Sarek

A portable workflow for WGS analysis of germline and somatic mutations

Maxime U. Garcia
maxulysse.github.io
@MaxUlysse
@gau

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Science for Life Laboratory

SciLifeLab

https://scilifelab.se/

SciLifeLab is a national centre for molecular biosciences with focus on health and environmental research

Karolinska Institutet

KTH VETENSKAP OCH KONST

Stockholms universitet

UPPSALA UNIVERSITET

SciLifeLab

https://scilifelab.se/

Infrastructure Services

Genomics	Proteomics	Metabolomics
Single Cell Biology	Bioimaging and Molecular Structure	Chemical Biology and Genome Engineering
Drug Discovery	Diagnostics	Bioinformatics

National Genomics Infrastructure

https://ngisweden.scilifelab.se/

- National resource

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- National resource
- State-of-the-art infrastructure
  - massively parallel DNA sequencing and SNP genotyping

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- National resource
- State-of-the-art infrastructure
  - massively parallel DNA sequencing and SNP genotyping
- Guidelines and support
  - sample collection, study design, protocol selection
  - bioinformatics analysis

National Bioinformatics Infrastructure Sweden

https://www.nbis.se/

- Swedish ELIXIR node

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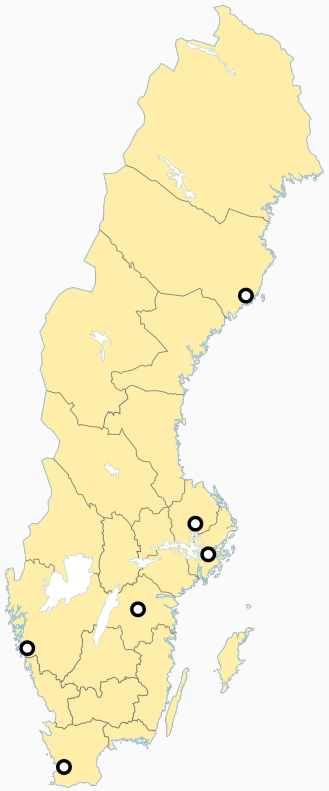
- Swedish ELIXIR node
- Bioinformatics support for Swedish researchers

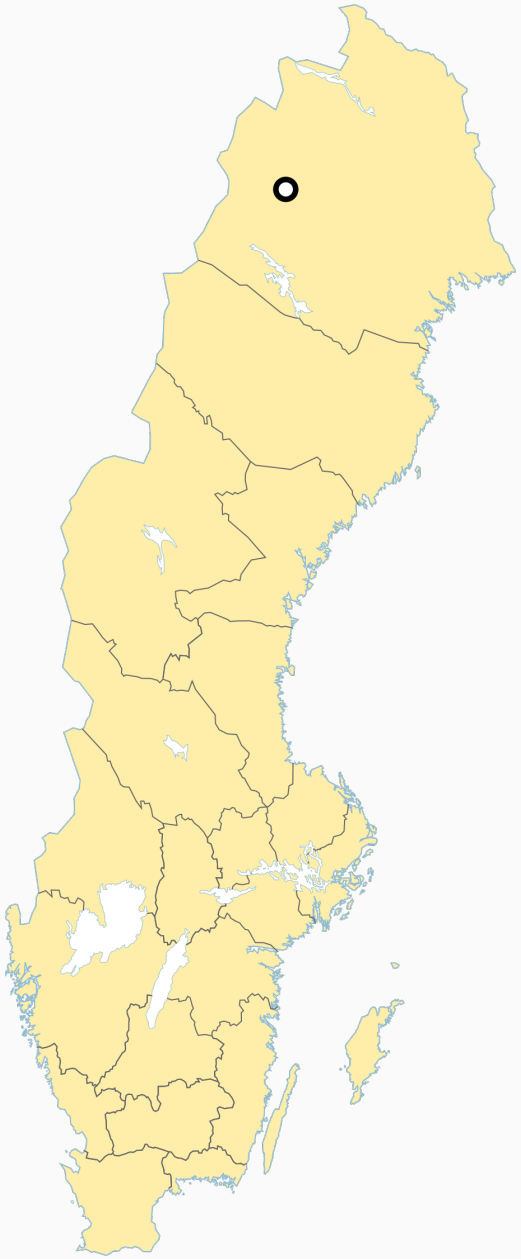
National Bioinformatics Infrastructure Sweden

NBIS
NATIONAL BIOINFORMATICS INFRASTRUCTURE SWEDEN

https://www.nbis.se/



Sarek



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?

http://opensource.scilifelab.se/projects/sarek/

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- Nextflow pipeline

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NATIONAL GENOMICS INFRASTRUCTURE

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NBIS NATIONAL BIOINFORMATICS INFRASTRUCTURE SWEDEN

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- Nextflow pipeline
- Developed at NGI
- In collaboration with NBIS
- Support from The Swedish Childhood Tumor Biobank

Nextflow

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- 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

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Preprocessing

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

Based on GATK Best Practices (GATK 3.8)

🔧 Switching to GATK 4.0

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- Reads mapped to reference genome with `bwa`

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gatk ☑ Best Practices

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- Recalibrate with `GATK BaseRecalibrator`

Germline Variant Calling

- SNVs and small indels:

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  - HaplotypeCaller
  - Strelka2

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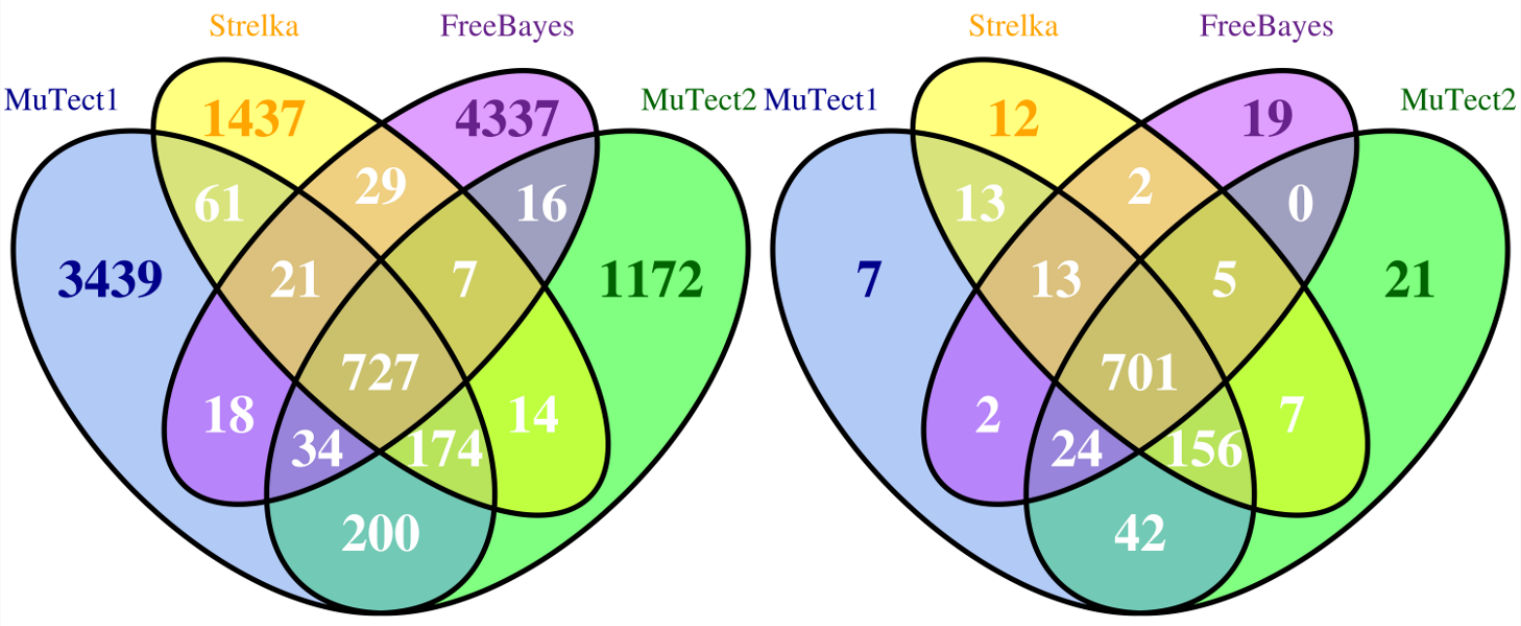
  - ASCAT
  - Control-FREEC (🔧 adding)

SNV Calling overlap



All calls True positives only

Number and overlap of somatic SNV calls from a WGS medulloblastoma dataset

Alioto TS et al. (2015) doi https://doi.org/10.1038/ncomms10001

Annotation

- VEP and SnpEff

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

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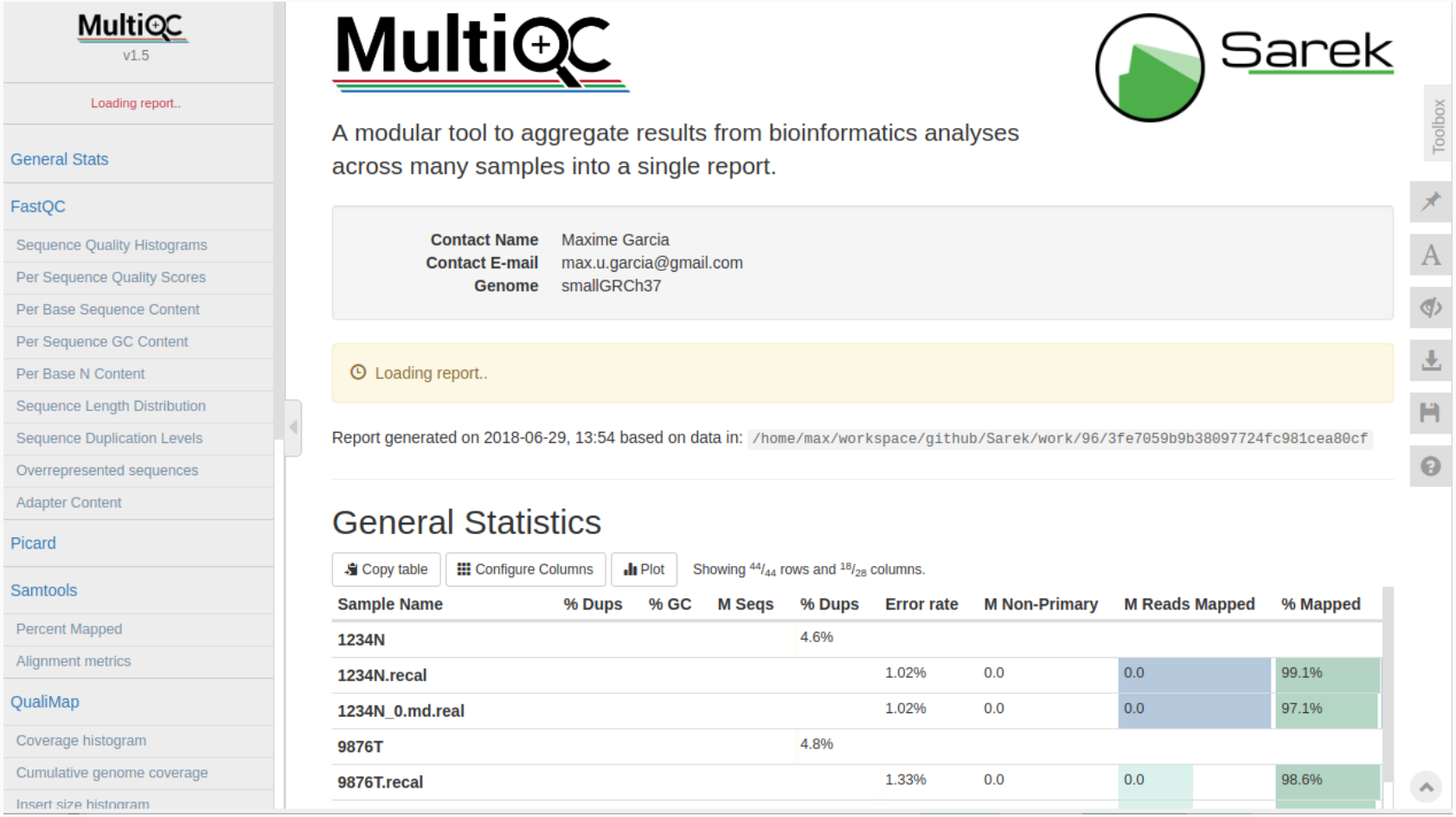
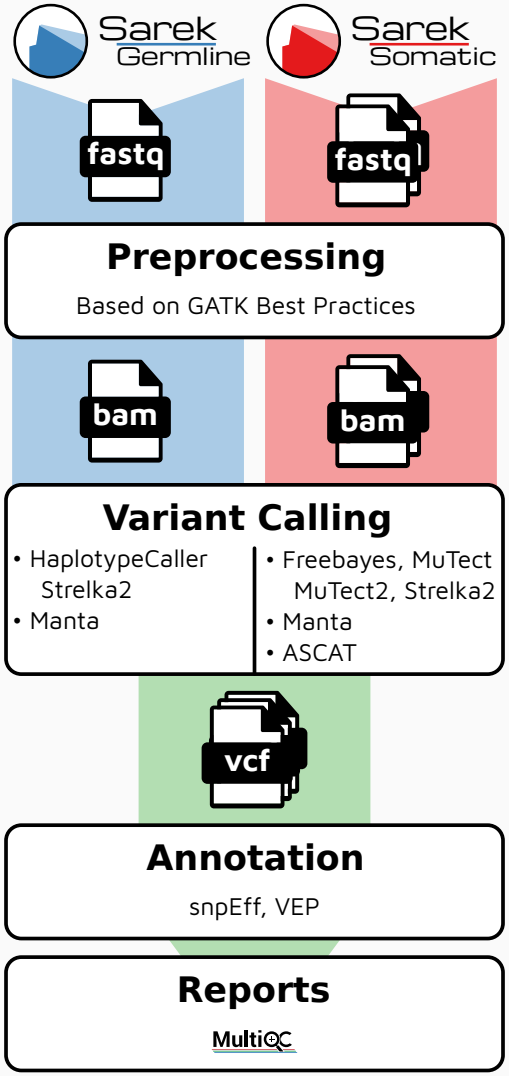
- Findings are ranked in three tiers
  - 1^{st} tier: well known, high-impact variants
  - 2^{nd} tier: variants in known cancer-related genes
  - 3^{rd} tier: the remaining variants

Reports



http://multiqc.info/

Workflow


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

- Preprocessing is done with the whole genome

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- Variant call only on the target regions

Reference genomes

- GRCh37 and GRCh38

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- Custom genome

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

Maxime Garcia, Szilveszter Juhos, Malin Larsson, Pall I Olason, Marcel Martin, Jesper Eisfeldt, Sebastian DiLorenzo, Johanna Sandgren, Teresita Diaz de Ståhl, Valtteri Wirta, Monica Nistèr, Björn Nystedt, Max Käller

https://doi.org/10.1101/316976

http://nf-co.re/

A community effort to collect a curated set of Nextflow analysis pipelines

- GitHub organisation to collect pipelines in one place
- No institute-specific branding
- Strict set of guideline requirements
- Automated testing for code style and function
- Conda environnment, Docker and Singularity container

Get involved!

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- We have gitter channels
  - `https://gitter.im/SciLifeLab/Sarek`
  - `https://gitter.im/nf-core/Lobby`

Acknowledgments

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Björn Nystedt
Markus Ringnér
Pall I Olason
Jonas Söderberg

Clinical Genomics
Kenny Billiau
Hassan Foroughi Asl
Valtteri Wirta

Clinical Genetics
Jesper Eisfeldt

Any questions?

- http://opensource.scilifelab.se/projects/sarek/
- https://github.com/SciLifeLab/Sarek
- https://maxulysse.github.io/jobim2018