hCNV Community

Standards and protocols for CNV discovery and data exchange

Andrew Stubbs
Antonio Rausell
Krzysztof Poterlowicz
Michael Baudis

www.elixir-europe.org

2025-05-15

hCNV products

- Resource (https://refcnv.org/) : Progenetix cancer CNV reference resource and upcoming refCNV for reference copy number data accessible via Beacon API - Michael
- Resource (htsget2Galaxy) : FAIR access to GA4GH databases - Andrew
- Resource (CNV 2 Galaxy Beacon) : integrate rare disease workflow with external data (e.g hCNV from refcnv) and Cancer data in Genomic Beacons. – Khaled / Krzys
- Resource: - bioinformatics and ML tools for CNV assessment, including a couple of slides opening to non-coding SNVs at the very end (which can be of interest for the rare-disease group even if is beyond the CNV scope). - Antonio
- Standards: Beacon, VRS and VCF support for CNV representation and querying

progenetix.org

Cancer Genomics Reference Resource

- ***open*** resource for oncogenomic profiles
- over **150'000 cancer CNV profiles**
- more than 9**00 diagnostic types**
- runs on a **Beacon API**
- inclusion of reference datasets (e.g. TCGA)
- support for SNV data (TCGA, cell lines...)
- standardized encodings (e.g. NCIt, ICD-O 3)
- identifier mapping for PMID, GEO, Cellosaurus, TCGA, cBioPortal where appropriate
- core clinical data (TNM, sex, survival ...)
- data mapping services

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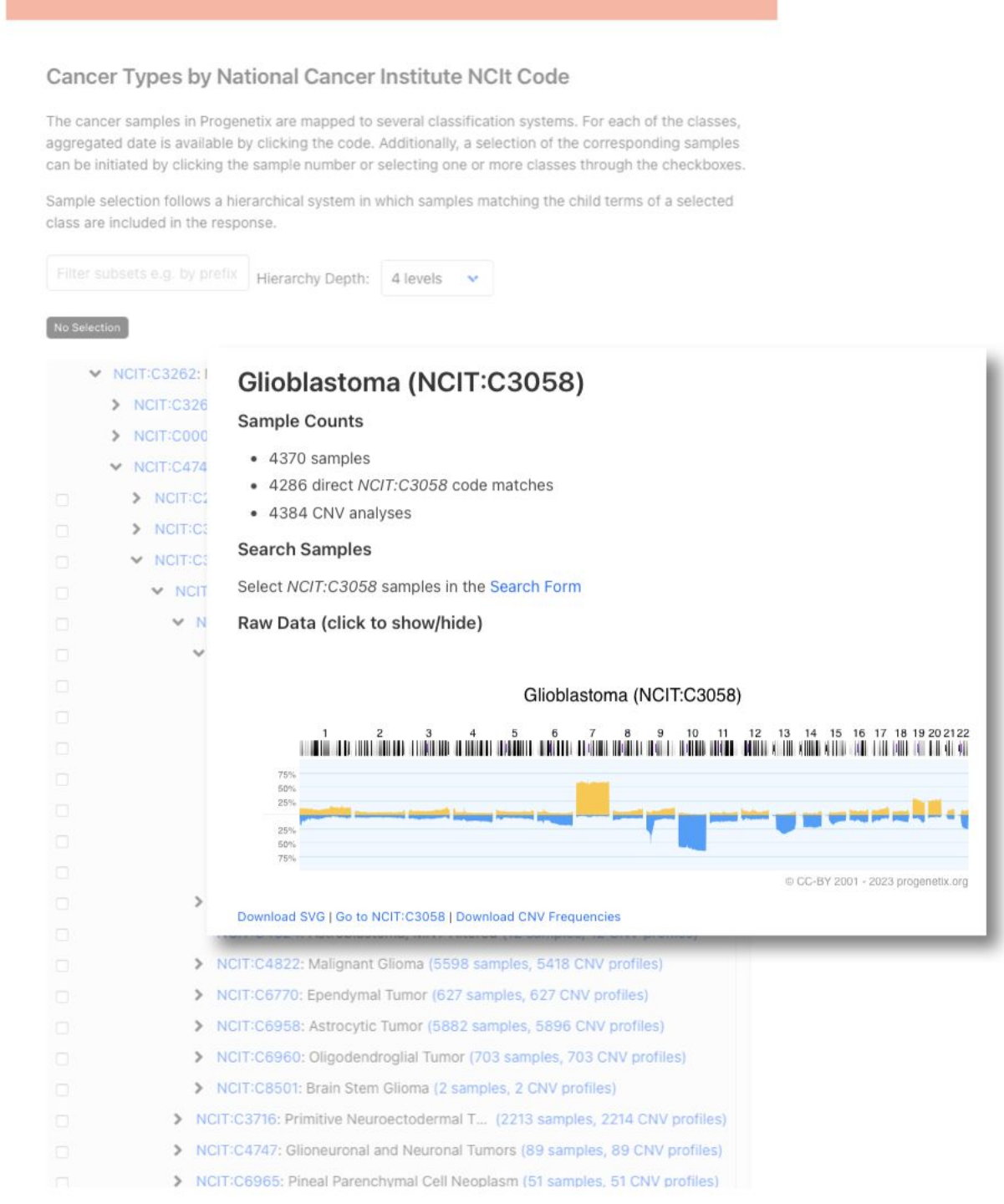

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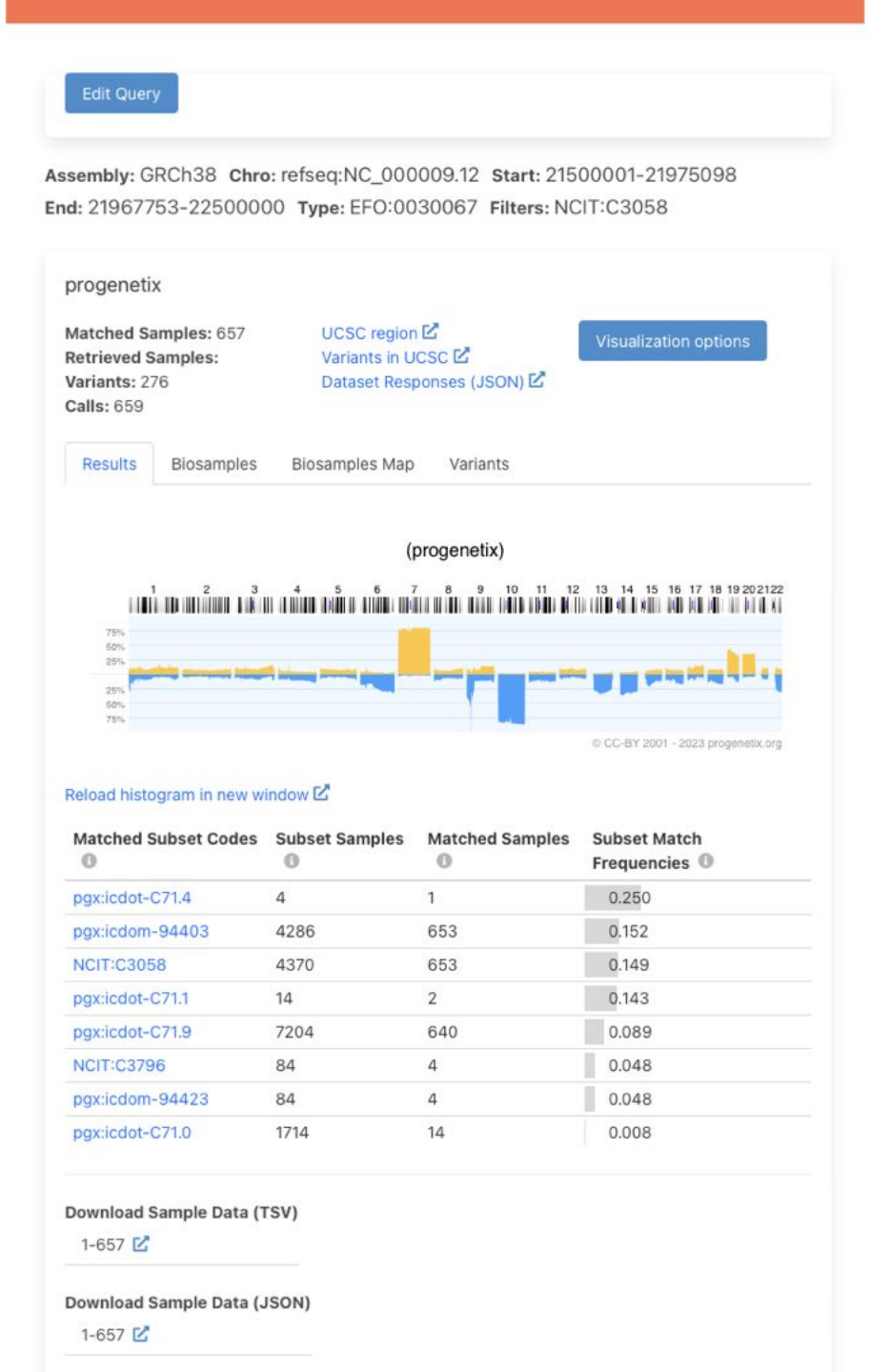

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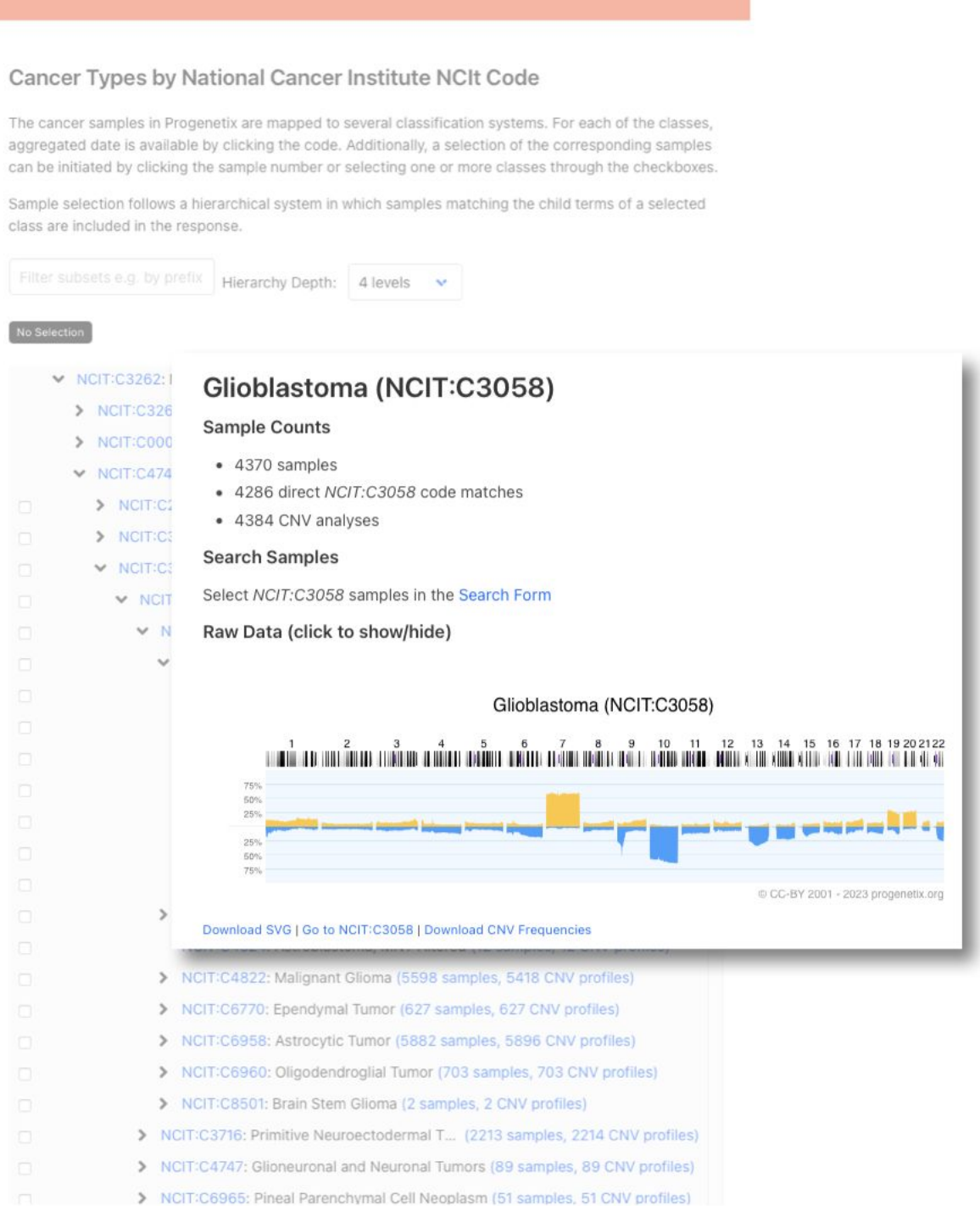

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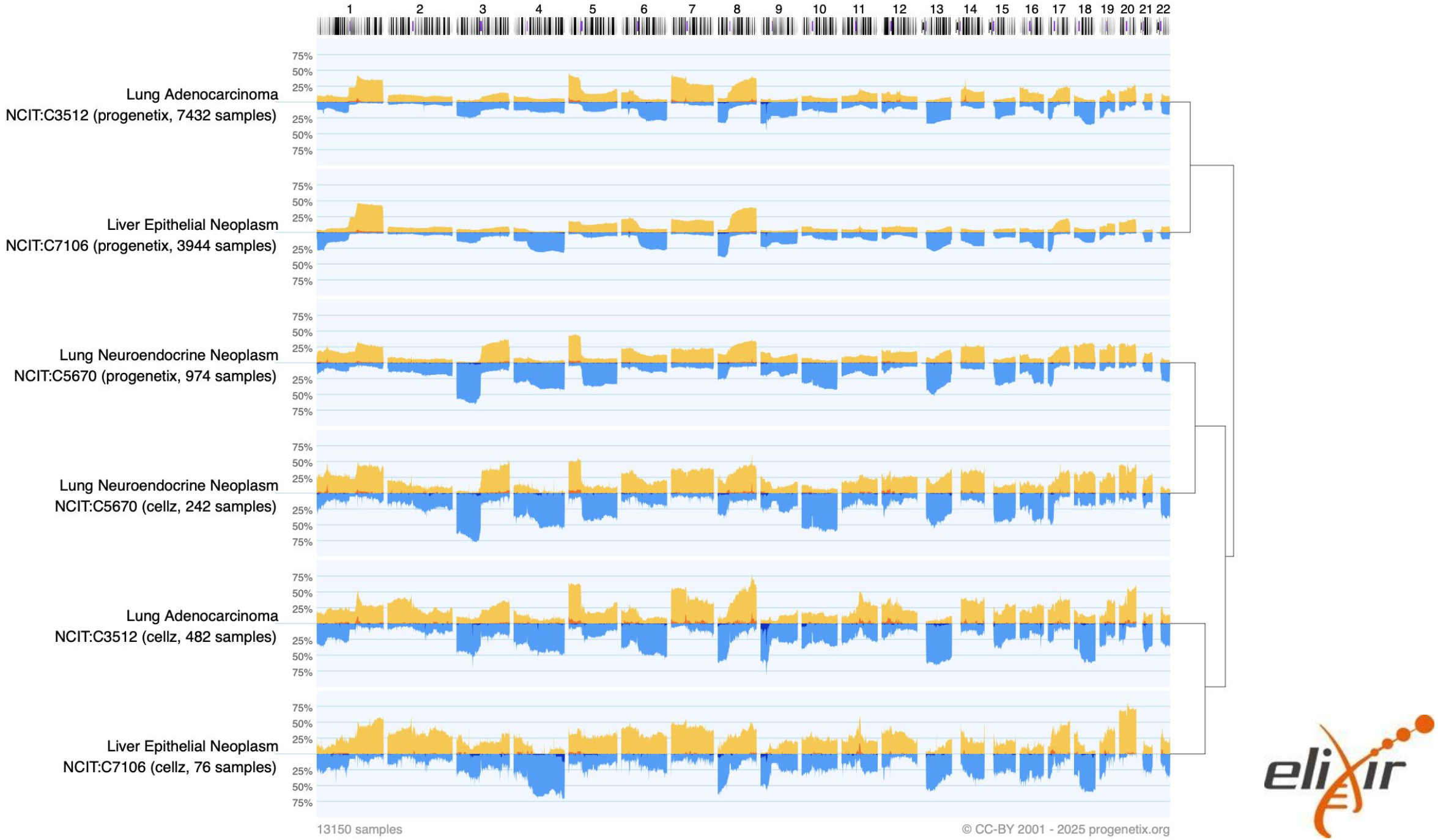
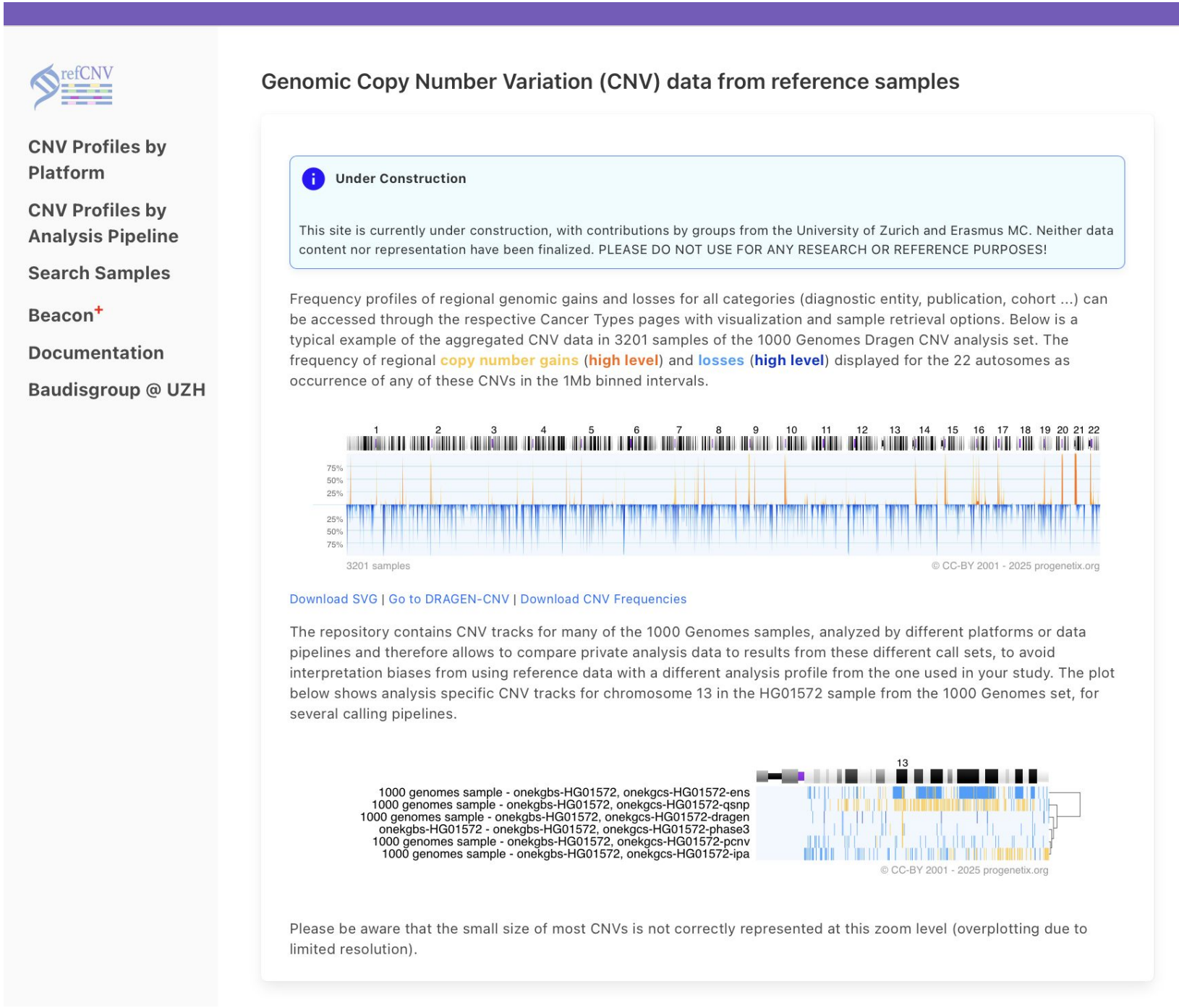

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Lung Adenocarcinoma
NCIT:C3512 (progenetix, 7432 samples)
Liver Epithelial Neoplasm
NCIT:C7106 (progenetix, 3944 samples)
Lung Neuroendocrine Neoplasm
NCIT:C5670 (progenetix, 974 samples)
Lung Neuroendocrine Neoplasm
NCIT:C5670 (cellz, 242 samples)
Lung Adenocarcinoma
NCIT:C3512 (cellz, 482 samples)
Liver Epithelial Neoplasm
NCIT:C7106 (cellz, 76 samples)
75%
50%
25%
13150 samples
© CC-BY 2001 - 2025 progenetix.org

refCNV
Germline CNVs…

- germline CNVs vary widely by genomic background but importantly also by technical assessment
  - sequencing & array
  - bioinformatics workflows
- frequency based information can be misleading
- starting from a benchmarking project (A. Stubbs et al.) we started to do a "non-judgemental" collection w/ technical annotations
- Beacon API, obviously …



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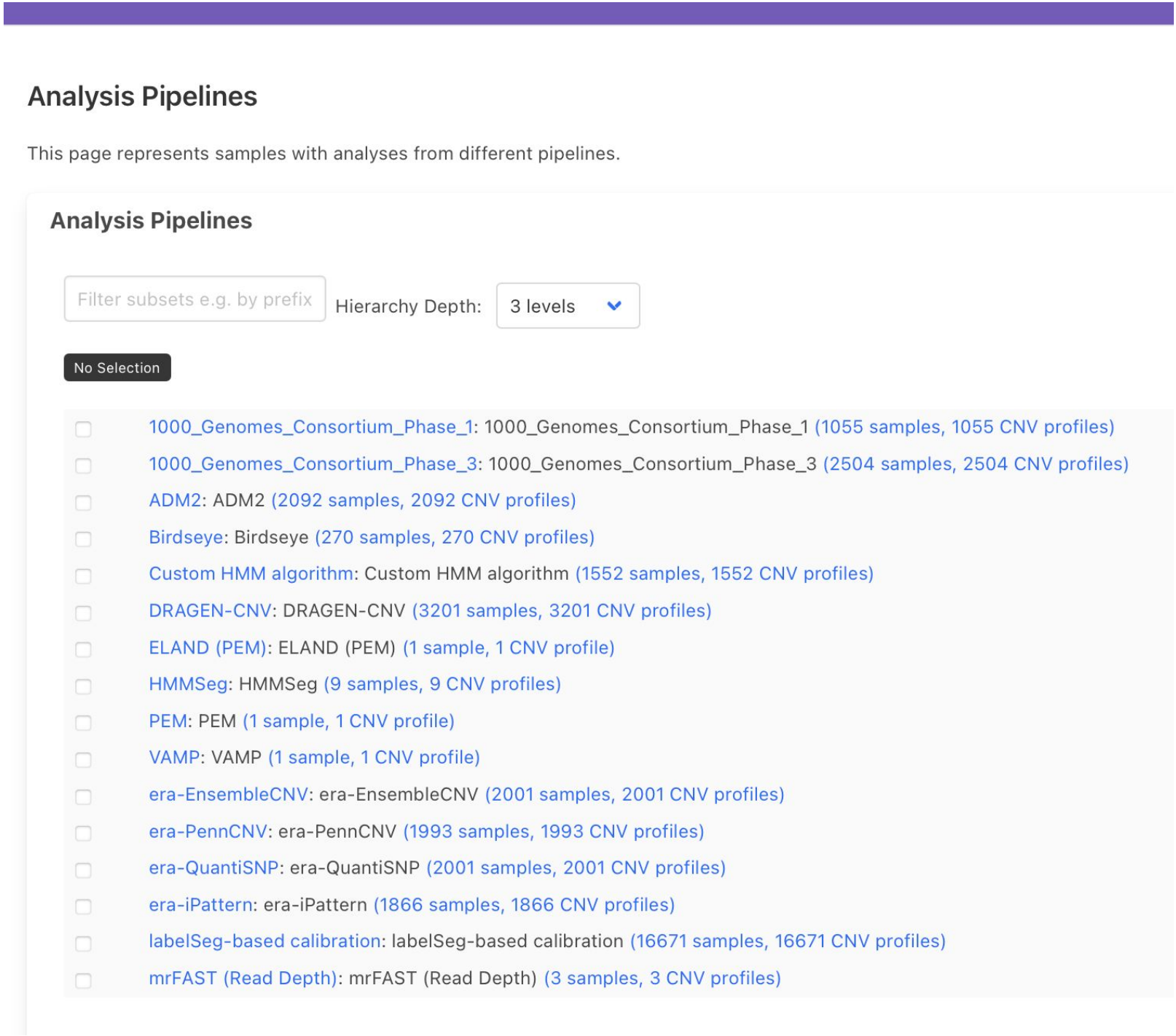
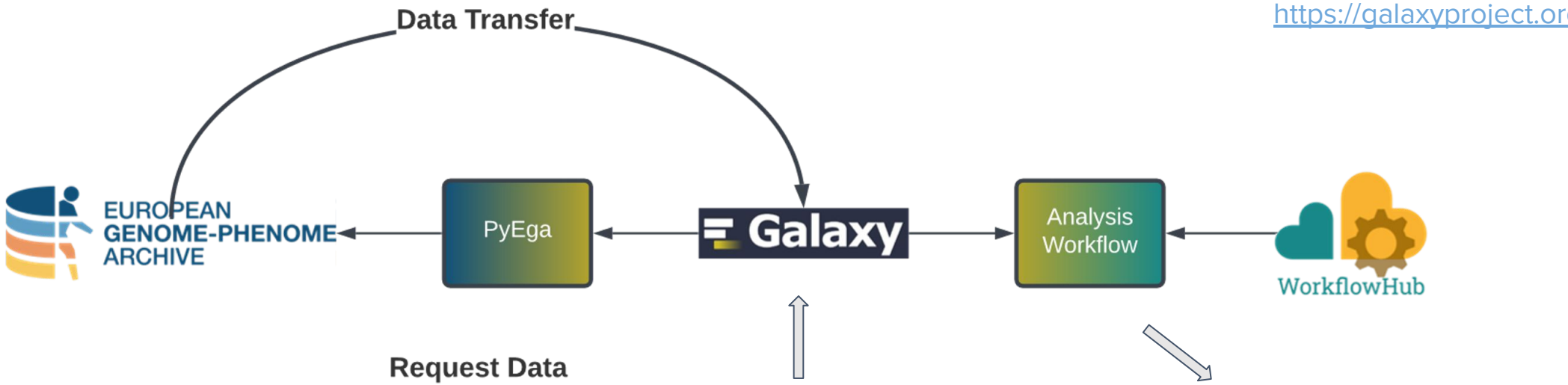


HTSgetGalaxy :FAIR CLOUD Analysis

Galaxy & GA4GH alignment:
https://galaxyproject.org/ga4gh/



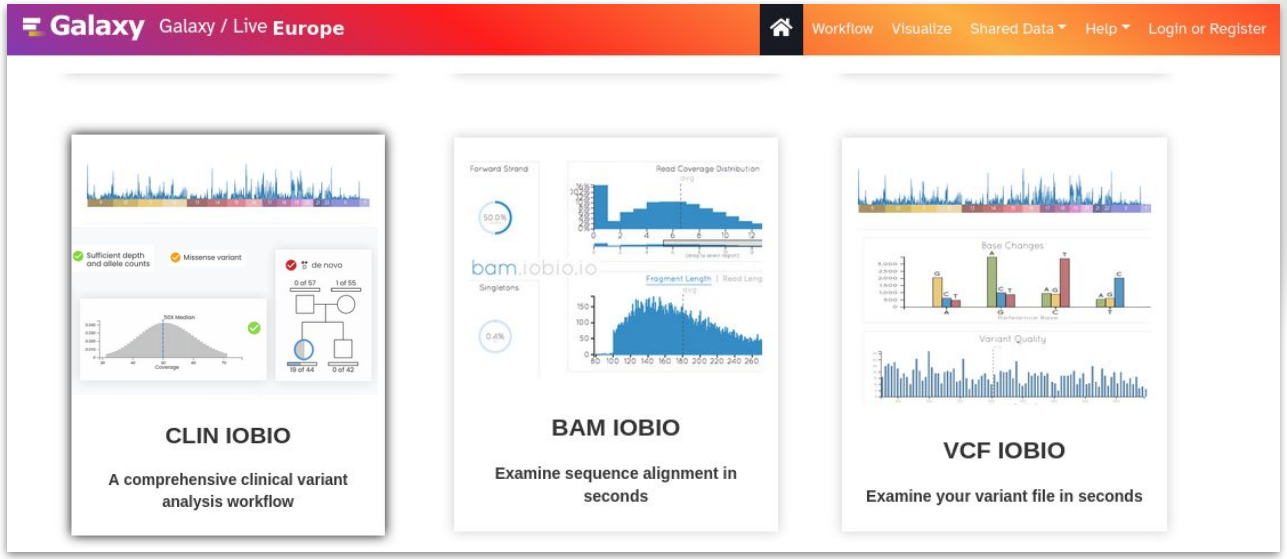
Log in with ELIXIR AAI

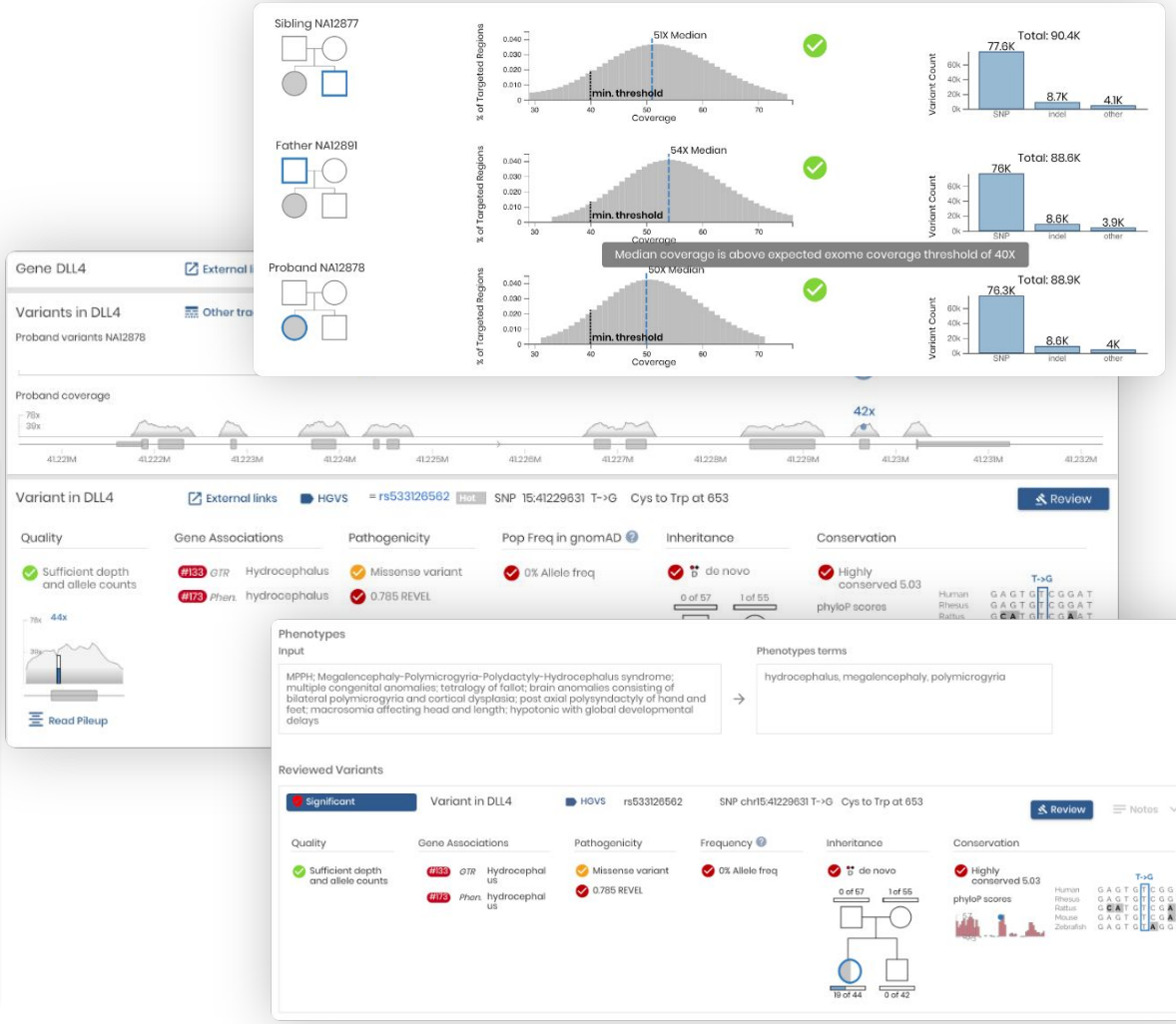
Authentication (passports/visa)

NOTE: Pilot implementation uses username/password for authentication, future release of Galaxy will support use of passports & visas

Data analysis & reporting: Galaxy clin.iobio trio analysis

- Galaxy Interactive Tool
- Docker based
- Interactive variant exploration

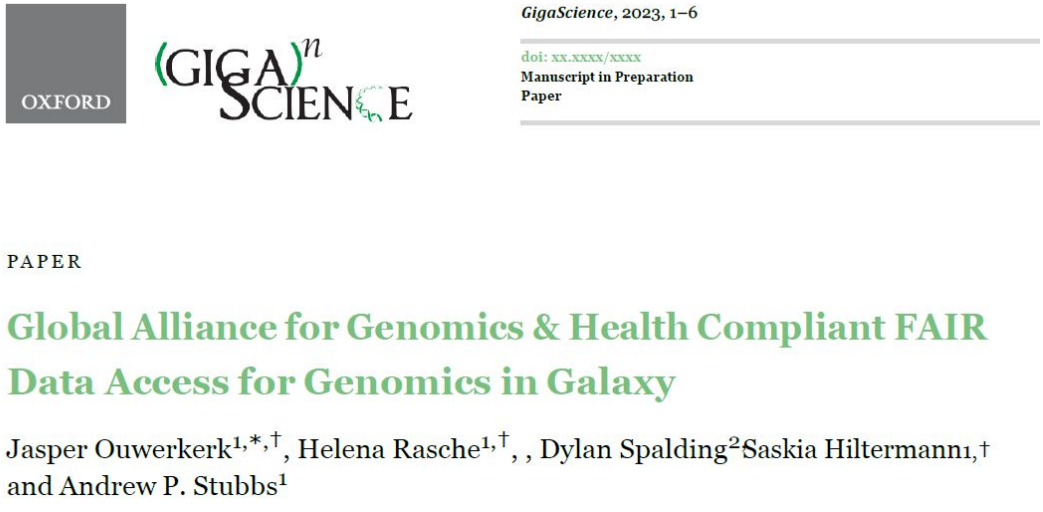


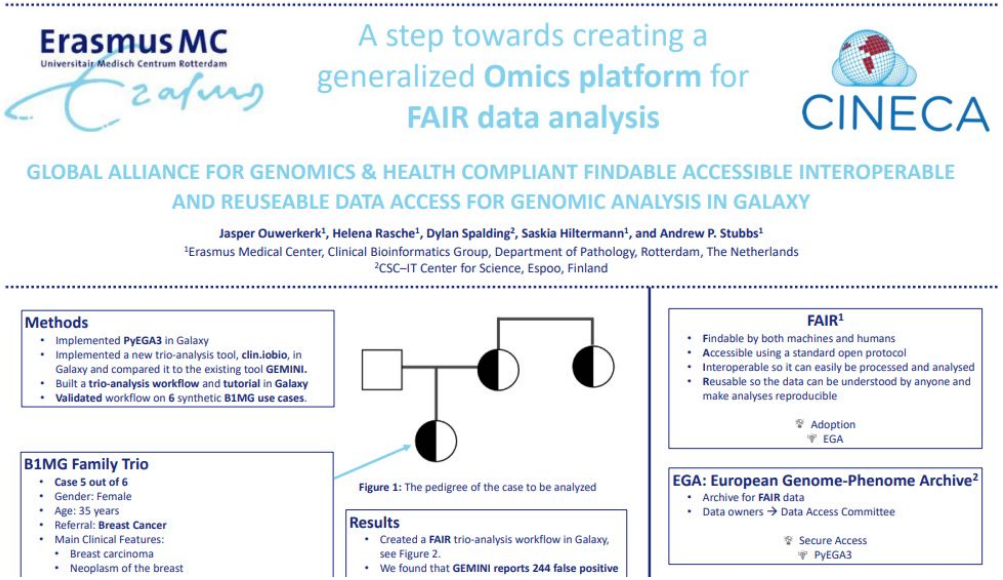


HTSgetGalaxy : Summary

We have implemented:

- Secure access to GA4GH EGA service using PyEGA3 Galaxy service
- Standard analysis for B1MG synthetic data (Filtering etc...)
- Interactive gene variant detection for trio-analysis with clin.iobio in Galaxy
- Related Galaxy Training Network (GTN)
- Single source of Cancer analysis tooling for scientific community – Cancer Galaxy (https://cancer.usegalaxy.eu/)





hCNV Galaxy and Nextflow

Galaxy

- Structural genomic variant calling tools with user-friendly interface for running tools and managing data.
- Galaxy is also a powerful platform for developing and sharing bioinformatics workflows deposited in the WorkflowHub.
- Galaxy training network tutorial (slides, hands on, workflows)

Nextflow

- Nextflow workflows/modules available to be used on a variety of compute platforms, including local machines, clusters, and clouds.
- Nextflow can be used to run hCNV on multiple samples in parallel, which can significantly reduce the amount of time required to analyze a large dataset.

Galaxy Training Network

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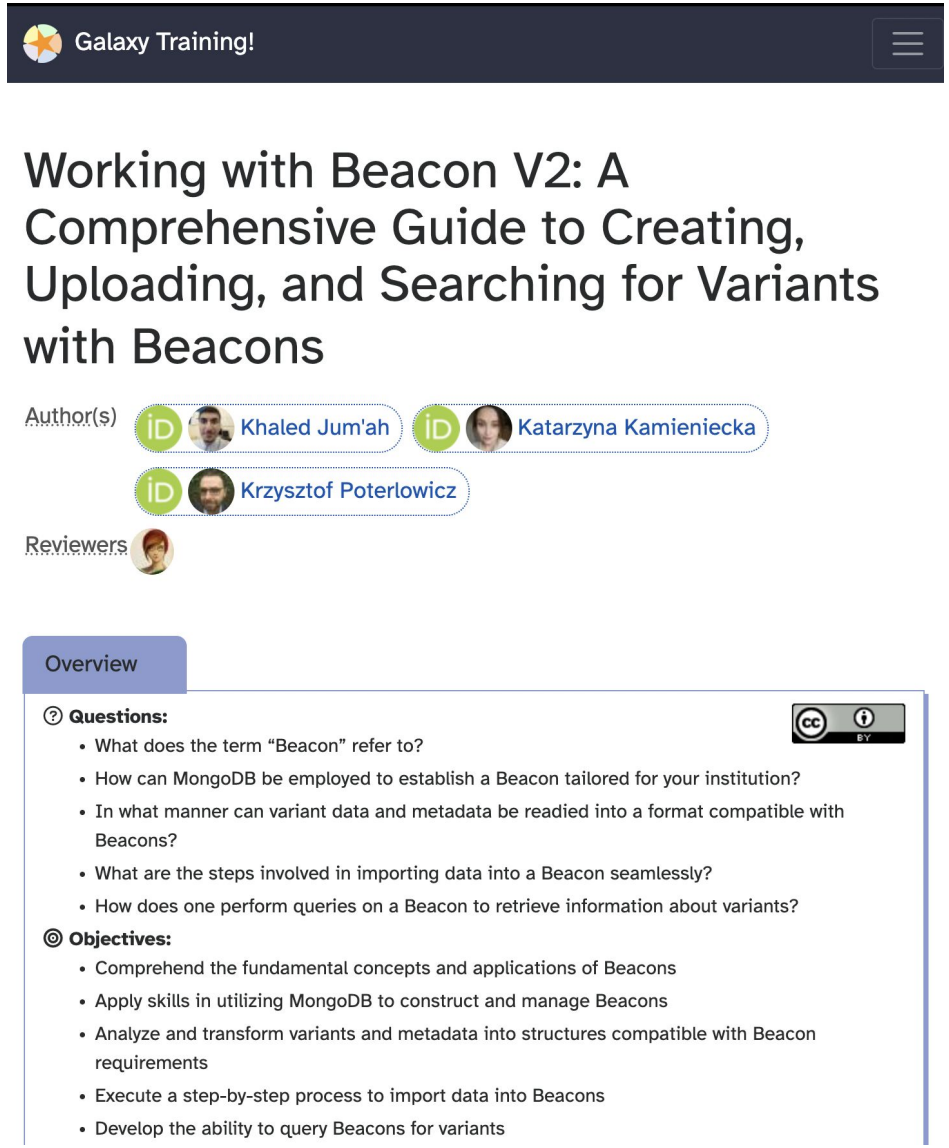
Control-FREEC Training material

- Define the specific challenges in locating human Copy Number Variances (hCNVs).
- Show how to pre-process the sequenced reads for hCNVs detection.
- Show an example on using Control-FREEC to detect the hCNVs from cancer dataset.
- Visualise the hCNVs' findings.

Control-FREEC workflow

- Publish the workflow on Galaxy and Workflow hub to be accessible by the community



Beacon v2 tools

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Beacon2 Import

Run Tool

Import JSON formatted datasets to beacon database
(Galaxy Version 1.0.7+galaxy0)

Tool Parameters

DATABASE HOST - optional

127.0.0.1

Hostname/IP of the beacon database (--db-host)

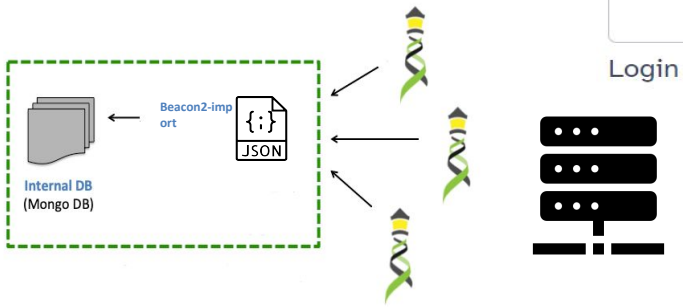
DATABASE PORT *

27017

Port of the beacon database (--db-port)

DATABASE PASSWORD - optional

Login password for the beacon database (--



Beacon2 Bracket

Run Tool

Specifies a sequence ranges for both the start and end positions of a genomic variation
(Galaxy Version 1.0.7+galaxy0)

Tool Parameters

DATABASE HOST - optional

127.0.0.1

Hostname/IP of the beacon database (--db-host)

Beacon2 Gene

Run Tool

Queries the beacon database and retrieve the genomic variants matching gene symbol
(Galaxy Version 1.0.7+galaxy0)

Tool Parameters

DATABASE HOST - optional

127.0.0.1

Hostname/IP of the beacon database (--db-host)

Beacon2 Sequence

Run Tool

Query for the existence of a specified sequence at a given genomic position
(Galaxy Version 1.0.7+galaxy0)

Tool Parameters

DATABASE HOST - optional

127.0.0.1

Hostname/IP of the beacon database (--db-host)

Beacon2 Range

Run Tool

Retrieve the genomic variants from the beacon database by specifying start and end positions
(Galaxy Version 1.0.7+galaxy0)

Tool Parameters

DATABASE HOST - optional

127.0.0.1

Hostname/IP of the beacon database (--db-host)

hCNV data analyses with Nextflow modules

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modules Public

Forked from nf-core/modules

Repository to host tool-specific module files for the Nextflow DSL2 community!

Star

biohackeu23 {B}{H} nf-core

Nextflow MIT License Updated last month

new module: beacon2-ri-tools #4264

Open **kkamieniecka** opened this issue last month · 0 comments

kkamieniecka commented last month Member

beacon2-ri-tools transform genomic variations data (VCF) to queryable data (MongoDB)
See extended documentation here.

+ Add tasklist

kkamieniecka added the new module label last month

elixir

bioinformatics and ML tools for CNV assessment

…. Antonio

CNV annotation & Query Standards Development

GA4GH VRS & Beacon Scouts

- unambiguous representation and recovery of genomic variation data still represent major problems in large scale genomic studies (meta-analyses and data federated data discovery)
- structural genome variants present additional challenges both on epistemic and technical levels
- GA4GH has emerged as the major driver for standards development and harmonization
- ELIXIR hCNV members contribute to the development and improvement of CNV representation and query options as well as associated vocabularies
  - VCF 4.4+ D and J flags (e.g. indicating dosage w/o locus assignment)
  - EFO relative copy number count term tree
  - VRS v1.3/v2 representation of copyNumberChange and copyNumberCount
  - Beacon query types specifically suited for CNV or "fuzzy location" events

CNV annotation & Query Standards Development

GA4GH VRS & Beacon Scouts: CNV Classes

GA4GH VRS1.3+	Beacon	VCF v4.4+	SO
EFO:0030070 gain	DUP or **EFO:0030070**	DUP SVCLAIM=D	SO:0001742 copy_number_gain
EFO:0030071 low-level gain	DUP or **EFO:0030071**	DUP SVCLAIM=D	SO:0001742 copy_number_gain
EFO:0030072 high-level gain	DUP or **EFO:0030072**	DUP SVCLAIM=D	SO:0001742 copy_number_gain
EFO:0030072 high-level gain	DUP or EFO:0030073	DUP SVCLAIM=D	SO:0001742 copy_number_gain
EFO:0030067 loss	DEL or **EFO:0030067**	DEL SVCLAIM=D	SO:0001743 copy_number_loss
EFO:0030068 low-level loss	DEL or **EFO:0030068**	DEL SVCLAIM=D	SO:0001743 copy_number_loss
EFO:0020073 high-level loss	DEL or **EFO:0020073**	DEL SVCLAIM=D	SO:0001743 copy_number_loss
EFO:0030069 complete genomic loss	DEL or **EFO:0030069**	DEL SVCLAIM=D	SO:0001743 copy_number_loss

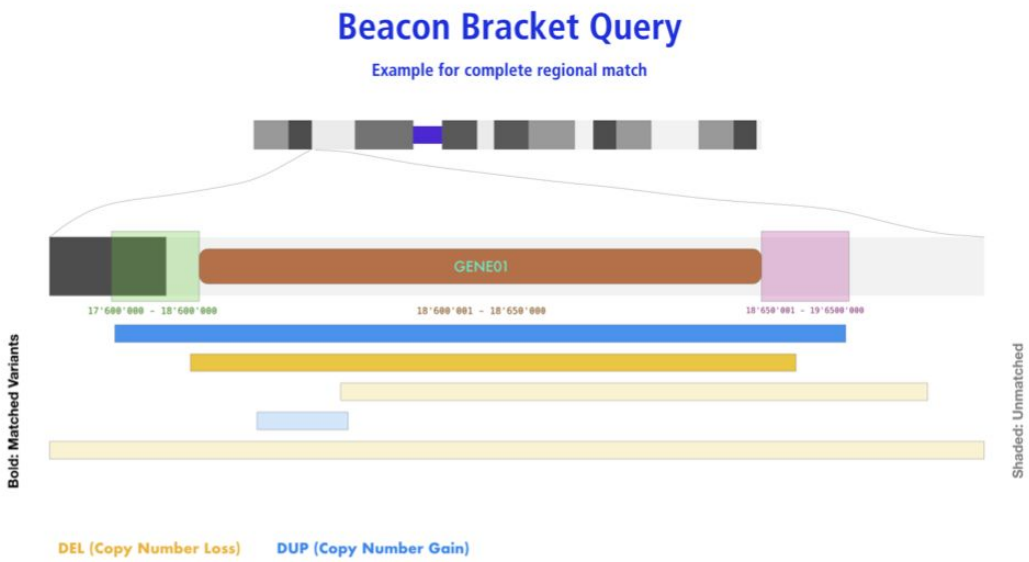
CNV annotation & Query Standards Development

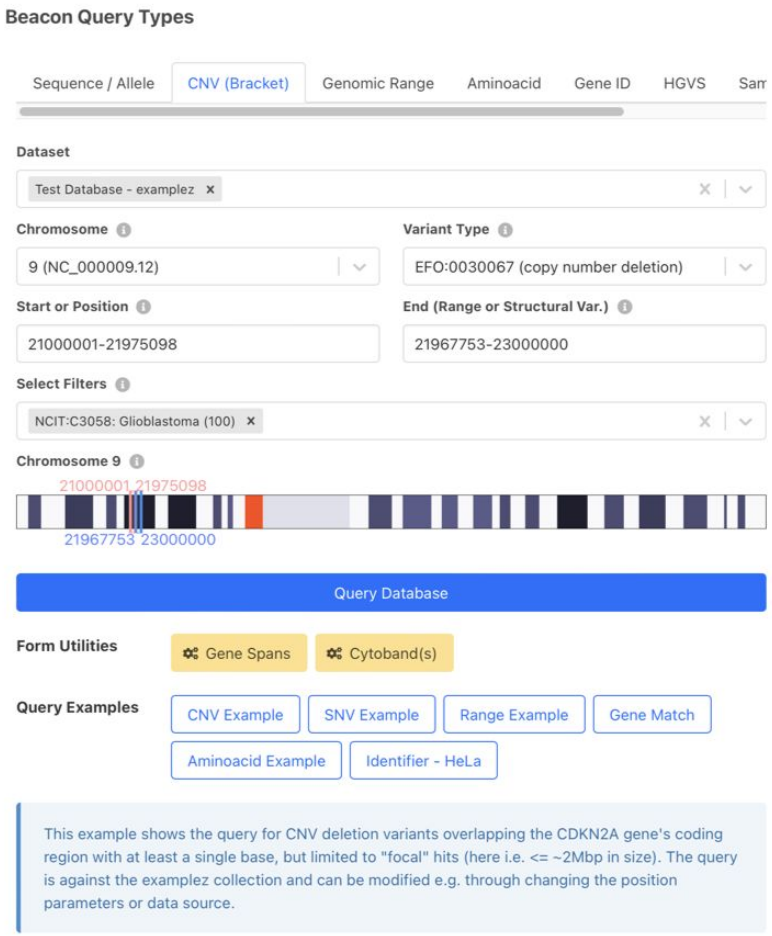
Beacon Scouts: CNV Queries

Variation Queries

Bracket ("CNV") Query

- defined through the use of 2 start, 2 end
- any contiguous variant...





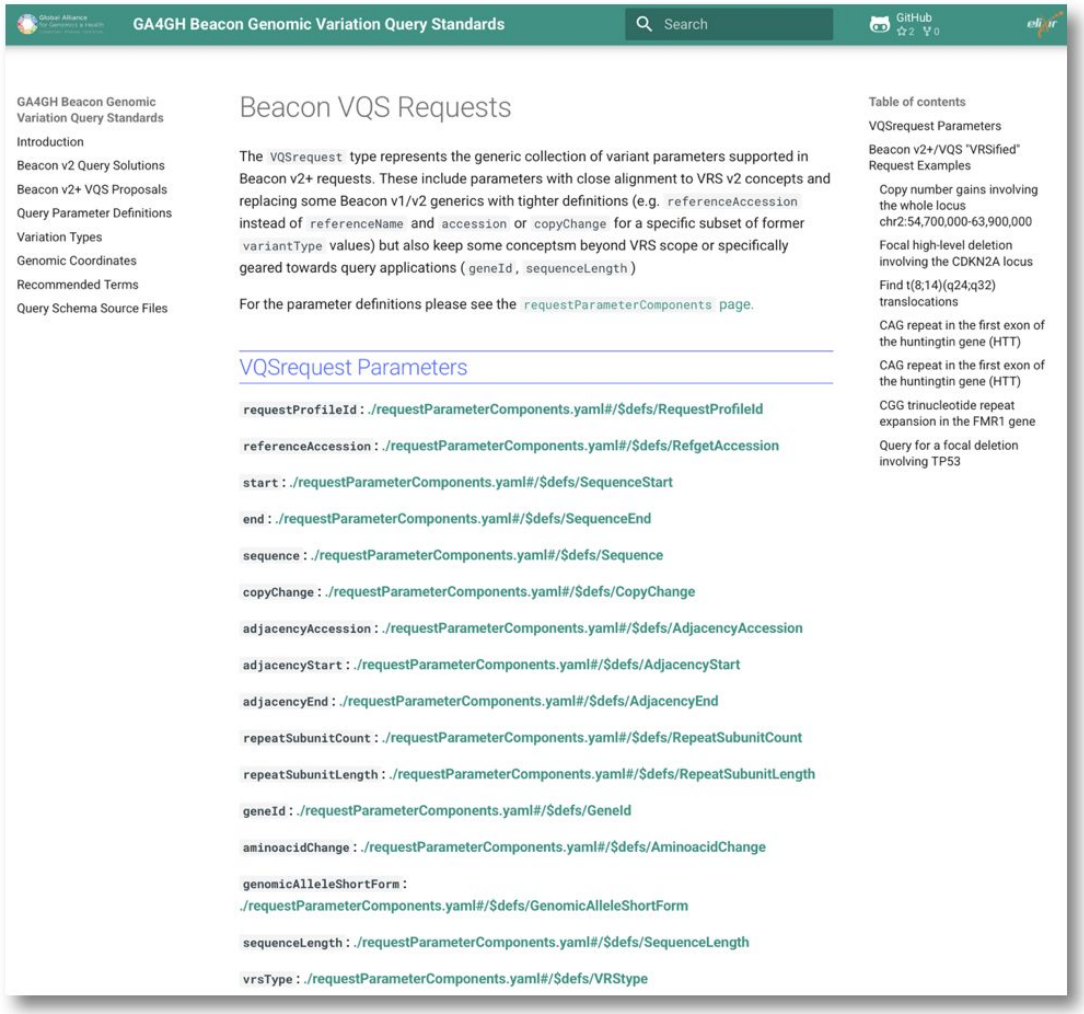
CNV annotation & Query Standards Development

Beacon Scouts: Moving Ahead

Beacon Scouts

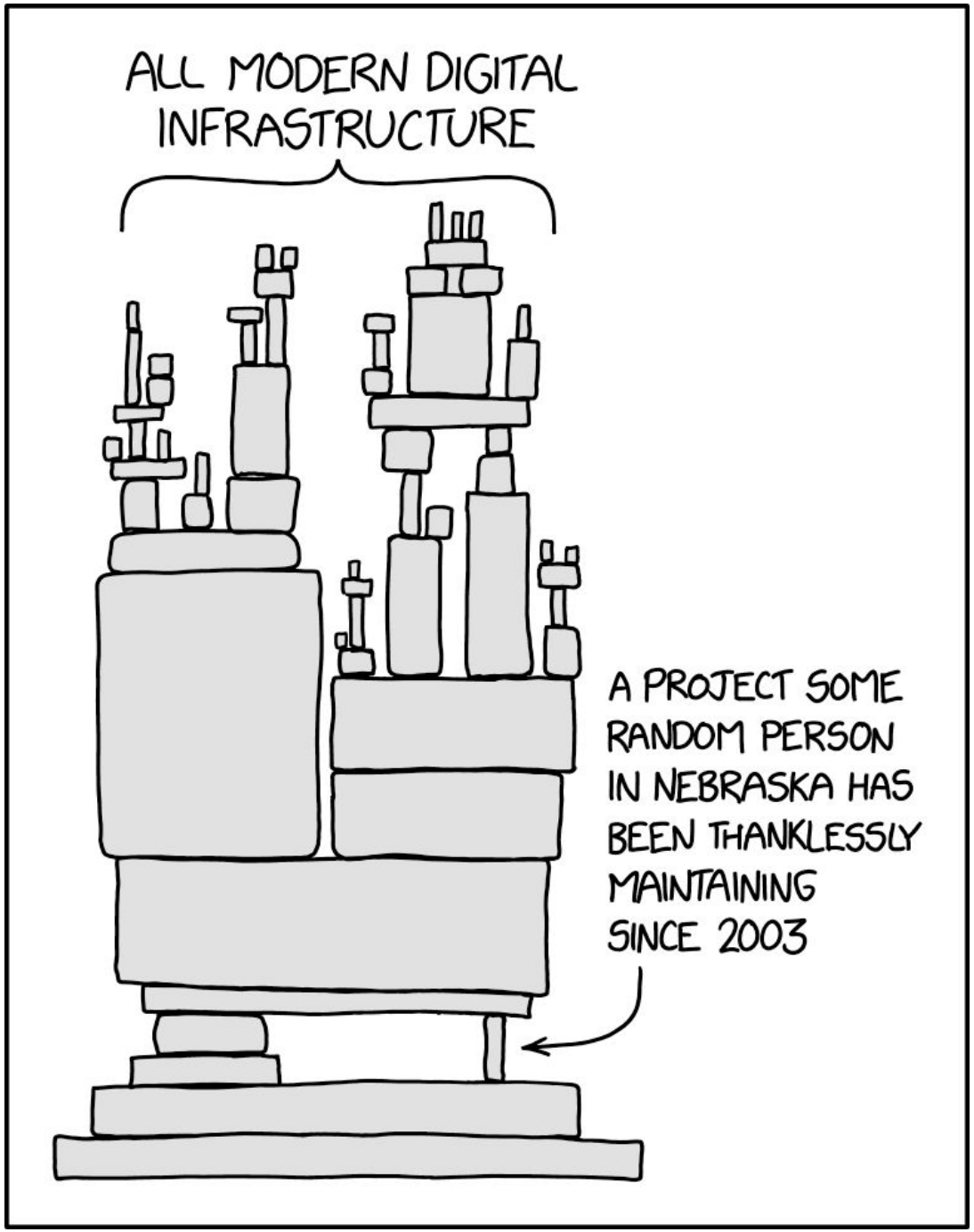
Finding the Paths to Beacon's Future

- Genomic Variation Scouts
  - ➡ extension to the query model based on assessed needs
    - fusions/breakpoints, cytogenetic annotations, repeats, categorical variants...
  - ➡ adoption of evolving VRS... standards for variant representation
    - adjacency, repeats…
    - re-use of parameters where clear (e.g. **`sequenceLength`** instead of **`variantMinLength`** + **`variantMaxLength`**)



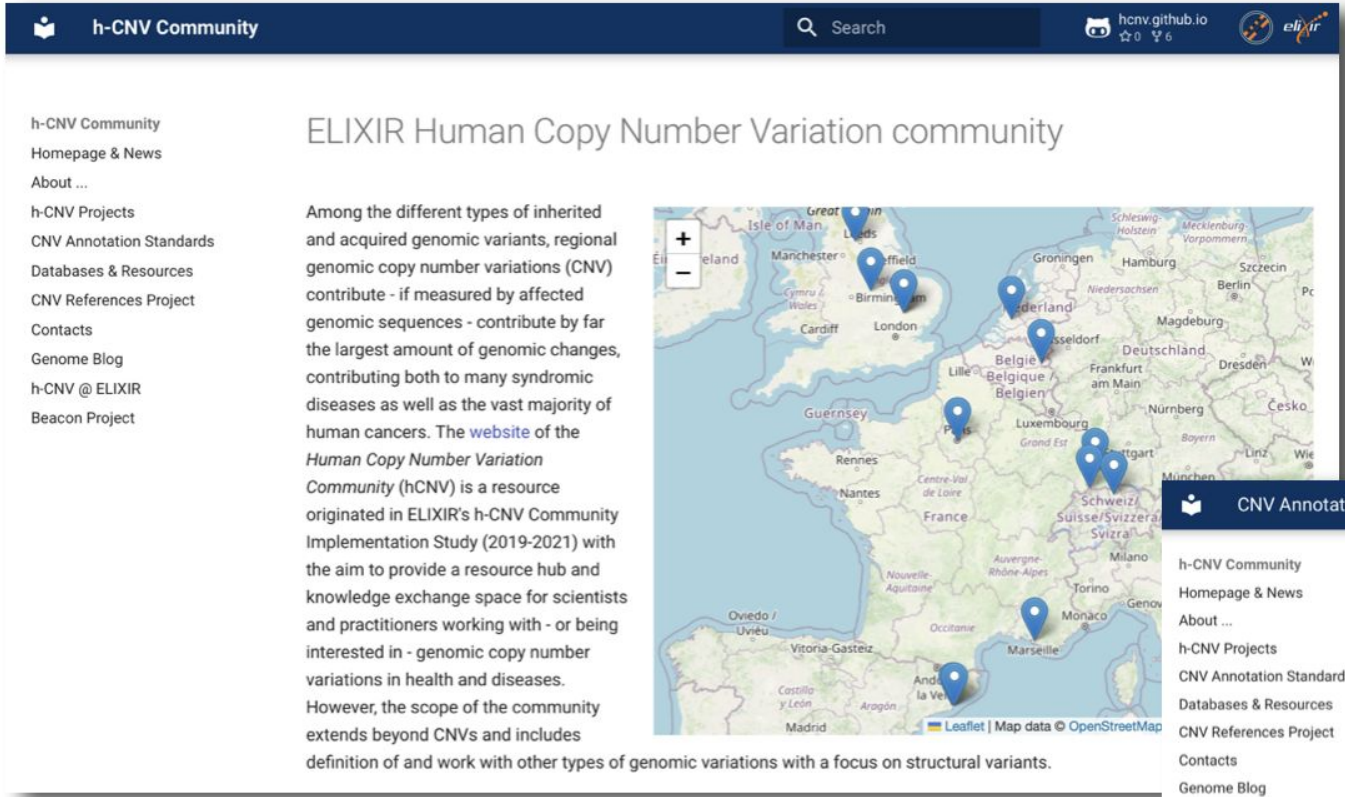
https://genomebeacons.org/variant-query-types/variant-scouts-home/

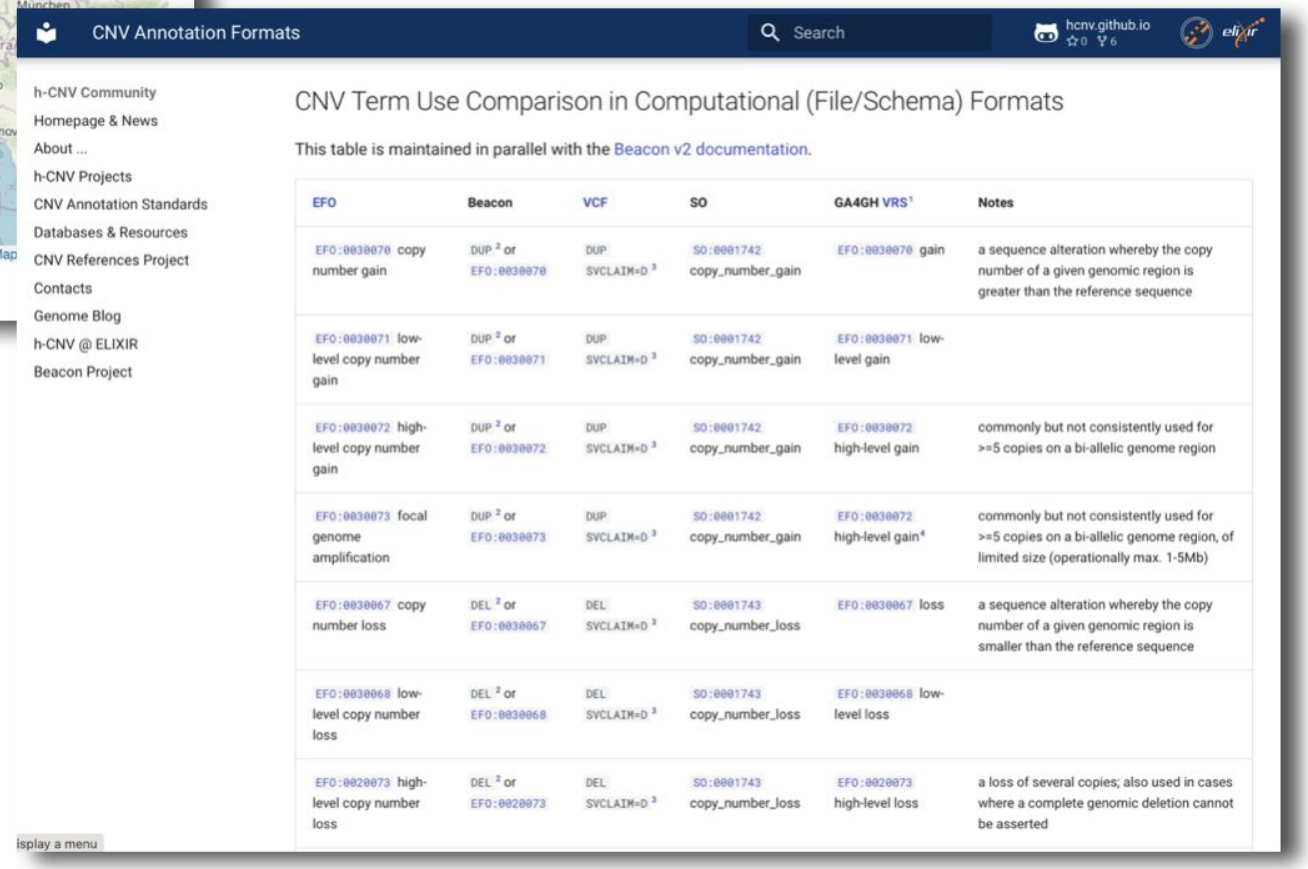
Contribute
Participate
Exchange
Maintain



ELIXIR hCNV Community

https://cnvar.org/





Thank you

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