



Global Alliance
for Genomics & Health



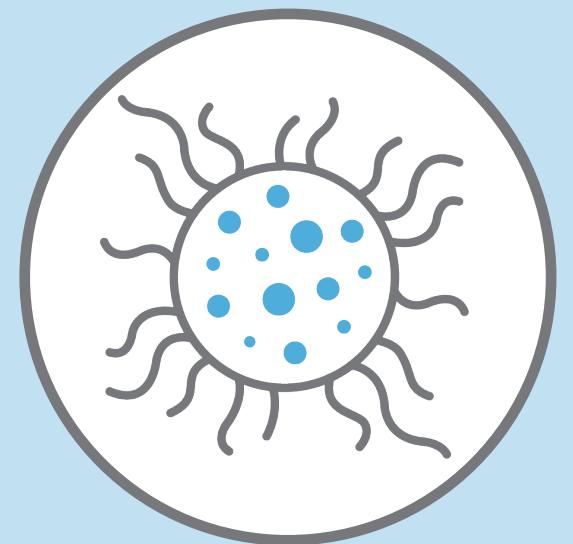
Open Reference Resource for Oncogenomic Copy Number Aberrations Implementing Emerging Global Standards **Progenetix - From Experiments to APIs**

Michael Baudis | EORTC-PAMM | Firenze December 2022

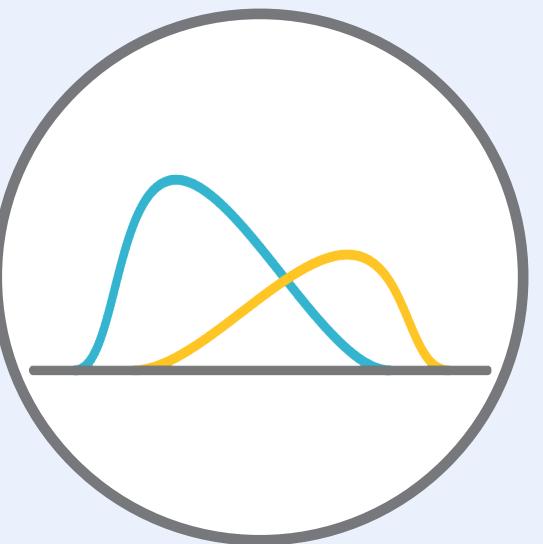
Genomic Data Aggregation Can...



Global Alliance
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Demonstrate
patterns in health
& disease



Increase statistical
significance of
analyses



Lead to
“stronger” variant
interpretations



Increase
accurate
diagnosis

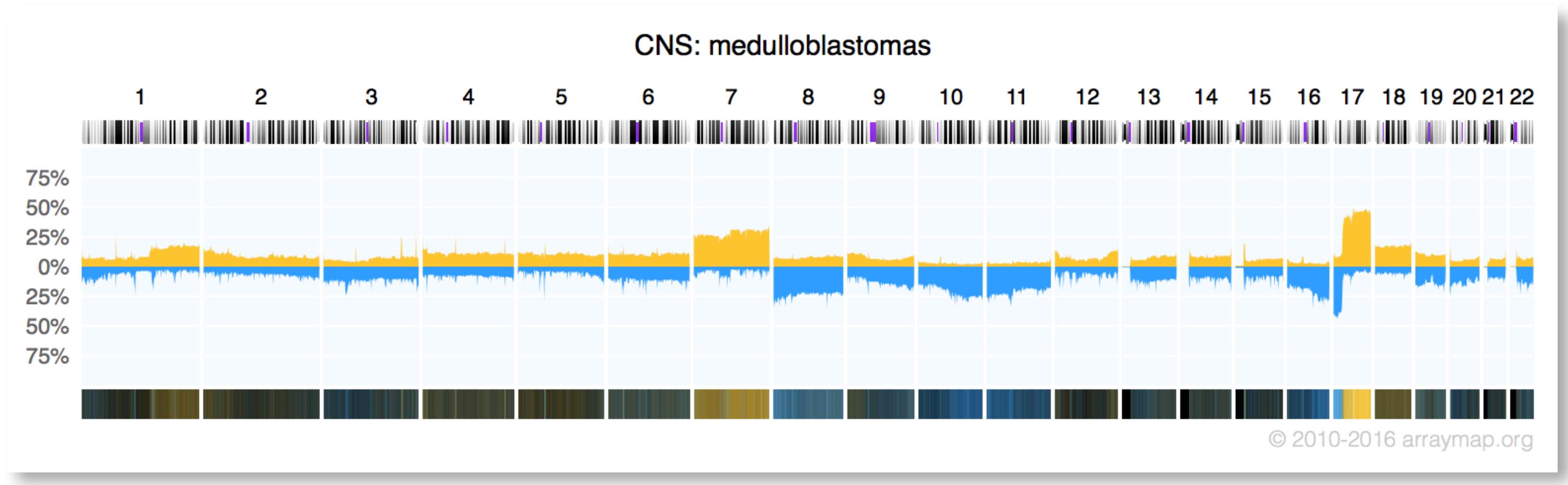


Advance
precision
medicine

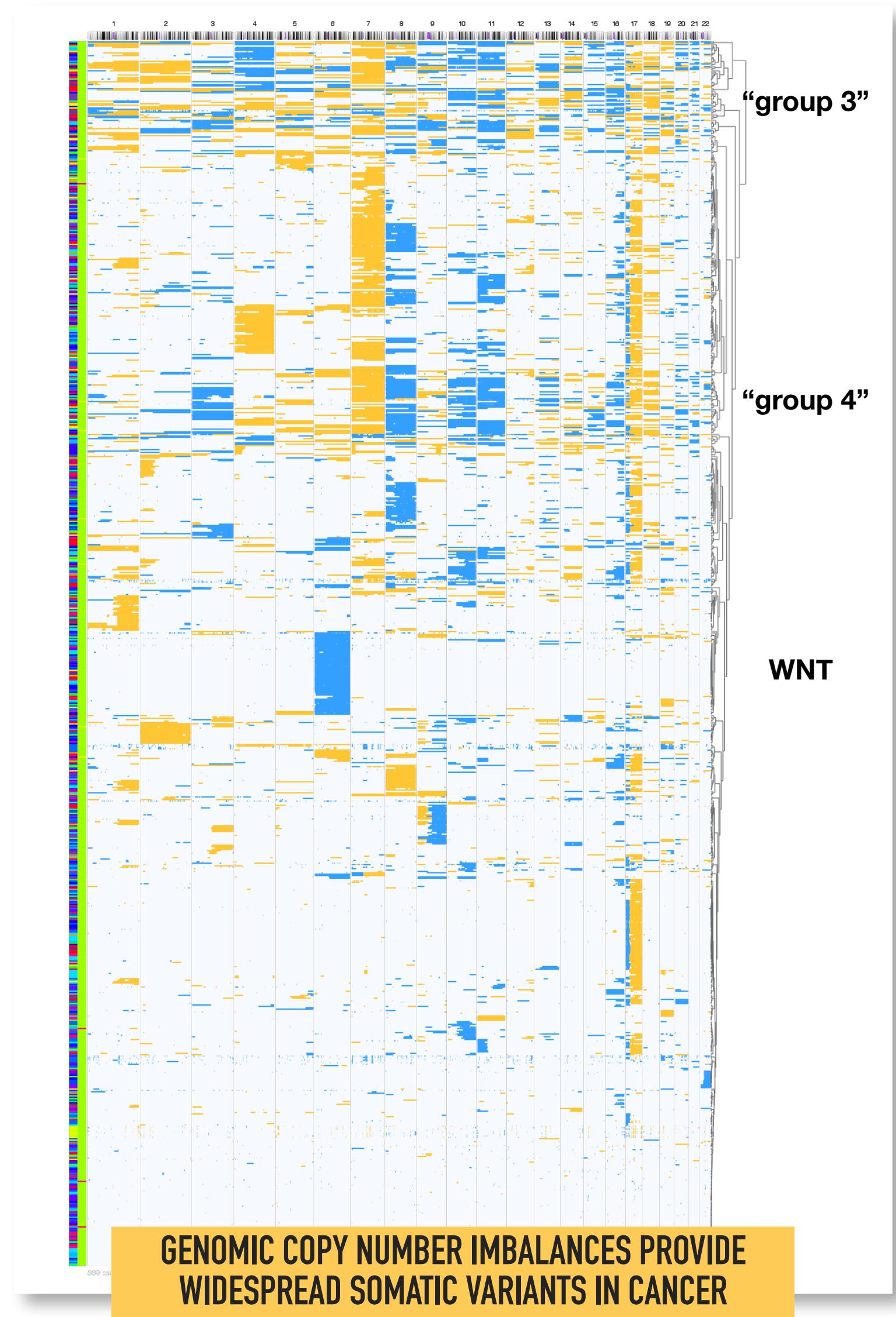
Somatic CNVs In Cancer

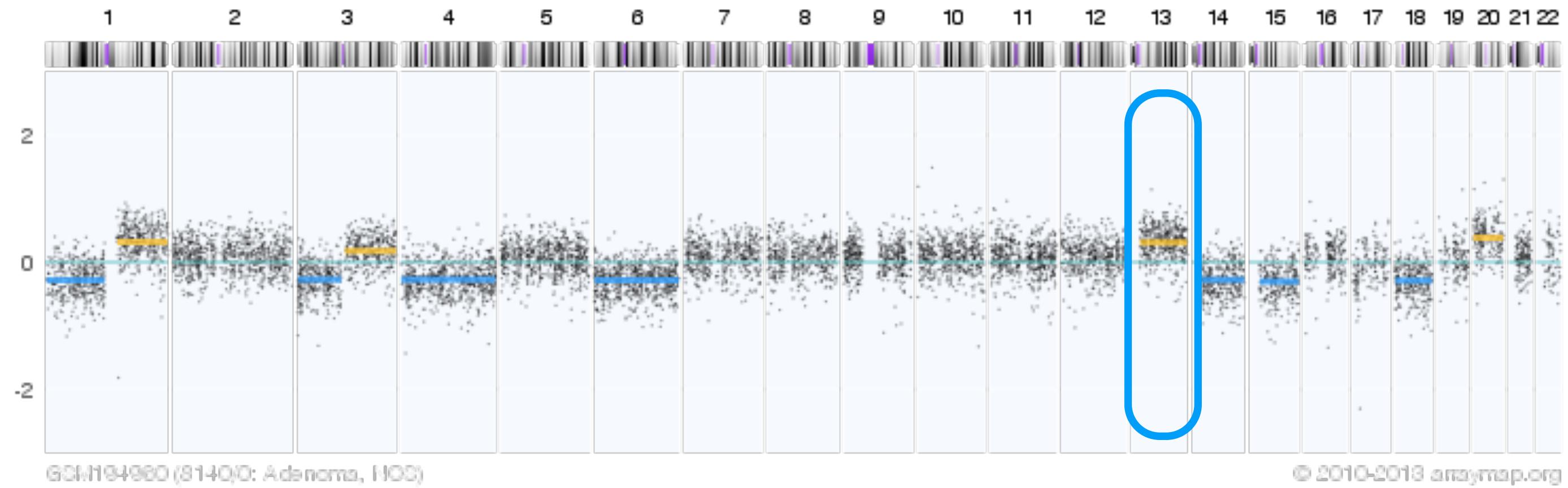
Recurrent mutation patterns

How can those patterns be used for classification and determination of biological mechanisms?

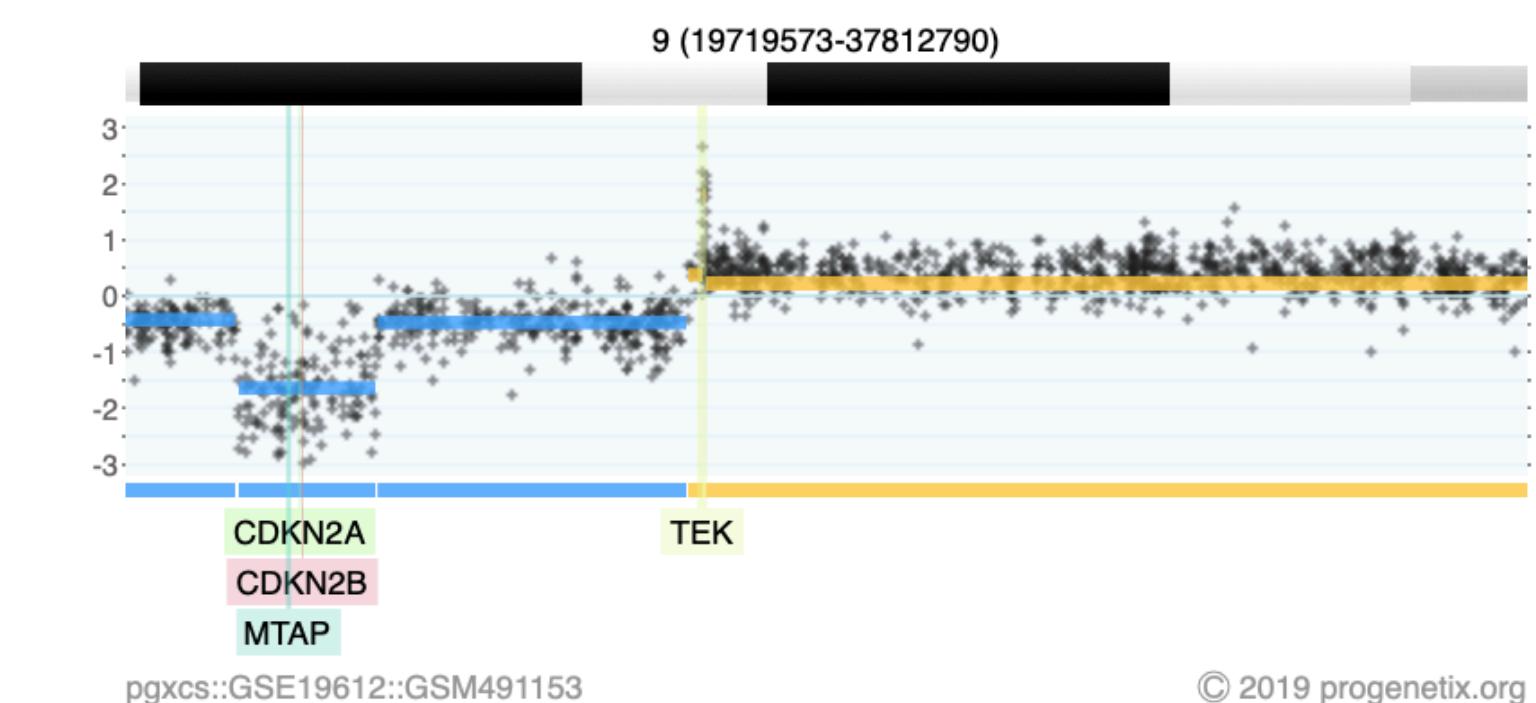


A genomic copy number histogram for malignant medulloblastomas, the most frequent type of pediatric brain tumors, displaying regions of genomic duplications and deletions. These can be decomposed into individual tumor profiles which segregate into several clusters of related mutation patterns with functional relevance and clinical correlation.





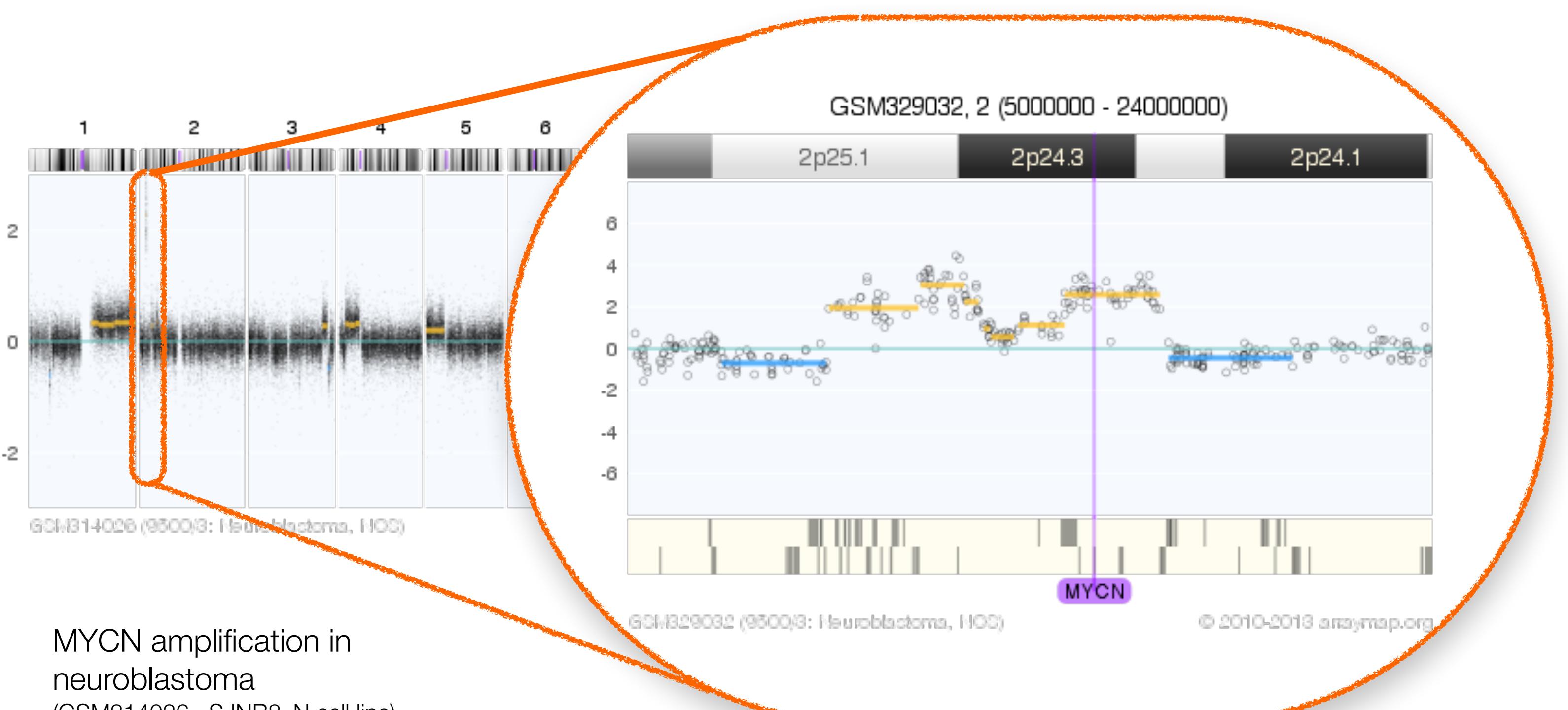
Gain of chromosome arm 13q in colorectal carcinoma



2-event, homozygous deletion in a Glioblastoma

CNVs Arrive in a Variety of Formats

- most available data is array/matrix based
- conversion of probe specific (ratio) values through normalization & segmentation



MYCN amplification in neuroblastoma (GSM314026, SJNB8_N cell line)

low level/high level copy number alterations (CNAs)

arrayMap



CNVs Arrive in a Variety of Formats

Text conversion from ISCN

- articles and supplements with **cytoband-based *rev ish* CGH** results are a great source of CNV data
- conversion by mapping cytoband locations (e.g. UCSC annotation files) to genome coordinates and assigning CNV types (enh, dim, amp are standard)

CGH AND FISH OF METASTATIC COLORECTAL CANCER

TABLE 3. Comparison of Primary Tumors and Metastases by CGH

Case	Gain in common	Loss in common	Primary tumor only	Metastasis only
108		18		
113	7, 8q24-qter, 13q11-qter, 20q11-qter, Xq11-Xter	1p33-pter, 2p21-pter, 4q24-qter, 15q11-q15, 17p11-pter, 18		
LM	12q22-qter, 15q23-qter, 17q11-ter, 20p11-p12, 20q11-ter, 22q11-ter	1p11-p32, 1q24-31, 4, 13q11-pter, 17p11-pter, 18, 20p11-ter	11p11-pter-	12+
145	4q26-q28, 6p11-p13, 8p11-p12, 920q11-qter	1p11-pter, 4q31-qter, 6q11-qter, 8p12-pter, 11, 15q11-qter, 16q11-qter, 17p11-pter, 18, 21q11-qter	13q21-qter+, 20p11-pter-	8q11-qter+, 10-, 6p21-pter-
53	7, 8q11-qter, 9q33-qter, 13q11-qter, 20p11-p12, 20q11-qter	4p13-pter, 4q21-qter, 8p12-pter, 15q14-qter, 18q11-qter, 20p12-pter	5p11-pter-, 5q13-qter-, 14q11-qter-	11+, 16p11-pter+, 17q11-qter+, 19+, 21q11-qter+, 22q11-qter+
147	7, 13q11-qter, 20q11-qter	8p21-pter, 18	4p14-pter-, 4q28-qter+, 8p11-21-, 17q11-q2+, 21q11-qter-	11q22-qter+, 16+, 1p11-33-

TABLE 1. Clinical Data

Case number	Age	Sex	Site	Stage ^a	Grade ^b	Diagnosis of metastatic disease ^c
2	40	M	Transverse colon	IV	3	Synchronous
6	79	M	Ascending colon	IV	2	Synchronous
9	73	M	Transverse colon	II	2	N/A
11	56	M	Rectosigmoid	IV	2	Metachronous
12	70	F	Sigmoid colon	IV	2	Synchronous
13	65	M	Descending colon	II	9	Synchronous
14	60	M	Rectum	III	3	Metachronous
15	51	F	Rectum	III	2	Metachronous
19	63	M	Rectosigmoid Junction	III	2	Synchronous
20	63	M	Rectum	IV	9	Metachronous
21	64	F	Sigmoid colon	IV	2	Synchronous
35	71	M	Rectum	III	9	Metachronous
49	72	M	Cecum	IV	3	Synchronous
53	72	F	Sigmoid colon	IV	2	Synchronous
104	61	M	Sigmoid colon	IV	2	Metachronous
105	58	M	Ascending colon	II	2	Metachronous
107	77	F	Cecum	IV	2	Metachronous
108	53	F	Splenic flexure	IV	2	Synchronous
112	68	M	Rectum	III	3	Synchronous
113	41	M	Splenic flexure	IV	2	Synchronous
114	49	M	Splenic flexure	IV	3	Synchronous
116	73	M	Rectosigmoid	III	9	Metachronous
120	24	F	Descending colon	IV	2	Synchronous
123	62	F	Rectum	III	2	Metachronous
124	42	M	Rectum	IV	9	Synchronous
145	70	M	Rectosigmoid	IV	2	Synchronous
147	86	F	Cecum	IV	2	Synchronous

^aAJCC/UICC staging system (Hutter and Sabin, 1986).

^bGrade of primary tumor: 1–3, low, moderate, high grade; 9, grading unknown.

^cSynchronous, diagnosis of metastatic disease within 12 months following diagnosis of primary tumor; metachronous, diagnosis of metastatic disease after 12 months or later.

GENES, CHROMOSOMES & CANCER 25:82-90 (1999)
Chromosome Arm 20q Gains and Other Genomic Alterations in Colorectal Cancer Metastatic to Liver, as Analyzed by Comparative Genomic Hybridization and Fluorescence In Situ Hybridization

W. Michael Korn,¹* Toru Yasutake,² Wen-Lin Kuo,¹ Robert S. Warren,³ Colin Collins,¹ Masao Tomita,² Joe Gray,¹ and Frederic M. Waidman¹

CNVs Arrive in a Variety of Formats: VCF

Issue 1: There are two fields to specify SV/CNV

#CHROM	POS	ID	REF	ALT	QUAL	FILTER	INFO
1	2827694	rs2376870	CGTGGATGCGGGAC	C	.	PASS	SVTYPE=DEL;END=282770
2	321682	.	T		6	PASS	SVTYPE=DEL;END=321887
2	14477084	.	C	<DEL:ME:ALU>	12	PASS	SVTYPE=DEL;END=144773
3	9425916	.	C	<INS:ME:L1>	23	PASS	SVTYPE=INS;END=942591
3	12665100	.	A	<DUP>	14	PASS	SVTYPE=DUP;END=126862
4	18665128	.	T	<DUP:TANDEM>	11	PASS	SVTYPE=DUP;END=186652

1) Symbolic allele (SA)

2) SVTYPE

- DEL Deletion relative to the reference
 - INS Insertion of novel sequence relative to the reference
 - DUP Region of elevated copy number relative to the reference
 - INV Inversion of reference sequence
 - CNV Copy number variable region (may be both deletion and duplication)
 - BND Breakend
- The CNV category should not be used when a more specific category can be applied. Reserved subtypes include:
- DUP:TANDEM Tandem duplication
 - DEL:ME Deletion of mobile element relative to the reference
 - INS:ME Insertion of a mobile element relative to the reference



- DEL: Deletion relative to the reference
- INS: Insertion of novel sequence relative to the reference
- DUP: Region of elevated copy number relative to the reference
- INV: Inversion of reference sequence
- CNV: Copy number variable region (may be both deletion and duplication)
- BND: Breakend



VCF v4.4 deprecate SVTYPE

#CHROM	POS	ID	REF	ALT	QUAL	FILTER	INFO	FOR
chrA	2	.	TGC	T	.	.	EVENT=DEL_seq	
chrA	2	.	T		.	.	SVLEN=2;SVCLAIM=DJ;EVENT=DEL_symbolic;END=4	
chrA	2	delbp1	T	T[chrA:5[.	.	.	MATEID=delbp2;EVENT=DEL_split_bp_cn	
chrA	2	delbp2	A]chrA:2]A	.	.	MATEID=delbp1;EVENT=DEL_split_bp_cn	
chrA	2	.	T		.	.	SVLEN=2;SVCLAIM=D;EVENT=DEL_split_bp_cn;END=4	
chrA	5	.	G	GAAA	.	.	EVENT=homology_seq	
chrA	5	.	G	<DUP>	.	.	SVLEN=3;CIPOS=0,5;EVENT=homology_dup	
chrA	14	.	T	<INS>	.	.	IMPRECISE;SVLEN=100;CILEN=-50,50;CIPOS=-10,10;END=14	
chrA	14	.	G	.CCCCCG	.	.	EVENT=single_breakend	

Symbolic allele (SA)

- DEL Region of lowered copy number relative to the reference, or a deletion breakpoint
 - INS Insertion of novel sequence relative to the reference
 - DUP Region of elevated copy number relative to the reference, or a tandem duplication breakpoint
 - INV Inversion of reference sequence
 - CNV Copy number variable region (may be both deletion and duplication)
- The CNV category should not be used when a more specific category can be applied.
- Implementations are free to define their own subtypes. The presence of a subtype does not change either the copy number or breakpoint interpretation of a symbolic structural variant allele. The following subtypes are recommended:
- DUP:TANDEM Tandem duplication
 - DEL:ME Deletion of mobile element relative to the reference
 - INS:ME Insertion of a mobile element relative to the reference

Note that the position of symbolic structural variant alleles is the position of the base immediately preceding the variant.

Reserved specific subtypes

Use Subtype to define new structural variant

- <DUP:TANDEM> precise form of duplication
- <DEL:ME:LINE>

Subtypes do not change the meaning symbolic allele.



- using genome positions (POS, INFO.END) for start, end mappings
- treatment of markers for imprecision during matching is left to the implementer
- DUP, DEL are interpreted as indicators for the type of copy number change

Progenetix Oncogenomics Resource

CNV Profiles for Most Cancer Entities from Individual Experiments

Progenetix in 2022

Cancer Genomics Reference Resource

- open resource for curated oncogenomic profiles
- **116'000+** cancer CNV profiles **800+** entities
- majority of data from genomic arrays; ~50% from SNP platforms with data re-processing
- standardized encodings (e.g. **NCIt**, **ICD-O 3**)
- identifier mapping for PMID, GEO, Cellosaurus, TCGA, cBioPortal where appropriate
- core biosample and technical metadata where accessible (TNM, sex, survival ...)
- cancer genome screening **publication DB**
- code mapping **services**



Cancer CNV Profiles

ICD-O Morphologies
ICD-O Organ Sites
Cancer Cell Lines
Clinical Categories

Search Samples

arrayMap
TCGA Samples
1000 Genomes
Reference Samples
DIPG Samples
cBioPortal Studies
Gao & Baudis, 2021

Publication DB

Genome Profiling
Progenetix Use

Services

NCIt Mappings
UBERON Mappings

Upload & Plot

Beacon⁺

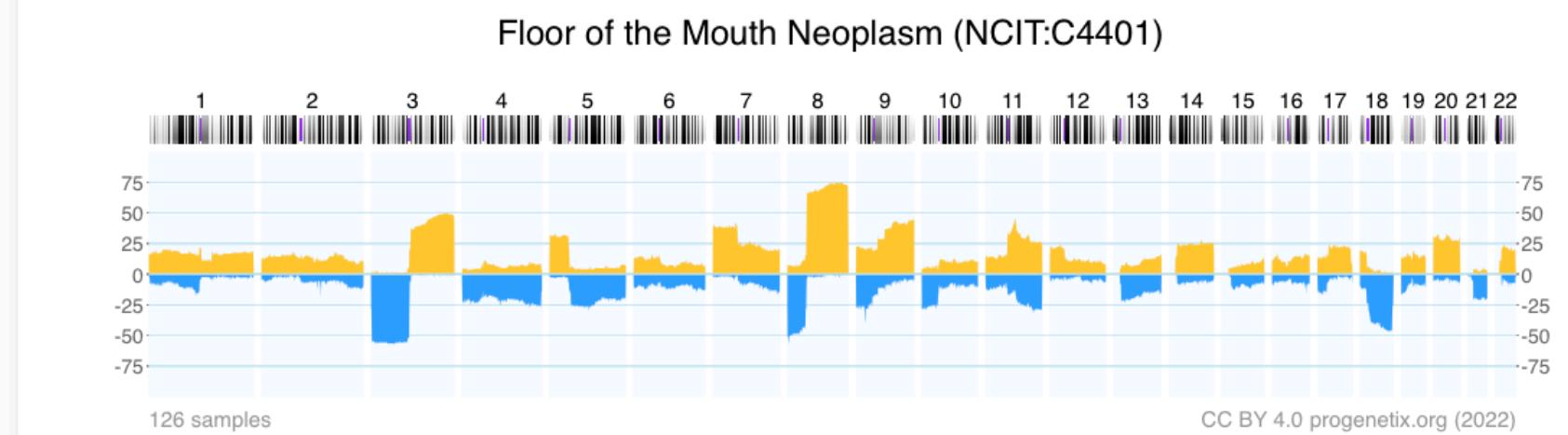
Documentation

News
Downloads & Use Cases
Sevices & API

Baudisgroup @ UZH

Cancer genome data @ progenetix.org

The Progenetix database provides an overview of mutation data in cancer, with a focus on copy number abnormalities (CNV / CNA), for all types of human malignancies. The data is based on *individual sample data* from currently **142063** samples.



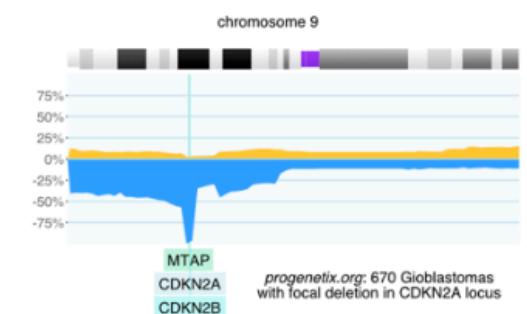
[Download SVG](#) | [Go to NCIT:C4401](#) | [Download CNV Frequencies](#)

Example for aggregated CNV data in 126 samples in Floor of the Mouth Neoplasm.
Here the frequency of regional **copy number gains** and **losses** are displayed for all 22 autosomes.

Progenetix Use Cases

Local CNV Frequencies

A typical use case on Progenetix is the search for local copy number aberrations - e.g. involving a gene - and the exploration of cancer types with these CNVs. The [\[Search Page \]](#) provides example use cases for designing queries. Results contain basic statistics as well as visualization and download options.



Cancer CNV Profiles

The progenetix resource contains data of **834** different cancer types (NCIt neoplasm classification), mapped to a variety of biological and technical categories. Frequency profiles of regional genomic gains and losses for all categories (diagnostic entity, publication, cohort ...) can be accessed through the [\[Cancer Types \]](#) page with direct visualization and options for sample retrieval and plotting options.

Cancer Genomics Publications

Through the [\[Publications \]](#) page Progenetix provides **4164** annotated references to research articles from cancer genome screening experiments (WGS, WES, aCGH, cCGH). The numbers of analyzed samples and possible availability in the Progenetix sample collection are indicated.

Progenetix in 2022

Cancer Genomics Reference Resource

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- cancer genome screening **publication DB**
- code mapping **services**

progenetix

Search Samples Modify Query

Assembly: GRCh38 Chro: 9 Start: 21500001-21975098 End: 21967753-22500000

Type: DEL Filters: NCIT:C3058

progenetix

Samples: 668 Variants: 286 Calls: 675

Found Variants (.pgxseg) All Sample Variants (.json) All Sample Variants (.pgxseg) Show Variants in UCSC

UCSC region JSON Response Visualization options

Results Biosamples Biosamples Map Variants

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22

75% 50% 25% 0% -25% -50% -75%

-75% -50% -25% 0% 25% 50% 75%

progenetix: 670 samples

CC BY 4.0 progenetix.org (2021)

Matched Subset Codes	Subset Samples	Matched Samples	Subset Match Frequencies
UBERON:0002021	4	1	0.250
icdot-C71.4	4	1	0.250
icdom-94403	4291	664	0.155
NCIT:C3058	4375	664	0.152
UBERON:0016525	14	2	0.143
icdot-C71.1	14	2	0.143
UBERON:0000955	7068	651	0.092
icdot-C71.9	7066	651	0.092
icdom-94423	84	4	0.048
NCIT:C3796	84	4	0.048
UBERON:0001869	1712	14	0.008
icdot-C71.0	1712	14	0.008

Progenetix in 2022

Cancer Genomics Reference Resource

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- cancer genome screening **publication DB**
- code mapping **services**



Cancer CNV Profiles

Search Samples

Studies & Cohorts

arrayMap

TCGA Samples

DIPG Samples

Gao & Baudis, 2021

Cancer Cell Lines

Publication DB

Genome Profiling

Progenetix Use

Services

NCIt Mappings

UBERON Mappings

Upload & Plot

Download Data

Beacon⁺

Progenetix Info

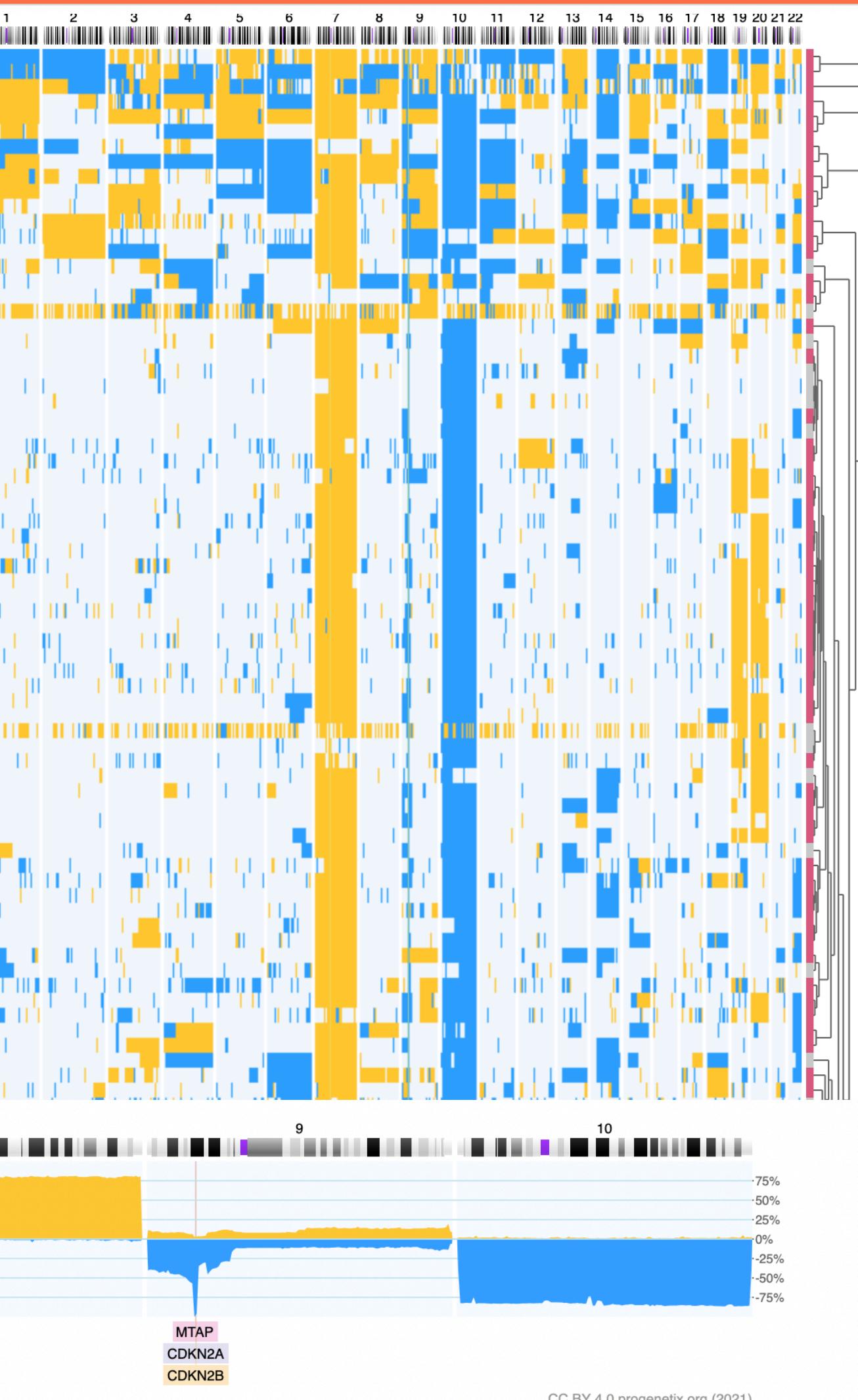
About Progenetix

Use Cases

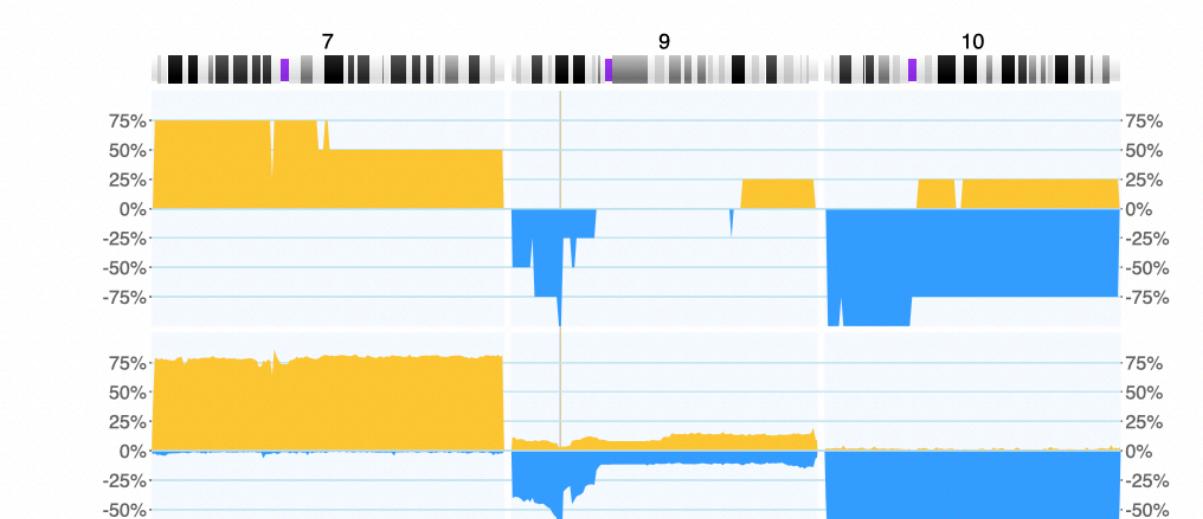
Documentation

Baudisgroup @ UZH

pgxcs-kftwze6
pgxcs-kftwz7d
pgxcs-kftwzab
pgxcs-kftwzum
pgxcs-kftw55qo
pgxcs-kftwulq
pgxcs-kftwuvof
pgxcs-kftw3hd8
pgxcs-kftw42q
pgxcs-kftw3596
pgxcs-kftwzkd4
pgxcs-kftw4gw1
pgxcs-kftwybtv
pgxcs-kftwuisse
pgxcs-kftwejw (20215515)
pgxcs-kftvh60
pgxcs-kftwuj1y
pgxcs-kftvmnxn (23079654)
pgxcs-kftw0u1d (18167341)
pgxcs-kftw60u2 (18167341)
pgxcs-kftwilia
pgxcs-kftwn4q (18077431)
pgxcs-kftwcov7 (21102433)
pgxcs-kftw6gv (19139420)
pgxcs-kftwur8g
pgxcs-kftw7w91 (18828157)
pgxcs-kftw1dk
pgxcs-kftw1zb
pgxcs-kftw3oev
pgxcs-kftwul0t
pgxcs-kftwukhg
pgxcs-kftw213x
pgxcs-kftw45dz
pgxcs-kftw2h1
pgxcs-kftwxez9
pgxcs-kftwukjd
pgxcs-kftwunck
pgxcs-kftw423r
pgxcs-kftwuldq
pgxcs-kftwyefi
pgxcs-kftrzbl
pgxcs-kftvazp
pgxcs-kftwx0a
pgxcs-kftwuk38
pgxcs-kftwuke1
pgxcs-kftvmn50 (23079654)
pgxcs-kftvmoav (23079654)
pgxcs-kftw52ga
pgxcs-kftw52d8
pgxcs-kftwupf9
pgxcs-kftwuk2a
pgxcs-kftwuiub
pgxcs-kftw8ja (21884817)
pgxcs-kftw3ji
pgxcs-kftw0acw
pgxcs-kftw0pv6
pgxcs-kftv40u
pgxcs-kftwuheo
pgxcs-kftvx29g
pgxcs-kftwummg
pgxcs-kftwizmk (23468990)
pgxcs-kftw16vy
pgxcs-kftw52z3
pgxcs-kftvz31
pgxcs-kftwugqy
pgxcs-kftwifv
pgxcs-kftwmtf (26629530)
pgxcs-kftw08qx
pgxcs-kftwuihs



Open Histogram



Progenetix in 2022

Cancer Genomics Reference Resource

- contains special data subsets, identified using the "cohorts" concept
 - ▶ TCGA CNV data
 - ▶ 1000Genomes germline CNVs (WGS)
 - ▶ Cancer cell line CNVs with addition of annotated SNV ... data
 - ▶ cBioPortal studies
 - ▶ ...

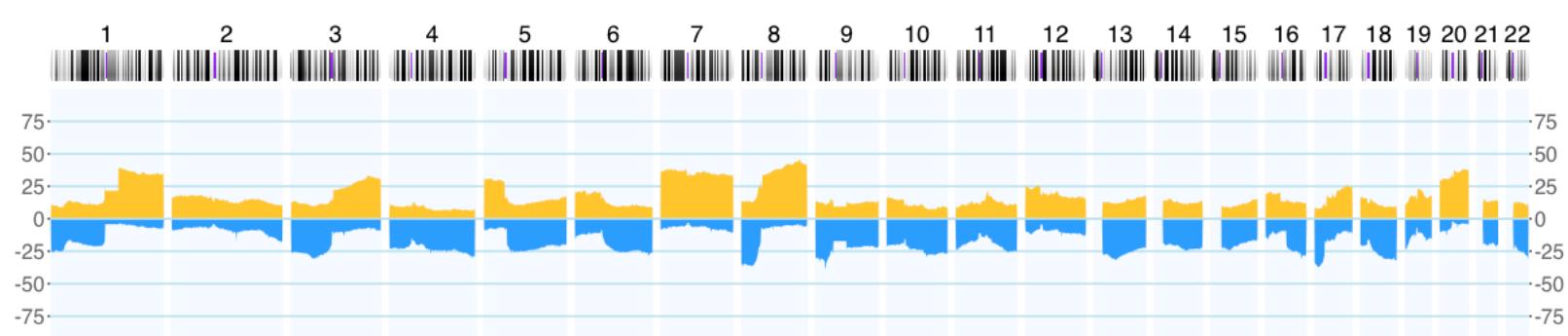


TCGA CNV Data

Search Genomic CNV Data from TCGA

This search page accesses the TCGA subset of the Progenetix collection, based on 22142 samples (tumor and references) from The Cancer Genome Atlas project. The results are based upon data generated by the [TCGA Research Network](#). Disease-specific subsets of TCGA data (aka. projects) can be accessed below.

TCGA Cancer samples (pgx:cohort-TCGAcancers)



11090 samples

CC BY 4.0 progenetix.org (2022)

[Download SVG](#) | [Go to pgx:cohort-TCGAcancers](#) | [Download CNV Frequencies](#)

[Edit Query](#)

Publication DB

- Genome Profiling
- Progenetix Use

Services

- NCIt Mappings
- UBERON Mappings

Upload & Plot

Beacon⁺

Documentation

News

Filter subsets e.g. by prefix

Hierarchy Depth: 2 levels

No Selection

- pgx:TCGA-ACC: TCGA ACC project (180 samples)
- pgx:TCGA-BLCA: TCGA BLCA project (810 samples)
- pgx:TCGA-BRCA: TCGA BRCA project (2219 samples)



Progenetix in 2022

Cancer Genomics Reference Resource

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 - ▶ ...

progenetix Cellosaurus

Cell Lines

Progenetix

Publication DB

Genome Profiling

Progenetix Use

Upload & Plot

Documentation

News

Downloads & Use Cases

Services & API

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Cancer Cell Lines

Cancer cell line CNVs

This search page uses Progenetix cell line copy number variation data. These data include cancer cell lines that have been mapped to [Cellosaurus](#) – a knowledge resource on cell lines.

CNV Frequency Plot

Cancer cell lines (pgx:cohort-celllines)

5752 samples

CC BY 4.0 progenetix.org (2022)

[Download SVG](#) | [Go to pgx:cohort-celllines](#) | [Download CNV Frequencies](#)

Edit Query

Cell Lines (with parental/derived hierarchies)

Filter subsets e.g. by prefix

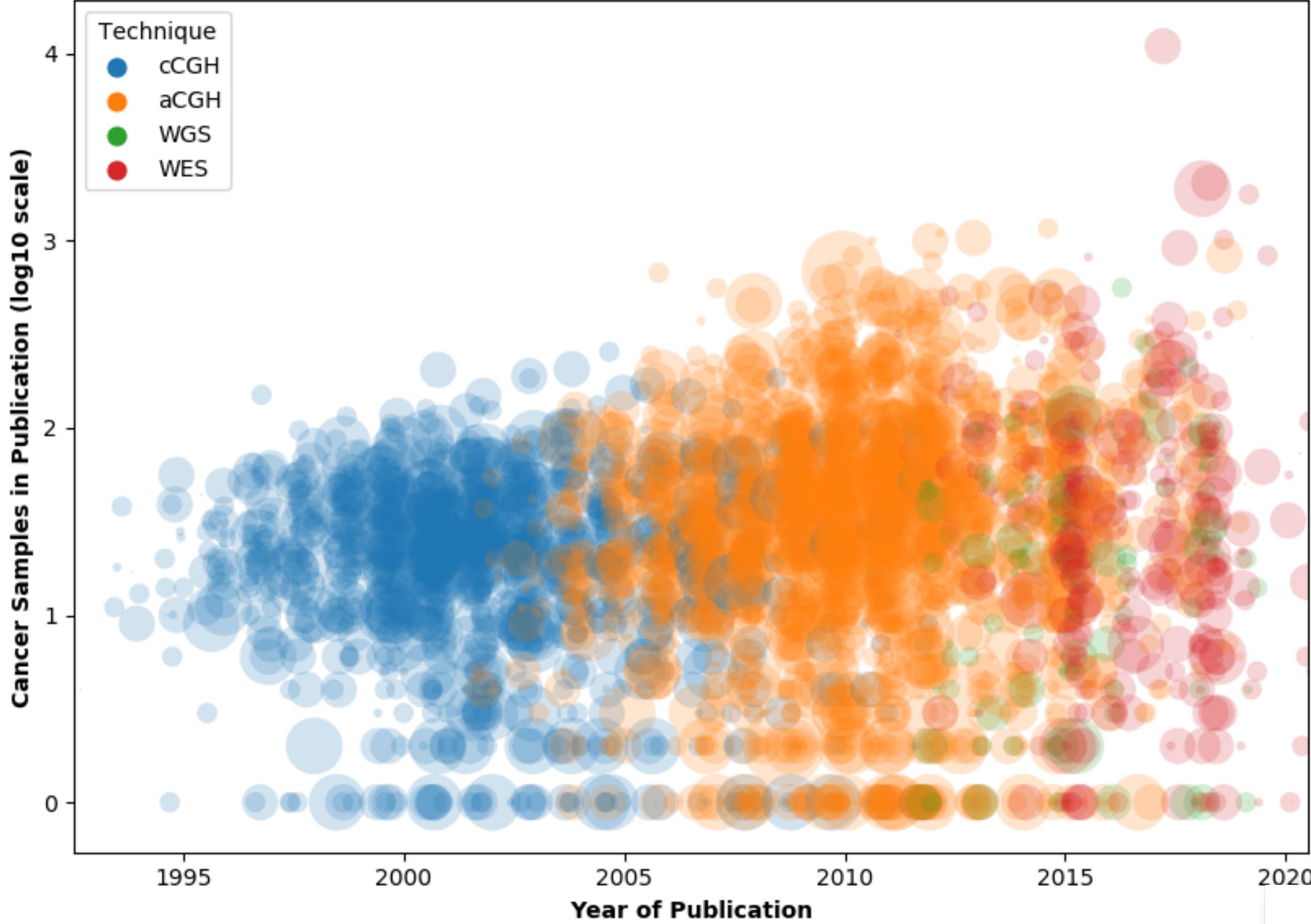
Hierarchy Depth: 2 levels

No Selection

cellosaurus:CVCL_0001: HEL (5 samples)

cellosaurus:CVCL_2481: HEL 92.1.7 (3 samples)

Number of tumor samples for each publication across the years



Map of the geographic distribution (by first author affiliation) of the 104'543 genomic array, 36'766 chromosomal CGH and 15'409 whole genome/exome based cancer genome datasets.

The numbers are derived from the 3'240 publications registered in the Progenetix database.



Progenetix Publication Collection

The current page lists articles describing whole genome screening (WGS, WES, aCGH, cCGH) experiments in cancer, registered in the Progenetix publication collection. For each publication the table indicates the numbers of samples analysed with a given technology and if sample profiles are available in Progenetix.

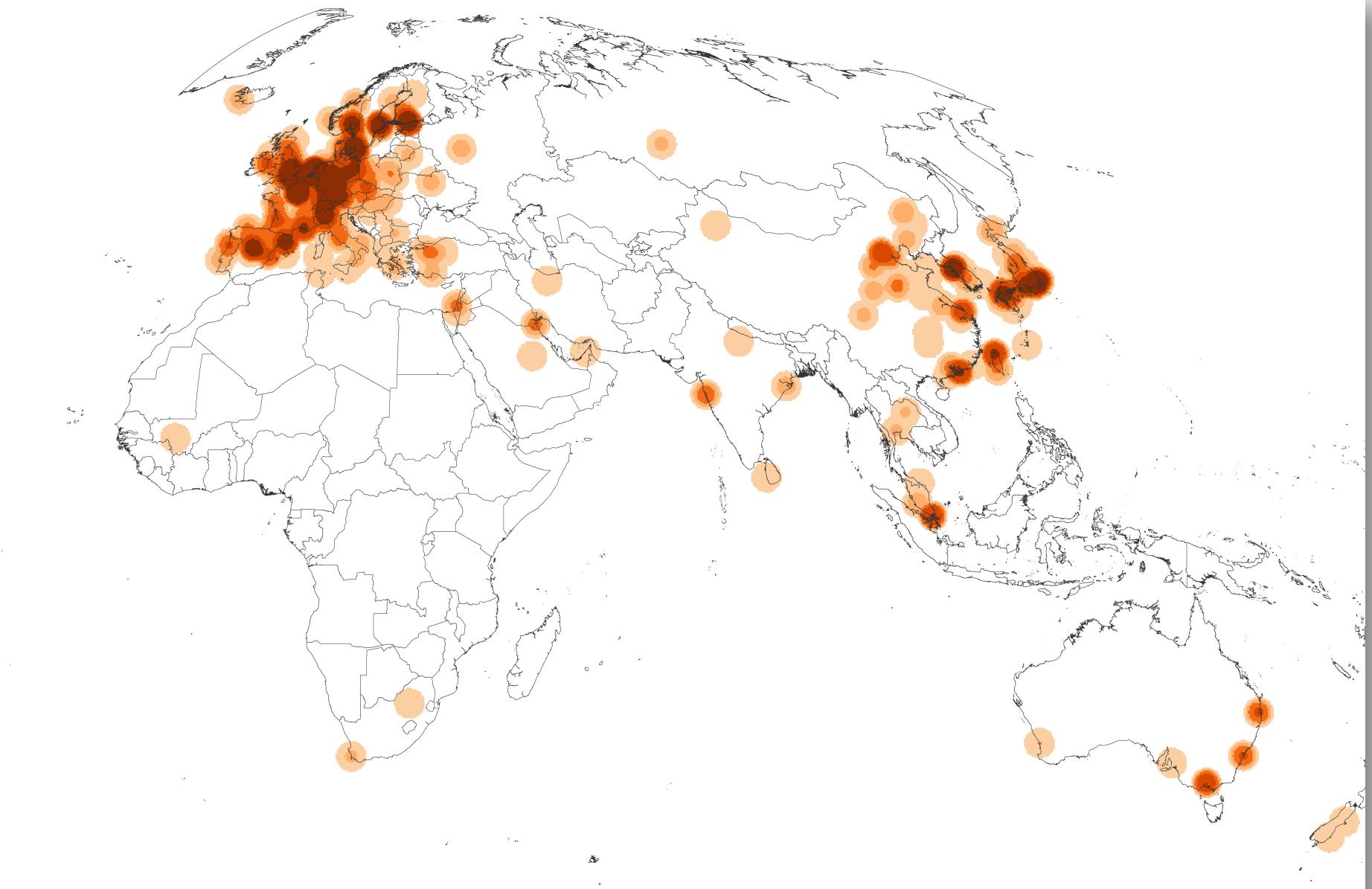
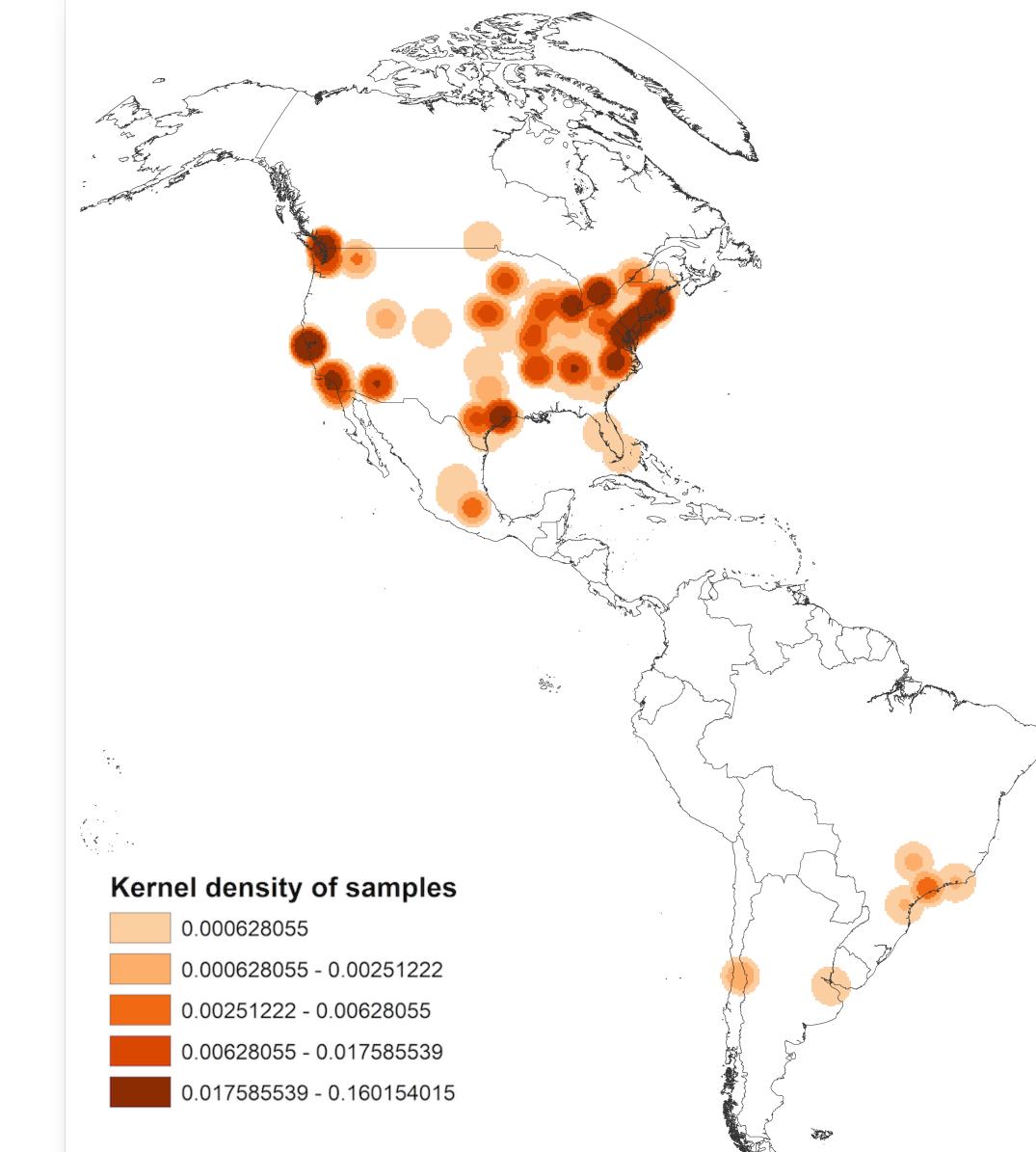
Please [contact us](#) to alert us about additional articles you are aware of. The inclusion criteria are described in the documentation [🔗](#).

Filter [i](#) City [i](#)

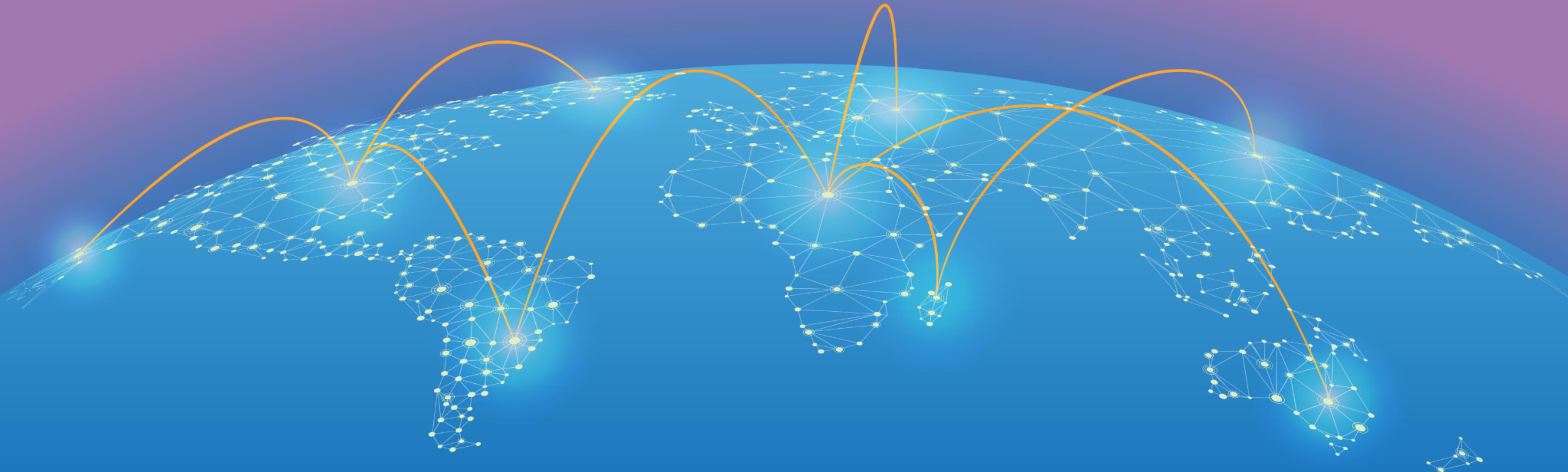
 Type to search... [▼](#)

Publications (3324)

id i ▾	Publication	cCGH	aCGH	WES	WGS	pgx
PMID:34103027	Peng G, Chai H, Ji W, Lu Y, Wu S et al. (2021) Correlating genomic copy number alterations with clinicopathologic findings in 75 cases of ... <i>BMC Med Genomics</i>	0	79	0	0	0
PMID:34059130	Tsui DWY, Cheng ML, Shady M, Yang JL et al. (2021) Tumor fraction-guided cell-free DNA profiling in metastatic solid tumor patients. ... <i>bioRxiv</i>	0	0	5	113	0

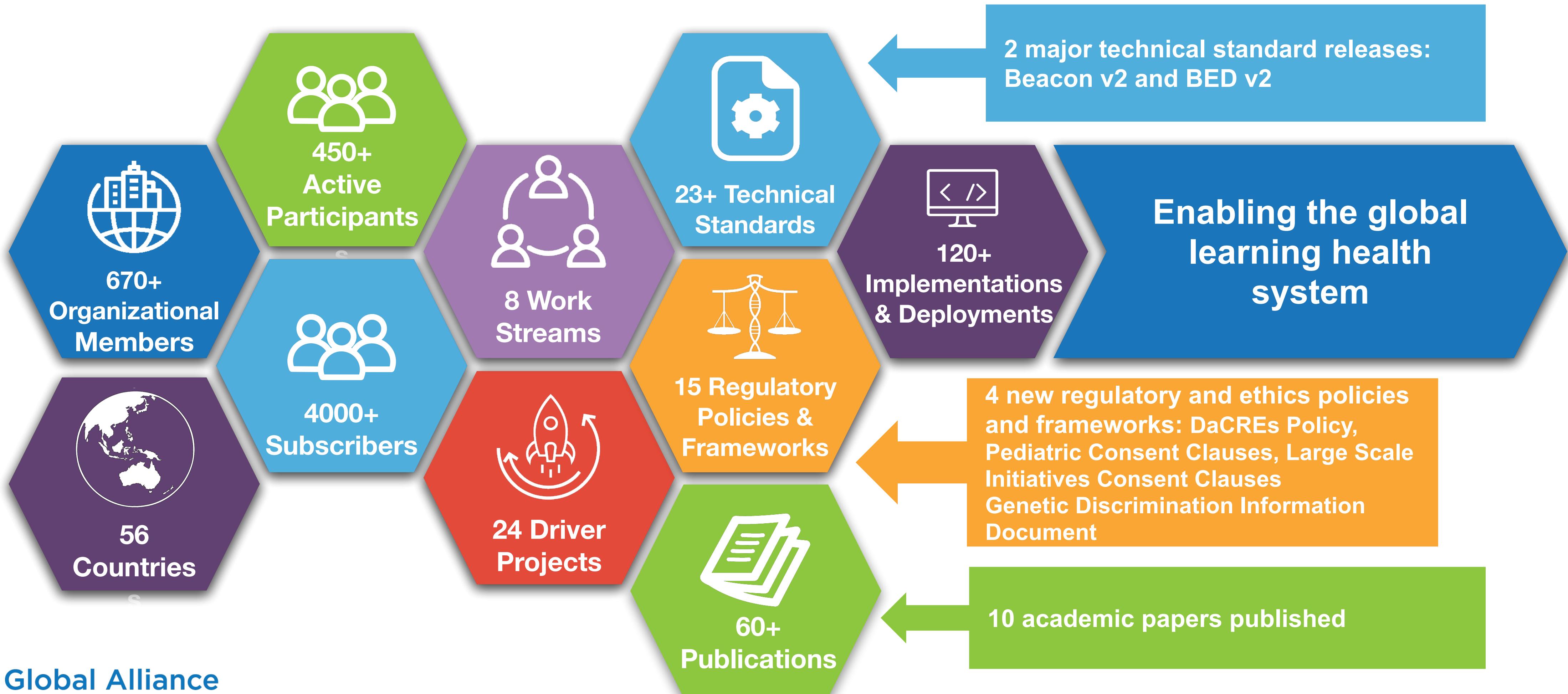


Since data is distributed globally, we need interoperable standards to answer research questions



Global Alliance for Genomics and Health (GA4GH)

Enabling responsible genomic data sharing for the benefit of human health



Global Alliance
for Genomics & Health

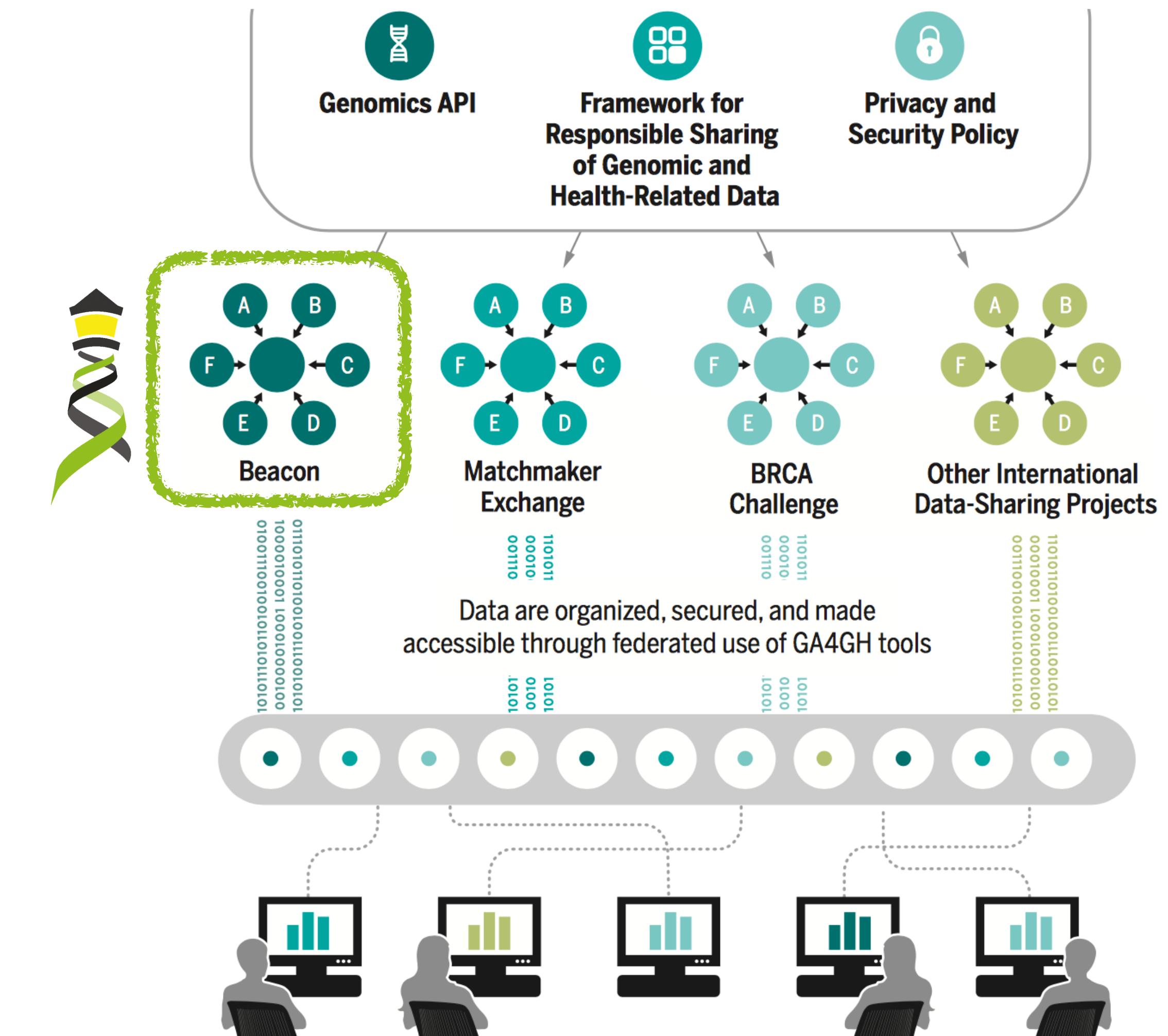


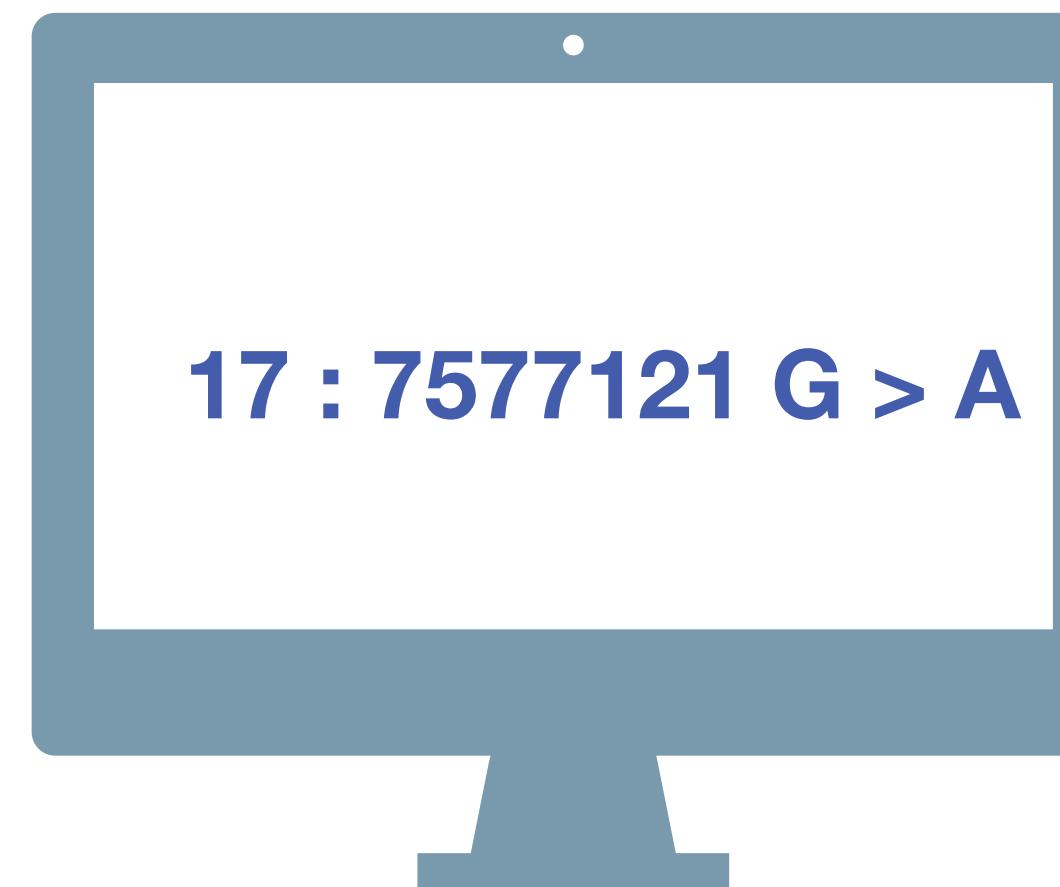
GENOMICS

A federated ecosystem for sharing genomic, clinical data

Silos of genome data collection are being transformed into seamlessly connected, independent systems

A federated data ecosystem. To share genomic data globally, this approach furthers medical research without requiring compatible data sets or compromising patient identity.





Have you seen this variant?
It came up in my patient
and we don't know if this is
a common SNP or worth
following up.

A Beacon network federates
genome variant queries
across databases that
support the **Beacon API**

Here: The variant has
been found in **few**
resources, and those
are from **disease**
specific **collections**.

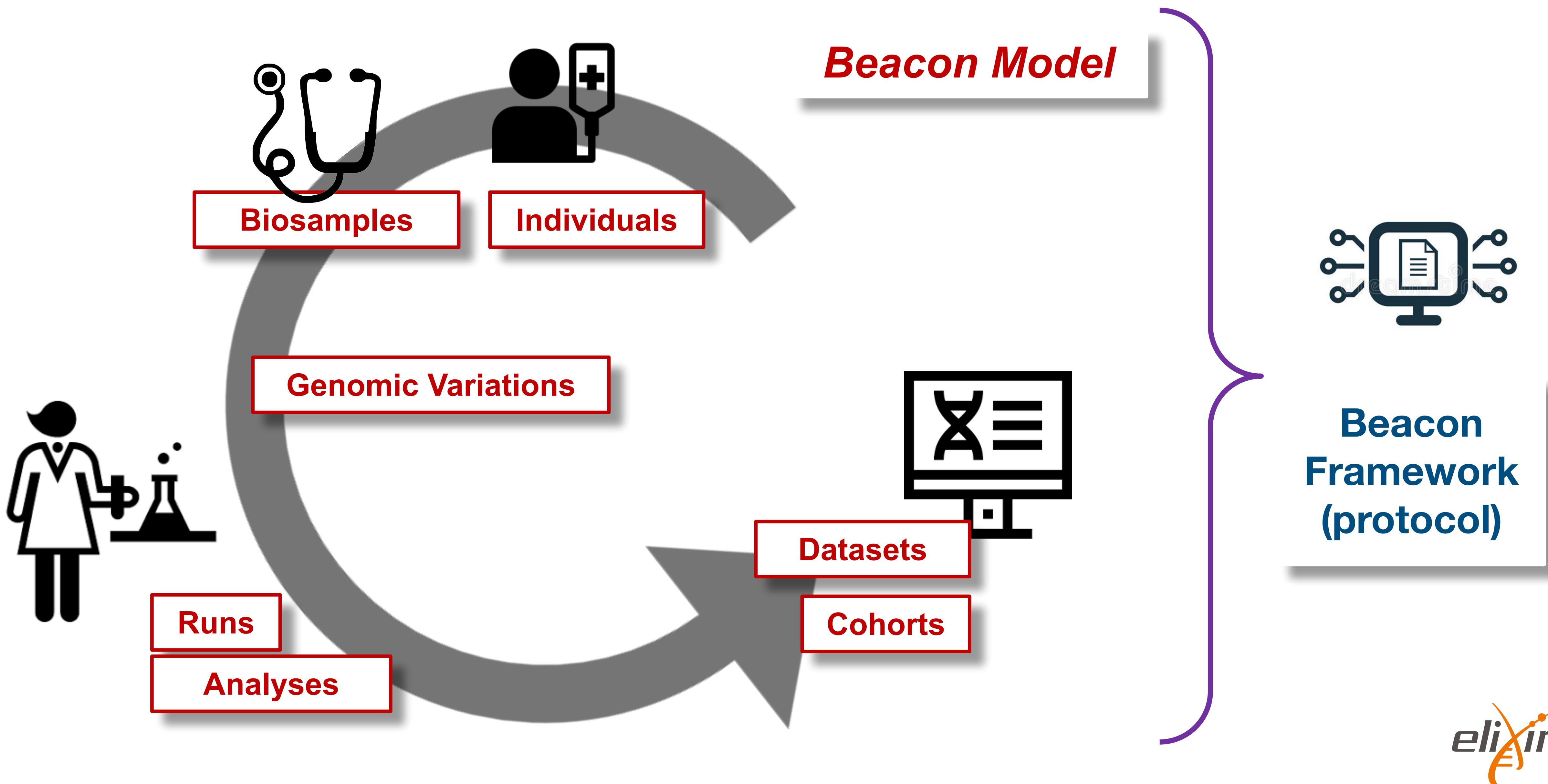


Making Beacons Biomedical - Beacon v2

- Scoping queries through "**biodata**" parameters
- Extending the queries towards **clinically ubiquitous variant formats**
 - ▶ cytogenetic annotations, named variants, variant effects
- Beacon queries as entry for **data delivery**
 - ▶ Beacon v2 permissive to respond with variety of data types
 - Phenopackets, biosample data, cohort information ...
 - ▶ handover to stream and download using htsgt, VCF, EHRs
- Interacting with **EHR standards**
 - ▶ FHIR translations for queries and handover ...
- Beacons as part of local, secure environments
- **Authentication** to enable non-aggregate, patient derived datasets
 - ▶ ELIXIR AAI with compatibility to other providers (OAuth...)

Beacon v2

docs.genomebeacons.org



Progenetix & GA4GH Beacon v2

A custom "full stack" implementation of a genomics resource
around Beacon data model & API



Onboarding

Demonstrating Compliance

- Progenetix Beacon+ has served as implementation driver since 2016
- Beacon v2 as service with protocol-driven registries for federation
- GA4GH approved Beacon v2 in April 2022



Beacon v2 GA4GH Approval Registry

Beacons:






European Genome-Phenome Archive (EGA)

GA4GH Approval Beacon Test

This [Beacon](#) is based on the GA4GH Beacon [v2.0](#)

BeaconMap	██████████
Bioinformatics analysis	██████████
Biological Sample	██████████
Cohort	██████████
Configuration	██████████
Dataset	██████████
EntryTypes	██████████
Genomic Variants	██████████
Individual	██████████
Info	██████████
Sequencing run	██████████

progenetix

Visit us
Beacon UI
Beacon API
Contact us

Theoretical Cytogenetics and Oncogenomics group at UZH and SIB

Progenetix Cancer Genomics Beacon+ provides a forward looking implementation of the Beacon v2 API, with focus on structural genome variants and metadata based on the...

BeaconMap	██████████
Bioinformatics analysis	██████████
Biological Sample	██████████
Cohort	██████████
Configuration	██████████
Dataset	██████████
EntryTypes	██████████
Genomic Variants	██████████
Individual	██████████
Info	██████████
Sequencing run	██████████

cnag

Centre Nacional Analisis Genomica (CNAG-CRG)

Beacon @ RD-Connect

This [Beacon](#) is based on the GA4GH Beacon [v2.0](#)

BeaconMap	██████████
Bioinformatics analysis	██████████
Biological Sample	██████████
Cohort	██████████
Configuration	██████████
Dataset	██████████
EntryTypes	██████████
Genomic Variants	██████████
Individual	██████████
Info	██████████
Sequencing run	██████████

University of Leicester

Cafe Variome Beacon v2

This [Beacon](#) is based on the GA4GH Beacon [v2.0](#)

BeaconMap	██████████
Bioinformatics analysis	██████████
Biological Sample	██████████
Cohort	██████████
Configuration	██████████
Dataset	██████████
EntryTypes	██████████
Genomic Variants	██████████
Individual	██████████
Info	██████████
Sequencing run	██████████

✓ Matches the Spec
 ✗ Not Match the Spec
 ⌚ Not implemented

Progenetix

Genomic resource utilizing Beacon v2 calls

- Progenetix uses Beacon v2 queries to drive its UI
- all individuals, biosamples, variants, analyses matched by a given query are stored by their object ids
- handovers for variant purposes (e.g. to retrieve all matched variants) are returned in the original response and asynchronously retrieved by the front end app

The screenshot shows the Progenetix UI with a search bar at the top. Below it, a summary box displays assembly information (GRCh38), chromosome (9), start (21500001-21975098), end (21967753-22500000), type (EFO:0030067), and filters (NCIT:C3058). A 'progenetix' logo is visible. The main area shows a histogram and a table of matched samples across various categories like UBERON codes and PGX access IDs. A yellow callout highlights a network request for biosamples: /beacon/biosamples/?requestedGranularity=record&limit=1000&skip=0&assemblyId=GRCh38&referenceName=9&variantType=EFO:0030067&start=21500000,21975098&end=21967753,22500000&filters=NCIT:C3058. A cyan callout highlights another request: /beacon/biosamples/?skip=0&limit=1000&accessid=fbffda57-0f41-4d6a-99fc-41d4cfdea9f6&requestedSchema=biosample. A pink callout highlights a request for genomic variations: /beacon/genomicVariations/?accessid=e2dadd91-9326-46de-97e4-6b88413b6bfe&requestedSchema=genomicVariant. At the bottom, download options are shown: Download Sample Data (JSON) and Download Sample Variants (JSON), both with a count of 1-660.

Assembly: GRCh38 Chro: 9 Start: 21500001-21975098 End: 21967753-22500000
Type: EFO:0030067 Filters: NCIT:C3058

progenetix

Matched Samples: 660 Retrieved Samples: 660 Variants: 279 Calls: 667

UCSC region Variants in UCSC Dataset Response (JSON)

Visualization options

Results Biosamples Biosamples Map Variants Annotated Variants

/beacon/biosamples/?requestedGranularity=record&limit=1000&skip=0&assemblyId=GRCh38&referenceName=9&variantType=EFO:0030067&start=21500000,21975098&end=21967753,22500000&filters=NCIT:C3058

Matched Subset Codes Subset Samples Matched Samples Subset Match Frequencies

Matched Subset Codes	Subset Samples	Matched Samples	Subset Match Frequencies
UBERON:0002021	14	1	0.025
pgx:icdot-C71.0	14	1	0.025
pgx:icdot-C71.0	14	1	0.025
NCIT:C3796	84	4	0.048
UBERON:0001869	1714	14	0.008
pgx:icdot-C71.0	1714	14	0.008

/beacon/genomicVariations/?accessid=e2dadd91-9326-46de-97e4-6b88413b6bfe&requestedSchema=genomicVariant

Download Sample Data (JSON)
Download Sample Variants (JSON)

Network Requests (Timeline View):

Name	Do...	T Transf...	T...	10.00s	20.00s	30.00s
biosamples	pro...	fr 5.14 KB	2...			
biosamples	lock	fr 52.60...	1...			
genomicVariations	lock	fr 25.99...	1...			
genomicVariations	lock	fr 3.98 KB	8...			
samplePlots.cgi	lock	fr 26.13 ...	2...			
collations	pro...	fr 199.4...	1...			

Beacon & CNVs

Open types w/ some definitions

- Beacon supports structural variant queries through the **variantType** parameter
- The default model **does not prescribe** which types can be used (but documents VCF derived DUP & DEL)
- CNV values are not (yet) supported but EFO offers common classes
- Progenetix supports EFO *relative CN terms* (but accepts & interpolates DUP & DEL)

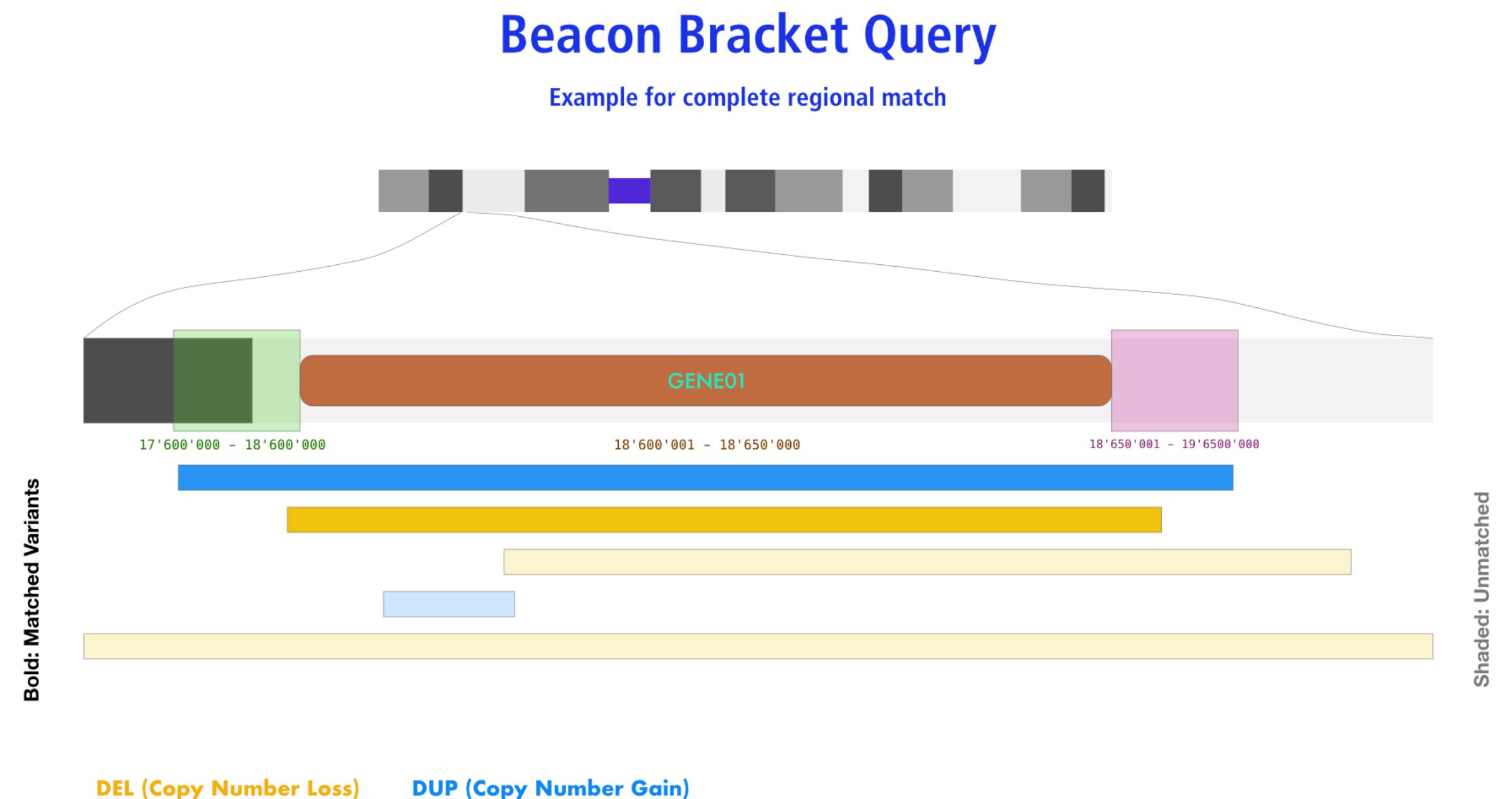
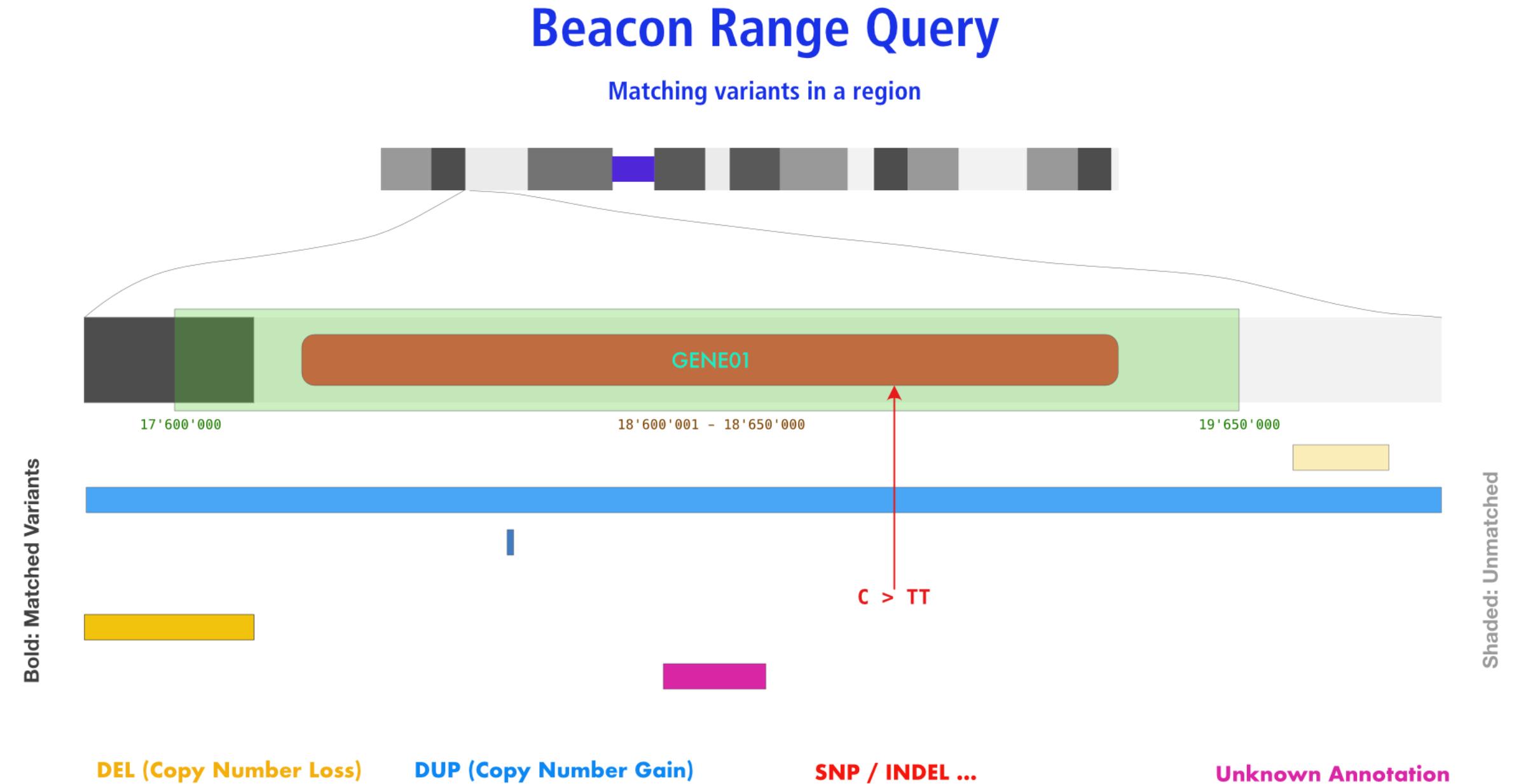
Beacon	VCF	SO	EFO	VRS	Notes
DUP	DUP ¹	SO:0001742 copy_number_gain	EFO:0030070 copy number gain	low-level gain (implicit)	a sequence alteration whereby the copy number of a given genomic region is greater than the reference sequence
DUP	DUP ¹	SO:0001742 copy_number_gain	EFO:0030071 low-level copy number gain	low-level gain	
DUP	DUP ¹	SO:0001742 copy_number_gain	EFO:0030072 high-level copy number gain	high-level gain	commonly but not consistently used for >=5 copies on a bi-allelic genome region
DUP	DUP ¹	SO:0001742 copy_number_gain	EFO:0030073 focal genome amplification	high-level gain	commonly but not consistently used for >=5 copies on a bi-allelic genome region, of limited size (operationally max. 1-5Mb)
DEL	DEL ¹	SO:0001743 copy_number_loss	EFO:0030067 copy number loss	partial loss (implicit)	a sequence alteration whereby the copy number of a given genomic region is smaller than the reference sequence
DEL	DEL ¹	SO:0001743 copy_number_loss	EFO:0030068 low-level copy number loss	partial loss	
DEL	DEL ¹	SO:0001743 copy_number_loss	EFO:0030069 complete genomic deletion	complete loss	complete genomic deletion (e.g. homozygous deletion on a bi-allelic genome region)

¹ VCFv4.4 introduces an SVCLAIM field to disambiguate between *in situ* events (such as tandem duplications; known adjacency/ break junction: SVCLAIM=J) and events where e.g. only the change in abundance / read depth (SVCLAIM=D) has been determined. Both J and D flags can be combined.

Positional Queries

Going beyond single positions...

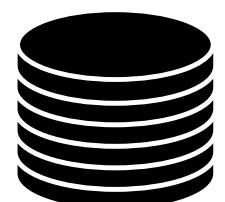
- Beacon v1 already provided support for "bracket" queries, e.g. for CNV queries - v2 improves documentation
- Use cases w/ focus on structural variants were evaluated by a Beacon "scout" team
- new "range" option
 - anything w/ overlap
 - matched variants can optionally be filtered by type, size, sequence
- query options are not hard defined but derived from parameters
 - Strong wish for defined types?



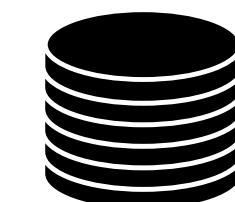
Progenetix Stack



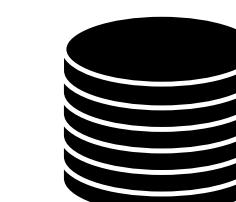
- JavaScript front-end is populated for query results using asynchronous access to multiple handover objects
 - ▶ biosamples and variants tables, CNV histogram, UCSC .bed loader, .pgxseg variant downloads...
- the complete middleware / CGI stack is provided through the *bycon* package 
 - ▶ schemas, query stack, data transformation (e.g. Phenopackets generation)...
- data collections mostly correspond to the main Beacon default model entities
 - ▶ no separate *runs* collection; integrated w/ analyses
 - ▶ *variants* are stored per observation instance



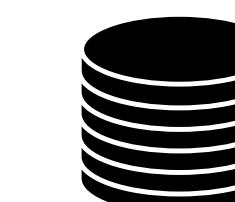
variants



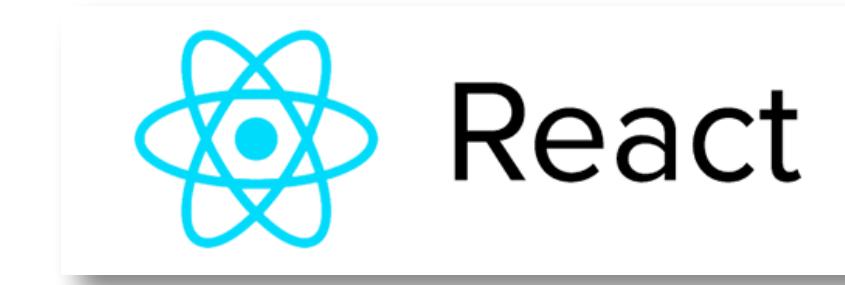
analyses



biosamples

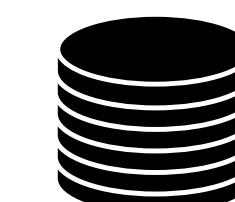


individuals

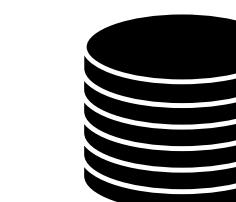


- *collations* contain pre-computed data (e.g. CNV frequencies, statistics) and information for all grouping entity instances and correspond to **filter values**
 - ▶ PMID:10027410, NCIT:C3222, pgx:cohort-TCGA, pgx:icdom-94703...
- *querybuffer* stores id values of all entities matched by a query and provides the corresponding access handle for **handover** generation

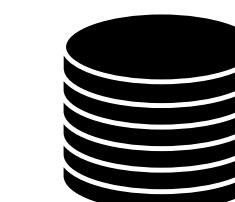
```
_id: ObjectId("6249bb654f8f8d67eb94953b"),
_id: '0765ee26-5029-4f28-b01d-9759abf5bf14',
source_collection: 'variants',
source_db: 'progenetix',
source_key: '_id',
target_collection: 'variants',
target_count: 667,
target_key: '_id',
target_values: [
  ObjectId("5bab578b727983b2e00ca99e"),
  ObjectId("5bab578d727983b2e00cb505")]
```



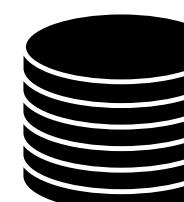
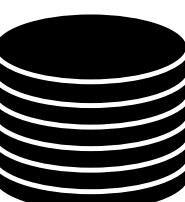
collations



geolocs



genespans publications



qBuffer

Entity collections

Utility collections

bycon

Progenetix' Beacon Stack

- Python-based software stack
- originally developed for in-house use
- public code base & increasingly sophisticated documentation

→ Happy about adoption & contributions!

progenetix / bycon Public

Code Issues Pull requests Actions Projects Wiki Security Insights Settings

main 1 branch 0 tags Go to file Add file Code About

mbaudis datatable parameter refinements 1d808c1 2 days ago 649 commits

beaconServer some refactoring 16 days ago

config datatable parameter refinements 2 days ago

lib datatable parameter refinements 2 days ago

rsrc/genomes reshuffle & variantType fix 3 months ago

schemas cytoband now in intervals 2 months ago

services datatable parameter refinements 2 days ago

.gitignore lib to package root 11 months ago

LICENSE Create LICENSE 2 years ago

README.md reshuffling and some args are back 7 months ago

__init__.py mostly handover stub for UCSC... 6 months ago

requirements.txt annotatedvariants handover 7 days ago

tests.md ... 12 days ago

README.md

License CC0 1.0

Bycon - a Python-based environment for the Beacon v2 genomics API

The `bycon` project - at least at its current stage - is a mix of *Progenetix* (i.e. GA4GH object model derived, *MongoDB* implemented) - data management, and the implementation of middleware & server for the Beacon API.

More information about the current status of the package can be found in the inline documentation which is also presented in an accessible format on the *Progenetix* website.

More Documentation

Services

The `bycon` environment - together with the *Progenetix* resource - provide a growing number of data services in (cancer) genomics and disease ontologies. `bycon`'s services are tools to enable the APIs.

Directory Structure

beaconServer

- web applications for data access
- Python modules for Beacon query and response functions in `lib`

services

Readme CC0-1.0 license 5 stars 4 watching 4 forks

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Contributors 4

mbaudis Michael Baudis

sofiapfund Sofia

qingyao

KyleGao Bo Gao

Languages

Python 99.5% Shell 0.5%

Progenetix Documentation

[Documentation Home](#)[Progenetix Source Code](#)[bycon](#)[progenetix-web](#)[PGX](#)[Additional Projects](#)[News & Changes](#)[Pages & Forms](#)[Services & API](#)[Use Case Examples](#)[Classifications, Ontologies & Standards](#)[Publication Collection](#)[Data Review](#)[Beacon+ & bycon](#)[Technical Notes](#)[Progenetix Data](#)[Baudisgroup @ UZH](#)

Rapidly evolving documentation of both the Beacon API itself and its use and technical implementation on [docs.genomebeacons.org](#) [docs.progenetix.org](#)

- for testing API responses

[/BIOSAMPLES/{ID}/G_VARIANTS](#)

- [/biosamples/pgxbs-kftva5c9/g_variants/](#)
- retrieval of all variants from a single biosample

[Base /individuals](#)[/INDIVIDUALS + QUERY](#)[• /individuals?filters=NCIT:C7541](#)Progenetix Source Code 

With exception of some utility scripts and external dependencies (e.g. [MongoDB](#)) the software (from database interaction to website) behind Progenetix and Beacon+ is implemented in Python.

[bycon](#)

- Python based service based on the [GA4GH Beacon protocol](#)
- software powering the Progenetix resource
- [Beacon+](#) implementation(s) use the same code base

[progenetix-web](#)

- website for Progenetix and its [Beacon+](#) implementations
- provides Beacon interfaces for the [bycon](#) server, as well as other Progenetix services (e.g. the [publications](#) service)
- implemented as [React / Next.js](#) project
- contains this documentation tree here as [mkdocs](#) project, with files in the [docs](#) directory

Org.progenetix

Search

beacon-v2
☆2 8

Base /biosamples

[/BIOSAMPLES + QUERY](#)

- [/biosamples?filters=cellosaurus:CVCL_0004](#)

• this example retrieves all biosamples having an annotation for the Cellosaurus CVCL_0004 identifier (K562)

[/BIOSAMPLES/{ID}](#)[/BIOSAMPLES/{ID}/G_VARIANTS](#)[/BIOSAMPLES/{ID}/TESTMODE](#)[/BIOSAMPLES?testMode=true](#)[/BIOSAMPLES?entityType=some_random_samples](#)

- for testing API responses

[/BIOSAMPLES/{ID}/G_VARIANTS](#)

- [/biosamples/pgxbs-kftva5c9/g_variants/](#)
- retrieval of all variants from a single biosample

[Base /individuals](#)[/INDIVIDUALS + QUERY](#)[• /individuals?filters=NCIT:C7541](#)

Shoutout to Laure(e)n Fromont & Manuel Rueda for being instrumental in the Beacon v2 documentation!

Beacon API

Beacon-style JSON responses

The Progenetix resource's API utilizes the [bycon](#) framework for data query and delivery and represents a custom implementation of the Beacon v2 API.

The standard format for JSON responses corresponds to a generic Beacon v2 response, with the [meta](#) and [response](#) root elements. Depending on the endpoint, the main data will be a list of objects either inside [response.results](#) or (mostly) in [response.resultSets.results](#). Additionally, most API responses (e.g. for biosamples or variants) provide access to data using [handover](#) objects.

Beacon v2 Documentation

Search

beacon-v2
☆2 8

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Progenetix & Beacon⁺

The Beacon+ implementation - developed in the Python & MongoDB based [bycon](#) project - implements an expanding set of Beacon v2 paths for the [Progenetix](#) resource [+](#).

Scoped responses from query object

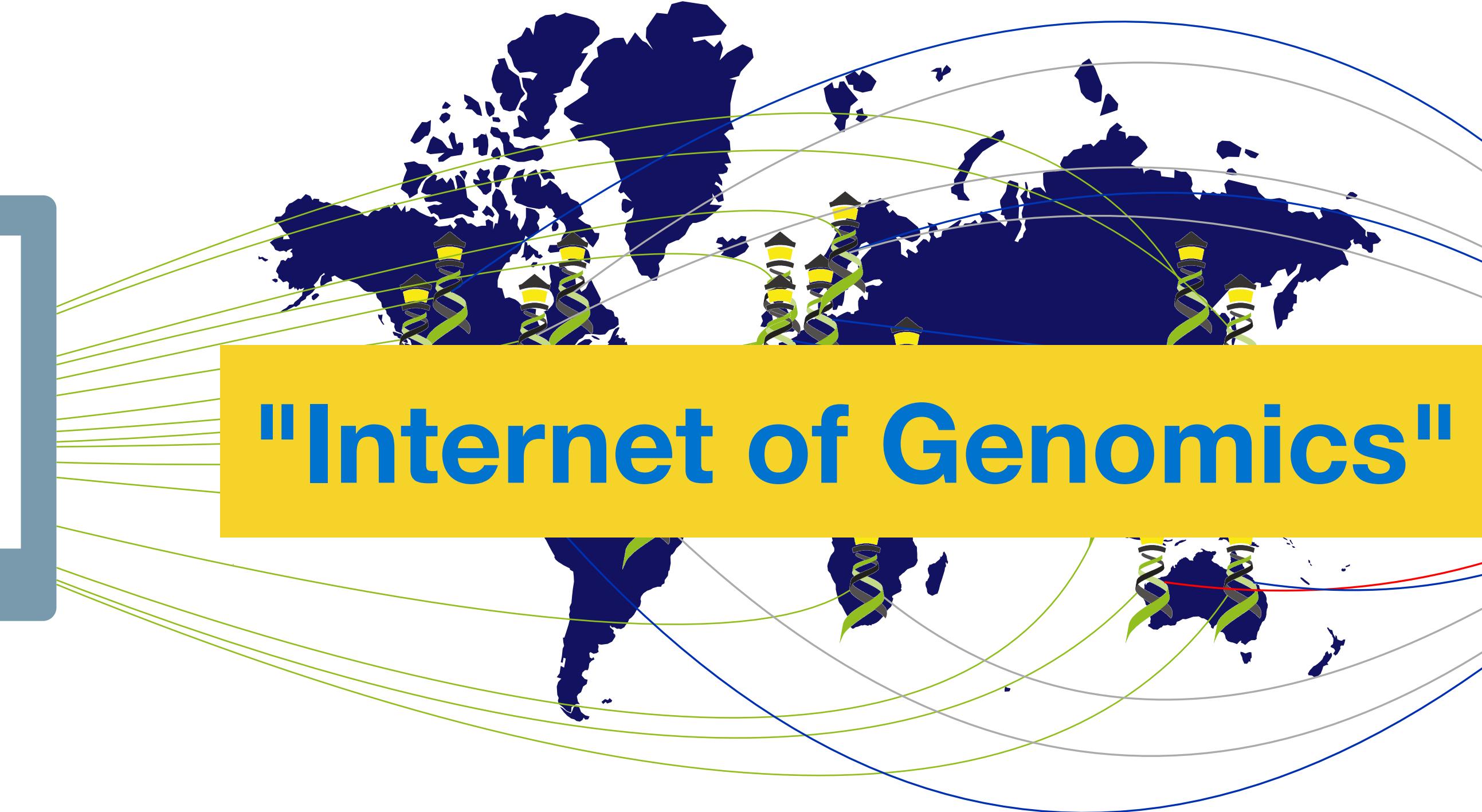
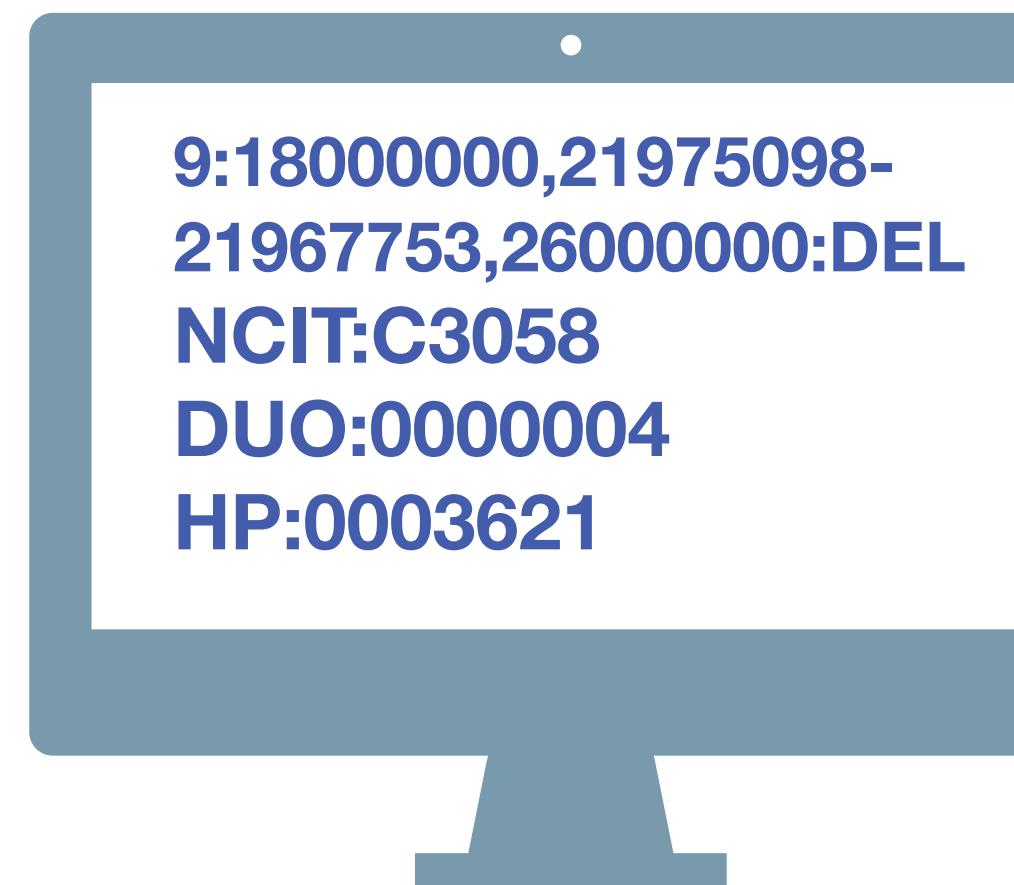
In queries with a complete [beaconRequestBody](#) the type of the delivered data is independent of the path and determined in the [requestedSchemas](#). So far, Beacon+ will compare the first of those to its supported responses and provide the results accordingly; it doesn't matter if the endpoint was [/beacon/biosamples/](#) or [/beacon/variants/](#) etc.

Below is an example for the standard test "small deletion CNVs in the CDKN2A locus, in gliomas" Progenetix test query, here responding with the matched variants. Exchanging the [entityType](#) entry to

- { "entityType": "biosample", "schema": "https://progenetix.org/services/schemas/Biosample/" }

would change this to a biosample response. The example can be tested by POSTing this as [application/json](#) to <http://progenetix.org/beacon/variants/> or <http://progenetix.org/beacon/biosamples/>.

```
{
  "$schema": "beaconRequestBody.json",
  "meta": {
    "apiVersion": "2.0",
    "requestedSchemas": [
      {
        "entityType": "genomicVariant",
        "schema": "https://progenetix.org/services/schemas/genomicVariant"
      }
    ],
    "query": {
      "requestParameters": {
        ...
      }
    }
  }
}
```



Have you seen deletions in this region on chromosome 9 in Glioblastomas from a juvenile patient, in a dataset with unrestricted access?



Beacon v2 API

The Beacon API v2 proposal opens the way for the design of a simple but powerful "genomics API".

Progenetix & Beacon v2⁺



A cancer genomics reference resource powered by GA4GH standards

Progenetix

- largest public resource for curated CNV in cancers (w/ increasing germline data)
- testbed for GA4GH standards development (e.g. **Beacon**, **Phenopackets**, **VRS**...)

Global Alliance for Genomics and Health (GA4GH)

- policies & technical standards with focus on *genomic data sharing*

Federated Data Access

- genomic complexity requires ***data access beyond individual resources***

Beacon v2

- main GA4GH **data discovery** and sharing protocol, developed with support from the European bioinformatics organization **ELIXIR**

GA4GH Genome Beacons
A Driver Project of the Global Alliance for Genomics and Health GA4GH and supported through ELIXIR

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GA4GH::SchemaBlocks
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specification teams v2 versions
website

beacon-project.io



Baudisgroup @ UZH

Ni Ai

Michael Baudis

Haoyang Cai

Paula Carrio Cordo

Bo Gao

Qingyao Huang

Saumya Gupta

Nitin Kumar

Rahel Paloots

Ziying Yang

Hangjia Zhao

Pierre-Henri Toussaint
Sofia Pfund



Beacon Protocol for Genomic Data Sharing
Beacons provide discovery services for genomic data using the Beacon API developed by the Global Alliance for Genomics and Health (GA4GH). The Beacon protocol itself is a standard for genomic data discovery. To provide a framework for publishing genomic data, the Beacon protocol defines a set of rules for publishing genomic data.

Samples
Request Allele Request Example

This example shows the query for CNV deletion variants overlapping the CDKN2A gene's coding region. The query is limited to hits that overlap with at least a single base, but limited to "focal" hits (here i.e. <= ~2Mbp in size). The query is against the Beacon API and can be modified e.g. through changing the assembly, the gene, or the size of the focal hit.

This query type is for copy number queries ("variantCNVRequest"). It uses the "start" and "end" positions to capture a set of similar variants.

Start Position: 21000001-21975098
End Position: 21967753-23000000
Classification(s): C3058: Glioblastoma (2119)

City: Select...
21000001 21975098
21967753 23000000

Query Beacon

beacon.progenetix.org/beaconPlus/

ELIXIR h-CNV
Christophe Béroux
David Salgado
many more ...

ga4gh-beacon / beacon-v2 Public

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main Go to file Add file Code

mbaudis Update ComplexValue.md ... 3 days ago 317

.github/workflows remove PDF; update variant table 3 months ago

bin Update README.md 7 days ago

docs Update ComplexValue.md 3 days ago

StringTerms description refinement 6 days ago

commonDefinitions.json 3 days ago

structuring intro pages 3 months ago

Revert "Update .gitignore" 3 days ago

repository changes moved to docs page 3 months ago

chatting 3 months ago

Initial commit 4 months ago

Update README.md 7 days ago

Creating the REST page last month

Switch to mermaid2 plugin 3 months ago

Beacon API Leads
Jordi Rambla
Anthony Brooks

Discovery WS
Michael Baudis (Beacon)
Marc Fiume (Networks)

Unified repository for Beacon v2 Code & Documentation

Description

This repository is a unified repository representing the different parts of the Beacon API:

- framework
- models
- Beacon v2 Documentation
 - authoritative source already in this repository [/docs](#)
 - rendered version through [here](#) (alternative address is [docs.genomebeacons.org](#))

github.com/ga4gh-beacon/

Get Involved! Visit GA4GH.ORG



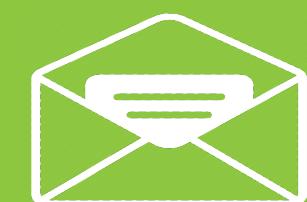
Global Alliance
for Genomics & Health

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DNA CLEANERS

AREA
RUGS
CLEANED LIKE
MAGIC

COMPUTERS
PLAID DOWN

TABLE CLOTHS
AND MORE

UPHOLSTERY
CHAIRS

744-4362

OPEN

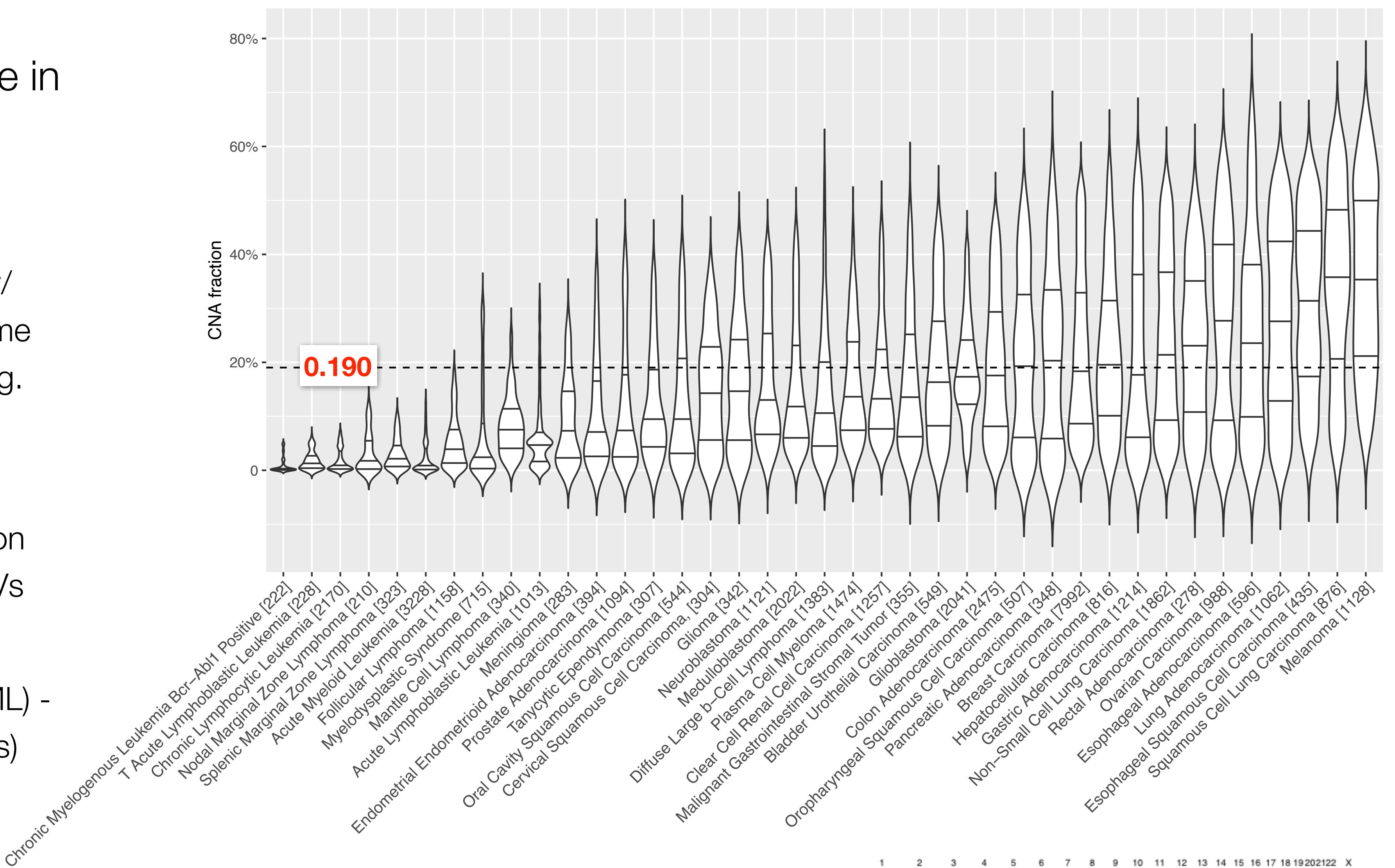
DNA CLEANERS

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Genome CNV coverage in Cancer Classes

- 43654 out of 93640 CNV profiles; filtered for entities w/ >200 samples (removed some entities w/ high CNV rate, e.g. sarcoma subtypes)
- Single-sample CNV profiles were assessed for the fraction of the genome showing CNVs (relative gains, losses)
- range of medians 0.001 (CML) - 0.358 (malignant melanomas)



Lowest / Highest CNV fractions =>

