Sarek

A portable workflow for WGS analysis of germline and somatic mutations

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@gau

SciLifeLab

NATIONAL GENOMICS INFRASTRUCTURE

Karolinska Institutet

DNA club

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://sarek.scilifelab.se/

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NATIONAL GENOMICS INFRASTRUCTURE

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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- Without the root user security problem
- Supported by Nextflow
- Can pull containers from Docker-hub

Sarek exists in multiple flavors

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Preprocessing

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

Based on GATK Best Practices (GATK 4.0)

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- Duplicates marked with `picard MarkDuplicates`

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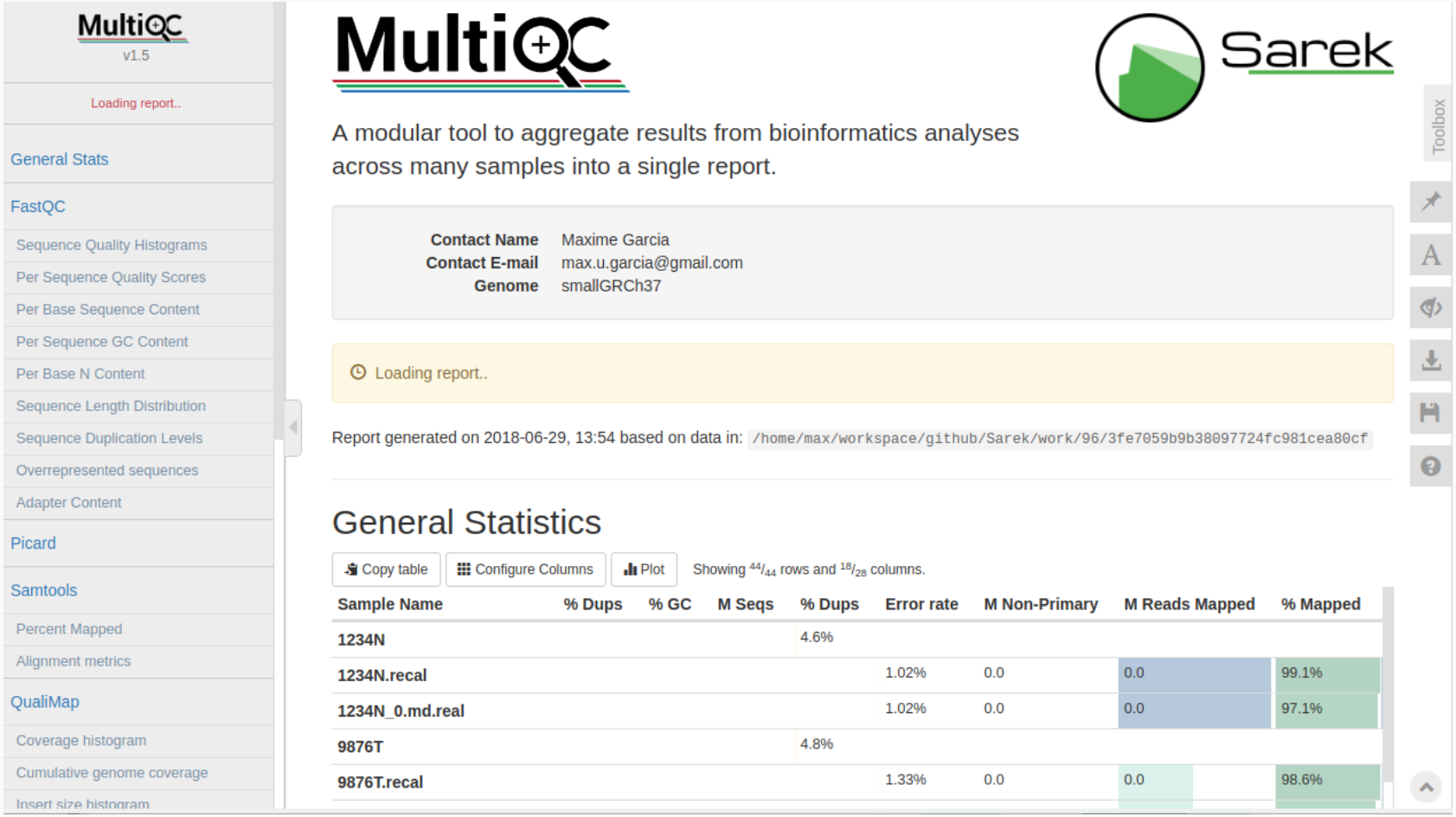
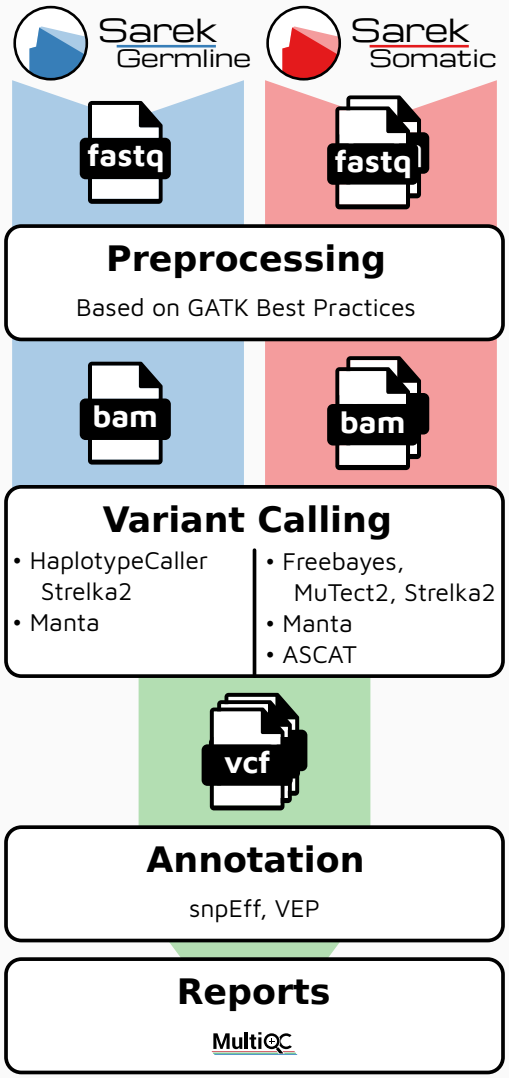
- Findings are ranked in three tiers
  - 1^{st} tier: well known, high-impact variants
  - 2^{nd} tier: variants in known cancer-related genes
  - 3^{rd} tier: the remaining variants

Reports



http://multiqc.info/

Workflow


Sarek Germline
Sarek Somatic
fastq
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Preprocessing
Based on GATK Best Practices
bam
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Variant Calling
• HaplotypeCaller
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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

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

Get involved!

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

Acknowledgments


Barntumörbanken	Elisa Basmaci	**NGI**	Johannes Alneberg	**NBIS**	Sebastian DiLorenzo
	Szilveszter Juhos		Anandashankar Anil		Malin Larsson
	Gustaf Ljungman		Franziska Bonath		Marcel Martin
	Monica Nistèr		Orlando Contreras-López		Markus Mayrhofer
	Gabriela Prochazka		Phil Ewels		Björn Nystedt
	Johanna Sandgren		Sofia Haglund		Markus Ringnér
	Teresita Díaz De Ståhl		Max Käller		Pall I Olason
	Katarzyna Zielinska-Chomej		Anna Konrad		Jonas Söderberg
			Pär Lundin		
Grupp Nistèr	Saad Alqahtani		Remi-Andre Olsen	**Clinical Genomics**	Kenny Billiau
	Min Guo		Senthilkumar Panneerselvam		Hassan Foroughi Asl
	Daniel Hägerstrand		Fanny Taborsak		Valtteri Wirta
	Anna Hedrén		Chuan Wang		
	Martin Proks			**Nextflow folks**	Paolo Di Tommaso
	Rong Yu				Sven Fillinger
	Jian Zhao	**Clinical Genetics**	Jesper Eisfeldt		Alexander Peltzer

Any questions?

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