University of Zurich[UZH]

BIO392
Bioinformatics of Genome Variations

Genomes: Core of "Personalized Health" & "Precision Medicine"

Michael Baudis **UZH SIB**
Computational Oncogenomics

BIO392: Course Schedule

https://compbiozurich.org/UZH-BIO392/

	Friday 2025-04-04	Tuesday 2025-04-08	Wednesday 2025-04-09	Thursday 2025-04-10	Friday 2025-04-11	Tuesday 2025-04-15	Wednesday 2025-04-16	Thursday 2025-04-17	Tuesday 2025-04-29	Wednesday 2025-04-30	Friday 2025-05-02	Tuesday 2025-05-06	Wednesday 2025-05-07
09:00 - 10:00	* Room information * Administrative - discuss times/days - exam		Jiahui: Terminal / Unix / Files	Hangjia: R enviroment introduction	Michael: Genoomic Resources & Data Sharing		Feifei: Sequence analysis practical. FastQC, trimmomatic, BWA-MEM2, SAMtools, GangSTR, BCFtools	Michael: Genomic Data & Privacy		Feifei & Ziying: survival	Feifei: population structure		Exam
10:00 - 11:00	Tina Siegenthaler: technical introduction (room, computer, accounts)		Jiahui: Terminal / Unix / Files	Hangjia: R exercise	Michael: Genoomic Resources & Data Sharing		Feifei:: Sequence analysis practical	Michael: Genomic Data & Privacy		Feifei & Ziying: survival	Feifei: population structure		Discussion
11:00 - 12:00	* explore course site * create Github accounts and forward to bio392@compbiozurich.org *feifei&jiahui: overall schedule of the course		jiahui: SIB online introduction to Unix		Michael: Genoomic Resources & Data Sharing		Feifei:: Sequence analysis practical	Michael: Genomic Data & Privacy		Feifei: survival	Feifei: population structure		
13:00 - 14:00	jiahui: Github	Michael: Introduction	Jiahui & Ziying: Python	Hangjia: CNV paper reading	Hangjia: Clinvar and Clingen	Feifei: Sequence analysis introduction. Overview of pipeline from raw reads -> variant calling & interpretation	Feifei:: STR reading up		Feifei:: analysis & interpretation. Parsing VCF (cyvcf2), UCSD genome browser, ENSEMBL variant effect predictor	Feifei: population structure	Feifei & others: Presentation & Discussion	Exam revision, Q&A	
14:00 - 15:00	jiahui: Github&Git exercise	Michael: Introduction	Exercise	Hangjia: Progenetix as tool for CNV frequencies etc.	Hangjia: blast	Feifei: Sequence analysis introduction	Feifei:: STR reading up		Feifei:: analysis & interpretation.	Feifei: population structure	Feifei & others: Presentation & Discussion		
15:00 - 16:30		Michael: Introduction			Hangija: Blast exercise				Feifei:: analysis & interpretation.	Feifei: population structure	Feifei & others: Presentation & Discussion		

https://drive.switch.ch/index.php/s/PB1czLjrjAKR6Q2

Let's Have Some Standards!

Genome Coordinates

More than one way to get them wrong

Product	"0-start, half-open"	"1-start, fully-closed"	Interbase
BAM/CRAM	X		
SAM		X	
VCF		X	
BCF	X		
htsget	X		
refget	X		
Beacon	X		
VMC			X

0-start, half-open genomic coordinate system

Definition

Two integers that define the start and end positions of a range of residues, possibly with length zero, and specified using "0-start, half-open" coordinates.

The following also applies to coordinates:

- Coordinates start at 0 and finish at the length of the sequence
- Start must be greater than 0
- End must be greater than the start
- The length of an interval is (end - start)
- The reverse start is (sequence length - end)
- The reverse end is (sequence length - (start-1))
- A zero-length interval (start == end) is a point between two residues
- An interval of length 1 is a residue position
- Two intervals are equal if their start and end are equal
- Two intervals intersect if start or end occurs between the start and end of the other
- Two intervals coincide if they intersect or if they are equal

GA4GH Recommendation

- We recommends the use of "**0-start, half-open**" (interbase) coordinate system in all systems
- This is not a retrospective recommendation for existing standards and products
- "**1-start, fully-closed**" should be used when displaying coordinates through a GUI or report

How '0-start, half-open' works

```
        G A G T G C
  G G T G G A G T G C G C C G C C A T G G
                    1 1 1 1 1 1 1 1 1 1 2
  0 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0
```

"0-start, half-open" breaks down into two integer positions. The first, "0-start", refers to the start coordinate and uses an indexing scheme starting at 0 to refer to bases within a sequence, similar to array indexes in most C based programming languages. The second, "half-open", refers to the end coordinate and is one higher than the start (effectively using an indexing system starting at 1).

This scheme makes sub-sequences very easy to define. In the above example we have highlighted the subsequence `GAGTGC`, which starts at position 4 and ends at position 10. Calculating the length of this subsequence is easily done by subtracting start from end e.g. (10-4) = 6. Other transformations are less prone to programming errors than the alternative system "1-start, fully-closed".

This same coordinate system can be used to flag insertions and deletions as a start and an end which equal each other refers to a space between two residues e.g. 4,4 would flag an event occurring between `GGTG` and `GAGTGC`.

https://genomestandards.org/standards/genome-coordinates/

Dates and Times

There is only the ISO way!

- Y = year
- M = month
- D = day
- H = hour
- M = minute
- S = second
- .S = decimal fraction of a second

The specification of a time point is given through the concatenation of

- a date in YYYY-MM-DD
- the designator "T" indicating a following time description
- the time of day in HH:MM:SS.SSS form, where "SSS" represents a decimal fraction of a second
- a time zone offset in relation to UTC

Examples¶

- year (YYYY)
  - 2015
  - Time points with year granularity are both common for obfuscated personal data as well as technical metadata (e.g. year of publication of an analysis).
- date (e.g. date of birth) in YYYY-MM-DD
  - 2015-02-10
  - This represents the standard way of representing a specific day, e.g. a date of birth.
- time stamp in milliseconds in YYYY-MM-DDTHH:MM:SS.SSS
  - 2015-02-10T00:03:42.123Z
  - Timepoints with millisecond granularity are typical use cases for timing computer generated entries, e.g. the time of a record's update ("updateTime").

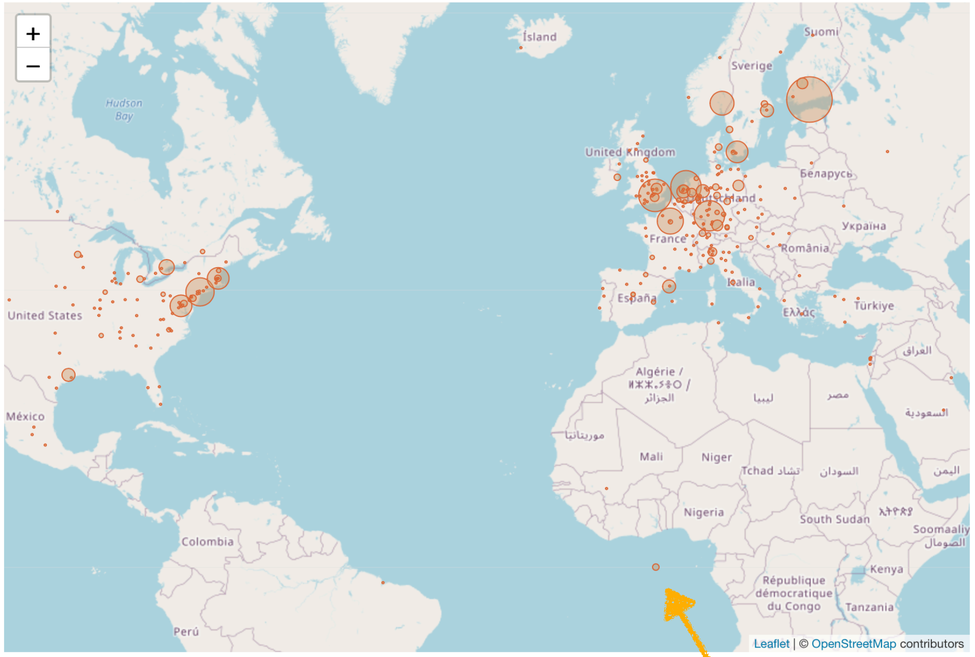
https://xkcd.com/1179/

Data Curation

Provide "clean and correct data" - but final verification of data from external resources lies with the user ...

- correct data is important for any type of scientific analysis
- errors in formats and values can occur during all steps between data acquisition and analysis (numerous "Excelgates"!)
- "meta"-resources and analyses are prone to erroneous data due to varying input formats and lack of source control

➡ always look for batch effects and outliers!



Geographic distribution (by corresponding author) of the **118554** genomic array, **36766** chromosomal CGH and **42105** whole genome/exome based cancer genome datasets from the **3306** listed publications. Area sizes correspond to the sample numbers reported from a given location.

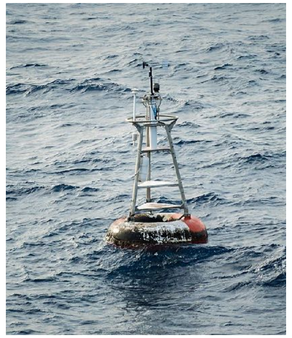
Progenetix publication collection
progenetix.org/publications/list
2020-11-28

25 / 3306 publications

Data Curation - Geolocations

Provide "clean and correct data" - but final verification of data from external resources lies with the user ...

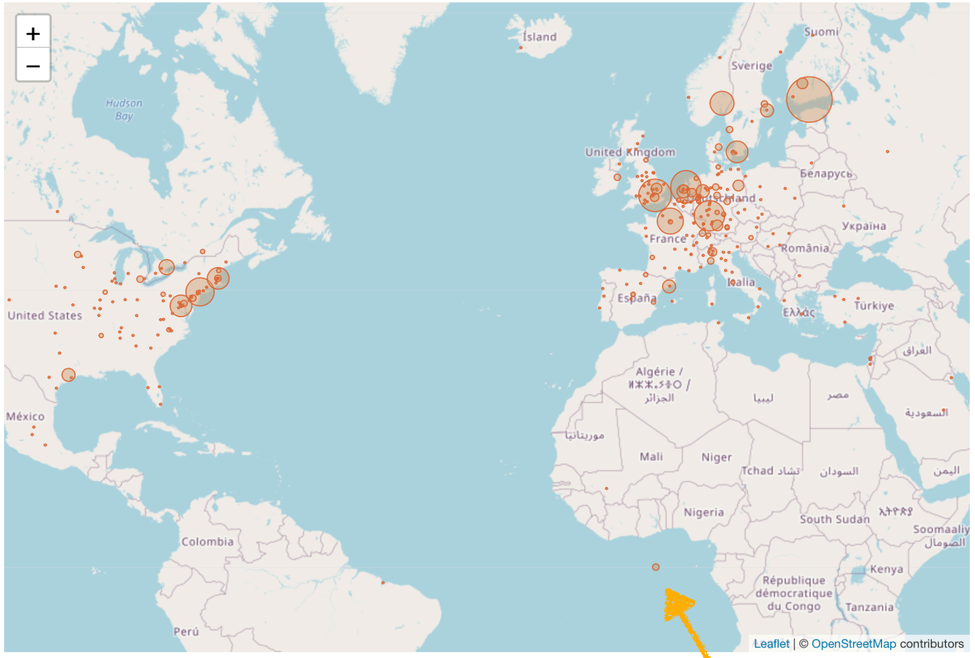
The most geo-tagged place on earth is Null Island



*A troubleshooting country has been added with an Indeterminate sovereignty class called **Null Island (1, 2)**. It is a fictional, 1 meter square island located off Africa where the equator and prime meridian cross. Being centered at 0,0 (zero latitude, zero longitude) it is useful for flagging geocode failures which are routed to 0,0 by most mapping services. Aside: "Null Islands" exist for all local coordinate reference systems besides WGS84 like State Plane (and global if not using modern Greenwich prime meridian). Null Island in Natural Earth is scaleRank 100, indicating it should never be shown in mapping. Side note: Rank 30 (zoom 29 in Google speak)*

https://en.wikipedia.org/wiki/Null_Island

Michael Szell: The Data Science Process 2
http://michael.szell.net/downloads/lecture26_datasciprocess2.pdf
2020-11-25



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25 / 3306 publications

Documentation Strategies

(Not so) Best Practices

```
f_d = f_d_s[c_t]
r = {}
for k in res_schema.keys():
    if k in f_d:
        r.update({k:f_d[k]})
```

- What is documentation? I'll remember this! ¯_(ツ)_/¯

mbaudis@netscape.net

- Just email me if help is needed, unexpectedly
- We had money for a chat bot.

```
normalize_variant_values_for_export(v, byc, drop_fields=None):
```

- Clean code documents itself - Just use explicit variable/function names.
- Clean code documents itself - Never use explicit variable/function names.
- Perl POD it is. There is a command to show the notes in your terminal…
- I wrote a paper about the resource. In 2001.
- Haven't you found the GoogleGroups account?
- Documentation? StackOverflow, whelp!

BIOINFORMATICS **APPLICATIONS NOTE** *Vol. 17 no. 12 2001*
Pages 1228–1229

Progenetix.net: an online repository for molecular cytogenetic aberration data

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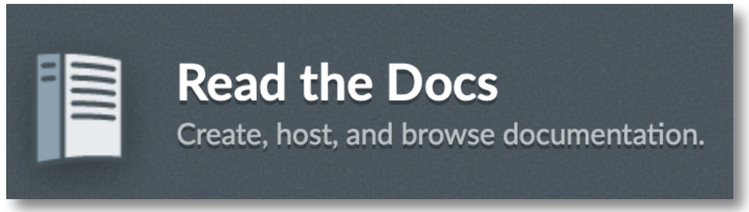
Received on July 5, 2001; revised on July 9, 2001; accepted on July 16, 2001

Documentation Strategies

Currently en Vogue

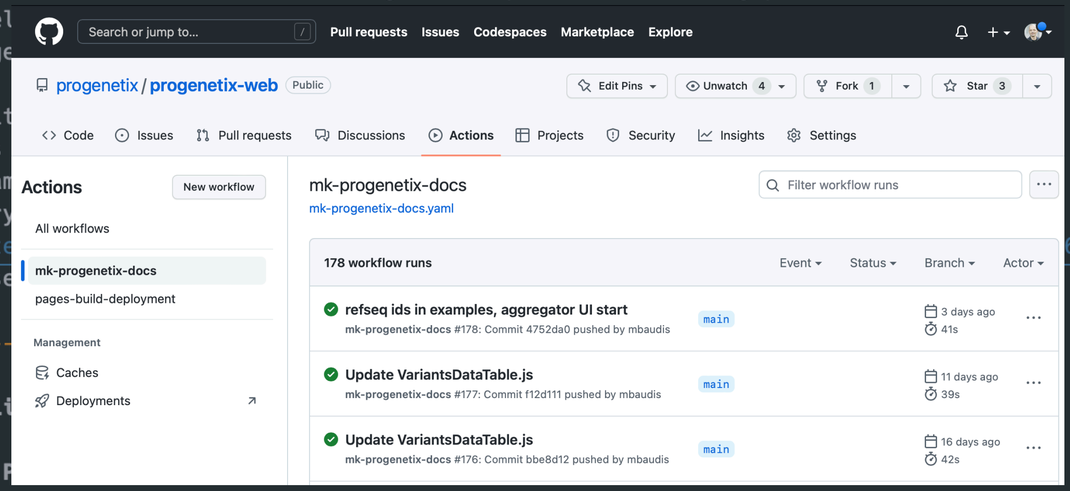
- Cloud-based documentation systems with online compilation
- written in simplified markup languages
  - ➡ Markdown (Yeah!)
  - ➡ Restructured Text (Meeh...)
- local and/or service based compilation and hosting
- build systems & output hosting
  - ➡ ReadTheDocs
    - direct building from .rst document tree or MkDocs based
  - ➡ Github Pages
    - direct using Jekyll or over MkDocs through GH actions

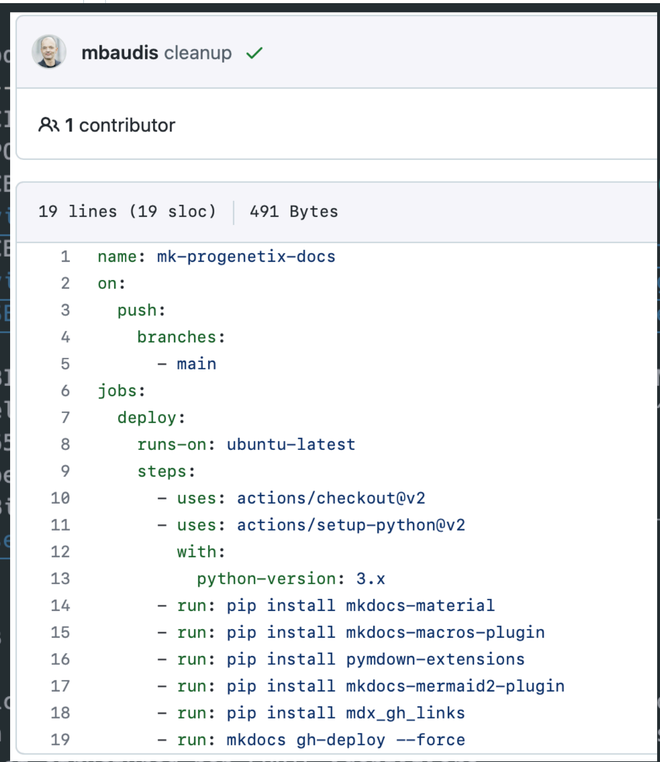


Local Testing

```
→  progenetix-web git:(main) mkdocs serve
INFO     -  Building documentation...
INFO     -  [macros] - Macros arguments: {'module_name': 'main',
           'modules': [], 'include_dir': '', 'include_yaml': [],
           'j2_block_start_string': '', 'j2_block_end_string': '',
           'j2_variable_start_string': '', 'j2_variable_end_string': '',
           'on_undefined': 'keep', 'on_error_fail': False, 'verbose': False}
INFO     -  [macros] - Extra variables (config file):
           ['excerpt_separator', 'blog_list_length', 'social']
INFO     -  [macros] - Extra filters (module): ['pretty']
INFO     -  MERMAID2  - Initialization arguments: {}
INFO     -  MERMAID2  - Using javascript library (8.8.0):
              https://unpkg.com/mermaid@8.8.0/dist/mermaid.min.js
INFO     -  Cleaning site directory
INFO     -  The following pages exist in the docs directory, but are not
           included in the "nav" configuration:
             - beaconplus.md
             - changelog.md
             - classifications-and-ontologies.md
             - progenetix-data-review.md
             - progenetix-website-builds.md
             - publication-collection.md
INFO     -  MERMAID2  - Found superfences config: {'custom_fences': [{'name':
           'mermaid', 'class': 'mermaid', 'format': <function fence_mermaid at
           0x104075ab0>}]}
INFO     -  MERMAID2  - Page 'Technical Notes': found 2 diagrams, adding scripts
INFO     -  Documentation built in 0.83 seconds
INFO     -  [09:05:32] Watching paths for changes: 'docs', 'mkdocs.yaml'
INFO     -  [09:05:32] Serving on http://127.0.0.1:8000/
INFO     -  [09:05:33] Browser connected:
           http://127.0.0.1:8000/classifications-and-ontologies/
```

Web Deployment (Github)

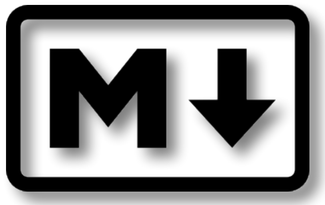




Documentation Strategies

Best Practices

- start early
- update often
- sometimes try to follow your own guide
- balance between inline documentation & doc system
- use Markdown
- plan for contingencies
  - ➡ cloud providers disappear | cancel services | change terms



https://en.wikipedia.org/wiki/List_of_defunct_social_networking_services

https://en.wikipedia.org/wiki/List_of_search_engines#Defunct_or_acquired_search_engines

Task: Reading up Some Standards...

- genome coordinates - take your time...
- Don't you want to rename all of your files "ISO style"?

  ➡ write your time-anchored age in ISO ...

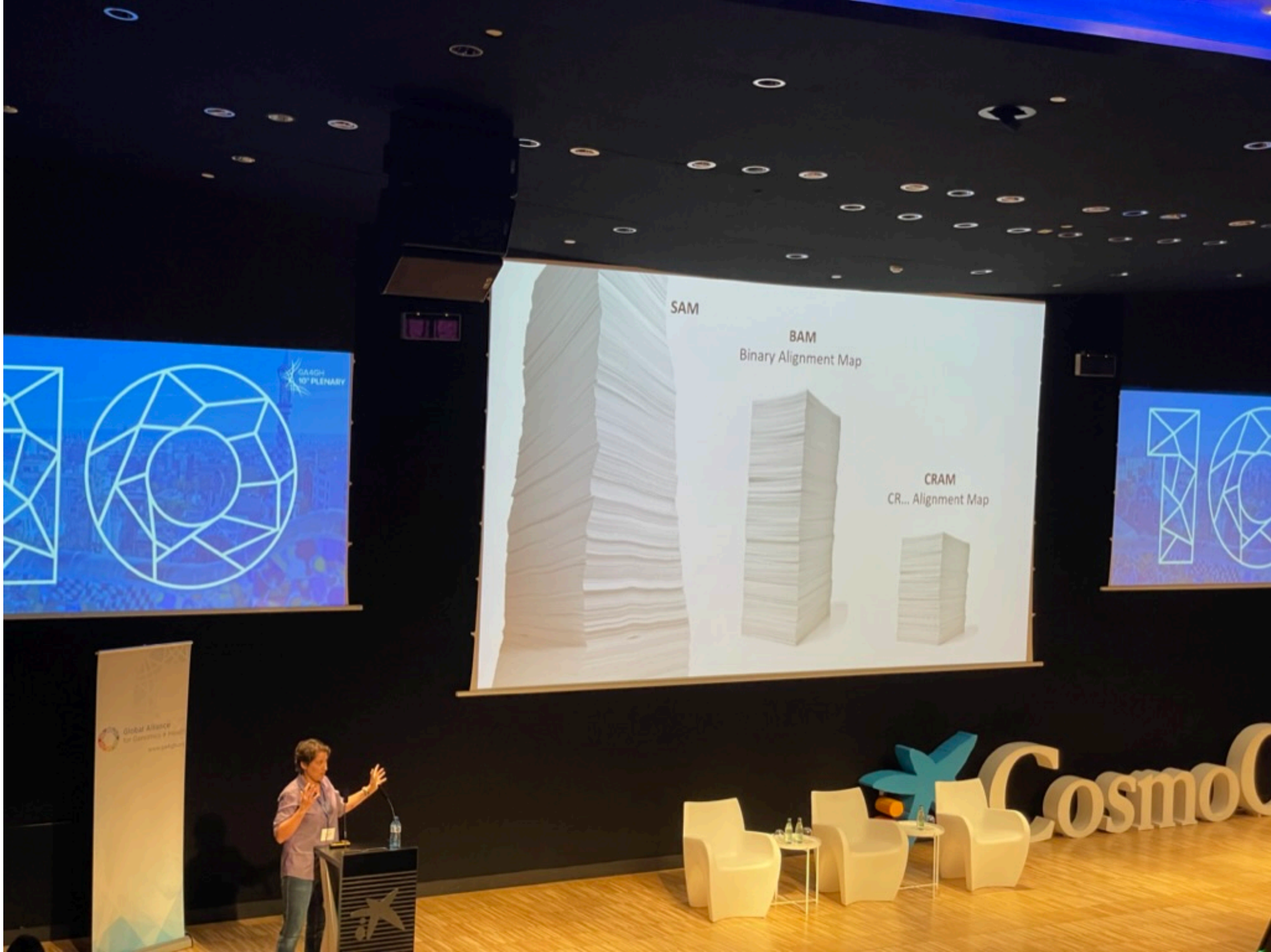
Task: Make some Docs

```
pip3 install mkdocs && mkdocs serve
```

- look up mkdocs

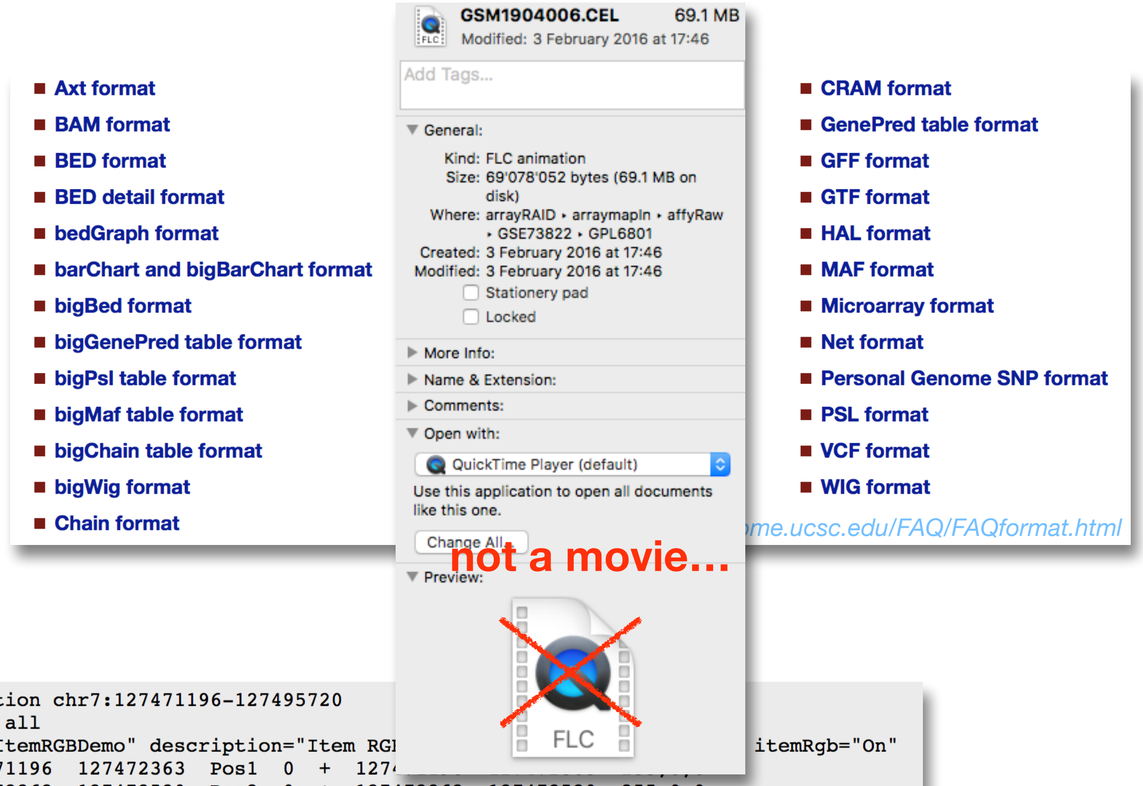
  ➡ extended https://squidfunk.github.io/mkdocs-material/

Genomic File Formats



Genomic File Formats

- **text** or **binary** file formats, optimised for specific types of biological data
- examples from genomics:
  - **BAM** - binary version of Sequence Alignment/Map (SAM)
  - CRAM - compressed version of BAM with multiple optimization and differential access options
  - **BED** (Browser Extensible Data) -flexible way to define the data lines in an genome browser annotation tracks
  - **VCF** (Variant Call Format)




```
browser position chr7:127471196-127495720
browser hide all
track name="ItemRGBDemo" description="Item RGB                                    itemRgb="On"
chr7    127471196  127472363  Pos1  0  +  127                                    ,
chr7    127472363  127473530  Pos2  0  +  127472363  127473530  255,0,0
chr7    127473530  127474697  Pos3  0  +  127473530  127474697  255,0,0
chr7    127474697  127475864  Pos4  0  +  127474697  127475864  255,0,0
chr7    127475864  127477031  Neg1  0  -  127475864  127477031  0,0,255
chr7    127477031  127478198  Neg2  0  -  127477031  127478198  0,0,255
chr7    127478198  127479365  Neg3  0  -  127478198  127479365  0,0,255
chr7    127479365  127480532  Pos5  0  +  127479365  127480532  255,0,0
chr7    127480532  127481699  Neg4  0  -  127480532  127481699  0,0,255
```

BED file example

Global Alliance for Genomics & Health

Collaborate. Innovate. Accelerate.

SAM/BAM and related specifications

These documents are maintained by the Large Scale Genomics work stream of the Global Alliance for Genomics & Health (GA4GH). Information on GA4GH procedures and how to get involved is available here. Lists of contributors and acknowledgements can generally be found in each individual specification document.

https://samtools.github.io/hts-specs/

Specifications:

- SAM v1
- SAM tags
- CRAM v2.1
- CRAM v3.x
- CRAM codecs
- BCF v1
- BCF v2.1
- CSI v1
- Tabix
- VCF v4.1
- VCF v4.2
- VCF v4.3
- VCF v4.4
- BED v1
- crypt4gh
- Htsget
- Refget

Alignment data files

SAMv1.tex is the canonical specification for the SAM (Sequence Alignment/Map) format, BAM (its binary equivalent), and the BAI format for indexing BAM files. **SAMtags.tex** is a companion specification describing the predefined standard optional fields and tags found in SAM, BAM, and CRAM files. These formats are discussed on the samtools-devel mailing list.

CRAMv3.tex is the canonical specification for the CRAM format, while **CRAMv2.1.tex** describes its now-obsolete predecessor. **CRAMcodecs.tex** contains details of the CRAM custom compression codecs. Further details can be found at ENA's CRAM toolkit page and GA4GH's CRAM page. CRAM discussions can also be found on the samtools-devel mailing list.

The **tabix.tex** and **CSIv1.tex** quick references summarize more recent index formats: the tabix tool indexes generic textual genome position-sorted files, while CSI is htslib's successor to the BAI index format.

Unaligned sequence data files

We do not define or endorse any dedicated unaligned sequence data format. Instead we recommend storing such data in one of the alignment formats (SAM, BAM, or CRAM) with the unmapped flag set. However for completeness, we list the commonest formats below with external links.

FASTA is an early sequence-only format originally defined by William Pearson's tool of the same name.

FASTQ was designed as a replacement for FASTA, combining the sequence and quality information in the same file. It has no formal definition and several incompatible variants, but is described in a paper by Cock et al.

Variant calling data files

VCFv4.4.tex is the canonical specification for the Variant Call Format and its textual (VCF) and binary (BCF) encodings, while **VCFv4.1.tex**, **VCFv4.2.tex** and **VCFv4.3.tex** describe their predecessors. These formats are discussed on the vcftools-spec mailing list.

BCFv1_qref.tex summarizes the obsolete BCF1 format historically produced by samtools. This format is no longer recommended for use, as it has been superseded by the more widely-implemented BCF2.

BCFv2_qref.tex is a quick reference describing just the layout of data within BCF2 files.

Discrete genomic feature data files

BEDv1.tex is the canonical specification for the GA4GH Browser Extensible Data (BED) format.

File encryption

crypt4gh.tex is the canonical specification of the crypt4gh format which can be used to wrap existing file formats in an encryption layer.

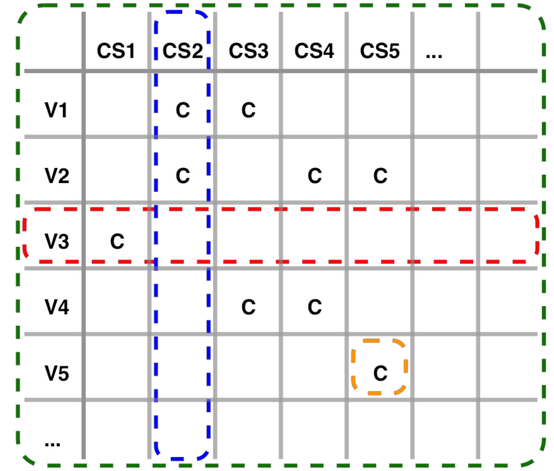
Transfer protocols

Htsget.md describes the *hts-get* retrieval protocol, which enables parallel streaming access to data sharded across multiple URLs or files.

Refget.md enables access to reference sequences using an identifier derived from the sequence itself.

The VCF file format

Standard for genomic variant representation



Example

VCF header

```
##fileformat=VCFv4.0
##fileDate=20100707
##source=VCFtools
##reference=NCBI36
##INFO=<ID=AA,Number=1,Type=String,Description="Ancestral Allele">
##INFO=<ID=H2,Number=0,Type=Flag,Description="HapMap2 membership">
##FORMAT=<ID=GT,Number=1,Type=String,Description="Genotype">
##FORMAT=<ID=GQ,Number=1,Type=Integer,Description="Genotype Quality (phred score)">
##FORMAT=<ID=GL,Number=3,Type=Float,Description="Likelihoods for RR,RA,AA genotypes (R=ref,A=alt)">
##FORMAT=<ID=DP,Number=1,Type=Integer,Description="Read Depth">
##ALT=<ID=DEL,Description="Deletion">
##INFO=<ID=SVTYPE,Number=1,Type=String,Description="Type of structural variant">
##INFO=<ID=END,Number=1,Type=Integer,Description="End position of the variant">
```

Body

#CHROM	POS	ID	REF	ALT	QUAL	FILTER	INFO	FORMAT	SAMPLE1	SAMPLE2
1	1	.	ACG	A,AT	.	PASS	.	GT:DP	1/2:13	0/0:29
1	2	rs1	C	T,CT	.	PASS	H2;AA=T	GT:GQ	0|1:100	2/2:70
1	5	.	A	G	.	PASS	.	GT:GQ	1|0:77	1/1:95
1	100		T	<DEL>	.	PASS	SVTYPE=DEL;END=300	GT:GQ:DP	1/1:12:3	0/0:20

Mandatory header lines

Optional header lines (meta-data about the annotations in the VCF body)

Reference alleles (GT=0)

Alternate alleles (GT>0 is an index to the ALT column)

Phased data (G and C above are on the same chromosome)

Deletion

SNP

Large SV

Insertion

Other event

Variant Call Format

- stores the results of a single or multiple interpretations of genome sequencing datasets, in comparison to a reference genome
- standard format for file-based storage of human genome variants

Global Alliance for Genomics & Health


24" Disk RAMAC
5MB/50 disks, 100 surfaces
100,000 6-bit char/disk

Storage


IBM 350

What is a PB, for human genomes?

It depends...

- 2 bits per base are sufficient to encode TCGA
  - using 00, 01, 10, 11
  - [TCGA]{3’000’000’000}
  - 2 * 3 * 10^9b = 6, 000, 000, 000 b
  - perfect genome (no overhead): ~715 MB
  - 1PB => ~1’400’000 genomes
- according to Swiss online store (Sep 2021) ~35'000CHF (65x16TB á CHF550)
- this is less than a PhD position per year in Switzerland …
- (real costs are 2x that, + duplication, facilities, service … => ~500’000CHF)
- **However: A single 30x BAM file => 100GB**
- Still: 500’000CHF => 1PB => 10’000 genomes => 50CHF/genome (BAM format)

Task: Estimate Storage Requirements for 1000 Genomes

How much computer storage is required for 1000 Genomes

- WES & WGS
- Different file formats
  - SAM
  - BAM
  - VCF
  - FASTA
- Associated costs
  - Cost factors
  - Raw Storage costs
- Familiarize with VCF format

  ➡specification in article collection

IBM-storage-unit-3500-Schiphol-1957

Please provide 1-page size estimates and reasoning for the use of the different file types (i.e. which would you use for storing called variants, which for full archival purposes, browser visualisation), for 3-5 formats. Submit your files (.md) per pull request to your Github directory.

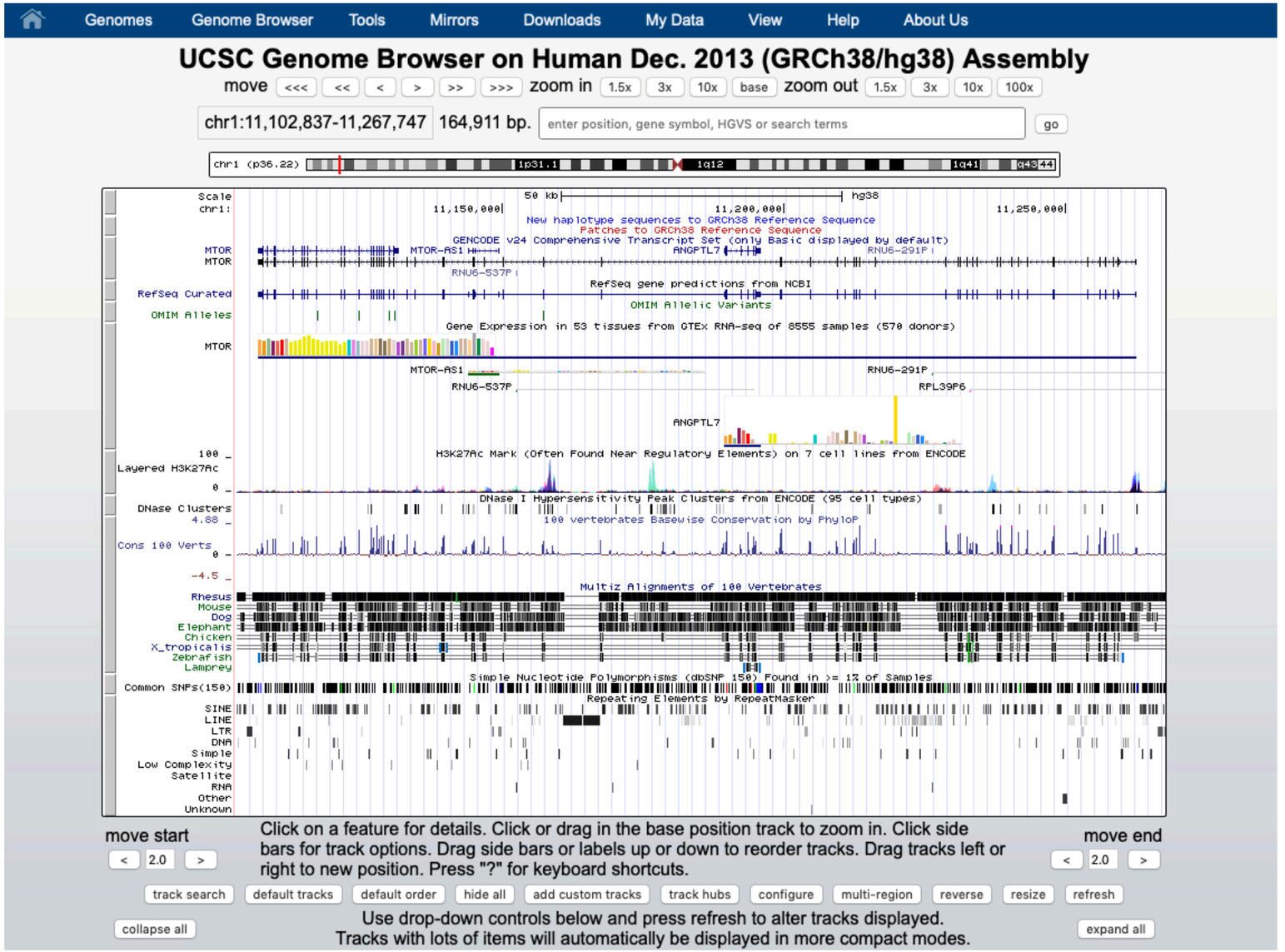
Genome Resources

Sequences | Variants | Interpretations

RESOURCES FOR GENOMICS: UCSC GENOME BROWSER

- Originated from the Human Genome Project
- Most widely used general genome browser
- many default tracks
- many species
- customization with "BED" files

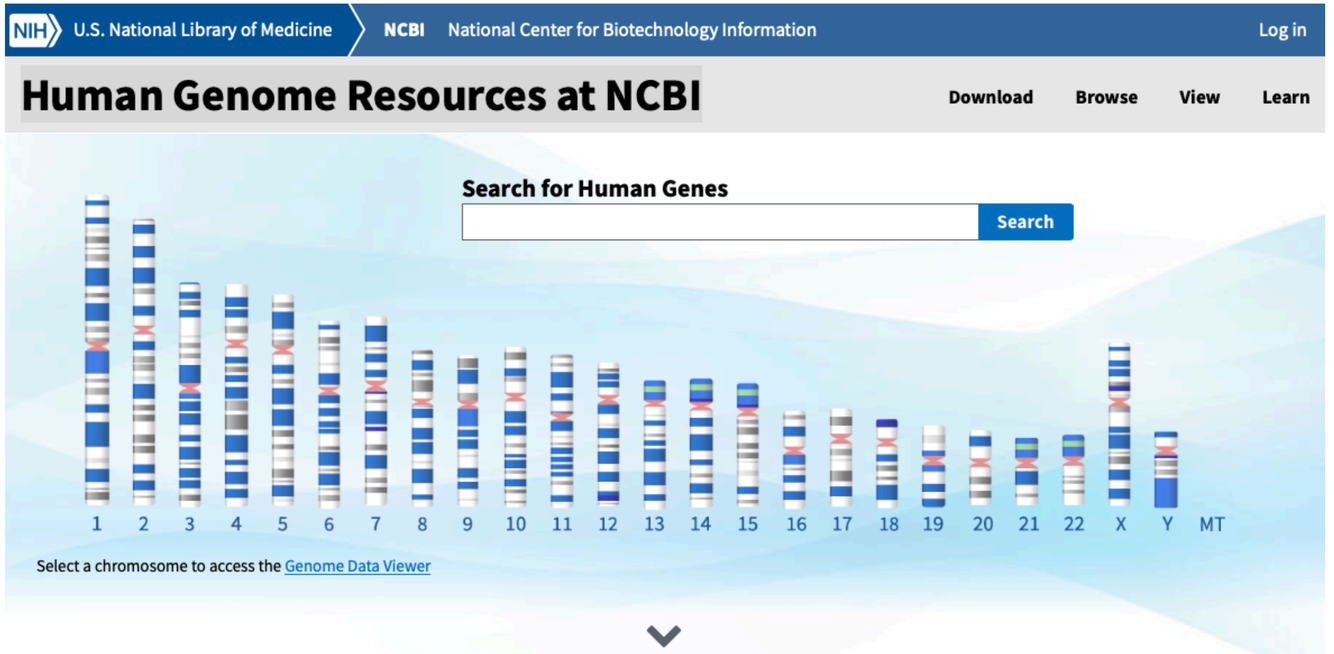
genome.ucsc.edu



RESOURCES FOR GENOMICS: HUMAN GENOME RESOURCES AT NCBI

- Entry point for genome reference data
- Human genome assemblies
- Human variant collections (dbVar, ClinVar, dbSNP) for download

www.ncbi.nlm.nih.gov/projects/genome/guide/human/



Download	GRCh38	GRCh37
Reference Genome Sequence	Fasta	Fasta
RefSeq Reference Genome Annotation	gff3	gff3
RefSeq Transcripts	Fasta	Fasta
RefSeq Proteins	Fasta	Fasta
ClinVar	vcf	vcf
dbSNP	vcf	vcf
dbVar	vcf	vcf

Where to find genome *variant* data ...

Reference Resources for Human Genome Variants

NCBI:dbSNP

- single nucleotide polymorphisms (SNPs) and multiple small-scale variations
- including insertions/deletions, microsatellites, non-polymorphic variants

NCBI:dbVAR

- genomic structural variation
- insertions, deletions, duplications, inversions, multinucleotide substitutions, mobile element insertions, translocations, complex chromosomal rearrangements

NCBI:ClinVar

- aggregates information about genomic variation and its relationship to human health

EMBL-EBI:EVA

- open-access database of all types of genetic variation data from all species

Ensembl

- portal for many things genomic...

RESOURCES FOR CANCER GENOMICS

COSMIC
Catalogue of somatic mutations in cancer

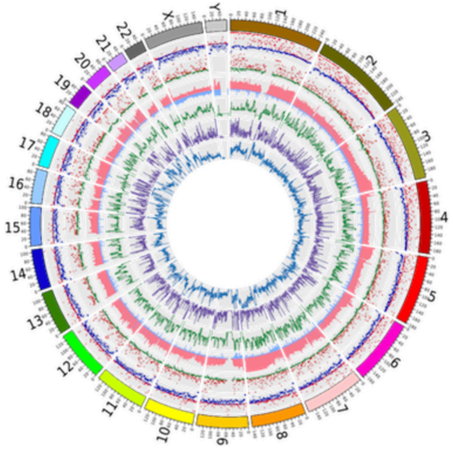
Home ▼ | Resources ▼ | Curation ▼ | Tools ▼ | Data ▼ | News ▼ | Help ▼ | About ▼ | Search COSMIC... | Login ▼

COSMIC v79, released 14-NOV-16

COSMIC, the Catalogue Of Somatic Mutations In Cancer, is the world's largest and most comprehensive resource for exploring the impact of somatic mutations in human cancer.

Start using COSMIC by searching for a gene, cancer type, mutation, etc. below, or by browsing a region of the human genome using the map to the right.

eg: Braf, COLO-829, Carcinoma, V600E, BRCA-UK, Campbell SEARCH



Browse the **genomic landscape** of cancer

R Resources

Key COSMIC resources

Cell Lines Project
COSMIC
Whole Genomes
Cancer Gene Census
Drug Sensitivity
Mutational Signatures
GRCh37 Cancer Archive

T Tools

Additional tools to explore COSMIC

Cancer Browser
Genome Browser
GA4GH Beacon
CONAN

C Expert Curation

High quality curation by expert postdoctoral scientists

Drug Resistance New
Cancer Gene Census
Curated Genes
Gene Fusions
Genome-Wide Screens

D Data

Further details on using COSMIC's content

Downloads
License
Submission
Genome Annotation
Datasheets
Help
FAQ

Cancer Gene Census Update

7 genes have been added to the Cancer Gene Census -

EPAS1 - Endothelial PAS domain protein 1.
PTPRT - Protein tyrosine phosphatase, receptor type T.
PPM1D - Protein phosphatase, Mg2+/Mn2+ dependent 1D.
BTK - Bruton tyrosine kinase.
PREX2 - Phosphatidylinositol-3,4,5-trisphosphate dependent Rac exchange factor 2.
TP63 - Tumour protein p63.
QKI - QKI, KH domain containing RNA binding.

For full details, see the Datasheet.

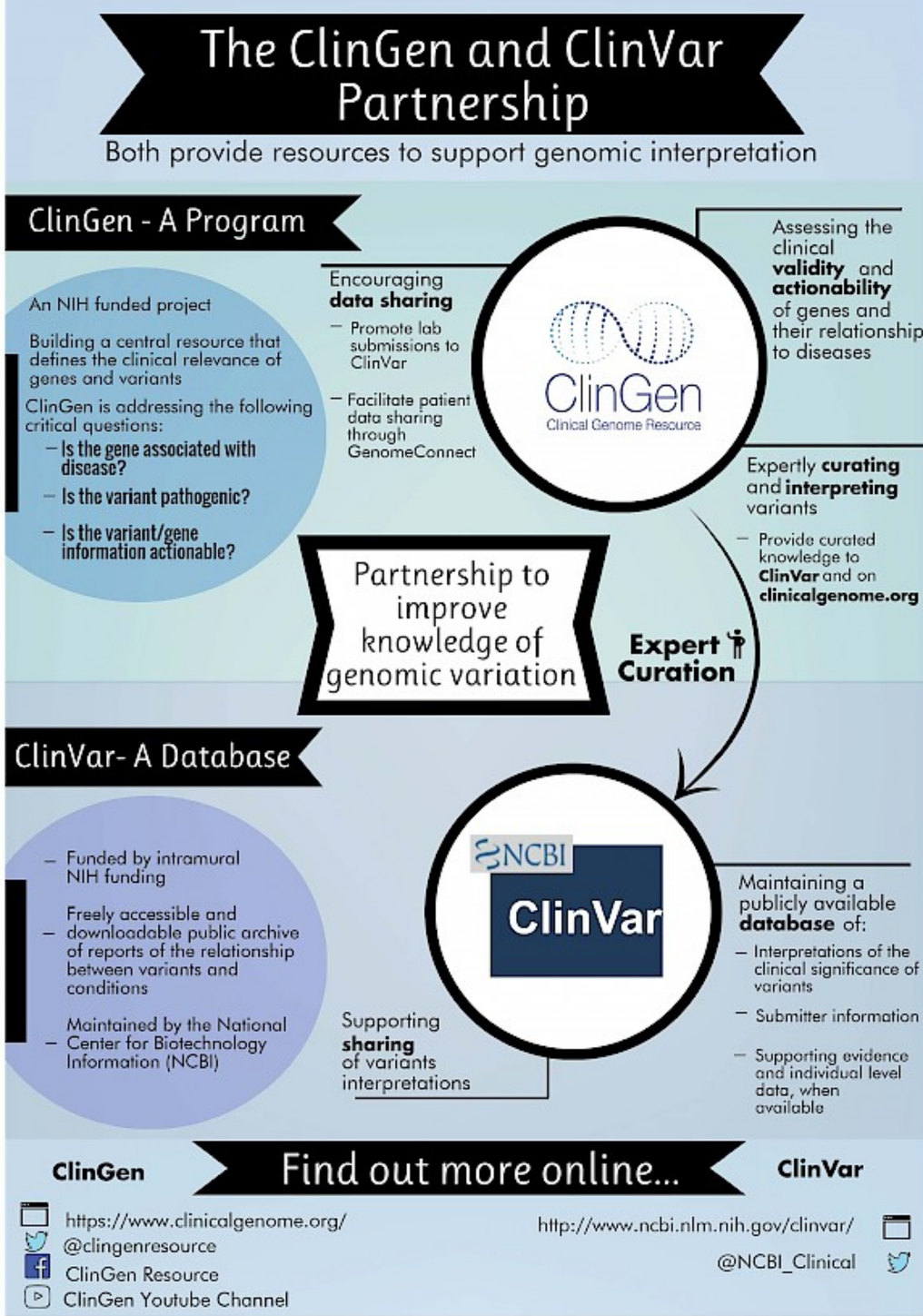
RESOURCES FOR GENOMICS: CLINGEN

- "The Genomic Variant WG brings together representatives from the Sequence and Structural Variant communities for focused discussions on resolving discrepancies in variant interpretation and creating consistent curation guidelines."
- Interpreted genome variants with disease association

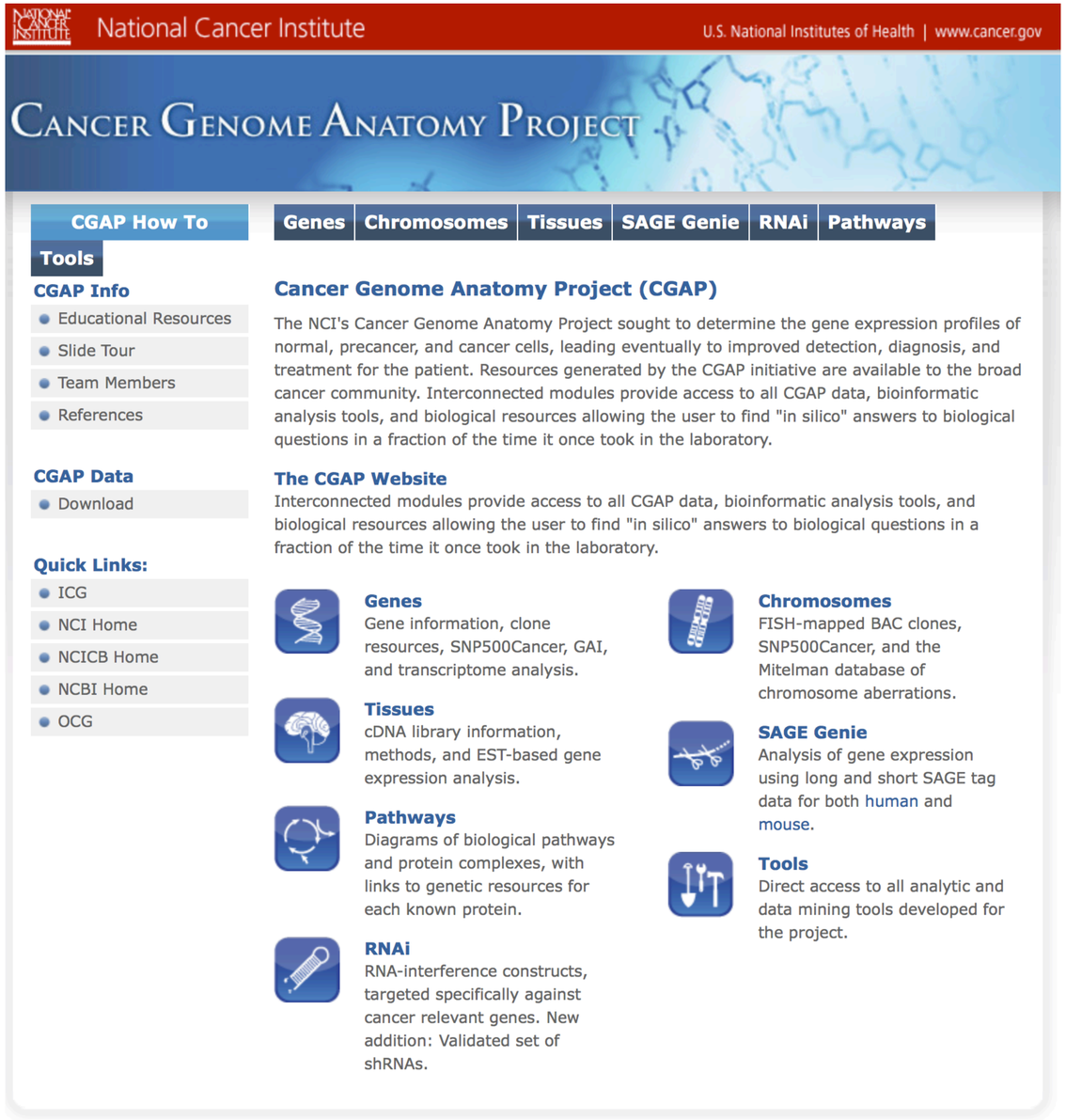
clinicalgenome.org

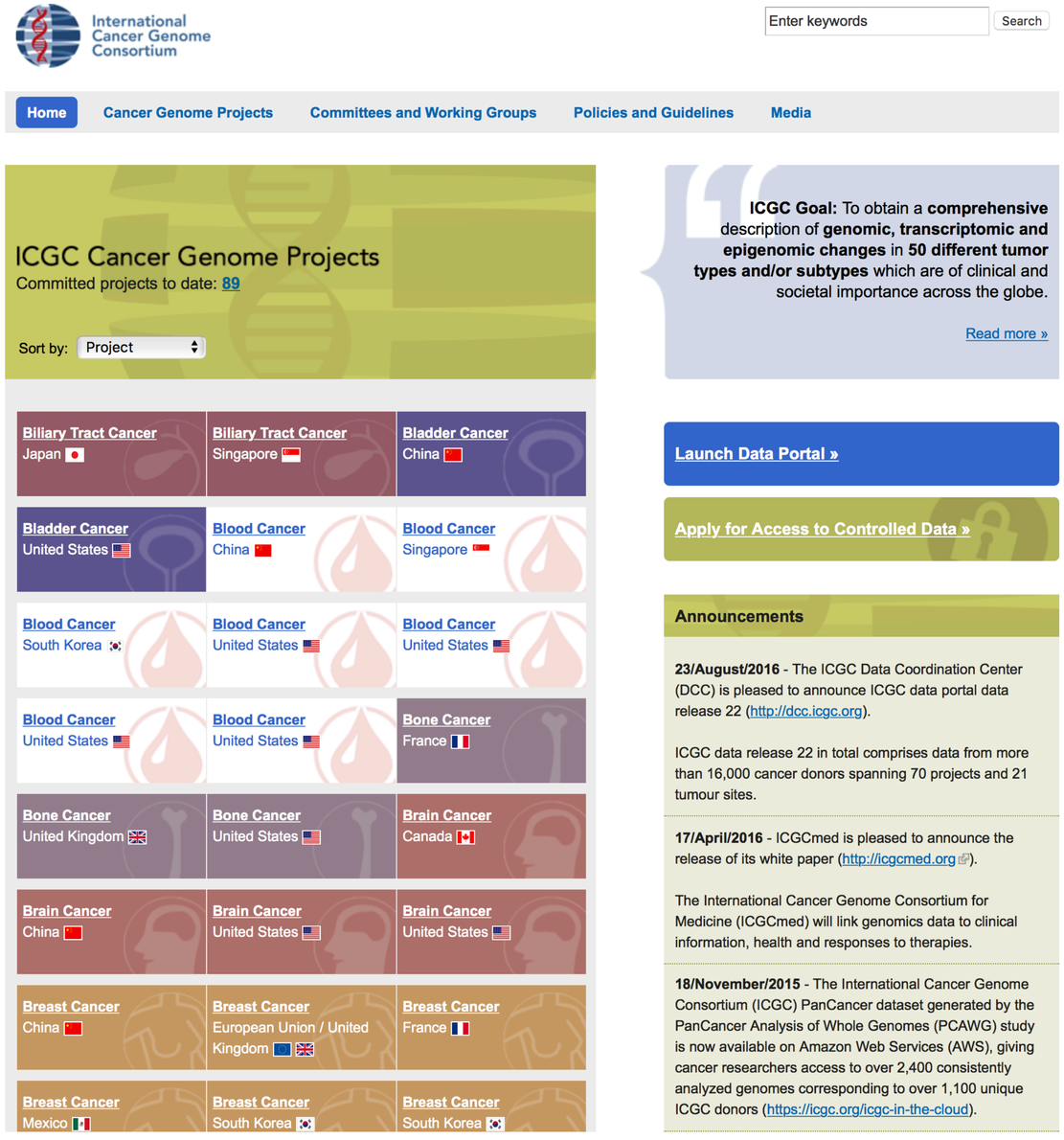
- ClinVar (an NCBI database/ resource) is used as basis for curated variant <-> disease associations in ClinGen
- ClinGen - a funded project (application/funding limited)
- ClinVar - an internal NIH resource (dependent on political "goodwill")

clinicalgenome.org



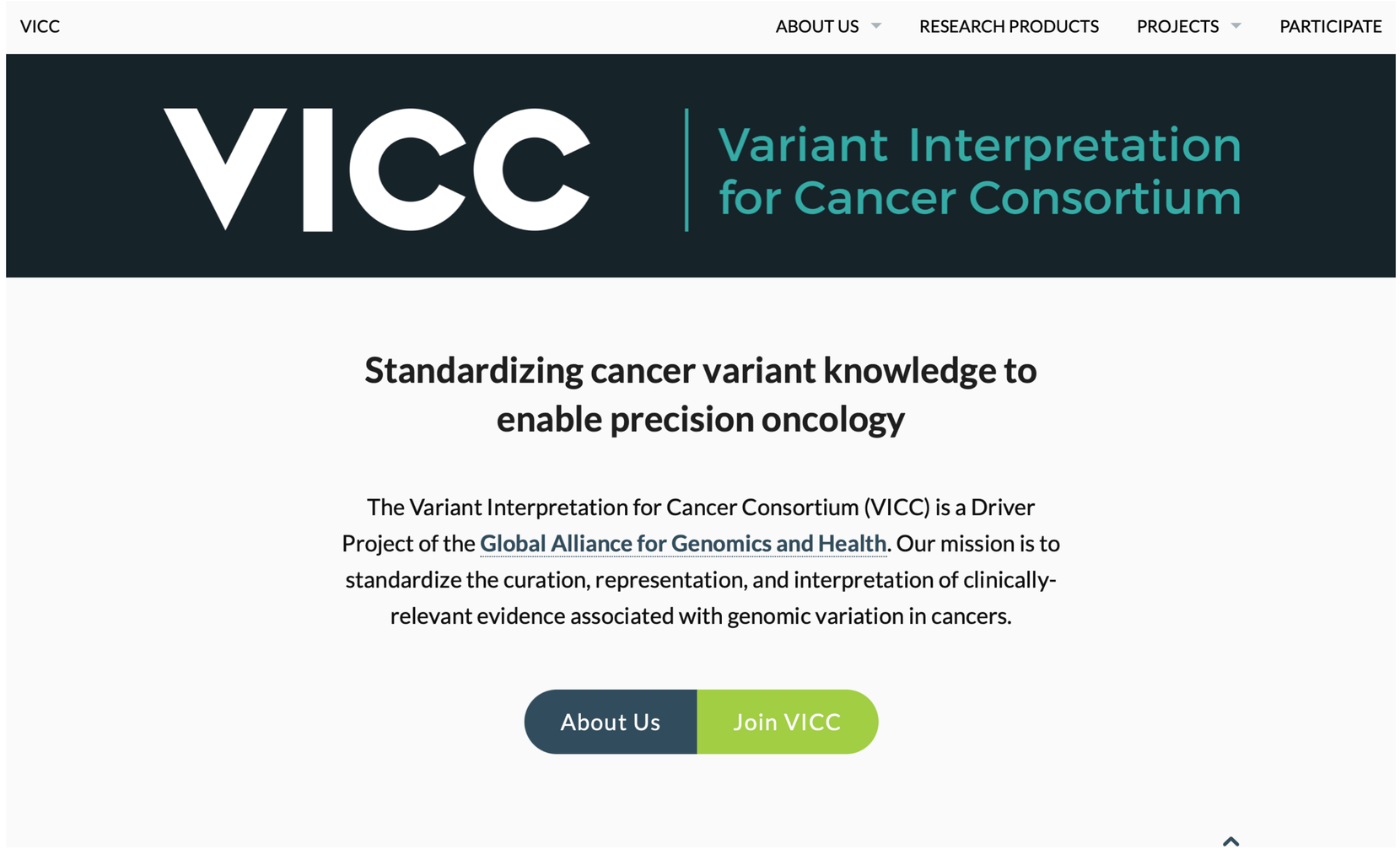
RESOURCES FOR CANCER GENOMICS





RESOURCES FOR CANCER GENOMICS

- The field of precision medicine aspires to a future in which a cancer patient's molecular information can be used to inform diagnosis, prognosis and treatment options most likely to benefit that individual patient. Many groups have created knowledgebases to annotate cancer genomic mutations associated with evidence of pathogenicity or relevant treatment options. However, clinicians and researchers are unable to fully utilize the accumulated knowledge derived from such efforts. Integration of the available knowledge is currently infeasible because each group curates their own knowledgebase without adherence to any interoperability standards. Therefore, there is a clear need to standardize and coordinate clinical-genomics curation efforts, to facilitate integration of the knowledge and evidence provided by institutions in academia, government, and industry alike.



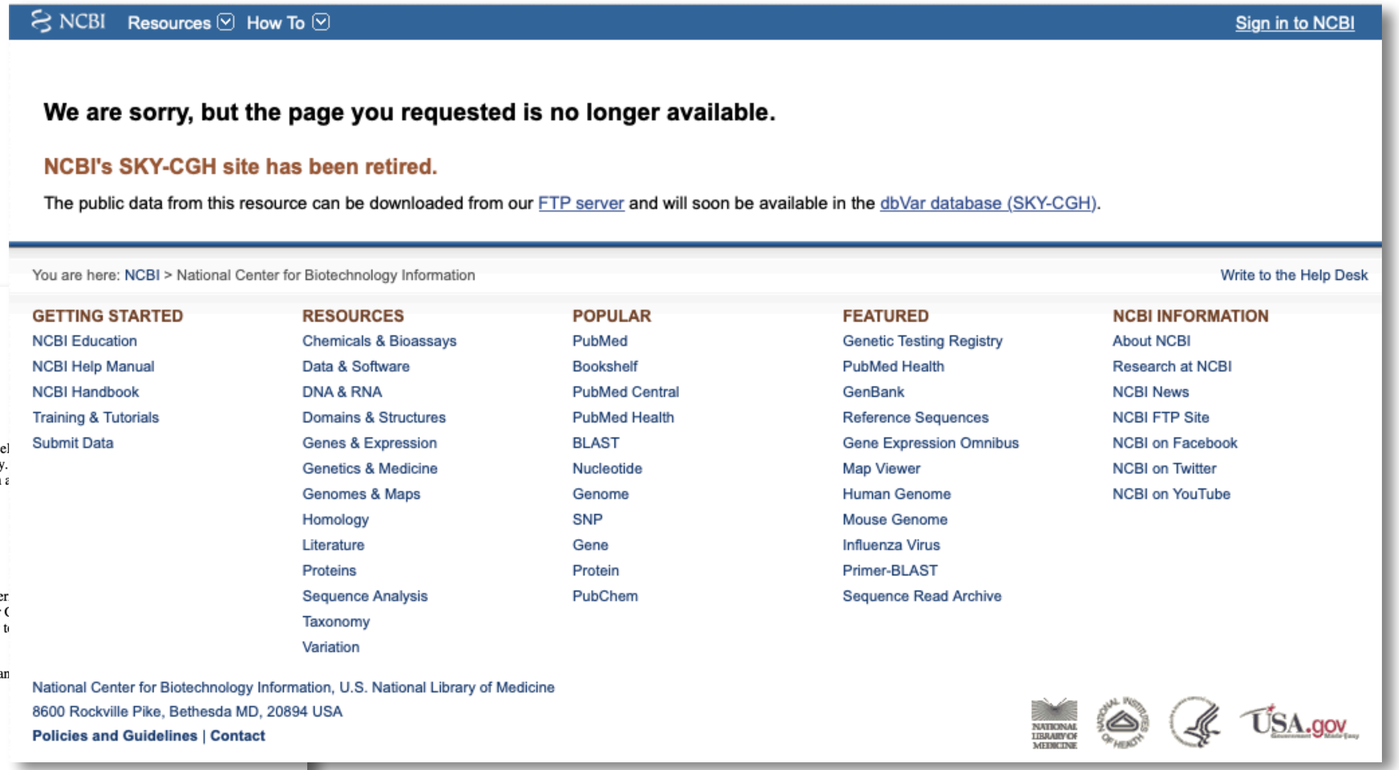
https://cancervariants.org/

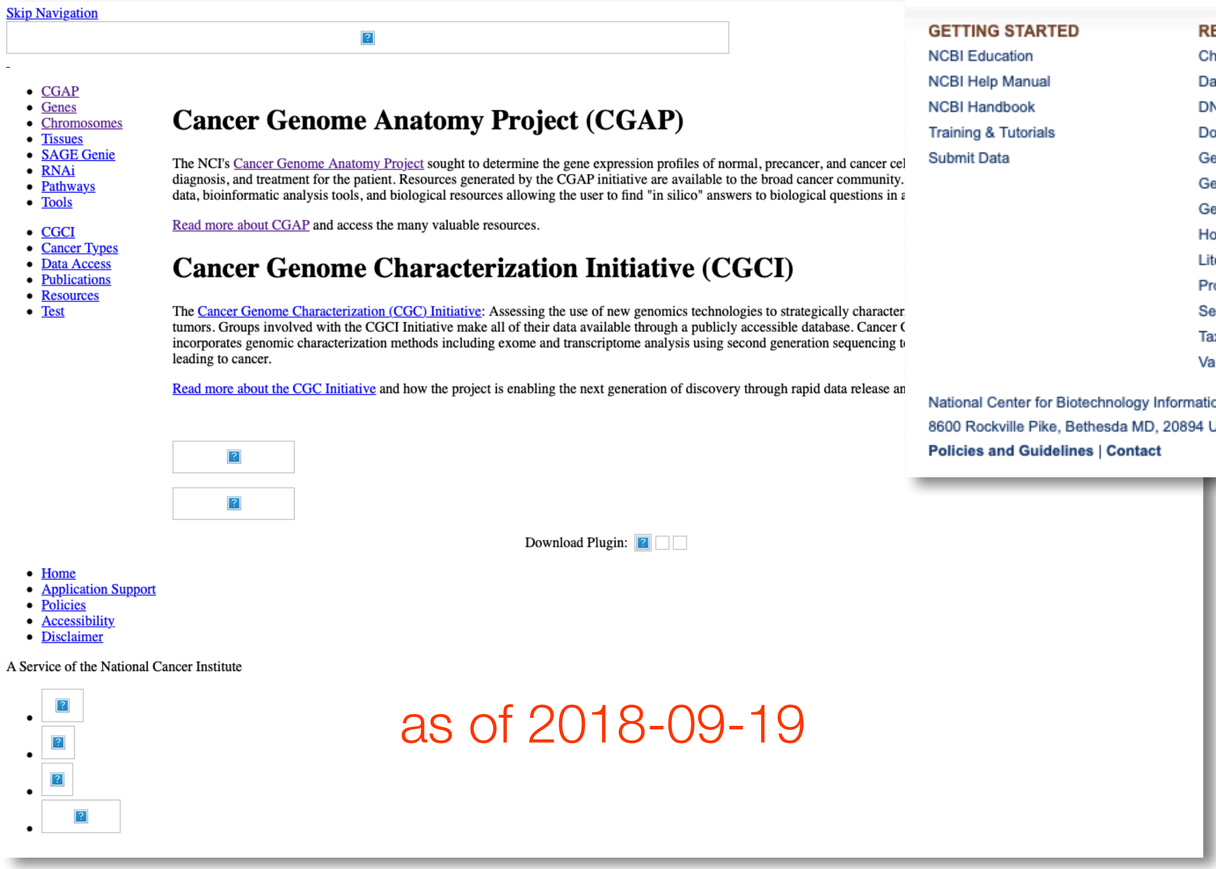
VARIANT RESOURCES FOR CANCER GENOMICS

Resource name	Primary institute	Constituent Knowledge base	Cancer focused	Therapeutic evidence	Predisp. evidence	Diagnostic evidence	Prognostic evidence	Variant emphasis	URL
Cancer Genome Interpreter (CGI)	Institute for Research in Biomedicine, Barcelona, Spain	x	x	x				Somatic	https://www.cancergenomeinterpreter.org/home
Clinical Interpretation of Variants in Cancer (CIViC)	Washington University School of Medicine (WashU)	x	x	x	x	x	x	All variants	www.civicdb.org
JAX Clinical Knowledgebase (CKB)	The Jackson Laboratory	x	x	x	x	x	x	Somatic	https://ckb.jax.org/
Molecular Match	Molecular Match	x	x	x			x	Somatic	https://app.molecularmatch.com/
OncoKB	Memorial Sloan Kettering Cancer Center	x	x	x				Somatic	http://oncokb.org/#/
Precision Medicine Knowledgebase (PMKB)	Weill Cornell Medical College	x	x	x	x	x	x	Somatic	https://pmkb.weill.cornell.edu/
BRCA exchange	GA4GH	x	x		x			Germline	http://brcaexchange.org/
Cancer Driver Log (CanDL)	Ohio State University (OSU) / James Cancer Hospital		x	x				Somatic	https://candl.osu.edu/
Gene Drug Knowledge Database	Synapse		x	x		x	x	Somatic	https://www.synapse.org/#!Synapse:syn2370773/wiki/62707
MatchMiner	Dana-Farber Cancer Institute		x					Somatic	http://bcb.dfci.harvard.edu/knowledge-systems/
COSMIC Drug Resistance Curation	Wellcome Trust Sanger Institute		x	x				Somatic	http://cancer.sanger.ac.uk/cosmic/drug_resistance
My Cancer Genome	Vanderbilt University		x	x		x	x	Somatic	https://www.mycancergenome.org/
NCI Clinical Trials	National Cancer Institute of the National Institutes of Health		x					Somatic	www.cancer.gov/about-cancer/treatment/clinical-trials
Personalized Cancer Therapy Database	MD Anderson Cancer Center		x	x	x	x	x	Somatic	https://pct.mdanderson.org/#/home
ClinGen Knowledge Base	ClinGen				x			Germline	https://www.clinicalgenome.org/resources-tools/
ClinVar	National Center for Biotechnology Information			x	x			All variants	http://www.ncbi.nlm.nih.gov/clinvar/
Pharmacogenomics Knowledgebase (PharmGKB)	Stanford University			x				Germline	https://www.pharmgkb.org/
The Human Gene Mutation Database (HGMD)	Institute of Medical Genetics in Cardiff				x			Germline	http://www.hgmd.cf.ac.uk

Wagner et al. A harmonized meta-knowledgebase of clinical interpretations of cancer genomic variants. Nature Genetics (under review 2018)

RESOURCES FOR GENOMICS - THEY MAY BREAK SOMETIMES ...





as of 2018-09-19

Beyond a Single Resource: Federation

Cell Genomics

CellPress
OPEN ACCESS

Commentary

International federation of genomic medicine databases using GA4GH standards

Adrian Thorogood,[1,2,*] Heidi L. Rehm,[3,4] Peter Goodhand,[5,6] Angela J.H. Page,[4,5] Yann Joly,[2] Michael Baudis,[7] Jordi Rambla,[8,9] Arcadi Navarro,[8,10,11,12] Tommi H. Nyronen,[13,14] Mikael Linden,[13,14] Edward S. Dove,[15] Marc Fiume,[16] Michael Brudno,[17] Melissa S. Cline,[18] and Ewan Birney[19]

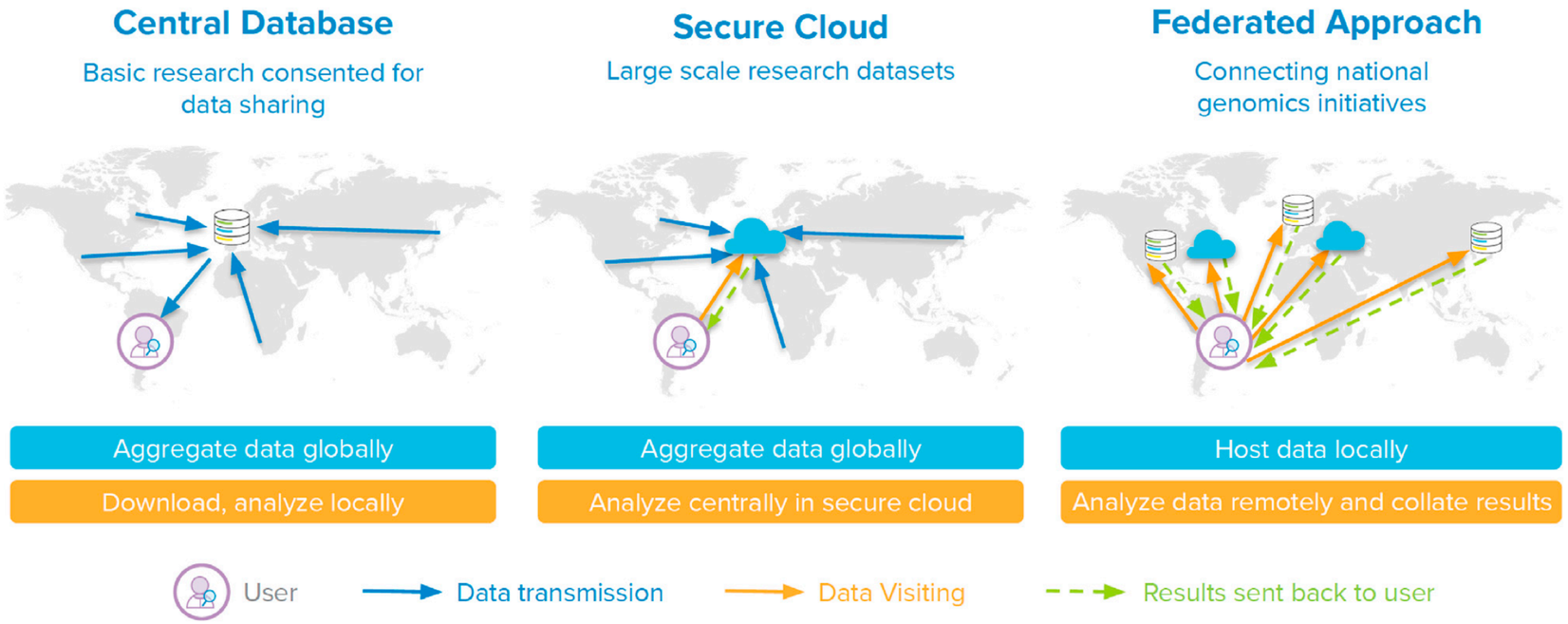


Figure 1. Data sharing approaches: Central database, secure cloud, and federated

Central database: Data from multiple sources are pooled in a central database. Researchers download copies of data and analyze them in their own computing environment.

Secure cloud: Data from multiple sources are pooled in a central cloud environment. Researchers remotely visit data and run their analyses in the cloud and download the result.

Federation: Data remain within locally controlled databases and computing environments, which may be cloud environments. Researchers remotely visit data, run their analyses at each site, and receive a local result, which can then be aggregated.

Task: Exploring Genome Resources

- primary deposition databases
- interpreted databases (e.g. variant annotations...)
- suggestion: VICC paper (Wagner et al.)
  - Wagner et al (2020): A harmonized meta-knowledgebase of clinical interpretations of somatic genomic variants in cancer
- make some notes about different genome resources and their primary use

  ➡Don't think only "human" ¯_(ツ)_/¯

BIO392: Course Schedule

https://compbiozurich.org/UZH-BIO392/

	Friday 2025-04-04	Tuesday 2025-04-08	Wednesday 2025-04-09	Thursday 2025-04-10	Friday 2025-04-11	Tuesday 2025-04-15	Wednesday 2025-04-16	Thursday 2025-04-17	Tuesday 2025-04-29	Wednesday 2025-04-30	Friday 2025-05-02	Tuesday 2025-05-06	Wednesday 2025-05-07
09:00 - 10:00	* Room information * Administrative - discuss times/days - exam		Jiahui: Terminal / Unix / Files	Hangjia: R enviroment introduction	Michael: Genoomic Resources & Data Sharing		Feifei: Sequence analysis practical. FastQC, trimmomatic, BWA-MEM2, SAMtools, GangSTR, BCFtools	Michael: Genomic Data & Privacy		Feifei & Ziying: survival	Feifei: population structure		Exam
10:00 - 11:00	Tina Siegenthaler: technical introduction (room, computer, accounts)		Jiahui: Terminal / Unix / Files	Hangjia: R exercise	Michael: Genoomic Resources & Data Sharing		Feifei:: Sequence analysis practical	Michael: Genomic Data & Privacy		Feifei & Ziying: survival	Feifei: population structure		Discussion
11:00 - 12:00	* explore course site * create Github accounts and forward to bio392@compbiozurich.org *feifei&jiahui: overall schedule of the course		jiahui: SIB online introduction to Unix		Michael: Genoomic Resources & Data Sharing		Feifei:: Sequence analysis practical	Michael: Genomic Data & Privacy		Feifei: survival	Feifei: population structure		
13:00 - 14:00	jiahui: Github	Michael: Introduction	Jiahui & Ziying: Python	Hangjia: CNV paper reading	Hangjia: Clinvar and Clingen	Feifei: Sequence analysis introduction. Overview of pipeline from raw reads -> variant calling & interpretation	Feifei:: STR reading up		Feifei:: analysis & interpretation. Parsing VCF (cyvcf2), UCSD genome browser, ENSEMBL variant effect predictor	Feifei: population structure	Feifei & others: Presentation & Discussion	Exam revision, Q&A	
14:00 - 15:00	jiahui: Github&Git exercise	Michael: Introduction	Exercise	Hangjia: Progenetix as tool for CNV frequencies etc.	Hangjia: blast	Feifei: Sequence analysis introduction	Feifei:: STR reading up		Feifei:: analysis & interpretation.	Feifei: population structure	Feifei & others: Presentation & Discussion		
15:00 - 16:30		Michael: Introduction			Hangija: Blast exercise				Feifei:: analysis & interpretation.	Feifei: population structure	Feifei & others: Presentation & Discussion		