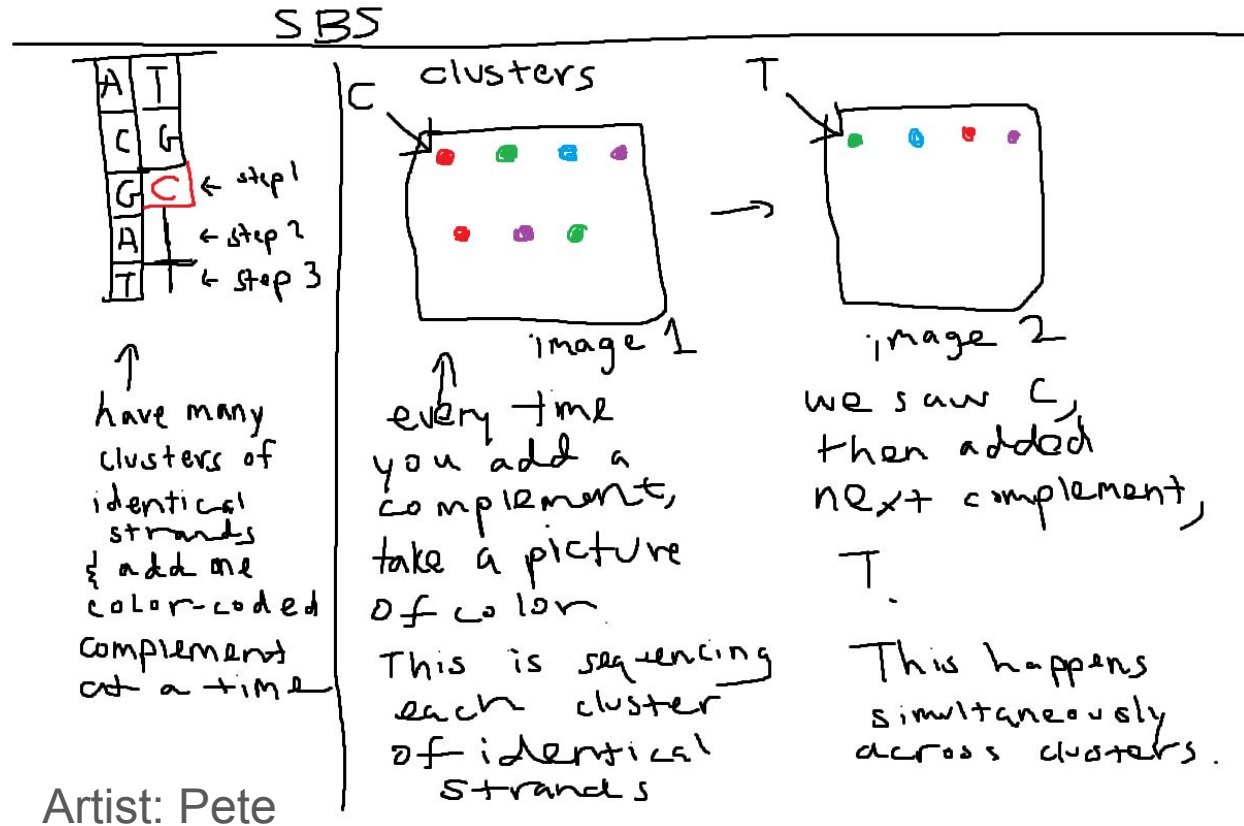
Artist: Pete

(*Important, Existential*) Student Question

From the VOX article, I keep wondering if our future will be like the one in Gattaca, where people simply pay for <u>choosing the optimal genes for their babies</u>. It sounds really scary to me because by then humans will play the role of God. Even it does become reality, how to simply switch the genes? <u>Using CRISPR</u>?