Lung Precancer Analysis

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Overview

Introduction

Lung Cancer

- Squamous cell carcinoma
- Adenocarcinoma

Precancer

Introduction

Study Objectives

Study Objectives

- Find different mutations
  - between WES
  - between WTS
  - from cancer
  - from precancer
- Pathway examine from the mutations
  - of WES
  - of RNA-seq
- Ultra-deep sequencing to find an *infinitesimal* quantity of Non-Circulating Tumor DNA
  - from blood
  - from urine
  - frrom bronchus
- Diagnostic performace

Materials

Lung Cancer Data

- WES + WTS
- Normal + {Primary, CIS + AIS, AAH, Dysplasia, MIA}
- Total 112 samples

Materials

Cancer Types

CIS + AIS

- Carcinoma *in situ* + Adenocarcinoma *in situ*

AAH

- Atypical adenomatous hyperplasia

Dysplasia

MIA

- Minimally invasive adenocarcinoma

Materials

Sample Count

Sample Count in WES

Sample Count in Transcriptome

Methods

Methods

Workflows

Data pre-processing for variant discovery

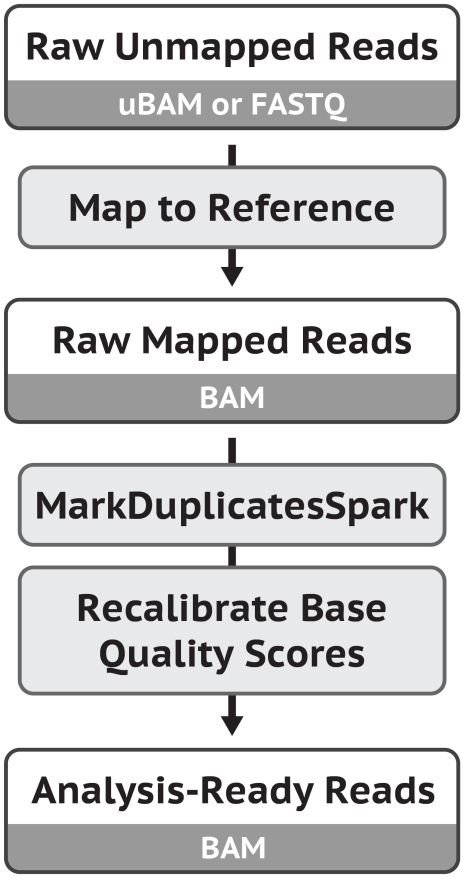

Figure: Data pre-processing for variant discovery (Van der Auwera et al., 2013; DePristo et al., 2011)

Somatic short variant discovery

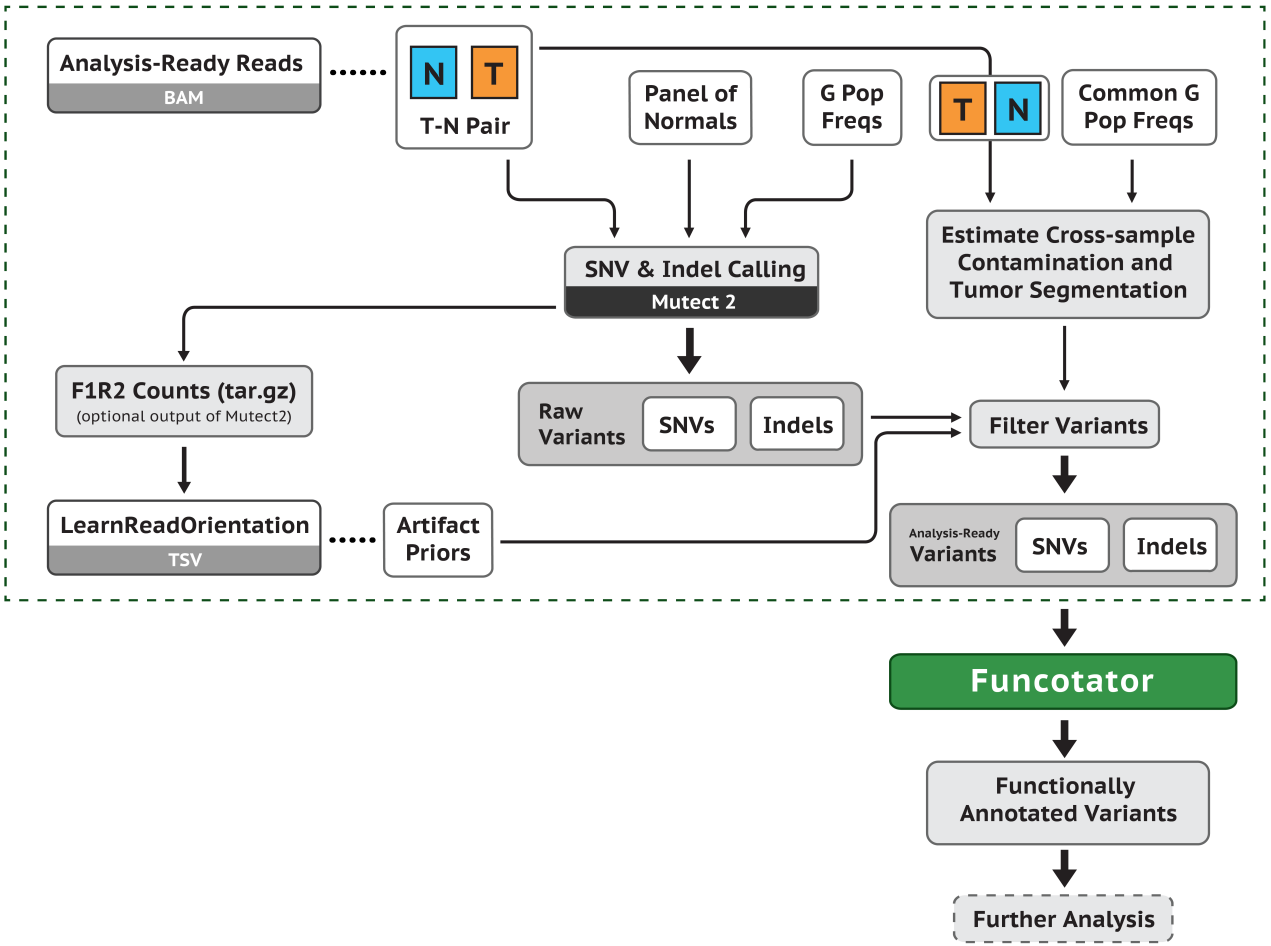

Figure: Somatic short variant (SNVs + Indels) discovery workflow (Van der Auwera et al., 2013; DePristo et al., 2011)

Germline short variant discovery

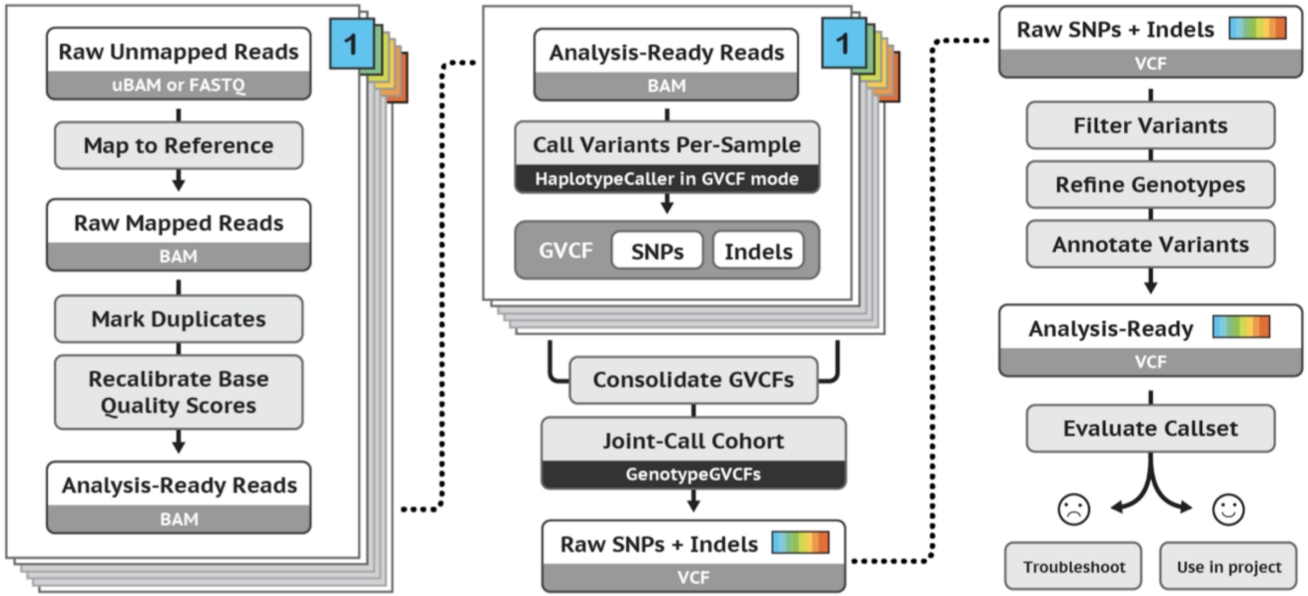

Figure: Germline short variant (SNVs + Indels) discovery workflow (Van der Auwera et al., 2013; DePristo et al., 2011)

RNA-seq short variant discovery

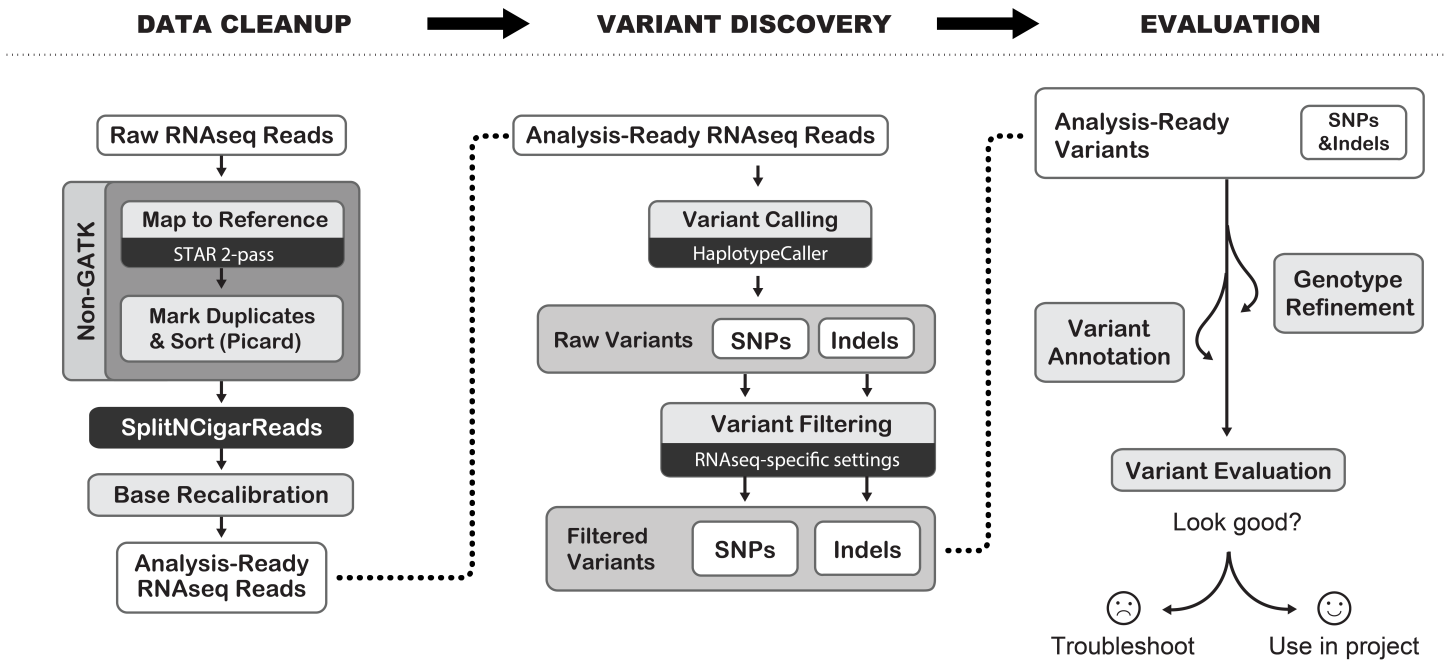

Figure: RNA-seq short variant (SNVs + Indels) discovery workflow (Van der Auwera et al., 2013; DePristo et al., 2011)

Methods

Miscellaneous

Used Bioinformatics Tools

- FastQC (Andrews et al., 2012)
- Sequenza (Favero et al., 2015)
- BWA (Li & Durbin, 2009; Li, 2013)
- STAR (Dobin et al., 2013)
- Bowtie2 (Langmead & Salzberg, 2012)
- Samtools (Li et al., 2009)
- GATK (Van der Auwera et al., 2013; DePristo et al., 2011)
- Picard (*Picard toolkit*, 2019)
- VCF2MAF (Kandoth et al., 2018)
- VEP (McLaren et al., 2016)

Python Packages

- Pandas (pandas development team, 2020; Wes McKinney, 2010)
- Sequenza-utils (Favero et al., 2015)
- Matplotlib (Hunter, 2007)
- Seaborn (Waskom & the seaborn development team, 2020)
- CoMut (Crowdis, He, Reardon, & Van Allen, 2020)

Results

Results

Quality Checks with FastQC

FastQC?

FastQC on WES

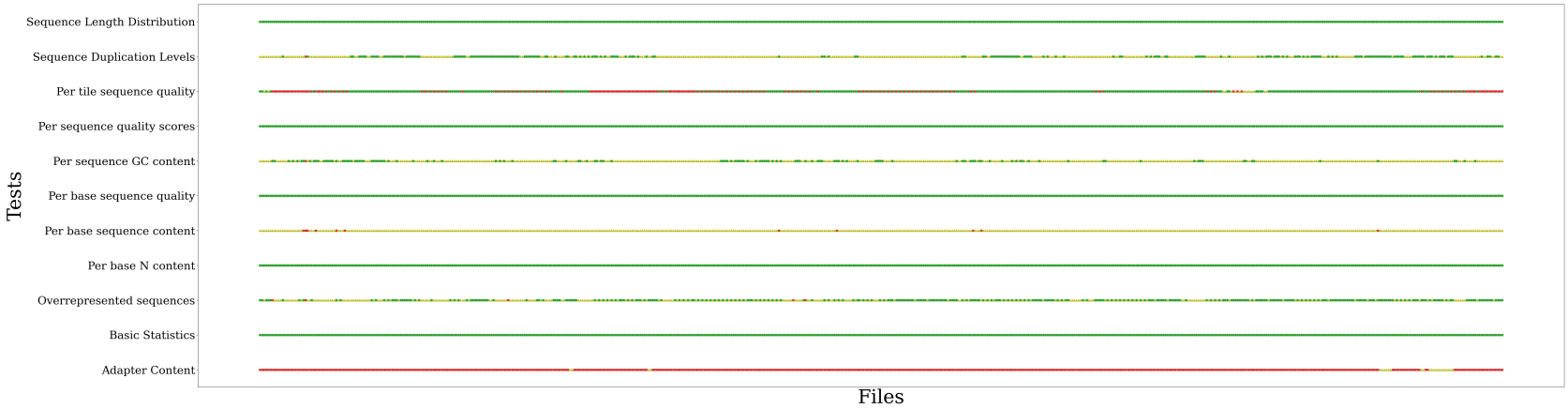

Figure: FastQC with WES data

∴ Only 33P1 has more than 3 failures: 6 FAILs.
∴ 33P1 is excluded at further analysis.

FastQC on WTS

Figure: FastQC with WTS data

$\therefore$ No sample has more than 5 failures.

$\therefore$ All sample are good to analysis.

Results

Quality Checks with Sequenza

Sequenza?

Cellularity & Ploidy on WES

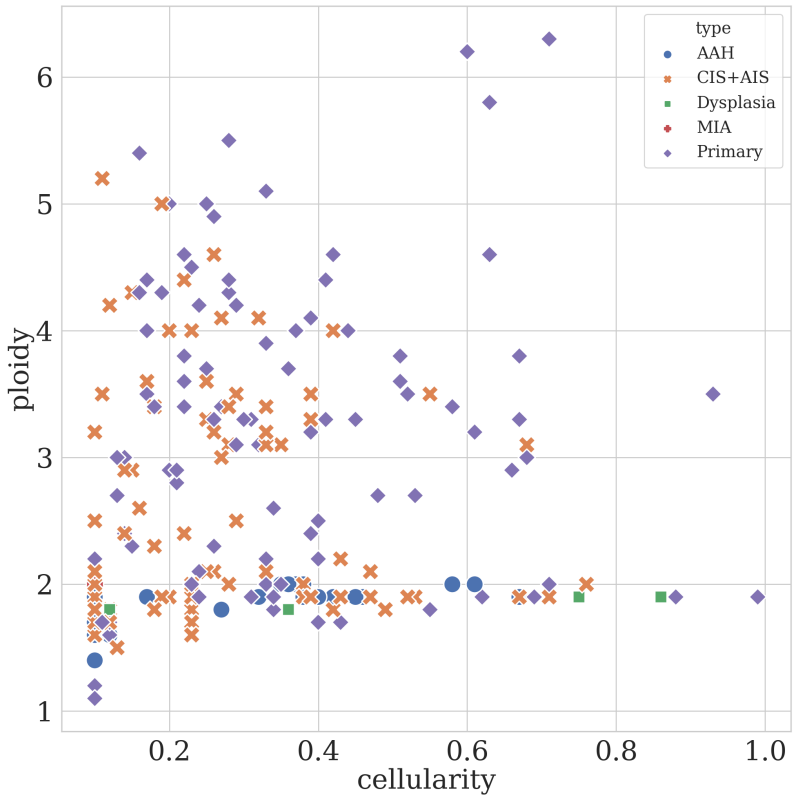

Figure: Cellularity and Ploidy from Sequenza

Copy Number Variation on WES

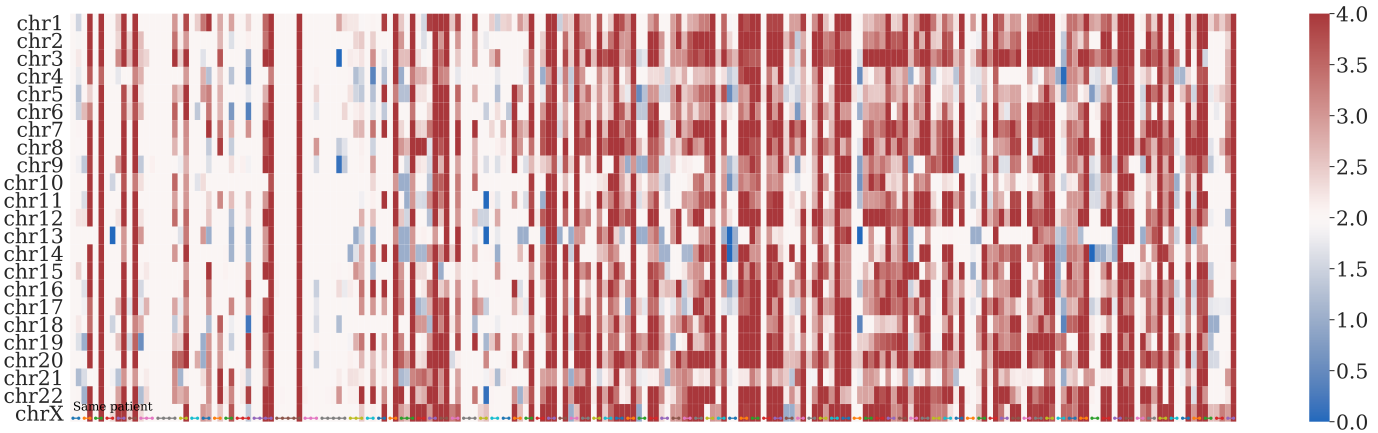

Figure: Copy Number Variation by patients and chromosomes

Results

Mutect2

Mutect2?

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