BMEG 3105 FALL 2022

Data analytics for personalized genomics and precision medicine Course introduction

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Course agenda:

- **Genome**

  Variant calling (very complicated)

  GWAS

- **RNA-seq**

  Gene-fusion—structural variant

- **Epigenome**

  Peak calling

Genome (genetic variant level to study cancer)

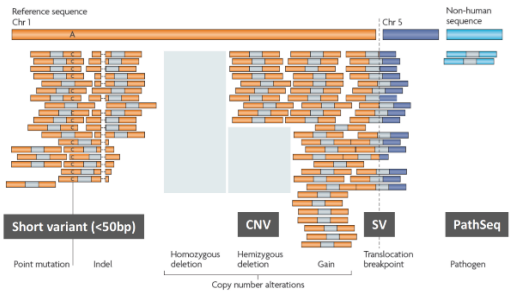
Why we care about variant?

- Human share 99.5% of genome, but the 0.5% difference could lead to lots of diseases and difference response to treatment.
- One of the examples is cancer which is caused by genome variant in multiple levels.

Types of genome variants:

- Short variant: point mutation, indel(<50bp)
- CNV: homozygous deletion, hemizygous deletion, gain
- SV: translocation breakpoint (gene shift from other location)
- PathSeq: pathogen (non-human)

Different types of genomic variants



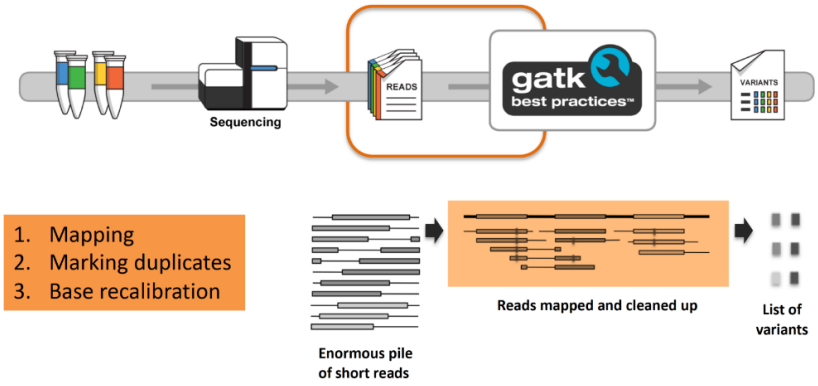
Ways to discover genetic variants:

- Library preparation (from gene bank sometimes)
- Sequencing (way similar to mapping)

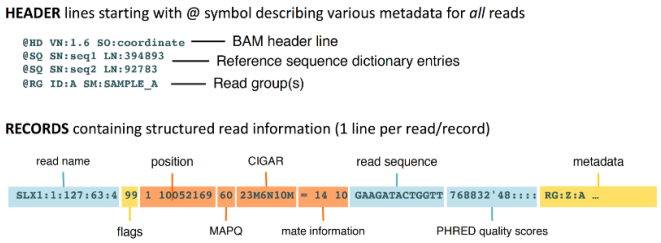
Variant VS error:

- Variant: real change
- Error: man-made and creep in on various experimental manipulations (PCR, sequencing, etc.)

Procedure for data pre-processing:



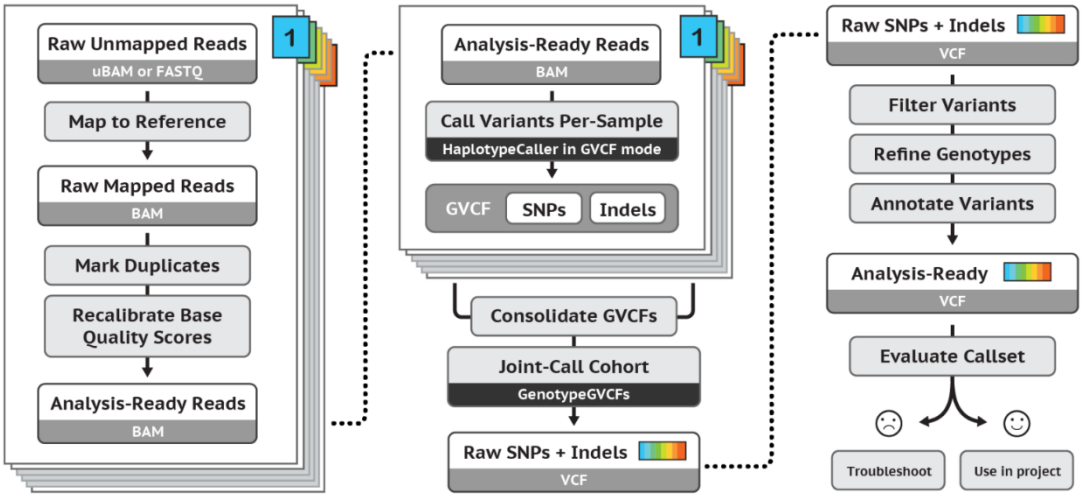
- Step1: map the reads produced by the sequence to the reference, with an input format named FASTQ, a text-based format for storing both a biological sequence and its corresponding quality scores. And output a sequence or binary alignment map with header and structured read information. The following pics is FASTQ and BAM format respectively:



- Step2: mark duplication to reduce duplications which come from some experimental manipulations.

Variant calling:

After analysis of data from the above operations, the variant calling details be like:(this is a procedure finding variants from reads)



- However, after analysis of genomes, we should joint some data together to conclude a result because a single genome data is unpowered, a joint call set will be more useful for data analysis.

Further downstream analysis for cancer diseases:

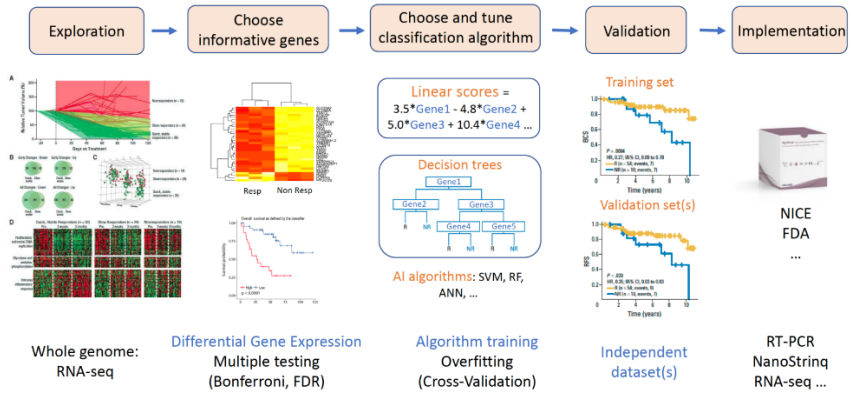
GWAS: a study about the SNPs which is of huge amount, trying to determine whether specific gene variant is related to a disease. For example: pot the variant that is common amongst all affected but absent in all unaffected.

To find the correlation between SNPs to diseases:

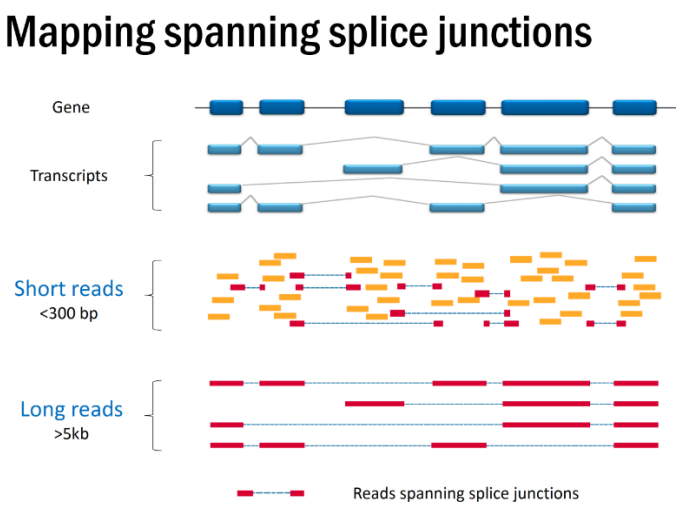
Bonferroni correction, is just to adjust P-value, suppose we have N SNPs, then the adjusted P-value is 0.05/N.

RNA-seq data analysis (genetic variant level to study cancer)

A basic procedure:



Mapping procedure which is helpful for identifying gene fusion



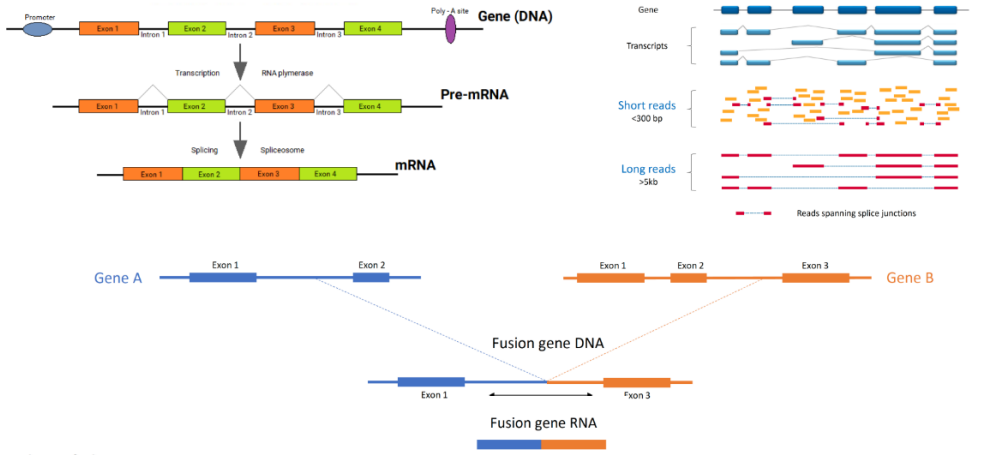
Gene fusion:

- Novel gene formed by fusion of two distinct wild type genes
- Is a specific kind of structural variant related to cancer
- In cancer: produced by somatic genome rearrangements

Advantage for RNA-Seq:

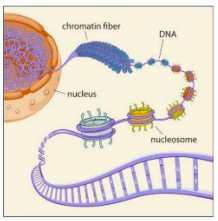
Detecting fusion in RNA-seq requires much less sequencing

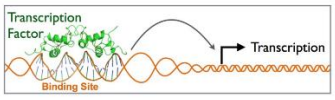
Principle for RNA-Seq detecting DNA fusion:

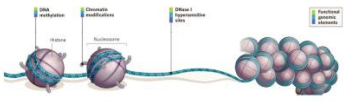


Epigenome (gene expression level to study cancer)

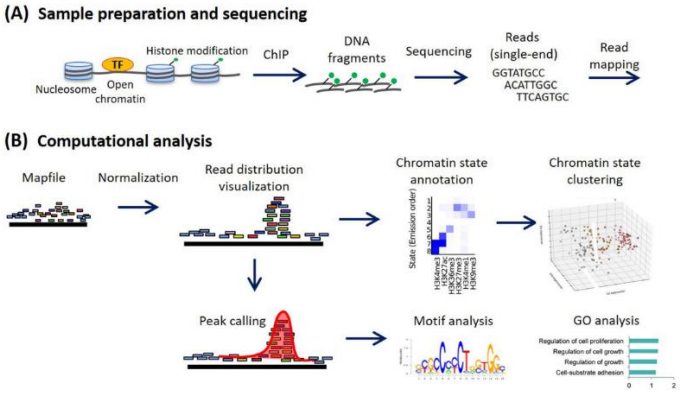
Structure of chromosome and co-factors give chance to regulate gene expression:



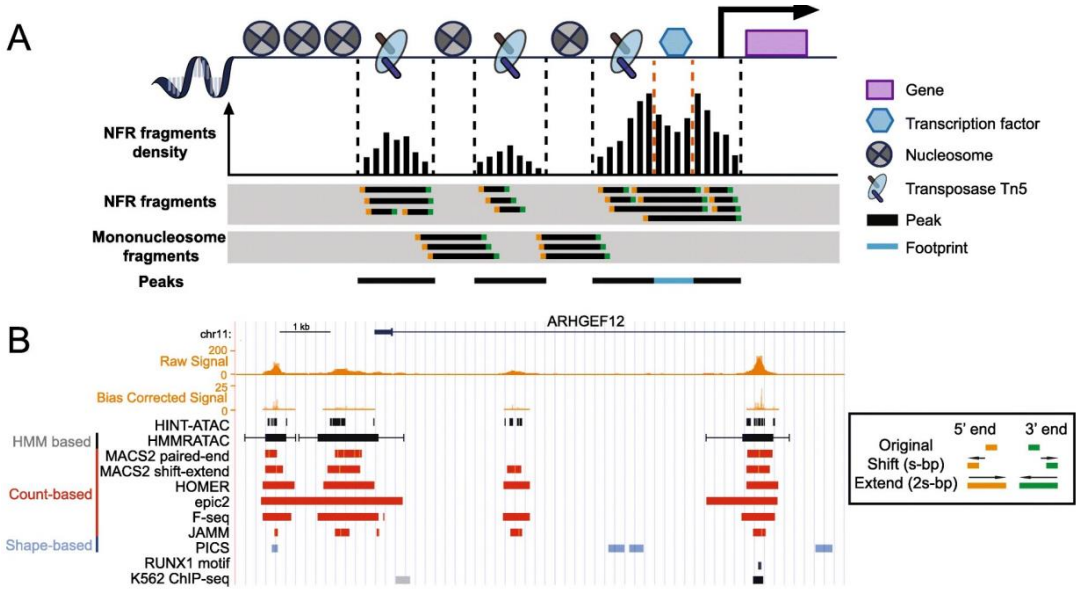




The overall data analytics pipeline for epigenetics



Peak calling



Peak shape is apparent in random background

The output of peak calling is BED file

Based on the chromosome, start of gene, end of gene and the label of gene

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chr7    127472363    127473530    Pos2    0    +    127472363    127473530    255,0,0
chr7    127473530    127474697    Pos3    0    +    127473530    127474697    255,0,0
chr7    127474697    127475864    Pos4    0    +    127474697    127475864    255,0,0
chr7    127475864    127477031    Neg1    0    -    127475864    127477031    0,0,255
chr7    127477031    127478198    Neg2    0    -    127477031    127478198    0,0,255
chr7    127478198    127479365    Neg3    0    -    127478198    127479365    0,0,255
chr7    127479365    127480532    Pos5    0    +    127479365    127480532    255,0,0
chr7    127480532    127481699    Neg4    0    -    127480532    127481699    0,0,255
```