ELIXIR ALL HANDS 2022

progenetix

Progenetix & Beacon+

An open cancer genomics resource on a stack of Beacon code...

Michael Baudis | ELIXIR All Hands | Amsterdam | 2022-06-07

elixir

Global Alliance “Beacon” - Jim Ostell, NCBI, March 7, 2014

Introduction

… I proposed a challenge application for all those wishing to seriously engage in ***international*** data sharing for human genomics. …

1. Provide a public web service
2. Which accepts a query of the form “Do you have any genomes with an “A” at position 100,735 on chromosome 3?”
3. And responds with one of “Yes” or “No” …

“Beacon” because … people have been scanning the universe of human research for ***signs of willing participants in far reaching data sharing***, but … it has remained a dark and quiet place. The hope of this challenge is to 1) ***trigger the issues*** blocking groups … in way that isn’t masked by the … complexities of the science, fully functional interfaces, and real issues of privacy, and to 2) in ***short order*** … see ***real beacons of measurable signal*** … from ***at least some sites*** … Once your “GABeacon” is shining, you can start to take the ***next steps to add functionality*** to it, and ***finding the other groups*** … following their GABeacons.

Utility

Some have argued that this simple example is not “useful” so nobody would build it. Of course it is not the first priority for this application to be scientifically useful. …intended to provide a ***low bar for the first step of real*** … ***engagement***. … there is some utility in …locating a rare allele in your data, … not zero.

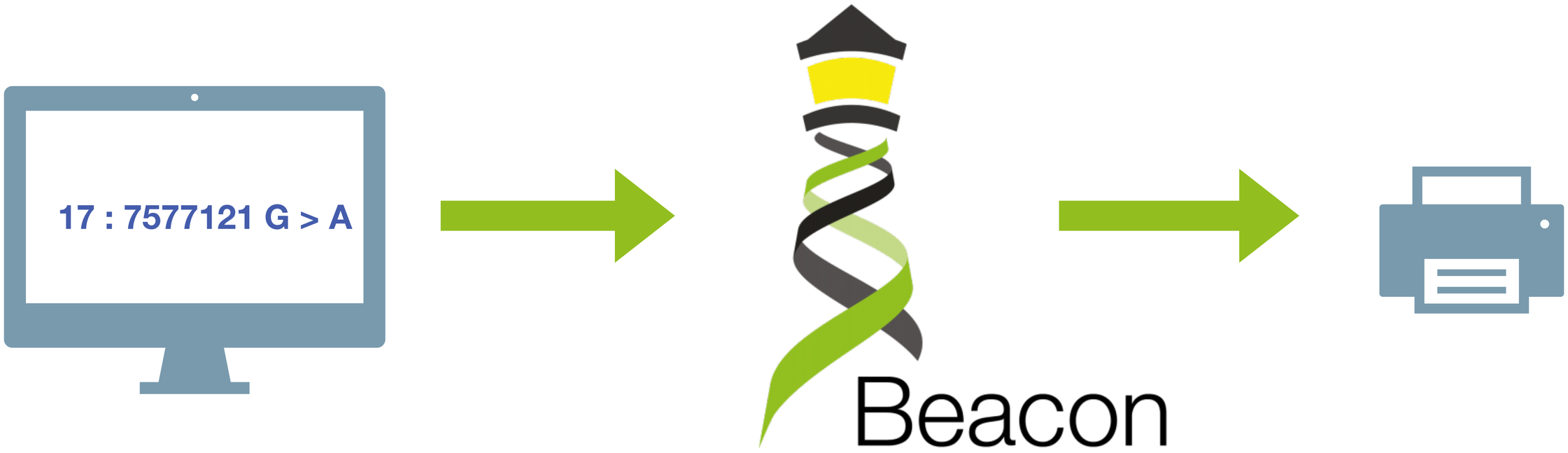
A number of more useful first versions have been suggested.

1. Provide ***frequencies of all alleles*** at that point
2. Ask for all alleles seen in a gene ***region*** (and more elaborate versions of this)
3. Other more complicated queries

"I would personally recommend all those be held for **version 2**, when the beacon becomes a service."
Jim Ostell, 2014

Implementation

1. Specifying the chromosome … The interface needs to specify the ***accession.version*** of a chromosome, or ***build number***…
2. Return values … right to ***refuse*** to answer without it being an error … DOS ***attack*** … or because …especially ***sensitive***…
3. Real time response … Some sites suggest that it would be necessary to have a ***“phone home” response*** …



A ***Beacon*** answers a query for a specific genome variant against individual or aggregate genome collections

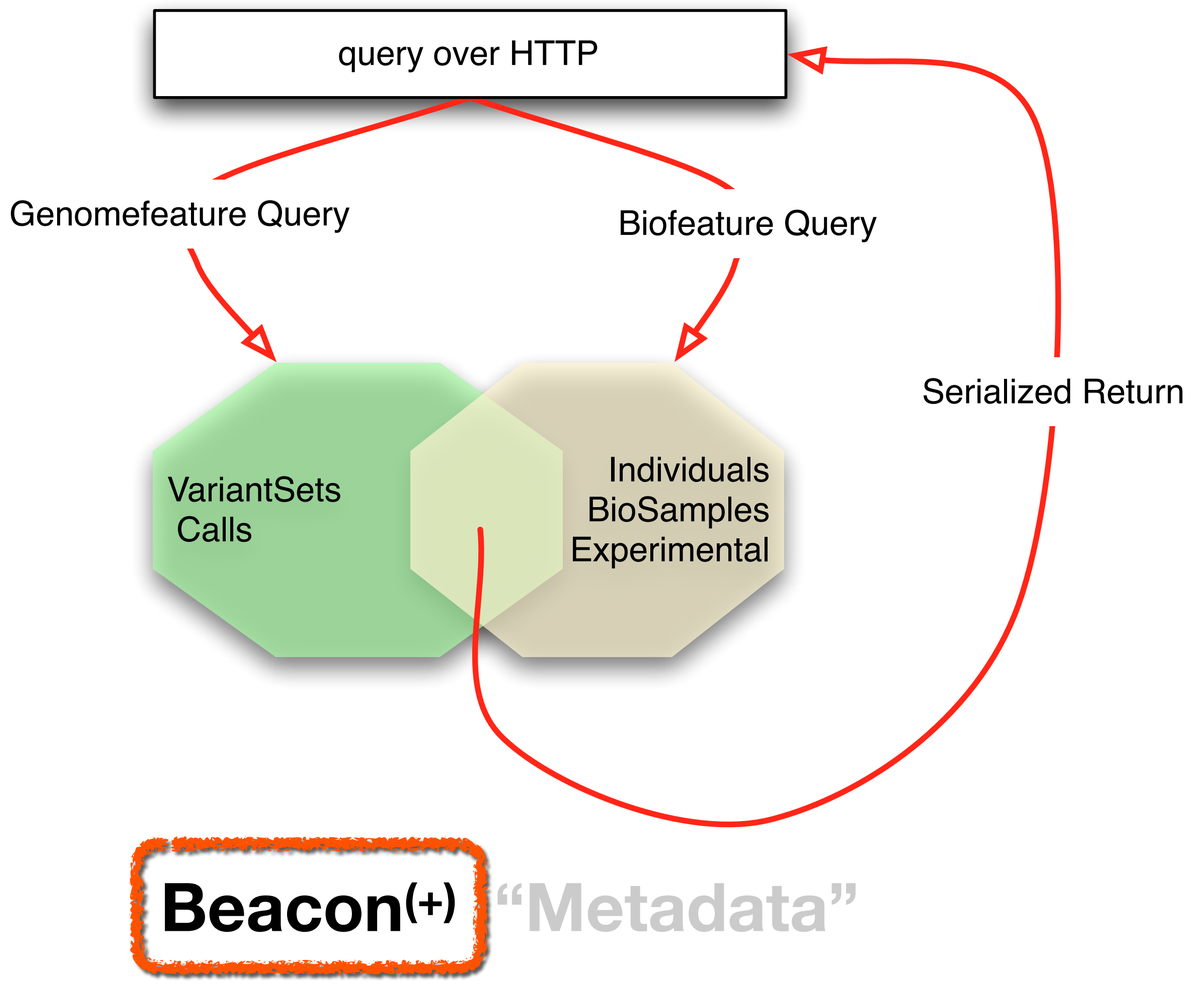
YES | **NO** | **\0**

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.

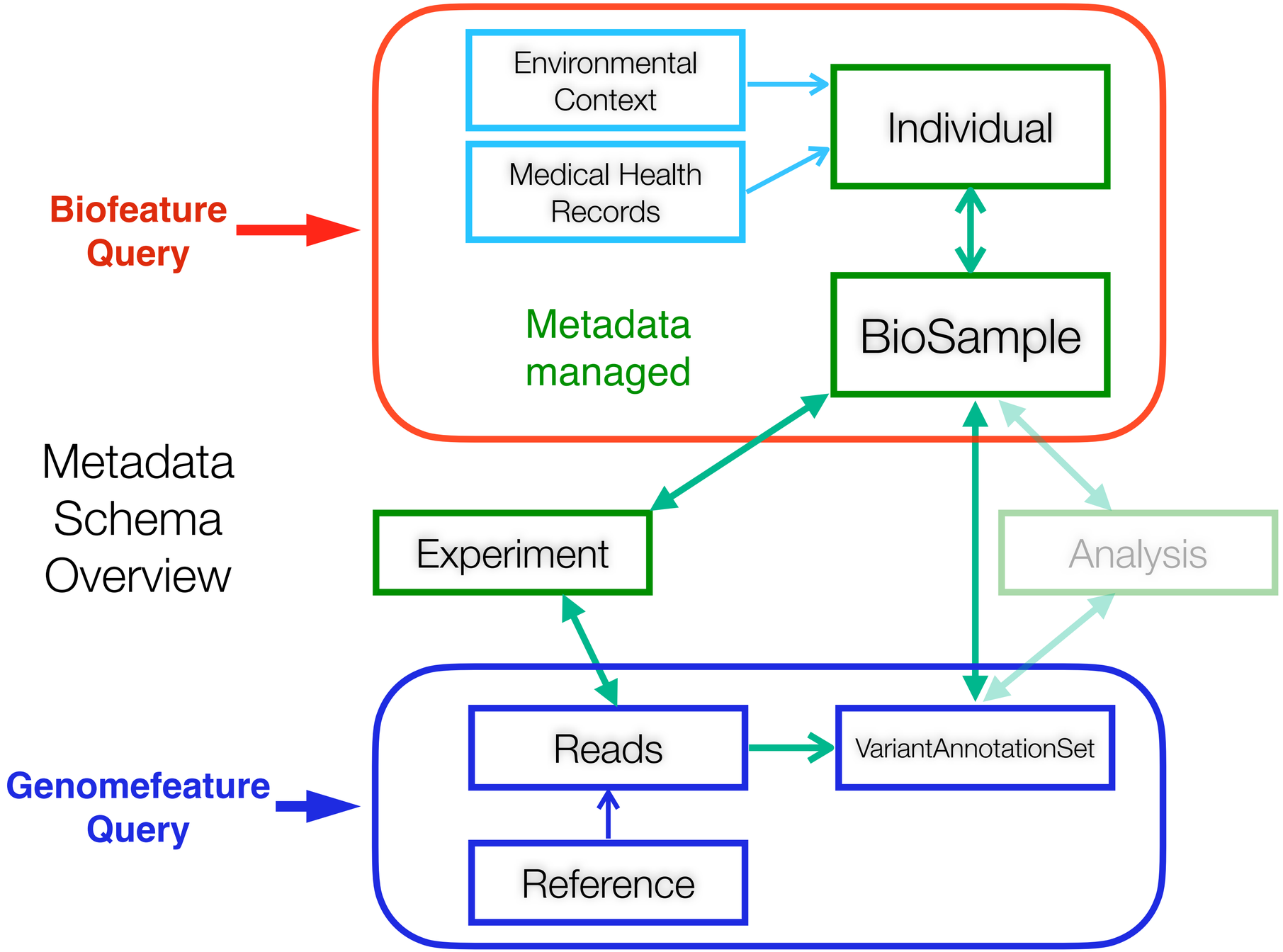
A Beacon network federates *genome variant queries* across databases that support the ***Beacon API***

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

Minimal GA4GH query API structure



Beacon+ in 2016 - Driving GA4GH implementations



beacon.progenetix.org

Beacon Implementations

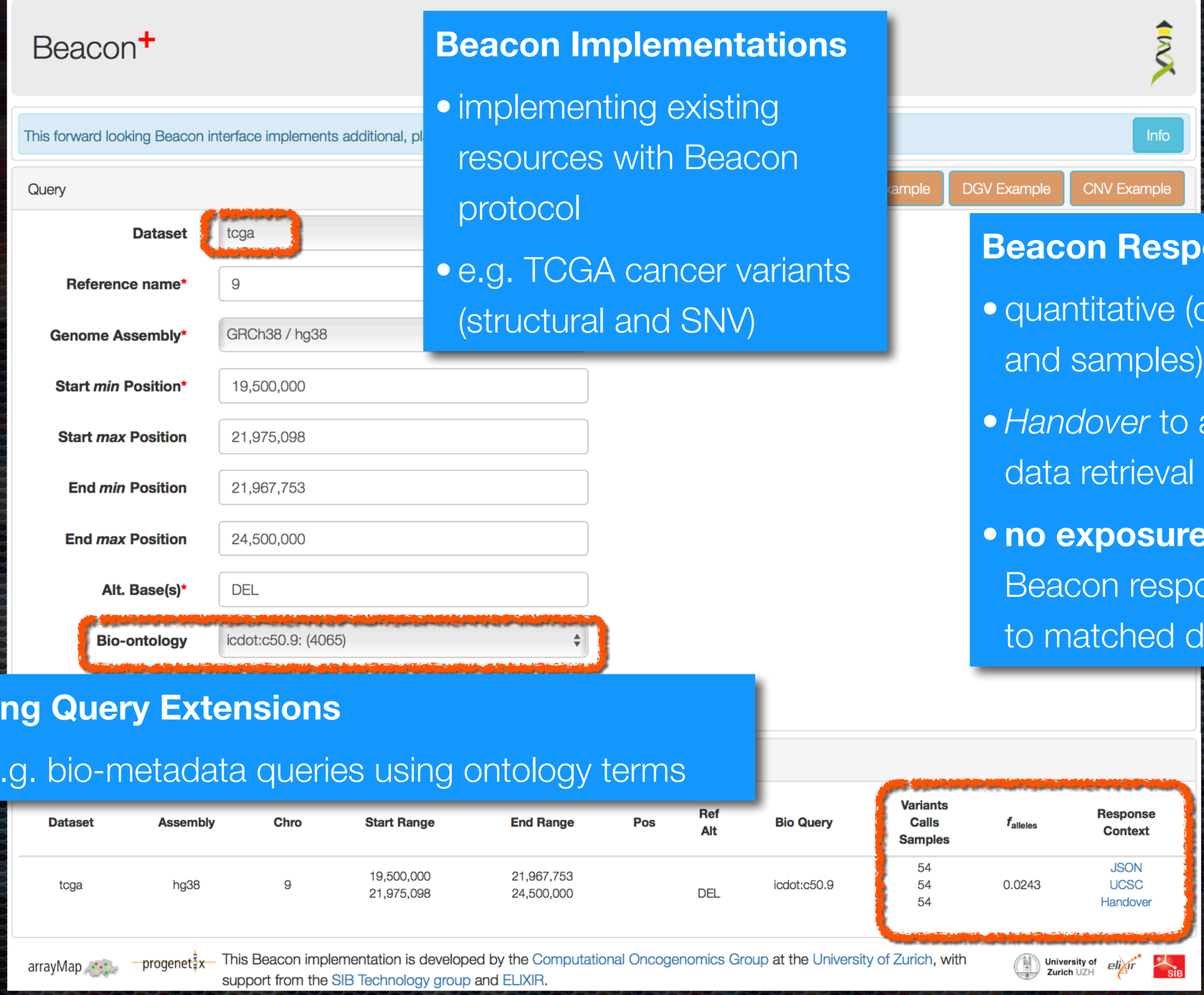
- implementing existing resources with Beacon protocol
- e.g. TCGA cancer variants (structural and SNV)

Beacon Response

- quantitative (counts for variants, callsets and samples)
- *Handover* to authentication system for data retrieval
- **no exposure** of data beyond standard Beacon response and additional pointer to matched data

Prototyping Query Extensions

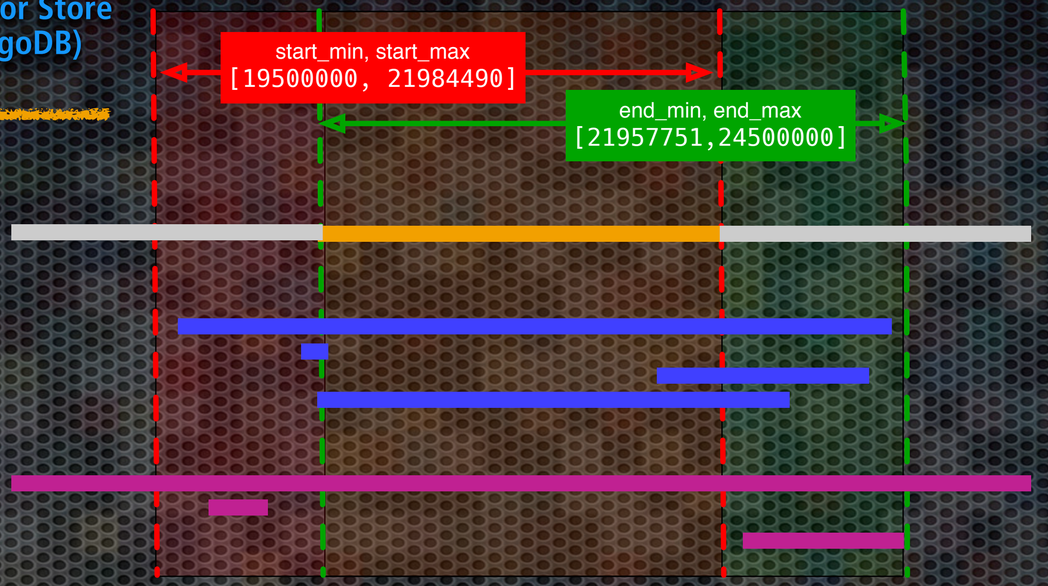
- testing e.g. bio-metadata queries using ontology terms



```
{
   "allele_request" : {
      "$and" : [
         { "reference_name" : “9" },
         { "variant_type" : “DEL" },
         { "start" : { "$gte" : 19500000 } },
         { "start" : { "$lte" : 21984490 } },
         { "end" : { "$gte" : 21957751 } },
         { "end" : { "$lte" : 24500000 } }
      ]
   },
   "api_version" : "0.4",
   "beacon_id" : "org.progenetix:progenetix-beacon",
   "exists" : true,
   "info" : {
      "query_string" :
"datasetId=arraymap&referenceName=chr9&assemblyId=GRCh38&variantType=DE
L&startMax=19000000&startMin=21984490&endMin=21900000&endMax=25000000&b
iosamples.bio_characteristics.ontology_terms.term_id=icdom:9440_3",
      "version" : "Beacon+ implementation based on a development branch
of the beacon-team project: https://github.com/ga4gh/beacon-team/pull/
94"
   },
   "url" : “http://progenetix.org/beacon/info/“,
   "dataset_allele_responses" : [
      {
         “datasetId" : "arraymap",
         "error" : null,
         "exists" : true,
         "external_url" : “http://arraymap.org",
         "sample_count" : 584,
         "call_count" : 3781,
         "variant_count" : 3244,
         "frequency" : 0.0094,
         "info" : {
           "description" : "The query was against database
\"arraymap_ga4gh\", variant collection \"variants_cnv_grch36\". 3781 /
59428 matched callsets for 3602919 variants. Out of 62105 biosamples in
the database, 2047 matched the biosample query; of those, 584 had the
variant.",
            "ontology_ids" : [
              "ncit:C3058",
              "pgx:icdom:9440_3",
              "pgx:icdot:C71.9",
              “pgx:icdot:C71.0"
            ]
         },
      }
   ],
```


start_min
start_max
end_min
end_max

Translation for Store (here MongoDB)



Match using query ranges “at least one base in interval affected”

Region of Interest, e.g. CDR of Gene (here: CDKN2A)

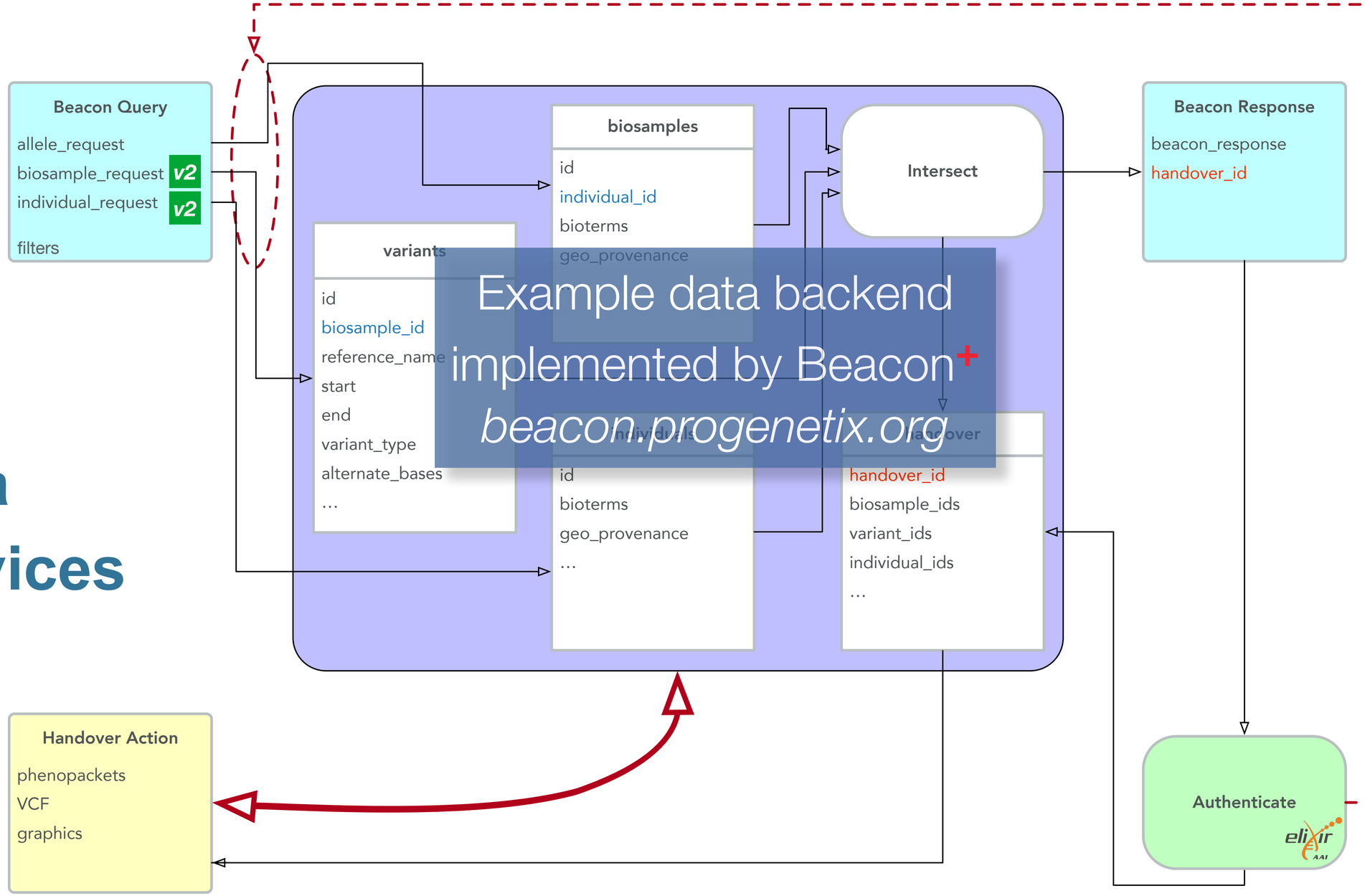
Example “focal” matches (overlap w/ size limit)

Mismatches
- too large
- end outside
- start outside

- Beacon+ **range queries** allow the definition of a genome region of interest, containing a specified variant (or other mappable feature)
- “fuzzy” matching of region ends is essential for features without base specific positions
- current Beacon implementation addresses CNV (DUP, DEL), as are specified in VCF && GA4GH variant schema

Beacon & Handover

Beacons v1.1 supports **data delivery services**



Beacon I/O

Handover

Authentication

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SIB

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elixir

Beacon Handover

- only exposure of access handle to data stored in secure system
- one-step authentication and selection of *handover* action; other scenarios possible / likely
- *handover* response **outside of Beacon protocol / system**


```
{
"alleleRequest": {
"endMax": "26000000",
"referenceName": "9",
"startMax": "21975098",
"endMin": "21967753",
"startMin": "18000000",
"alternateBases": "N",
"variantType": "DEL",
"referenceBases": "*"
},
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"beaconId": "progenetix-beacon",
"datasetAlleleResponses": [
{
"externalUrl": "https://beacon.progenetix.org/beacon/info/",
"datasetId": "arraymap",
"variantCount": 588,
"info": {
"distinctVarCount": 551,
"description": "The query was against database \"arraymap\", variant collection \"variants\". 588 matched callsets for 588 distinct variants."},
"error": null,
"exists": true,
"datasetHandover": [
  {
    "url": "https://beacon.progenetix.test/beaconplus-server/beacondeliver.cgi?do=biosamplesdata&accessid=5d76f88d-4012-11e9-a0b4-d9893b611ec4",
    "handoverType": { "label": "Biosamples", "id": "pgx:handover:biosamplesdata" },
    "description": "retrieve data of the biosamples matched by the query"
  },
  {
    "url": "https://beacon.progenetix.test/beaconplus-server/beacondeliver.cgi?do=callsetsvariants&accessid=5d77fb88-4012-11e9-a0b4-bb5a9c8cf98a",
    "description": "export all variants of matched callsets - potentially huge dataset...",
    "handoverType": { "label": "Callsets Variants", "id": "pgx:handover:callsetsvariants" }
  },
  {
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    "description": "create a CNV histogram from matched callsets",
    "url": "https://beacon.progenetix.test/beaconplus-server/beacondeliver.cgi?do=cnvhistogram&accessid=5d77fb88-4012-11e9-a0b4-bb5a9c8cf98a"
  },
  {
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    "url": "https://beacon.progenetix.test/beaconplus-server/beacondeliver.cgi?do=variantsdata&accessid=5d6e982b-4012-11e9-a0b4-c5ce5cc21906"
  }
],
"callCount": 588,
"varResponses": [
"9:21773941-21968713:DEL",
"9:21732467-23813102:DEL",
"9:21785019-21968713:DEL",
"9:21968713-22031006:DEL",
```

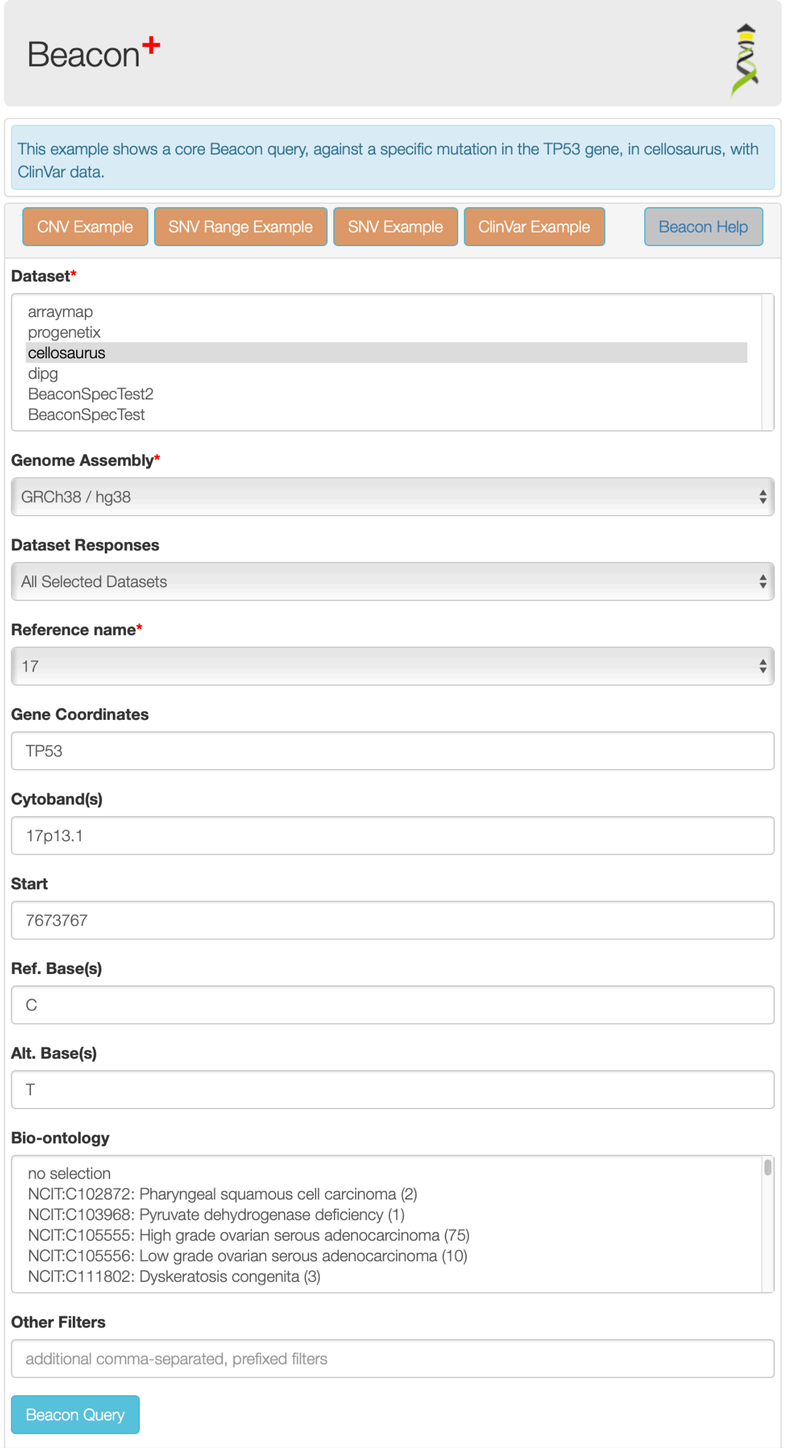

Beacon+
Flexible Modeling of New Features

Our Beacon platform is being used for the rapid testing of queries and responses - both v1.n and v2.0.a - against a number of partially large-scale genome datasets.

- Progenetix (>100000 cancer CNV profiles)
- DIPG (childhood brain tumor study)
- NEW: Cellosaurus ClinVar annotations for evidence representation
- Brewing: COVID-19

Currently running on a ~~Perl~~+MongoDB stack, a Python-based OS solution is in early development.

progenetix SIB SPHN


```
[
  {
    "callset_id": "cs-cellosaurus:CVCL_EI02",
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        "origin": "germline;somatic",
        "phenotype": "Hereditary cancer-predisposing syndrome;Li-Fraumeni
syndrome;PARP Inhibitor response;not provided",
        "clinical_significance": "Pathogenic/Likely pathogenic",
        "clinvar_full_name": "NM_001126112.2(TP53):c.853G&gt;A (p.Glu285Lys)"
      }
    },
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    ],
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    "variantset_id": "cellosaurus_clinvar_GRCH38",
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    "start_max": 7673766
  },
  {
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      "T"
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        "cell_line": "BT-474 Clone 5",
        "id": "CVCL_AQ07"
      },
      "clinvar": {
        "assembly": "GRCh38",
        "allele_id": "410258",
        "gene_id": "7157",
        "cytoband": "17p13.1",
        "variant_type": "single nucleotide variant",
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syndrome;PARP Inhibitor response;not provided",
        "origin": "germline;somatic",
        "clinvar_full_name": "NM_001126112.2(TP53):c.853G&gt;A (p.Glu285Lys)",
        "clinical_significance": "Pathogenic/Likely pathogenic"
      }
    },
    "end_min": 7673767,
    "biosample_id": "bios-cellosaurus:CVCL_AQ07",
    "reference_name": "17"
  },
  {
    "alternate_bases": [
      "T"
    ],
    "reference_bases": "C",
    "digest": "17_7673767_C_T",
    "end_max": 7673767,
    "variantset_id": "cellosaurus_clinvar_GRCH38",
    "start_max": 7673766,
    "callset_id": "cs-cellosa
```

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	Beacon v1 Development	Beacon v2 Development	Related ...
2014	**GA4GH founding event; Jim Ostell proposes Beacon concept including "more features ... version 2"**		
2015	• beacon-network.org aggregator created by DNAstack		• ELIXIR starts Beacon project support
2016	• Beacon v0.3 release • work on queries for structural variants (brackets for fuzzy start and end parameters...)	• Beacon+ concept implemented on progenetix.org • concepts from GA4GH Metadata (ontologies…) • entity-scoped query parameters ("individual.age")	
2017	• OpenAPI implementation • integrating CNV parameters (e.g. "startMin, statMax")	• Beacon+ demos "handover" concept	• GA4GH re-structuring (workstreams...) • Beacon part of Discovery WS
2018	• Beacon v0.4 release in January; feature release for GA4GH approval process • GA4GH Beacon v1 approved at Oct plenary		• new Beacon website (March)
2019	• ELIXIR Beacon Network	• Beacon hackathon Stockholm; settling on "filters" • Barcelona goes Zurich developers meeting • Beacon API v2 Kick off • adopting "handover" concept	• Beacon publication at Nature Biotechnology
2020		• "Scouts" teams working on different aspects - filters, genomic variants, compliance ... • discussions w/ clinical stakeholders	
2021		• framework + models concept implemented • range and bracket queries, variant length parameters • starting of GA4GH review process	
2022		• further changes esp. in default model, aligning with Phenopackets and VRS • unified beacon-v2 code & docs repository • Beacon v2 approved at Apr GA4GH Connect	• *docs.genomebeacons.org*

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Beacon v1 Development

Beacon v2 Development

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- *docs.genomebeacons.org*

Thank You!

... and many more!

Global Alliance for Genomics & Health

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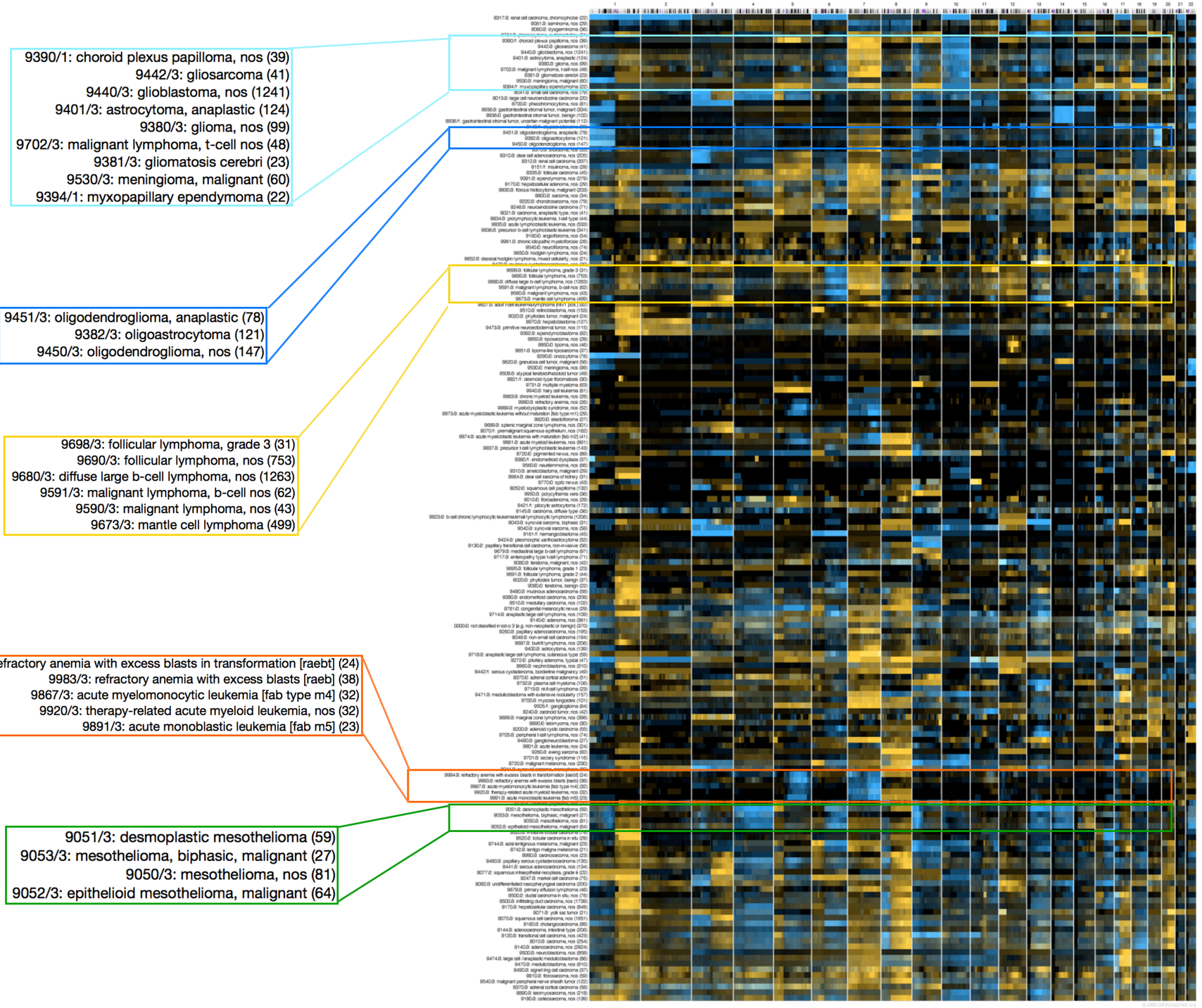
Progenetix Genomics Resource

From Genomic Experiments to Experimenting with the Beacon API

progenetix

Somatic Mutations In Cancer: Patterns
Making the case for genomic classifications
Some related cancer entities show similar copy number profiles



arrayMap

Progenetix in 2022

Cancer Genomics Reference Resource

- largest open resource for curated cancer genome profiles
- focus on copy number variations (CNV)
- >116'000 cancer CNV profiles, from >800 NCIt codes
- majority of data from genomic arrays with ~50% overall from SNP platforms with original data re-processing
- structured diagnostic encodings for NCIt, ICD-O 3, UBERON
- identifier mapping for PMID, GEO, Cellosaurus, TCGA, cBioPortal where appropriate
- core biosample and technical metadata annotations where accessible (TNM, genotypic sex, survival ...)
- publication database and code mapping services

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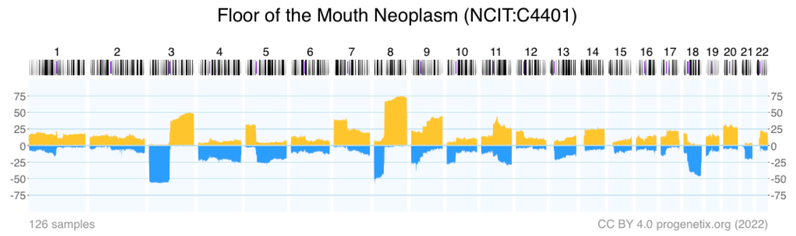
Cancer genome data @ progenetix.org

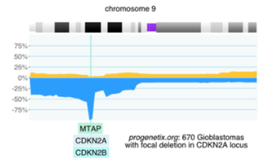
The Progenetix database provides an overview of mutation data in cancer, with a focus on copy number abnormalities (CNV / CNA), for all types of human malignancies. The data is based on *individual sample data* from currently **142063** samples.



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.

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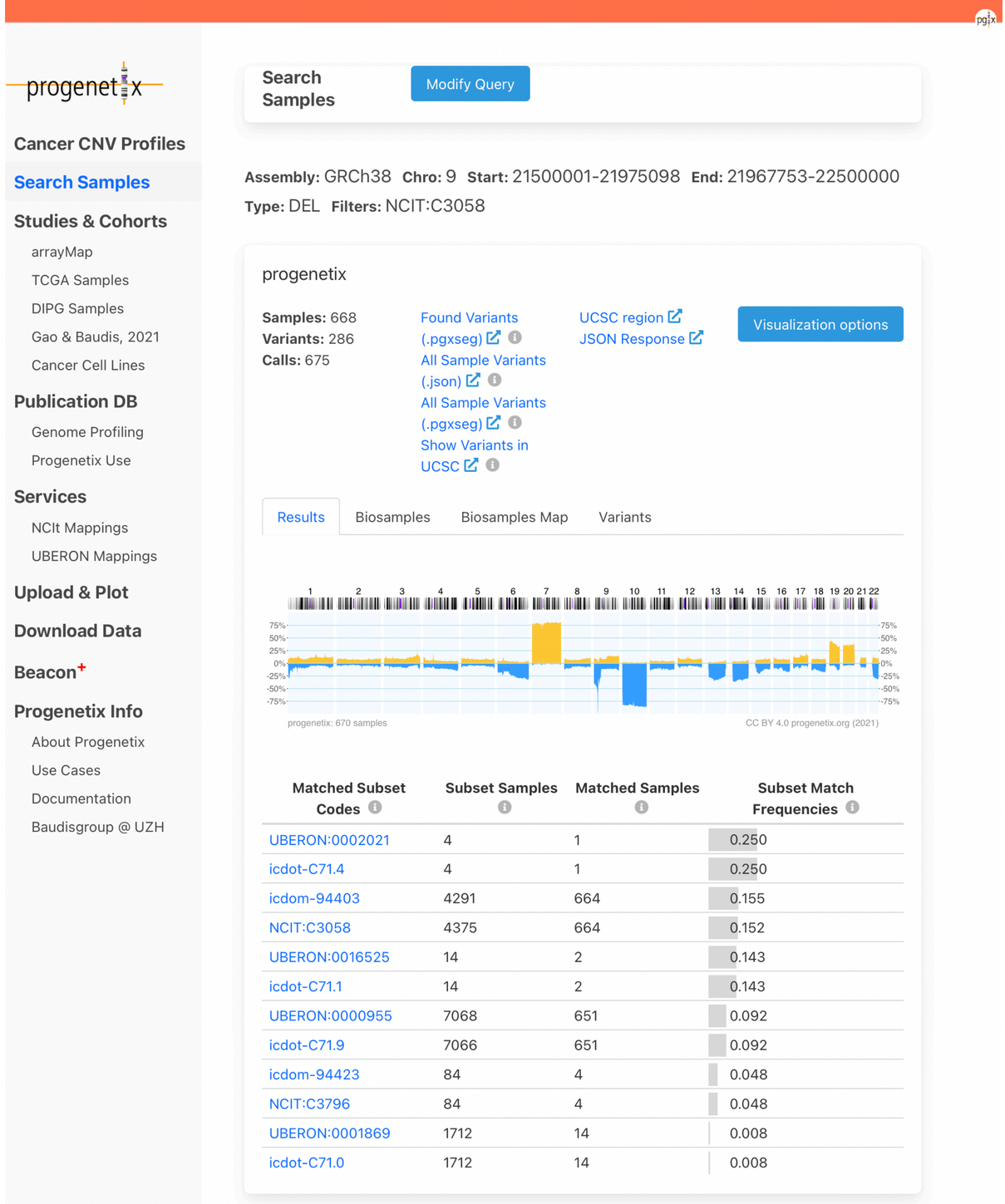

Progenetix in 2022

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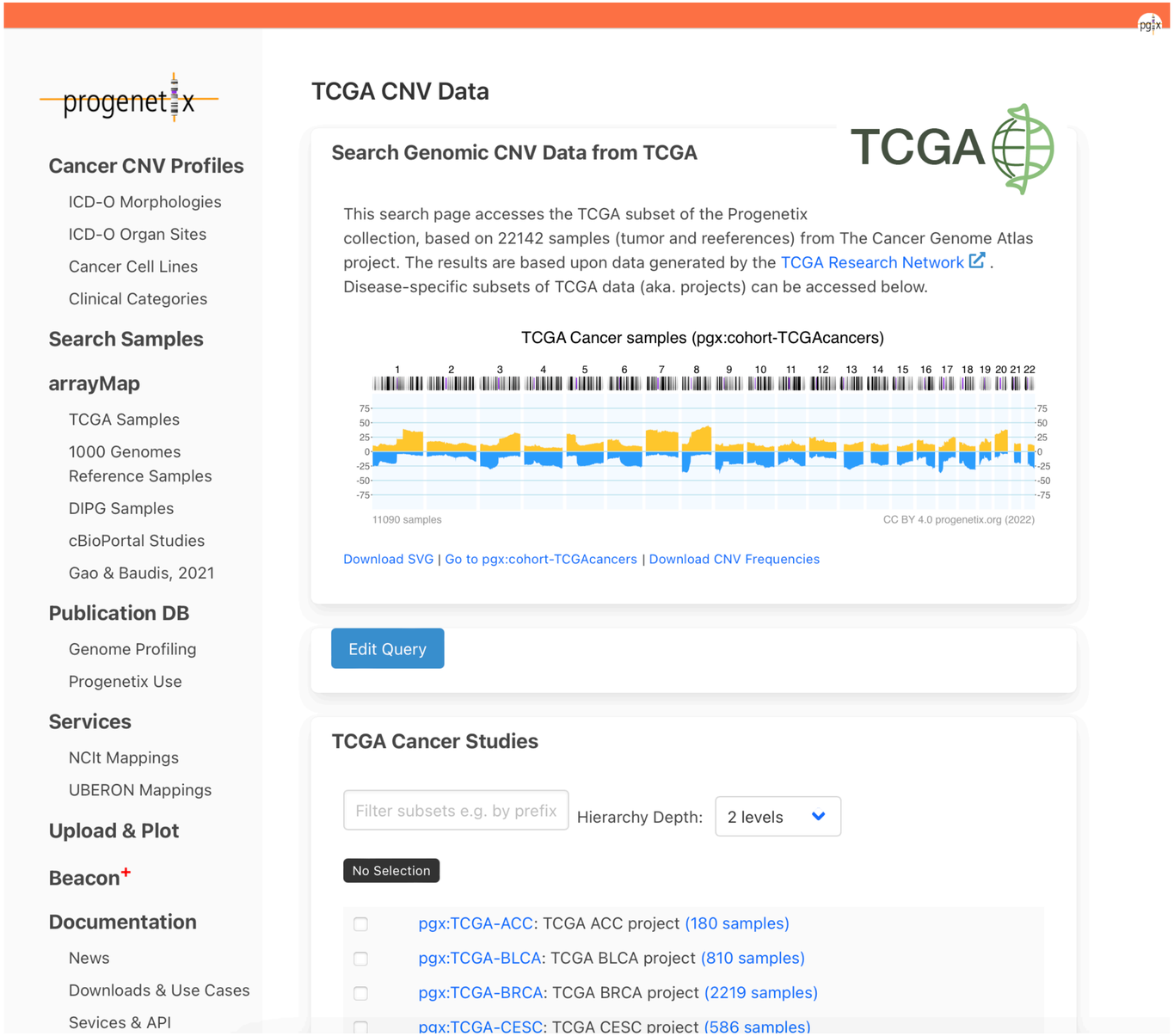
- contains special data subsets, identified using the "cohorts" concept
  - TCGA CNV data
  - 1000Genomes germline CNVs (WGS)
  - Cancer cell line CNVs with upcoming addition of annotated SNV ... data
  - cBioPortal studies
  - ...



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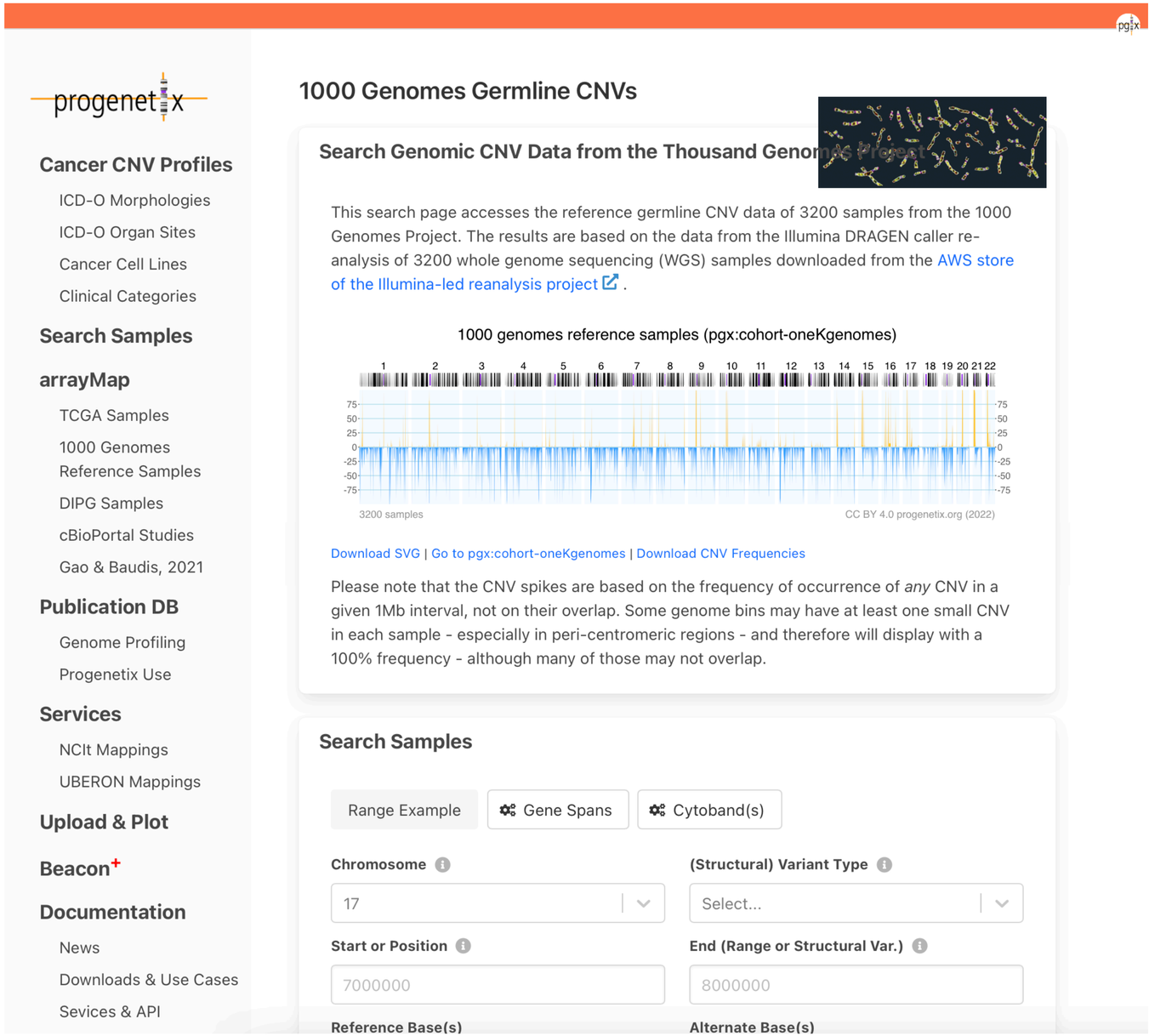

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Database, 2021, **2021(0)**, 1–9
DOI: https://doi.org/10.1093/database/baab043
Database update

The Progenetix oncogenomic resource in 2021

Qingyao Huang[1,2], Paula Carrio-Cordo[1,2], Bo Gao[1,2], Rahel Paloots[1,2] and Michael Baudis[1,2,*]

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[2]Swiss Institute of Bioinformatics, Winterthurerstrasse 190, Zurich 8057, Switzerland

*Corresponding author: Tel: +41 44 635 34 86; Email: michael.baudis@mls.uzh.ch

Citation details: Huang, Q., Carrio-Cordo, P., Gao, B. *et al.* The Progenetix oncogenomic resource in 2021. *Database* (2021) Vol. 2021: article ID baab043; DOI: https://doi.org/10.1093/database/baab043

Abstract

In cancer, copy number aberrations (CNAs) represent a type of nearly ubiquitous and frequently extensive structural genome variations. To disentangle the molecular mechanisms underlying tumorigenesis as well as identify and characterize molecular subtypes, the comparative and meta-analysis of large genomic variant collections can be of immense importance. Over the last decades, cancer genomic profiling projects have resulted in a large amount of somatic genome variation profiles, however segregated in a multitude of individual studies and datasets. The Progenetix project, initiated in 2001, curates individual cancer CNA profiles and associated metadata from published oncogenomic studies and data repositories with the aim to empower integrative analyses spanning all different cancer biologies. During the last few years, the fields of genomics and cancer research have seen significant advancement in terms of molecular genetics technology, disease concepts, data standard harmonization as well as data availability, in an increasingly structured and systematic manner. For the Progenetix resource, continuous data integration, curation and maintenance have resulted in the most comprehensive representation of cancer genome CNA profiling data with 138 663 (including 115 357 tumor) copy number variation (CNV) profiles. In this article, we report a 4.5-fold increase in sample number since 2013, improvements in data quality, ontology representation with a CNV landscape summary over 51 distinctive National Cancer Institute Thesaurus cancer terms as well as updates in database schemas, and data access including new web front-end and programmatic data access.

Database URL: progenetix.org

Table 1. Statistics of samples from various data resources

Data source	GEO	ArrayExpress	cBioPortal	TCGA	Total
No. of studies	898	51	38	33	1939
No. of samples	63 568	4351	19 712	22 142	138 663
Tumor	52 090	3887	19 712	11 090	115 357
Normal	11 478	464	0	11 052	23 306
Classifications					
ICD-O (Topography)	100	54	88	157	209
ICD-O (Morphology)	246	908	265	140	491
NCIt	346	148	422	182	788
Collections					
Individuals	63 568	4351	19 712	10 995	127 549
Biosamples	63 568	4351	19 712	22 142	138 663
Callsets[a]	63 568	4351	19 712	22 376	138 930
Variants	5 514 126	118 4170	1 778 096	2 654 065	10 716 093

[a]set of variants from one genotyping experiment; ICD-O, International Classification of Diseases for Oncology; NCIt, National Cancer Institute Thesaurus.

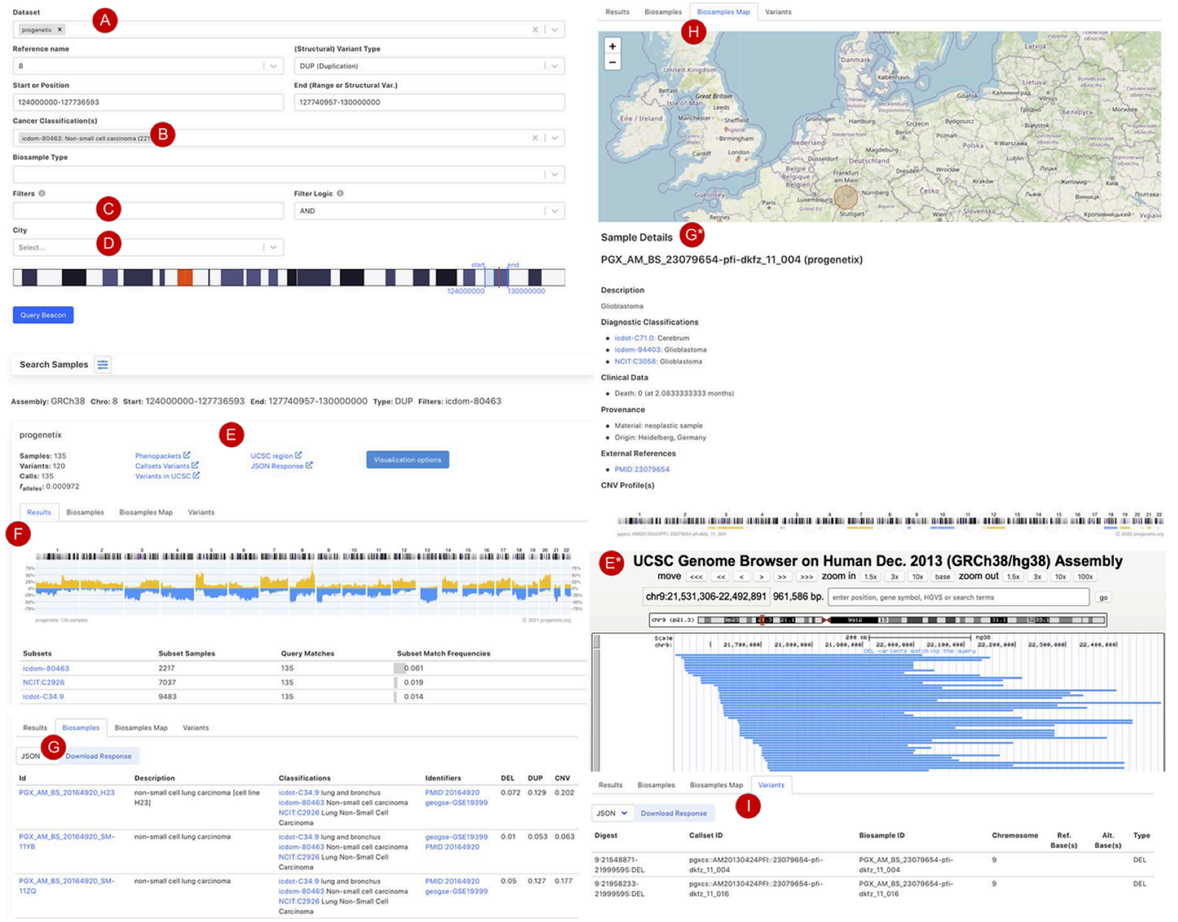

Figure 3. Beacon-style query using fuzzy ranges to identify biosamples with variants matching the CNA range This example queries for a continuous, focal duplication covering the complete MYC gene's coding region with < = 6 Mb in size. A: Filter for dataset; B: filter for cancer classification (NCIt and ICD-O-3 ontology terms available); C: additional filter, e.g. Cellosaurus; D: additional filter for geographic location; E: external link to UCSC browser to view the alignment of matched variants; F: cancer type classification sorted by frequency of the matched biosamples present in the subset; G: list of matched biosamples with description, statistics and reference. More detailed biosample information can be viewed through 'id' link to the sample detail page; H: matched variants with reference to biosamples can be downloaded in json or csv format.

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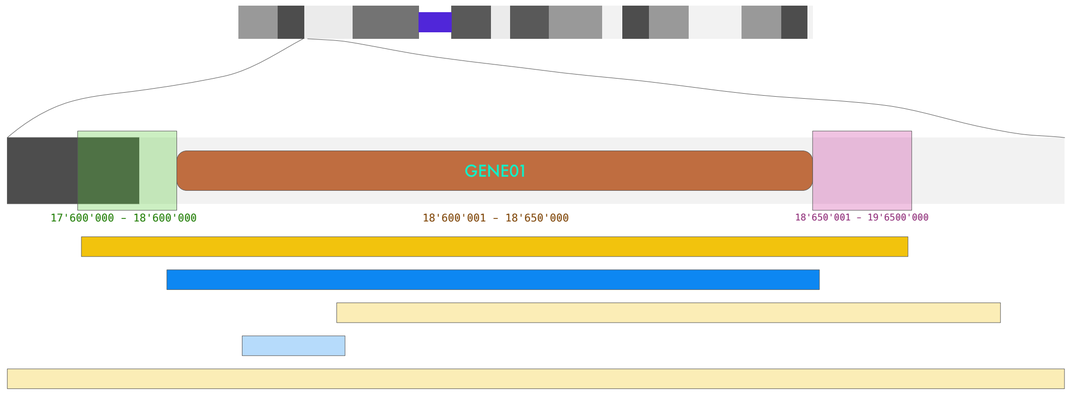
Progenetix in 2022

Variant and Metadata for Sample Discovery

- positional queries for genomic variants using the **GA4GH Beacon protocol**
- metadata queries (diagnoses, identifiers, clinical classes ...) using **Beacon "filters"**

Genome Bracket Query
(full match)



Bold: Matched Variants

Shaded: Unmatched

DEL (Copy Number Loss) DUP (Copy Number Gain)

progenetix

- Cancer CNV Profiles
- Search Samples
- Studies & Cohorts
  - arrayMap
  - TCGA Samples
  - DIPG Samples
  - Gao & Baudis, 2021
  - Cancer Cell Lines
- Publication DB
- Services
  - NCIt Mappings
  - UBERON Mappings
- Upload & Plot
- Download Data
- Beacon+
- Progenetix Info
  - About Progenetix
  - Use Cases
  - Documentation
  - Baudisgroup @ UZH

Search Samples

CDKN2A Deletion Example | MYC Duplication | TP53 Del. in Cell Lines | K-562 Cell Line

Gene Spans | Cytoband(s)

This example shows the query for CNV deletion variants overlapping the CDKN2A gene's coding region with at least a single base, but limited to "highly focal" hits (here i.e. <= ~1Mbp in size). The query can be modified e.g. through changing the position parameters or diagnosis.

Gene Symbol: Select...

Chromosome: 9

(Structural) Variant Type: DEL (Deletion)

Start or Position: 21500001-21975098

End (Range or Structural Var.): 21967753-22500000

Minimum Variant Length

Maximal Variant Length

Reference ID(s): Select...

Cancer Classification(s): NCIT:C3058: Glioblastoma (4375)

Clinical Classes: Select...

Genotypic Sex: Select...

Biosample Type: Select...

Filters

Filter Logic: AND

Filter Precision: exact

City: Select...

Chromosome 9

Query Database

ELIXIR ALL HANDS 2022

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

Global Alliance for Genomics & Health

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Beacon v2 Conformity and Extensions in Progenetix

Putting the + into Beacon ...

- support & use of standard Beacon v2 PUT & GET variant queries, filters and meta parameters
  - ➡ variant parameters, geneId, lengths, EFO & VCF CNV types, pagination
  - ➡ widespread, self-scoping filter use for bio-, technical- and and id parameters with switch for descending terms use (globally or per term if using POST)
- extensive use of handovers
  - ➡ asynchronous delivery of e.g. variant and sample data, data plots
- + extensions of query logic
  - ➡ optional use of OR logic for filter combinations (global)
- + extension of query parameters
  - ➡ geographic queries incl. $geonear and use of GeoJSON in schemas
- ┐(ツ ▽ ツ)┌ no implementation of authentication on this open dataset

Progenetix provides a number of additional services and output formats which are initiated over the / services path or provided as request parameters and are not considered Beacon extensions (though they follow the syntax where possible).

progenetix

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

React

APACHE HTTP SERVER PROJECT

python™

mongoDB

- *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"),
```

variants analyses biosamples individuals

Entity collections

collations geolocs genespans publications qBuffer

Utility collections

Documentation Home

Search

progenetix-web
☆3 1

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

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 Beac

`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 sevices (e.g. the publicat
- 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)

es/pgxbs-kftva5c9

a single biosample

MODE=TRUE

es?testMode=true

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

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

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

Org.progenetix

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 ccan 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": {
```

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pgxRpi

An interface API for analyzing Progenetix CNV data in R using the Beacon+ API

Beacon Path: Retrieve variants by biosample id(s)

```
https://progenetix.org/beacon/g_variants/
?biosampleIds=pgxbs-kftvh94d,pgxbs-kftvh94g,pgxbs-kftvh972
&output=pgxseg
```

Beacon Path: Get biosamples by filter(s)

```
http://progenetix.org/beacon/biosamples/
?filters=NCIT:C3697&output=datatable
```

Service Path: Retrieve CNV frequencies by filter(s)

```
http://www.progenetix.org/services/intervalFrequencies/
?id=NCIT:C4323&output=pgxseg
```

Author: Hangjia Zhao | @hangjiaz

README.md

pgxRpi

This is an API wrapper package to access data from Progenetix database.

You can install this package from GitHub using:

```
install.packages("devtools")
devtools::install_github("progenetix/pgxRpi")
```

If you are interested in accessing CNV variant data, get started from this vignette

If you are interested in accessing CNV frequency data, get started from this vignette

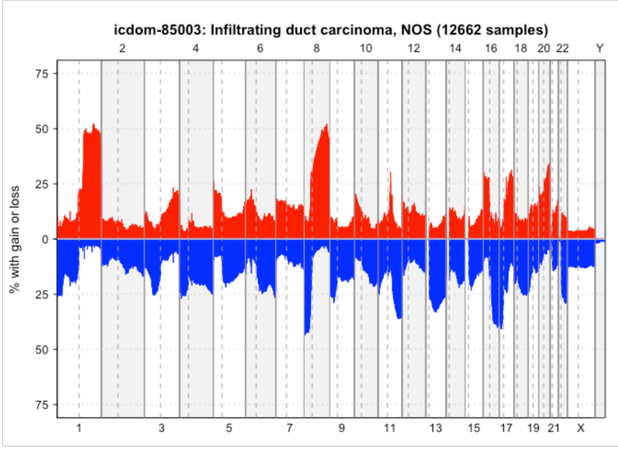
When you face problems, try to reinstall the latest version. If reinstallation doesn't help, please contact us.

```
variant_1 <- pgxLoader(type="variant", biosample_id = biosample_id)
```

```
biosamples <- pgxLoader(type="biosample", filters = "NCIT:C3059",codematches = TRUE,
                        biosample_id = c("pgxbs-kftva5zv","pgxbs-kftva5zw"))
```

```
freq_pgxseg <- pgxLoader(type="frequency", output ='pgxseg',
                         filters=c("NCIT:C4038","pgx:icdom-85003"),
                         codematches = TRUE)
```

```
pgxFreqplot(freq_pgxseg, filters='pgx:icdom-85003')
```



Beacon+: Phenopackets

Testing alternative response schemas...

http://progenetix.org/beacon/biosamples/pgxbs-kftvhyvb/phenopackets

- the v2 default schemas are mostly aligned w/ Phenopackets v2
- creating phenopackets can be done mostly by re-wrapping of Beacon entities (individual, biosample)
- variants can be included through file resource URLs; in Beacon+ this is done through *ad hoc* handover URIs


```
"id": "pgxpxf-kftx3tl5",
"metaData": {
  "phenopacketSchemaVersion": "v2",
  "resources": [
    {
      "id": "NCIT",
      "iriPrefix": "http://purl.obolibrary.org/obo/NCIT_",
      "name": "NCIt Plus Neoplasm Core",
      "namespacePrefix": "NCIT",
      "url": "http://purl.obolibrary.org/obo/ncit/neoplasm-core.c
      "version": "2022-04-01"
    },

"subject": {
  "dataUseConditions": {
    "id": "DUO:0000004",
    "label": "no restriction"
  },
  "diseases": [
    {
      "clinicalTnmFinding": [],
      "diseaseCode": {
        "id": "NCIT:C3099",
        "label": "Hepatocellular Carcinoma"
      },
      "onset": {
        "age": "P48Y9M26D"
      },
      "stage": {
        "id": "NCIT:C27966",
        "label": "Stage I"
      }
    }
  ],
  "id": "pgxind-kftx3tl5",
  "sex": {
    "id": "PATO:0020001",
    "label": "male genotypic sex"
  },
  "updated": "2018-12-04 14:53:11.674000",
  "vitalStatus": {
    "status": "UNKNOWN_STATUS"
  }
}

"biosamples": [
  {
    "biosampleStatus": {
      "id": "EFO:0009656",
      "label": "neoplastic sample"
    },
    "dataUseConditions": {
      "id": "DUO:0000004",
      "label": "no restriction"
    },
    "description": "Primary Tumor",
    "externalReferences": [
      {
        "id": "pgx:TCGA-0004d251-3f70-4395-b175-c94c2f5b1b81",
        "label": "TCGA case_id"
      },
      {
        "id": "pgx:TCGA-TCGA-DD-AAVP",
        "label": "TCGA submitter_id"
      },
      {
        "id": "pgx:TCGA-9259e9ee-7279-4b62-8512-509cb705029c",
        "label": "TCGA sample_id"
      },
      {
        "id": "pgx:TCGA-LIHC",
        "label": "TCGA LIHC project"
      }
    ],
    "files": [
      {
        "fileAttributes": {
          "fileFormat": "pgxseg",
          "genomeAssembly": "GRCh38"
        },
        "uri": "https://progenetix.org/beacon/biosamples/pgxbs-kftvhyvb/variants/?output=pgxseg"
      }
    ],
    "histologicalDiagnosis": {
      "id": "NCIT:C3099",
      "label": "Hepatocellular Carcinoma"
    },
    "id": "pgxbs-kftvhyvb",
    "individualId": "pgxind-kftx3tl5",
    "pathologicalStage": {
      "id": "NCIT:C27966",
      "label": "Stage I"
    },
    "sampledTissue": {
      "id": "UBERON:0002107",
      "label": "liver"
    },
    "timeOfCollection": {
      "age": "P48Y9M26D"
    },
```

Beacon+: Phenopackets

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```
"id": "pgxpxf-kftx3tl5",
"metaData": {
  "phenopacketSchemaVersion": "v2",
  "resources": [
    {
      "id": "NCIT",
      "iriPrefix": "http://purl.obolibrary.org/obo/NCIT_",
      "name": "NCIt Plus Neoplasm Core",
      "namespacePrefix": "NCIT",
      "url": "http://purl.obolibrary.org/obo/ncit/neoplasm-core.owl",
"files": [
  {
    "fileAttributes": {
      "fileFormat": "pgxseg",
      "genomeAssembly": "GRCh38"
    },
    "uri": "https://progenetix.org/beacon/biosamples/pgxbs-kftvhyvb/variants/?output=pgxseg"
  }
],
      },
      "onset": {
        "age": "P48Y9M26D"
      },
      "stage": {
        "id": "NCIT:C27966",
        "label": "Stage I"
      }
    }
  ],
  "id": "pgxind-kftx3tl5",
  "sex": {
    "id": "PATO:0020001",
    "label": "male genotypic sex"
  },
  "updated": "2018-12-04 14:53:11.674000",
  "vitalStatus": {
    "status": "UNKNOWN_STATUS"
  }
}
"biosamples": [
  {
    "biosampleStatus": {
      "id": "EFO:0009656",
      "label": "neoplastic sample"
    },
    "dataUseConditions": {
      "id": "DUO:0000004",
      "label": "no restriction"
    },
    "description": "Primary Tumor",
    "externalReferences": [
      {
        "fileAttributes": {
          "fileFormat": "pgxseg",
          "genomeAssembly": "GRCh38"
        },
        "uri": "https://progenetix.org/beacon/biosamples/pgxbs-kftvhyvb/variants/?output=pgxseg"
      }
    ],
    "histologicalDiagnosis": {
      "id": "NCIT:C3099",
      "label": "Hepatocellular Carcinoma"
    },
    "id": "pgxbs-kftvhyvb",
    "individualId": "pgxind-kftx3tl5",
    "pathologicalStage": {
      "id": "NCIT:C27966",
      "label": "Stage I"
    },
    "sampledTissue": {
      "id": "UBERON:0002107",
      "label": "liver"
    },
    "timeOfCollection": {
      "age": "P48Y9M26D"
    },
```

Beacon+: Phenopackets

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```
bios_s = data_db["biosamples"].find({"individual_id":ind["id"]})

for bios in bios_s:

    bios.update({
        "files": [
            {
                "uri": "{}/beacon/biosamples/{}/variants/?output=pgxseg".format(server, bios["id"]),
                "file_attributes": {
                    "genomeAssembly": "GRCh38",
                    "fileFormat": "pgxseg"
                }
            }
        ]
    })
    for k in bios_pop_keys:
        bios.pop(k, None)

    clean_empty_fields(bios)

    pxf_bios.append(bios)
```

```
def remap_phenopackets(ds_id, r_s_res, byc):

    if not "phenopacket" in byc["response_entity_id"]:
        return r_s_res

    mongo_client = MongoClient()
    data_db = mongo_client[ds_id]
    pxf_s = []

    for ind_i, ind in enumerate(r_s_res):

        pxf = phenopack_individual(ind, data_db, byc)
        pxf_s.append(pxf)

    return pxf_s
```

Future?

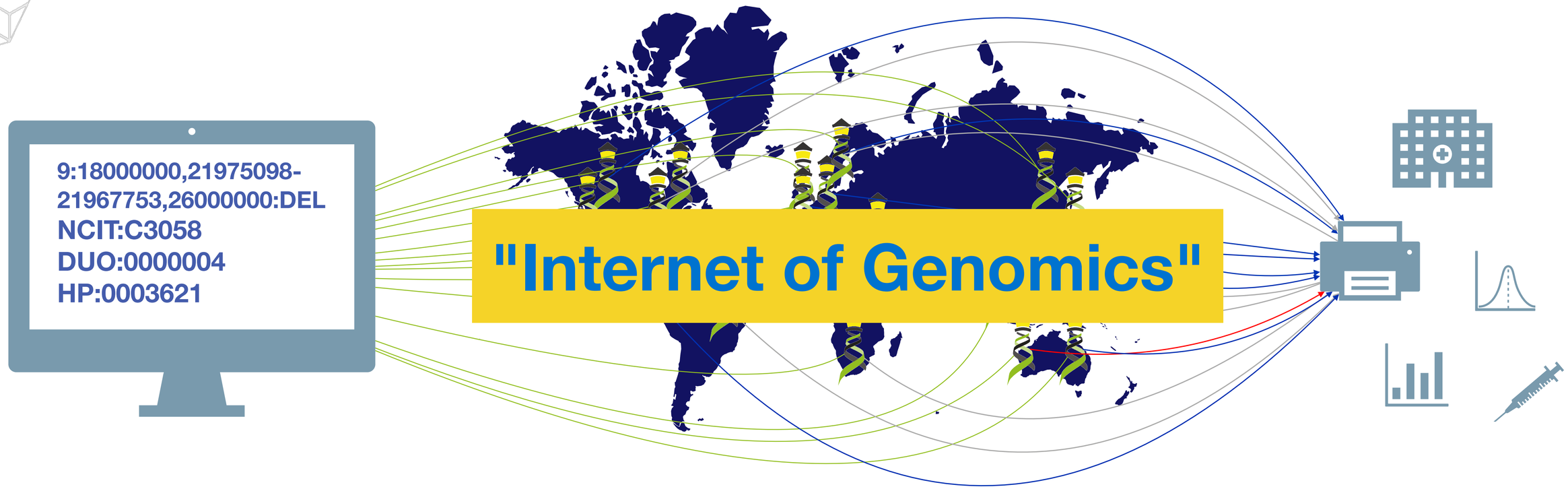
Some proposals for a stepwise Beacon protocol extension

- Boolean options for chaining filters

  ➡ use of heterogeneous/alternative annotations within and across resources

- Phenopackets support as a (the?) default format for biodata export
- PXF as request documents
- Focus on service & resource discovery
- ELIXIR Beacon Network, including translations for federated queries to Beacon and Beacon-like resources


FUTURE



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**".

hCNV Implementation Studies 2021-2023

Focus on Integration with ELIXIR Platforms and Communities - and beyond

- original 2019-2021 implementation study provided visibility and established connections for new studies
- instrumental were Biohackathons, use case & standards surveys and co-participation of group members
- future work plans to leverage the resources of participants through pre-established interactions and synergies
- 2 independent studies provide clearer definitions of deliverables and individual scopes

Michael Baudis	CH
Christophe Béroud	FR
David Salgado	FR
Alexander Kanitz	CH
Anthony Brookes	UK
Babita Singh	ES
Björn Grüning	DE
Jordi Rambla	ES
Kirill Tsukanov	EMBL-EBI
Krzysztof Poterlowicz	UK
Salvador Capella-Gutierrez	ES
Sergi Beltran	ES
Steven Laurie	ES
Tim Beck	UK
Timothee Cezard	EMBL-EBI

Thank You!

...all Beacon developers, managers, contributors & users!

...**current** + former Progenetix contributors, especially
Haoyang Cai, Bo Gao, Linda Grob, Saumya Gupta, Qingyao Huang,
Nitin Kumar, **Rahel Paloots**, Prisni Rath, **Ziying Yang** & **Hangjia Zhao**

elixir

SIB

University of Zurich[UZH]

SPHN Swiss Personalized Health Network

Global Alliance for Genomics & Health


HIER WOHNTE
V. 21. FEBR. 1916 BIS 2. APRIL 1917
LENIN
DER FÜHRER DER RUSSISCHEN
REVOLUTION