

CAB  
HMH

# Applying cancer subpopulations analysis methods to metagenomic series

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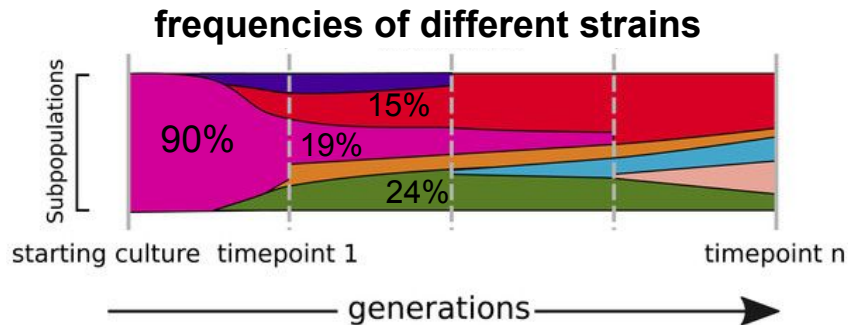
# Problem

## Input:

- metagenomic series data
- reference genome

## Output:

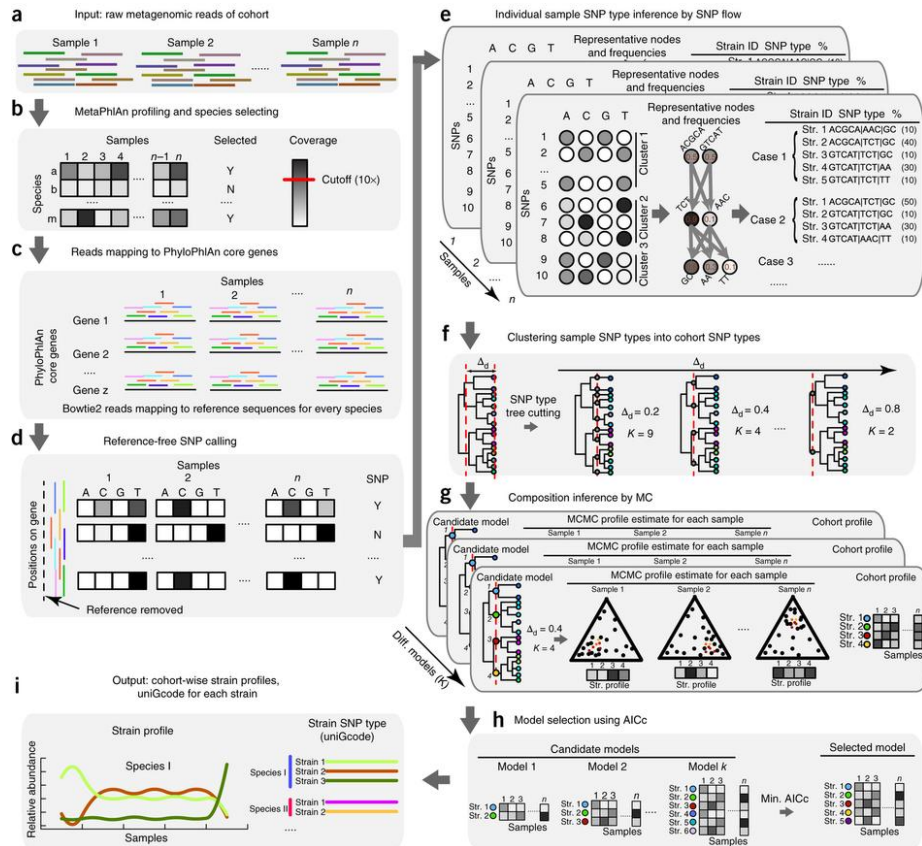
- the number of related strains
- their relative abundances across the samples



# ConStrains [Luo et. al, 2015]

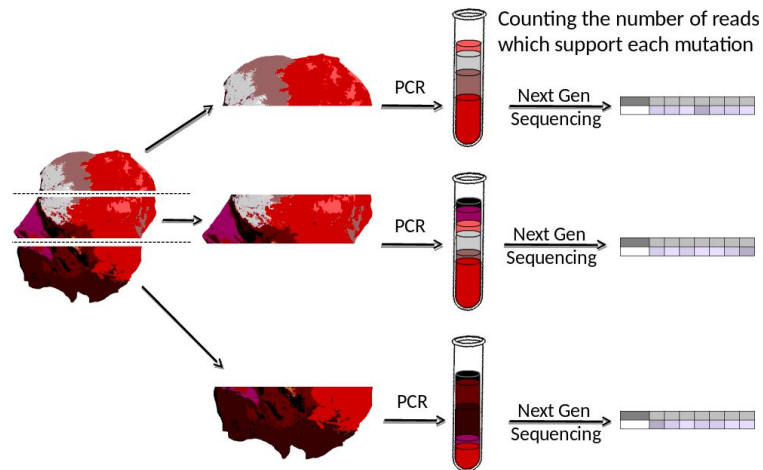
Questionable computational model!

Could not reproduce results from the paper

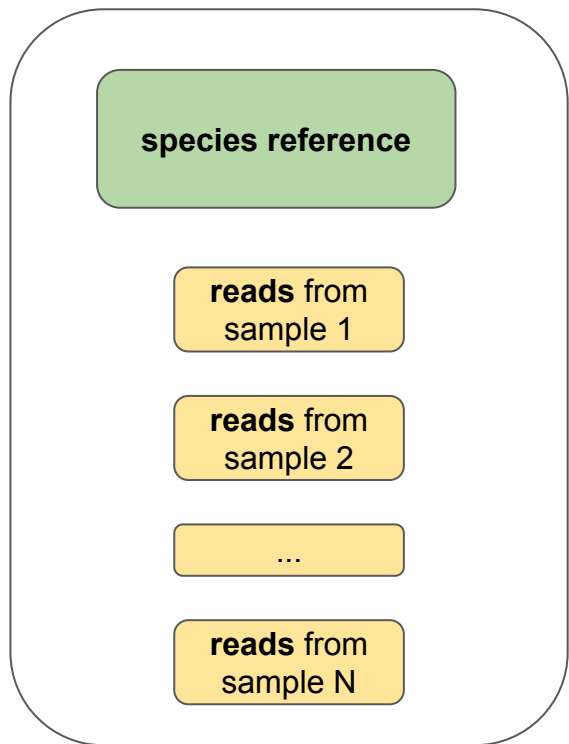


# Subpopulation analysis in multiple tumor samples

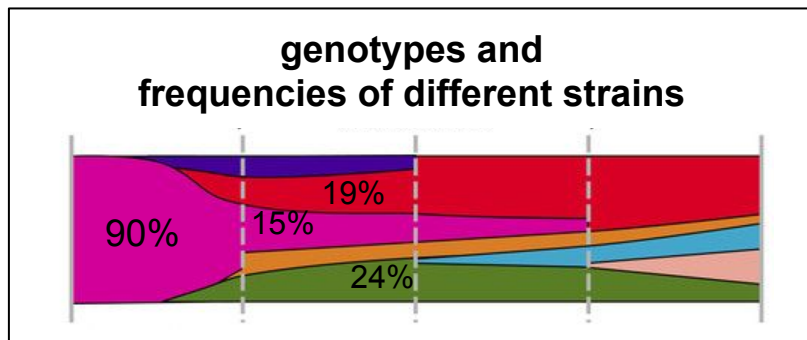
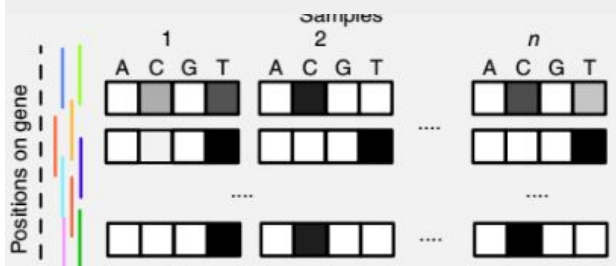
- **Clomial** [Zare et al, 2014]
  - Matrix decomposition with EM
- PyClone [Roth et al, 2014]
- **PhyloWGS** [Deshwar et al, 2015]
  - MCMC on phylogenies
- AncesTree [Beerenwinkel et al, 2015]
- LICHeE [Popic et al, 2015]
- ...



# General approach for *de novo* strain analysis



SNPs:

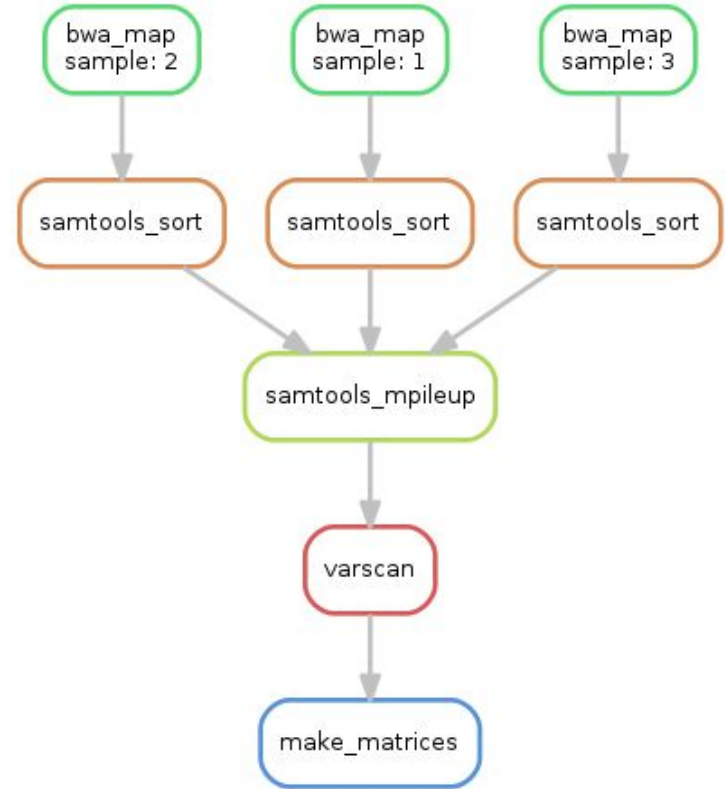


# Step 1: SNPs calling

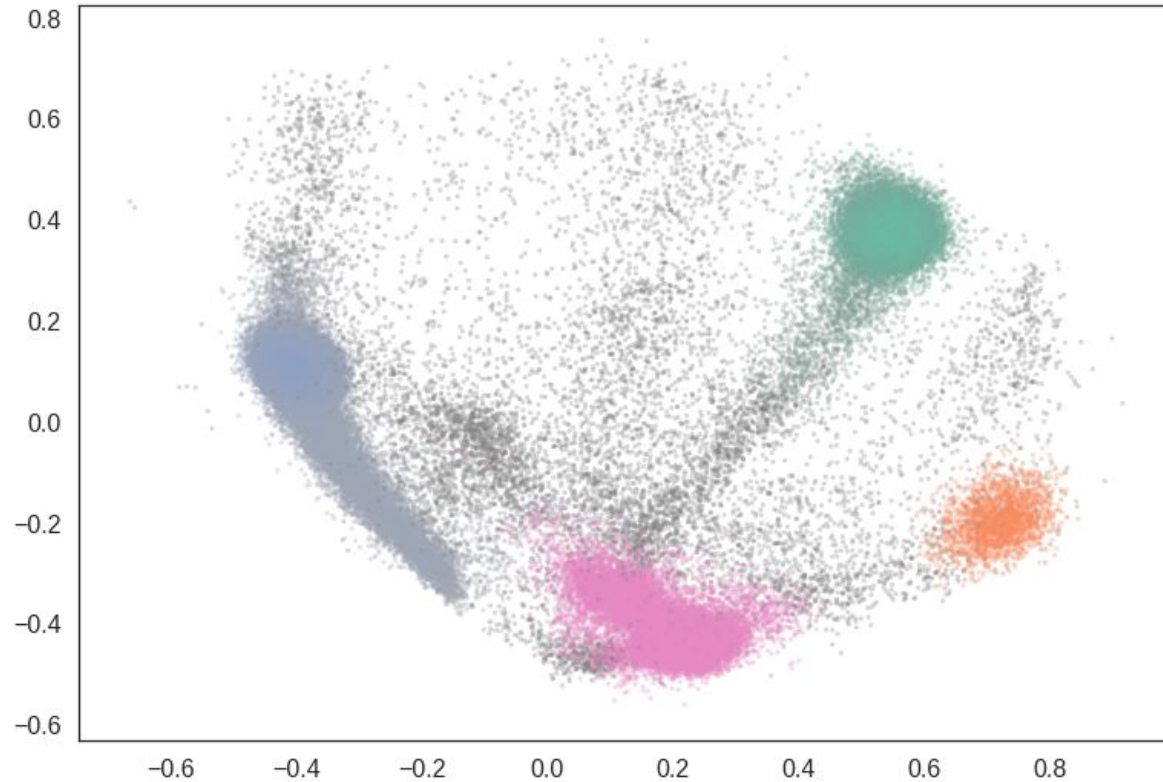
- BWA + samtools mpileup + VarScan wrapped in SnakeMake

## Problem:

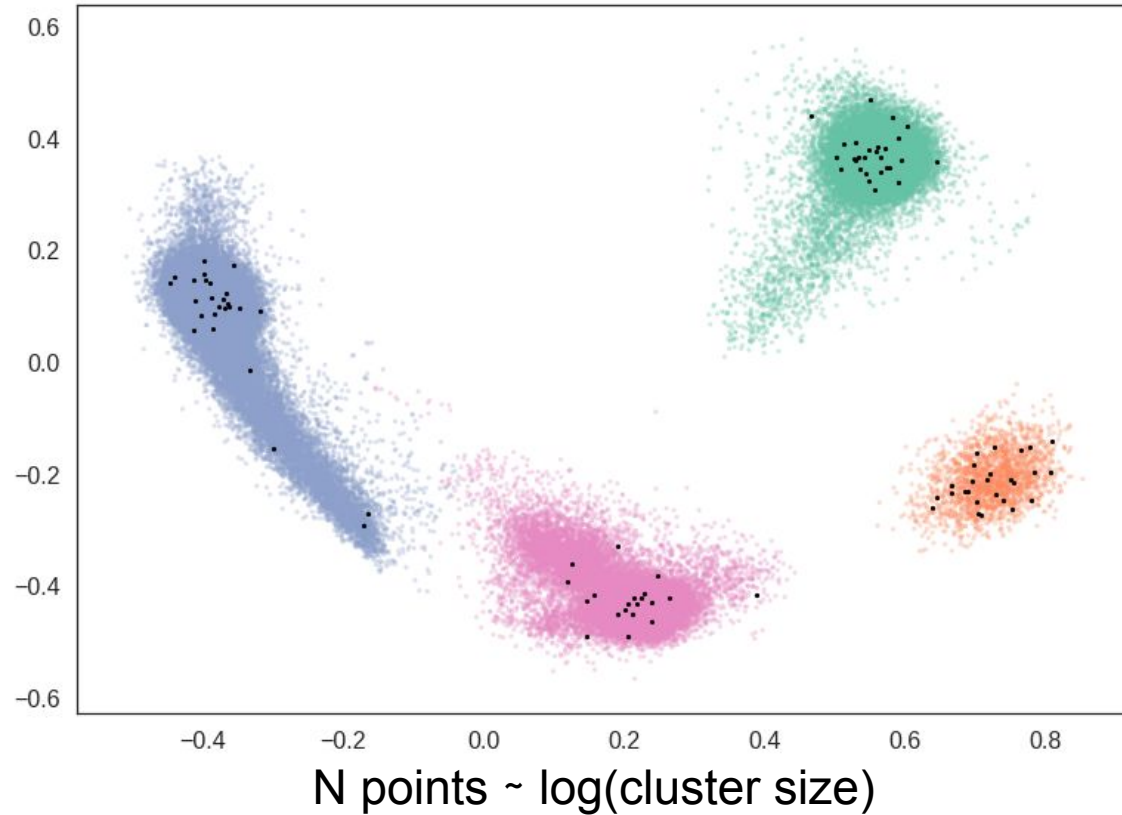
Clomial and PhyloWGS can't work with **too many SNPs**



## Step 2: SNPs clusterisation



# Step 3: SNPs subsampling





## Step 4: run cancer tools

- **PhyloWGS** finished only on simple data with high coverage and produced poor results
- **Clomial** results are in good agreement with ground truth

Further results concern Clomial

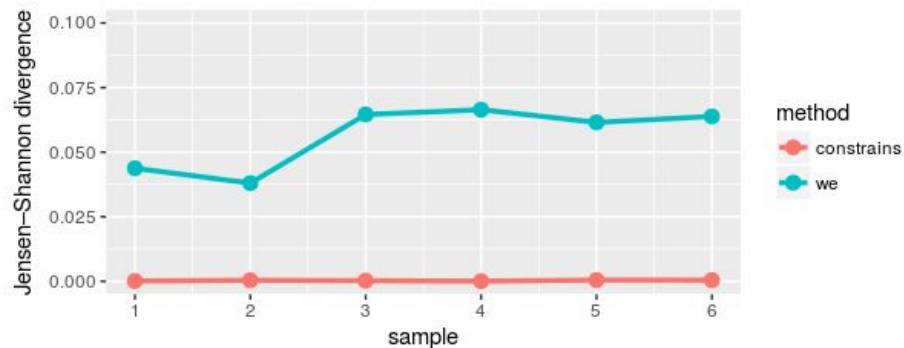
# Datasets

- Synthetic data
  - 4 datasets: 2 - 5 strains, 6 samples in each
  - frequencies from ConStrains paper
- Real data
  - Infant gut [Sharon et al, 2013]
  - known abundances of the *Staphylococcus epidermidis* strains

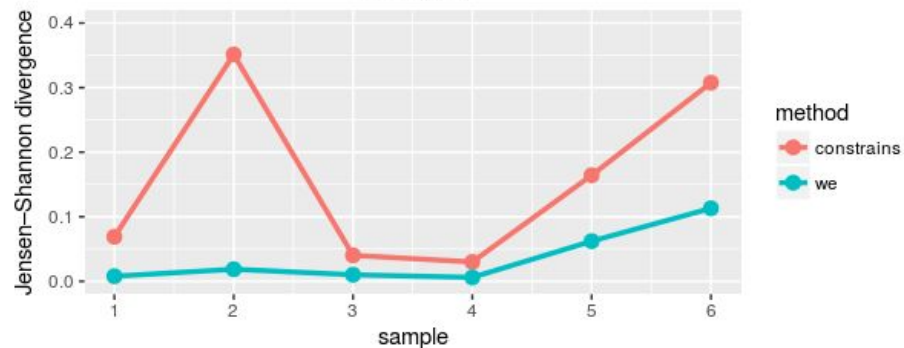
**Benchmarking:** count Jensen-Shannon divergence between predicted and real frequencies

# Results: synthetic data

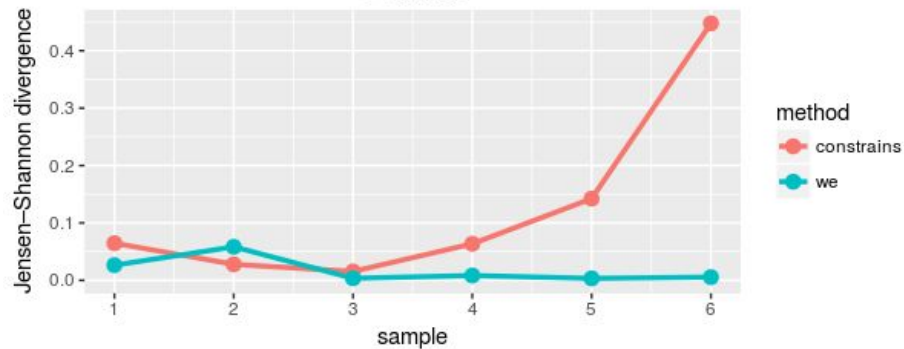
## 2 strains



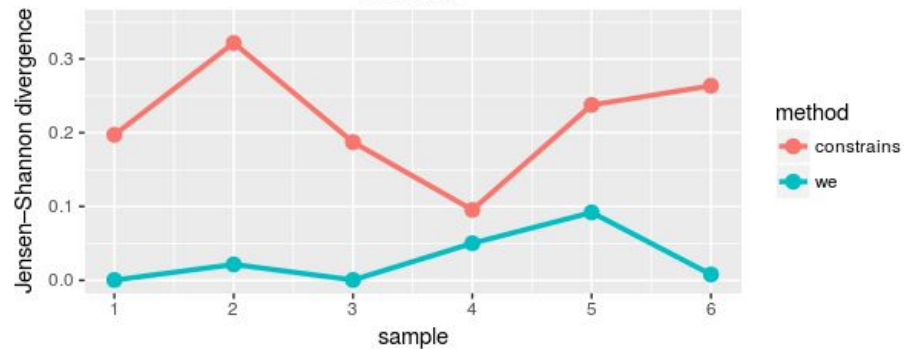
## 4 strains



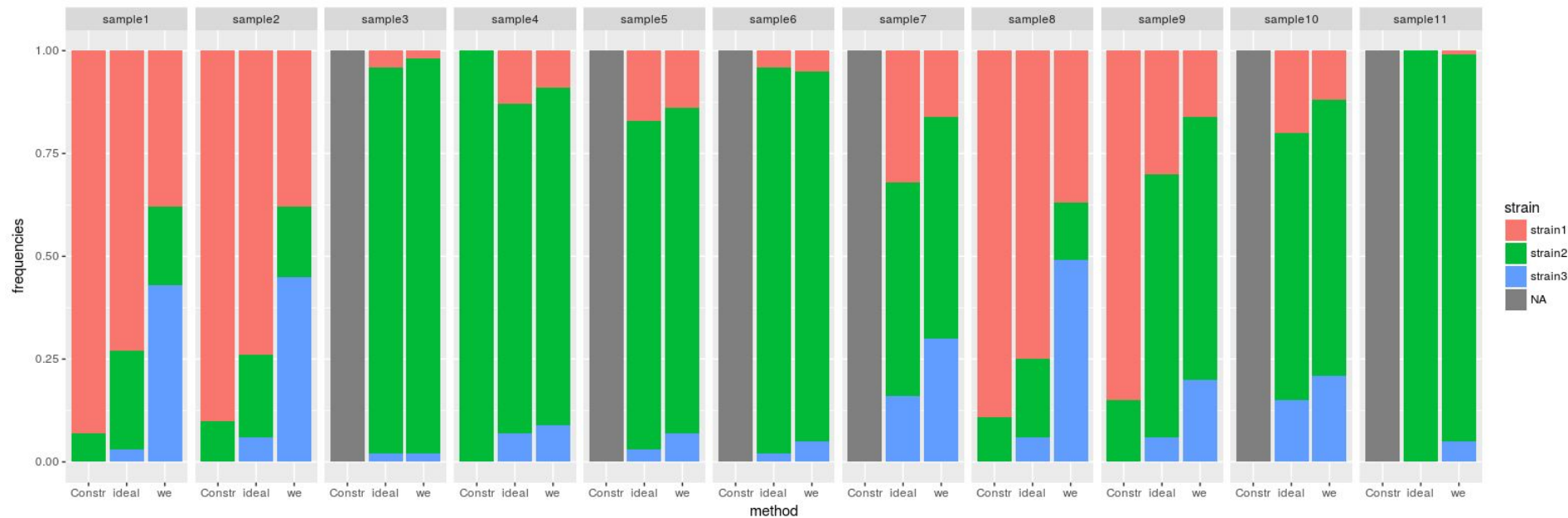
## 3 strains



## 5 strains



# Results: infant gut



ConStrains found 2 out of 3 strains and failed in 6 out of 11 samples

# Results

- SNP detection pipeline
- SNP clustering and subsampling
- Benchmarking framework
- Clomial and PhyloWGS were applied to metagenomic series data
- Clomial produced reasonable results, beating the ConStrains baseline

# Further plans

- Improve current pipeline
  - determine number of strains
  - study the correctness of resulting genotypes
- Integrate with existing metagenomic pipelines (MIDAS, metaPhlan)
- Test stability with rare strains contamination
- Come up with reference-free analysis
- Try other cancer tools (AncesTree, LICHeE, ...)

# Thank you!



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