Sarek

A portable workflow for WGS analysis of germline and somatic mutations

Maxime U. Garcia

maxulysse.github.io

@MaxUlysse

@gau

SciLifeLab

GANATIONALCTAC ATCAGENOMICSGT INFRASTRUCTURE

Karolinska Institutet

DNAclub

Sarek

Sarek, the National Park in Northen Sweden

The most dramatic and grandiose of all

- Long, deep, narrow valleys and wild, turbulent water.
- **A tortuous delta landscape.**
- Completely lacking in comfortable accommodations.
- Sarek is one of Sweden's **most inaccessible national parks**
- **There are no roads leading up to the national park**.

Sarek National Park website

Where we're going we don't need roads

What is Sarek?

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http://sarek.scilifelab.se/

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NATIONAL GENOMICS INFRASTRUCTURE

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- Support from The Swedish Childhood Tumor Biobank

NATIONAL GENOMICS INFRASTRUCTURE

NBIS NATIONAL BIOINFORMATICS INFRASTRUCTURE SWEDEN

Nextflow

https://www.nextflow.io/

- Data-driven workflow language

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- Shareable and reproducible (with containers)

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https://singularity.lbl.gov/

- Docker-like container engine
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- Supported by Nextflow
- Can pull containers from Docker-hub

Sarek exists in multiple flavors

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Sarek Germline

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Sarek Somatic

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Sarek Germline

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Sarek Exome

Preprocessing

gatk ☑ Best Practices

https://software.broadinstitute.org/gatk/best-practices/

Based on GATK Best Practices (GATK 4.0)

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Based on GATK Best Practices (GATK 4.0)

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Based on GATK Best Practices (GATK 4.0)

- Reads mapped to reference genome with `bwa`
- Duplicates marked with `picard MarkDuplicates`
- Recalibrate with `GATK BaseRecalibrator`

Germline Variant Calling

- SNVs and small indels:

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  - HaplotypeCaller
  - Strelka2

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  - ASCAT
  - Control-FREEC (🔧 adding)

Annotation

- VEP and SnpEff

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- ClinVar, COSMIC, dbSNP, GENCODE, gnomAD, polyphen, sift, etc.

Prioritization

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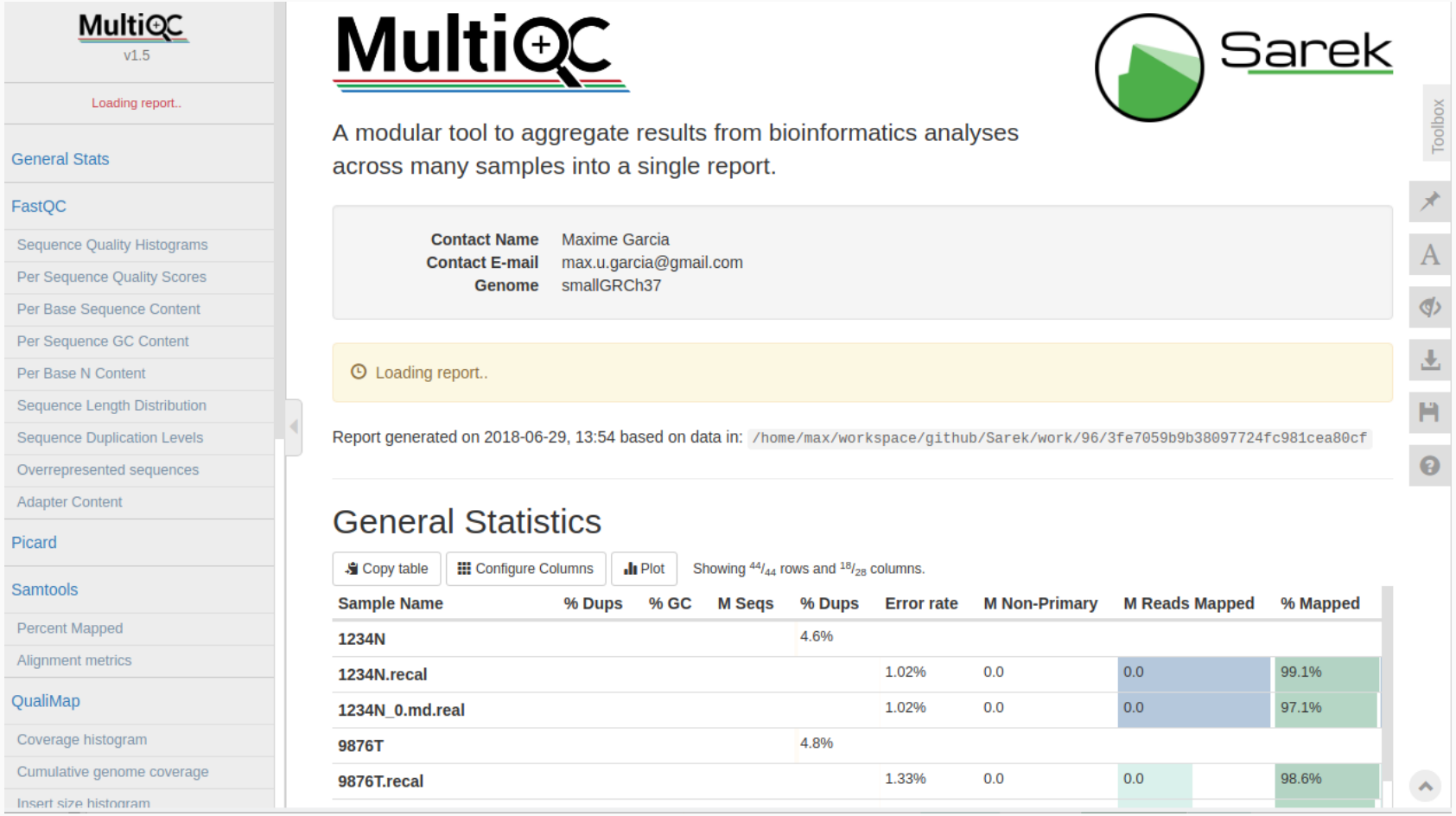
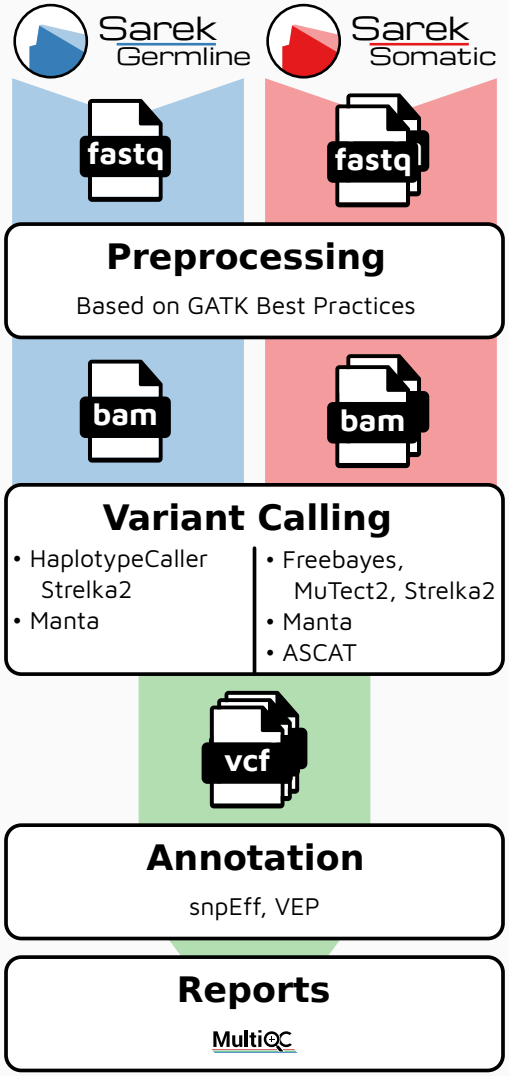
- Findings are ranked in three tiers
  - 1st tier: well known, high-impact variants
  - 2nd tier: variants in known cancer-related genes
  - 3rd tier: the remaining variants

Reports



http://multiqc.info/

Workflow


Sarek Germline
Sarek Somatic
fastq
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Preprocessing
Based on GATK Best Practices
bam
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Variant Calling
• HaplotypeCaller Strelka2
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vcf
Annotation
snpEff, VEP
Reports
MultiQC

Reference genomes

- GRCh37 and GRCh38

Reference genomes

- GRCh37 and GRCh38
- Custom genome

Reference genomes

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- Custom genome
- 🔧 Other organisms

More AWS testing

Production ready

Sarek at work

- 50 tumor/normal pairs with GRCh37 reference

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- 50 tumor/normal pairs with GRCh37 reference
- 90 tumor/normal pairs (with some relapse) with GRCh38 reference
- The whole SweGen dataset with GRCh38 reference
  - 1 000 samples in germline settings
- 4 clinical samples
  - more coming with Genomic Medicine Sweden initiative

Preprint available at BioRxiv

Sarek: A portable workflow for whole-genome sequencing analysis of germline and somatic variants

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Get involved!

- Our code is hosted on Github
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- We have gitter channels
  https://gitter.im/SciLifeLab/Sarek
  https://gitter.im/nf-core/Lobby

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Any questions?

- http://sarek.scilifelab.se/
- https://github.com/SciLifeLab/Sarek
- https://maxulysse.github.io/dnaclub2018