

Standard FHIR Clinical Genomic Operations for retrieving genetic data

Bret Heale – Humanized Health Consulting/ELIMU



HL7 FHIR DevDays International 2022 | Hybrid Edition, Cleveland, OH | June 6–9, 2022 | @HL7 | @FirelyTeam | #fhirdevdays | www.devdays.com

ORGANIZED BY

firely

HL7[®]
International

Who am I?

Collaborator on specification: <http://build.fhir.org/ig/HL7/genomics-reporting/operations.html>

Bret Heale

Founding Biomedical Informaticist, Humanized Health Consulting

Senior Medical Informaticist, ELIMU

Member, HL7 Clinical Genomics

Father, Family



RoadMap

- Intro
- Operations making life eas(ier)
- Things you would do with Operations
- Reference Implementation

Operations in FHIR

Specification

<http://build.fhir.org/ig/HL7/genomics-reporting/operations.html>

“To drive precision medicine, we need to provide developers with easy access to complex omic data”

- FHIR is a very versatile tool, and genomics is a space where many formats are currently used to communicate genomic data in clinical genomic reports.
- Operations extend the FHIR specification to reduce complex or processive tasks.
- Genomics Operations make it simpler/easier to get genomic data out of a FHIR server.

Accessing Genomic Data 101

\$find-subject-variants

- The code below is all you need to get all variants for patient HG00403 in the LDLR gene

```
range="NC_000019.9:11200138-11244496"
```

```
subject="HG00403"
```

```
url='https://fhir-gen-ops.herokuapp.com/subject-operations/genotype-operations/$find-subject-variants?subject='+subject+'&ranges='+range+'&includeVariants=true'
```

Working example: [https://fhir-gen-ops.herokuapp.com/subject-operations/genotype-operations/\\$find-subject-variants?subject=HG00403&ranges=NC_000019.9:11200138-11244496&includeVariants=true](https://fhir-gen-ops.herokuapp.com/subject-operations/genotype-operations/$find-subject-variants?subject=HG00403&ranges=NC_000019.9:11200138-11244496&includeVariants=true)

Variant Normalization - solved by Operations

\$find-subject-specific-variants

Variants can be represented in various ways. The following, using the Clinical Genomics FHIR Variant Profile components, are synonymous.

- component:coding-hgvs: HGVS = NM_001195798.2:c.12G>A

Variant Normalization - solved by Operations

\$find-subject-specific-variants

Variants can be represented in various ways. The following, using the Clinical Genomics FHIR Variant Profile components, are synonymous.

- component:coding-hgvs: HGVS = NM_001195798.2:c.12G>A
- component:genomic-hgvs: HGVS = NC_000019.9:g.11200236G>A

Variant Normalization - solved by Operations

\$find-subject-specific-variants

Variants can be represented in various ways. The following, using the Clinical Genomics FHIR Variant Profile components, are synonymous.

- component:coding-hgvs: HGVS = NM_001195798.2:c.12G>A
- component:genomic-hgvs: HGVS = NC_000019.9:g.11200236G>A
- component:genomic-hgvs: HGVS = NC_000019.10:g.11089560G>A

Variant Normalization - solved by Operations

\$find-subject-specific-variants

Variants can be represented in various ways. The following, using the Clinical Genomics FHIR Variant Profile components, are synonymous.

- component:coding-hgvs: HGVS = NM_001195798.2:c.12G>A
- component:genomic-hgvs: HGVS = NC_000019.9:g.11200236G>A
- component:genomic-hgvs: HGVS = NC_000019.10:g.11089560G>A
- Using Multiple components (VCF-like):
 - component:genomic-ref-seq: NC_000019.10
 - component:ref-allele: G
 - component:alt-allele: A
 - component:coordinate-system: 0-based interval counting
 - component:exact-start-end: start = 11089559

Variant Normalization - solved by Operations

\$find-subject-specific-variants

- Summary note
 - To be complete, a FHIR query would need to comprehensively include all the different HGVS for a variant, the VCF-like use of multiple components, and perhaps even a list of variants that contain the variant of interest as input parameters. The genomic operations use a single format for input parameters and guarantee that the search will cover all the possible HGVS and other formatting options. Implicit in these FHIR Genomics operations is that variants in requested regions are returned regardless of how they are formatted/represented/stored in a server.
 - See: <https://build.fhir.org/ig/HL7/genomics-reporting/branches/operations/operations.html#expectation-of-normalized-variant-search> for more information. 'Liftover' is also performed by the server providing the operations.

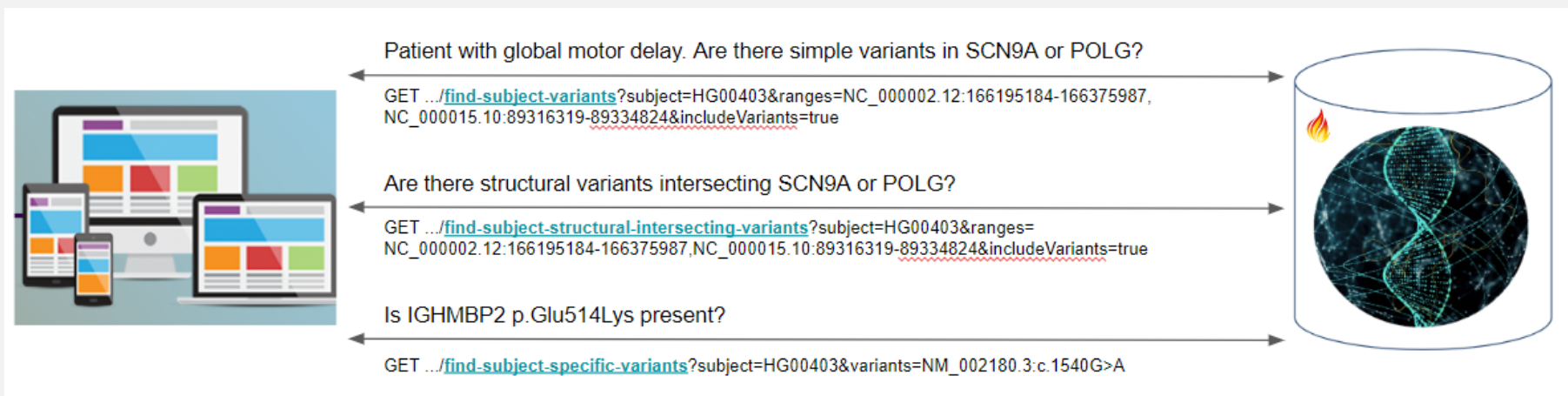
Populations too

\$find-population-specific-variants

- An exercise to learn why genomic operations make life better
 - Here is the base-URL for a public FHIR server that has a result for each of the possible formats previously mentioned:
'https://api.logicahealth.org/FHIRgenomics2Test/open/'
 - Patient m123 has a variant profile for each format. There are additional patients as well. Using FHIR queries, find all the patients' results in the FHIR server with base-URL 'https://api.logicahealth.org/FHIRgenomics2Test/open/'
- The FHIR operations normalize, e.g. \$find-population-specific-variants, making finding all the patients with a variant easier. Also, the FHIR operation normalizes the output so you don't need to parse all the various formats, which makes using the data easier. Great news for an app developer, analyst or data engineer.

Things you would do with Genomic Operations

- Diagnostic odyssey
 - Objective: Identify causative variant for rare disease
 - structural variant operations support search based on intersection or subsumption of a region of interest
 - find-subject-specific-variants supports searching for specific SNPs, useful when computing polygenic risk scores



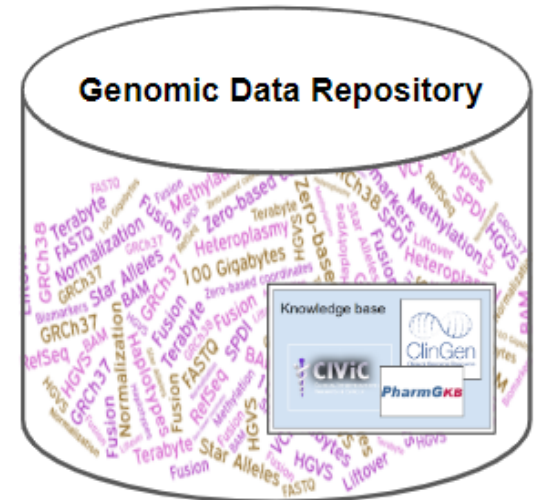
Things you would do with Genomic Operations

- Cancer therapeutics
 - Objective: Identify molecularly-guided treatment options
 - Operations can dynamically compute implications.



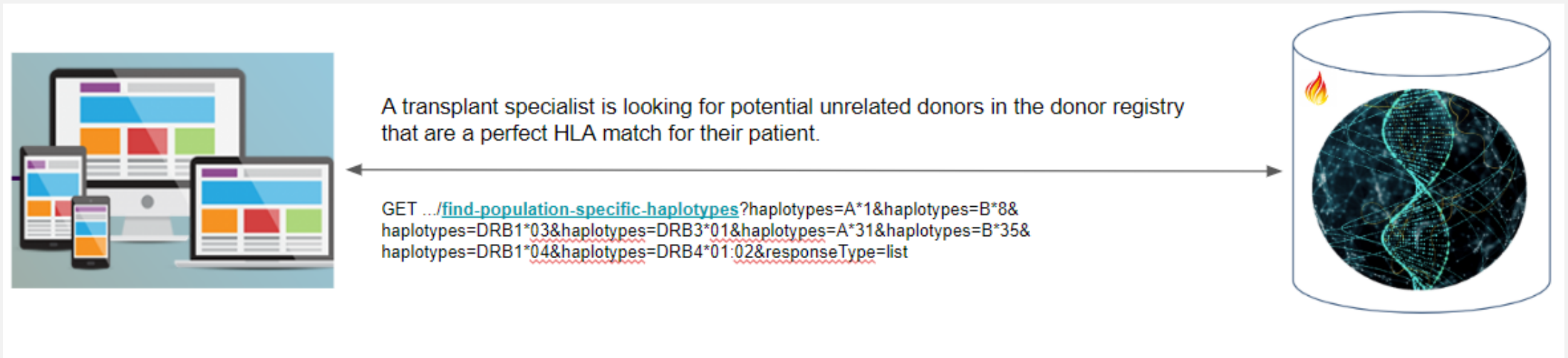
Patient HG00403 has metastatic breast cancer.
 Targeted sequencing of a tumor biopsy specimen shows ERBB2 (HER2) variant NM_004448.4:c.2264_2278del.
 What are the potential treatment options?

`GET .../find-subject-tx-implications?subject=HG00403&variants=NM_004448.4:c.2264_2278del&conditions=http://snomed.info/sct|372137005`



Things you would do with Genomic Operations

- Transplant donor matching
 - Objective: Determine if HLA-matched subjects are present
 - Population queries support 'patients like me' functionality



Reference Implementation – check out the code!!!!

- Reference Implementation – Exercises, Examples, Sample Apps
 - open-source git-repo: <https://github.com/FHIR/genomics-operations>
 - **WIKI** <https://github.com/FHIR/genomics-operations/wiki>
 - In connecathon 30, many of the operations were tested out by using either the swagger interface (<https://fhir-gen-ops.herokuapp.com/>) to the reference implementation or Postman (https://github.com/FHIR/genomics-operations/blob/main/FHIRGenomicsOperations.postman_collection.json).
 - EXAMPLE APPS - [5. Genomics apps · FHIR/genomics-operations Wiki · GitHub](#)
- SPECIFICATION: <http://build.fhir.org/ig/HL7/genomics-reporting/operations.html>

GenomeX

- Proposed as one of the initial Use Cases within GenomeX
 - “Enabling Access to Complex Genomic Information through FHIR Genomics Operations”
 - Part of CodeX FHIR Accelerator
 - <https://confluence.hl7.org/display/COD/Enabling+Access+to+Complex+Genomic+Information+through+FHIR+Genomics+Operations>



To do list

- Visit WIKI for Reference Implementation
 - Write a genomics app against reference implementation
 - Write a genomics app against your own implementation
- Check out HL7 Clinical Genomics WG Specification
 - Including operations and profiles for genetic data
- Join HL7 Clinical Genomics WG (Zulip and list-serv)
- Join Genomx Operations use case (“Enabling Access to Complex Genomic Information through FHIR Genomics Operations”) community
 - Intent is to be tightly focused and accelerate

Contact

- During DevDays, you can find / reach me here:
 - Via Whova App – Speaker’s Gallery
 - bheale@humanizedhealthconsulting.com
 - Zulip
 - LinkedIn
 - ..

Q&A

- Thank you for your time!
- QUESTIONS?

ORGANIZED BY



Bonus Slide - Helpful utility from the Reference Implementation

- get-feature-coordinates
 - Feature Coordinate Utility: This utility returns genomic feature coordinates and other annotations. (e.g. Gene range with reference accession id)
 - All data are from NCBI Human Genome Resources. For chromosomes, build 37 and build 38 reference sequences are returned. For genes, genomic coordinates are returned, along with a list of transcripts. MANE transcript is flagged. For transcripts, genomic coordinates are returned, along with the gene name and composite exons, along with exon coordinates. For proteins, the corresponding transcript is returned.
- <https://github.com/FHIR/genomics-operations/wiki/2.-Getting-Started#utilities>