CanDIG

Jonathan Dursi, Hospital for Sick Children

CanDIG

National Analysis of Distributed Private Genomic Data

The CanDIG Platform

Goal:

- A **Canadian** approach to analysis of health research data:
  - **National**-scale populations
  - **Respecting** provincial, institutional stewards **local control** over their data, users.

Project:

- Funded 4 year cyberinfrastructure project, ~5 FTEs and staffing up

The CanDIG Platform

SickKids®
RESEARCH INSTITUTE

PRINCESS MARGARET GENOMICS CENTRE

McGill University and Génome Québec
Innovation Centre
Innovation in action

Canada's Michael Smith
Genome Sciences Centre

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National Analysis of Distributed Private Genomic Data

Health Care Data is Provincial

- Each province has made it's own decisions about privacy trade-offs
- Putting data in one place challenging even if it scaled

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Health Care Data is Provincial

- National-scale data needed for:
  - Population-scale studies (*e.g.*, cancers)
  - Supporting researchers with national projects

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National Analysis of Distributed Private Genomic Data

Health Care Data is Everywhere

- Torrent of next-generation sequencing data:
  - How to discover it?
  - How to analyze it?
  - How to make it accessible while still maintaining security, privacy?

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National Analysis of Distributed Private Genomic Data

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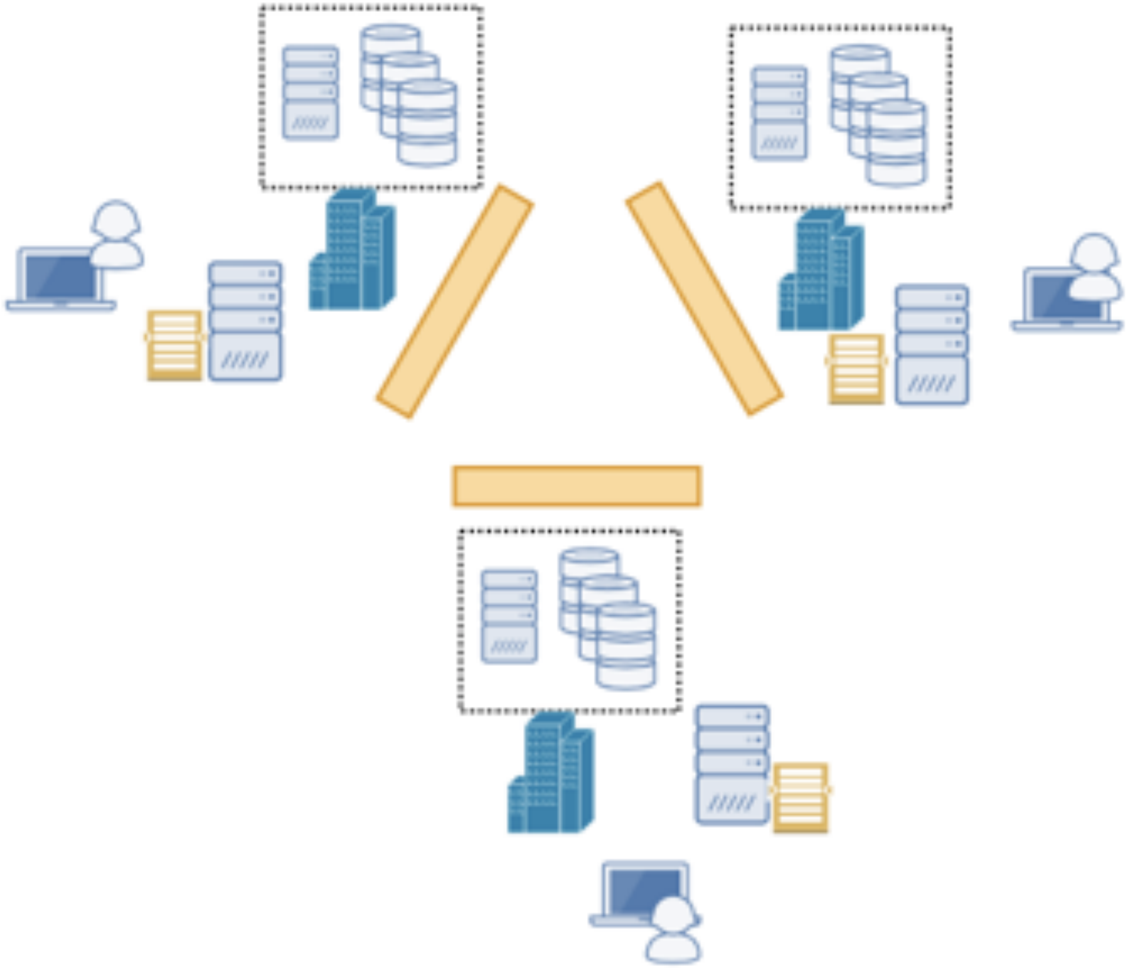
- Allow each site to control its own data, users
- Trust authentication of users from other sites, but make own authorization decisions
  - Users may be able to see everything in one set (Co-Is on a national project), only little, with differential privacy, or nothing
- Researchers send queries, aggregate intermediate results to get final answers



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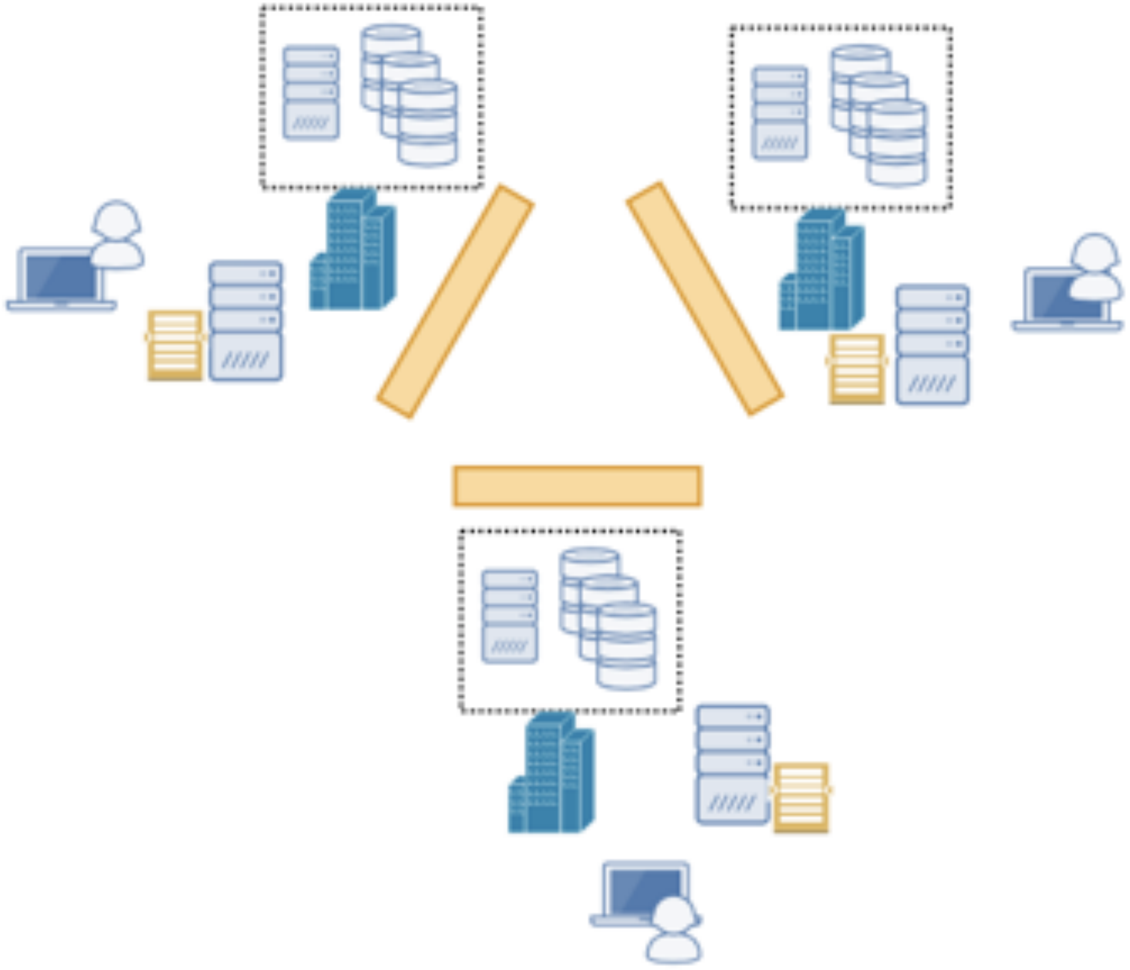
National Analysis of Distributed Private Genomic Data

Platform Principles

- As decentralized as possible
  - Local control of data
  - Minimize centralized infrastructure (maintenance, security)

Distributed Infrastructure for Genomics

- **Fully** distributed
- Participating sites: data providers, compute providers, source of user requests
- Access to data through API requests, directly or via pipelines
- Local sites control access to their data
- Sites authenticate their users
- Researcher queries need only ever see intermediate results, aggregated.



CanDIG *National Analysis of Distributed Private Genomic Data*

Platform Principles

- As decentralized as possible
  - Local control of data
  - Minimize centralized infrastructure (maintenance, security)
- Reduce, reuse, recycle
  - Lots of interesting and new work to do, including challenging algorithmic/privacy work
  - Don’t add to that by re-inventing wheels

CanDIG and the GA4GH

- CanDIG makes use of APIs and data standards from GA4GH (Global Alliance for Genomics and Health)
  - RESTful APIs for variants, reads data, metadata…
  - Schemas for data exchange
  - Security best practices
- Part of several successful projects
- Google Genomics, Microsoft, …

Global Alliance
for Genomics & Health

Matchmaker Exchange

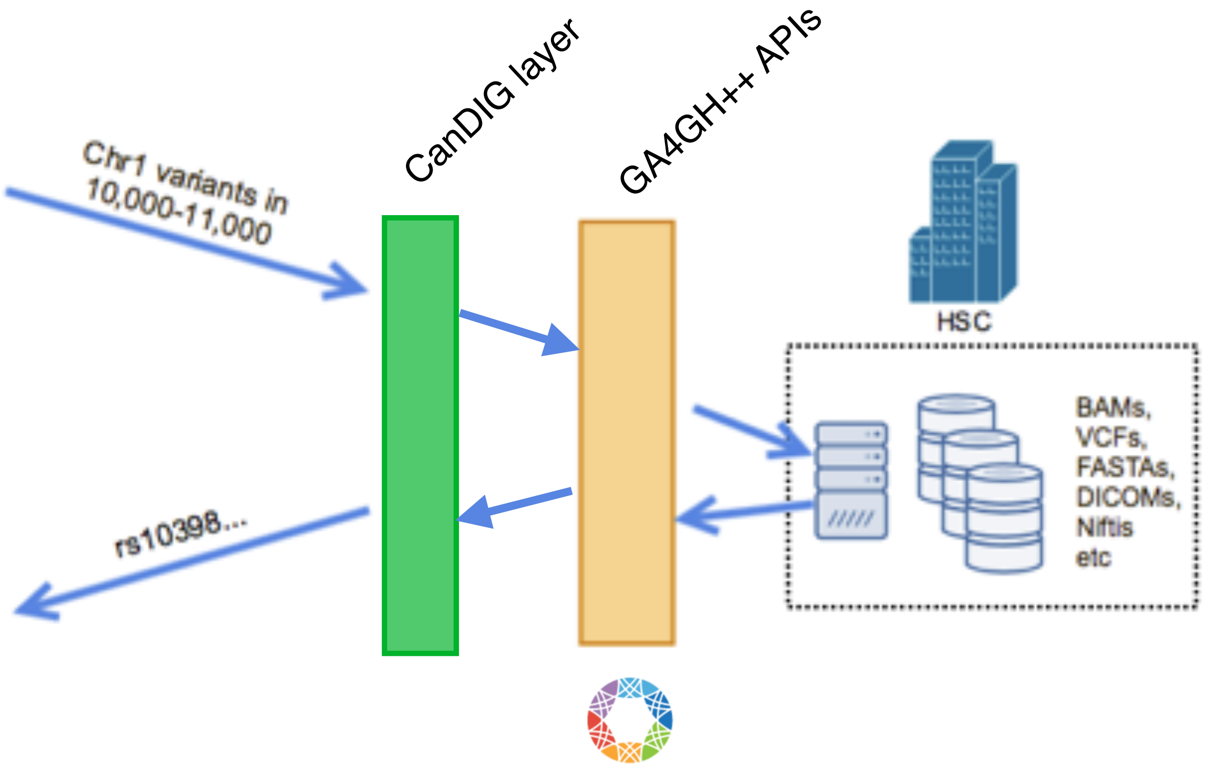
BRCA CHALLENGE

Beacon

Cancer Gene Trust

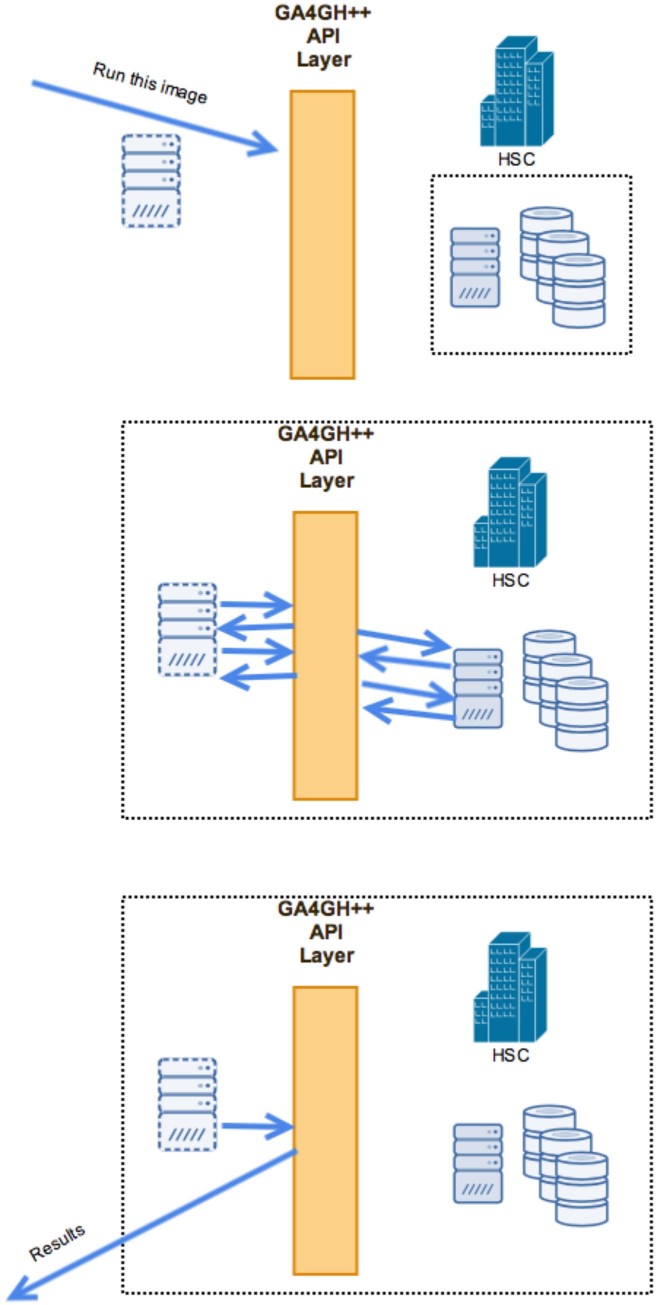
CanDIG and the GA4GH

- All access to data through API.
- Allows abstraction of underlying data store, fine-grained permissions to particular data
- Thin CanDIG layer on top:
  - Richer queries
  - Federation of queries
  - Authentication/Authorization
  - Differential Privacy



CanDIG and the GA4GH

- Queries can be simple queries, handled by the API layer immediately
- Or analyses requiring substantial computation
  - Task Executor Service: run one (or chain) of images against local data
  - Return results through API



CanDIG and OpenID Connect

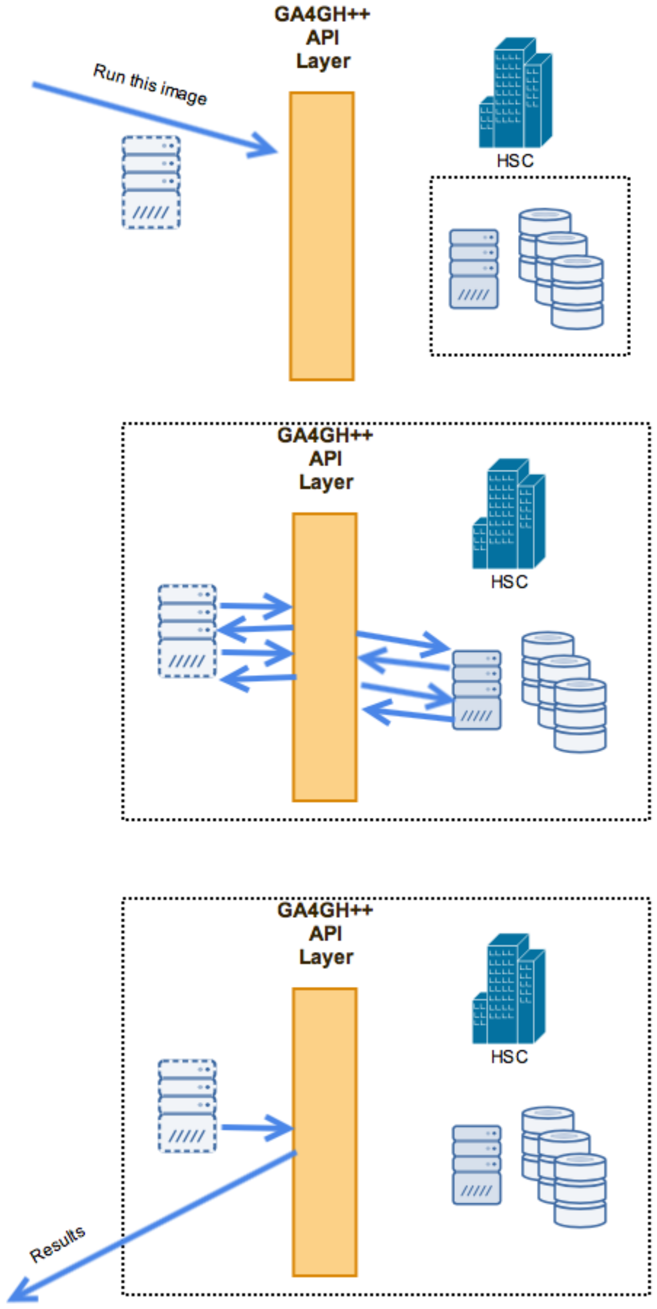
- Use existing well-tested web technologies
  - OpenID Connect for federated authentication
  - KeyCloak to serve OIDC from existing LDAP/AD/etc for each IdP

Platform Principles

- As decentralized as possible
  - Local control of data
  - Minimize centralized infrastructure (maintenance, security)
- Reduce, reuse, recycle
  - Lots of interesting and new work to do, including challenging algorithmic/privacy work
  - Don’t add to that by re-inventing wheels
- Start simple
  - Get simple, working things up and running first
  - Iterate towards desired applications

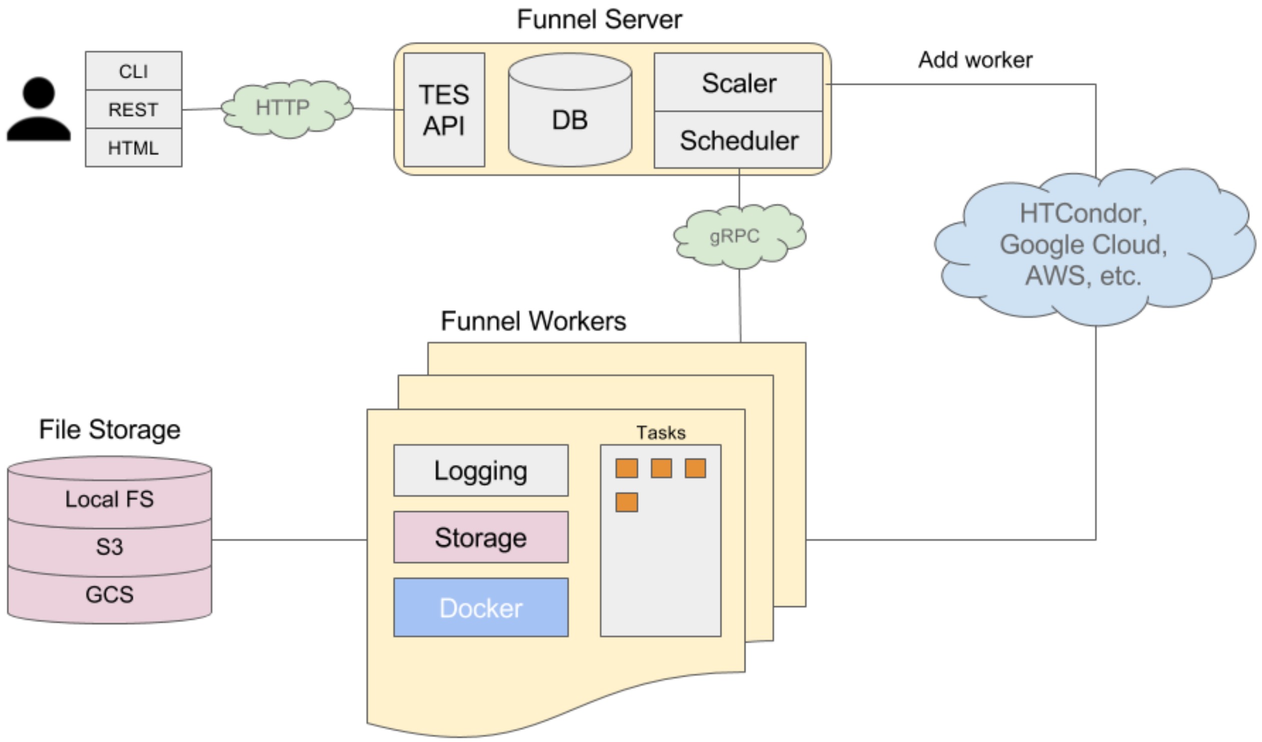
Remote Task Execution

- Want to be able to:
  - Authenticate in
  - Run a bioinformatics task against one of the remote data sets
  - Work done by Steven Li, co-op student, UHN



Remote Task Execution

- Using Funnel, an implementation of GA4GH Task executor definition
- Using Keycloak for OIDC authentication
  - Access to underlying LDAP
- Proof of concept completed



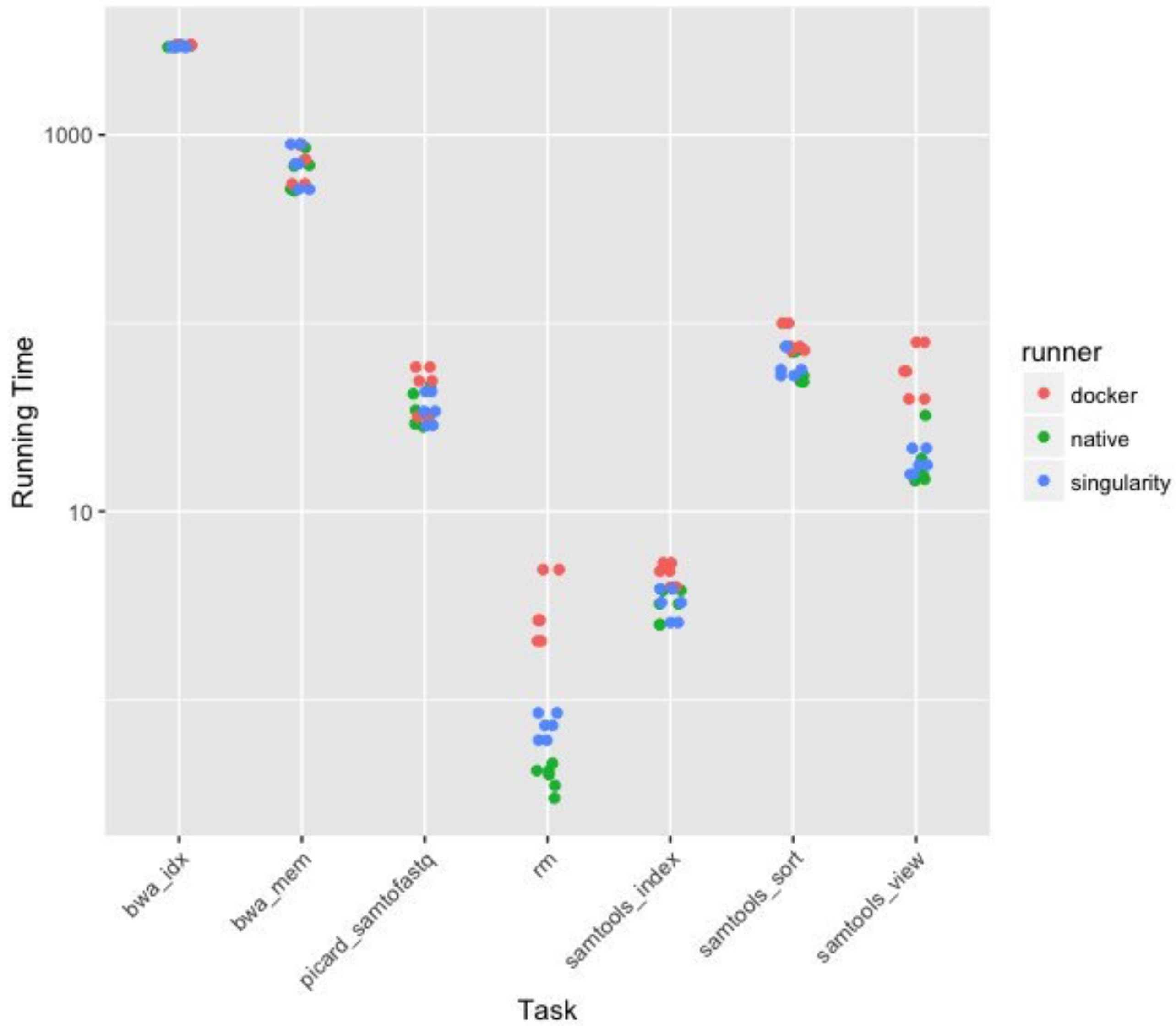
https://ohsu-comp-bio.github.io/funnel/

Containers

- For tasks to be cataloged, distributed, and run on several systems, must be bundled
- Looked at VMs, Docker, rkt, Singularity, Intel Clear Containers
- Need some sort of packaging
- Don’t necessarily need isolation; can handle that at job running time w/ unprivileged users, sandboxes

Containers

- VMs are an awkward fit for discrete, short-lived jobs
- With different container options, performed some benchmarking (https://github.com/CanDIG/images_bakeoff)
- Modest startup cost for docker, perhaps some very modest I/O penalty
- Otherwise quite good performance across all solutions



Singularity or Rkt

- Docker gives us lots of great tooling, and we will use it in the short term (*e.g.*, funnel support)
- But medium term will move to Singularity or Rkt
  - Focus on packaging rather than isolation
  - rkt can easily dial up/down isolation w/o root daemons
- If really needed VM-like isolation, Intel clear containers would be a good choice.

Privacy and Queries

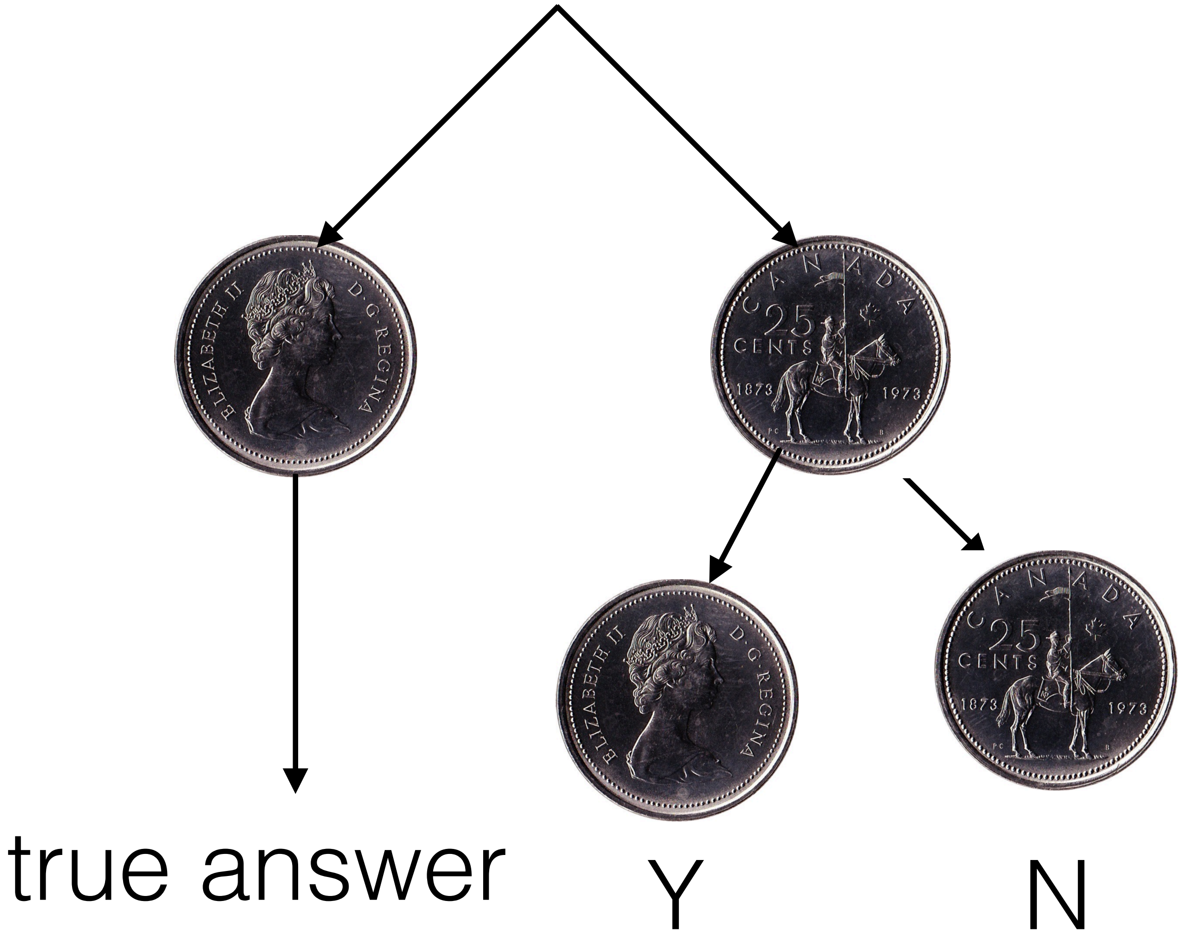
- In many cases, a researcher in a particular project will have complete access to data set
- In other cases, data set can only be accessed at all if privacy of all individuals can be guaranteed
- How can we allow analysis of data while not exposing information of any individual?

Privacy and Queries

- Two approaches:
  - Build queries and applications that only the minimal results are returned - don’t leak extraneous data
  - Add differential privacy for sensitive data sets

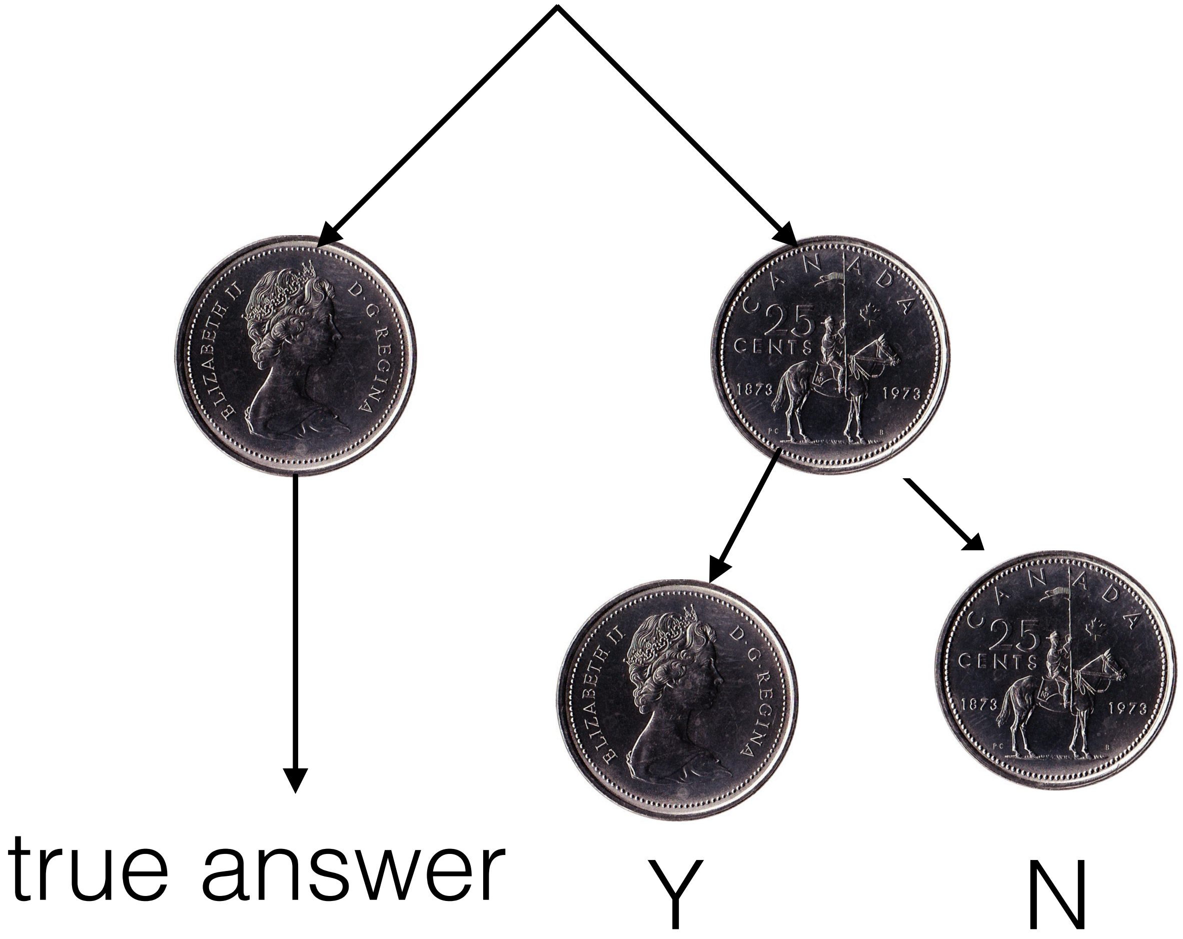
Randomized Response

- Old technique for surveying for behaviours which are illegal or have other stigma attached.
- “Have you, in the last week, listened to Nickleback.”
- p = 0.5 - true answer
- p = 0.5 - random answer
- “bad” answer occurs w/ p = 0.25; “plausible deniability” for any survey respondent.



Randomized Response

- But at the same time, can estimate true *overall* frequencies (and correlations!) knowing the noise model.
- If obtain a frequency f' from the survey instrument, can calculate true frequency f = 2(f' - 1/4)
- Need more samples for given variance, but can get accurate results while protecting each individual's privacy.

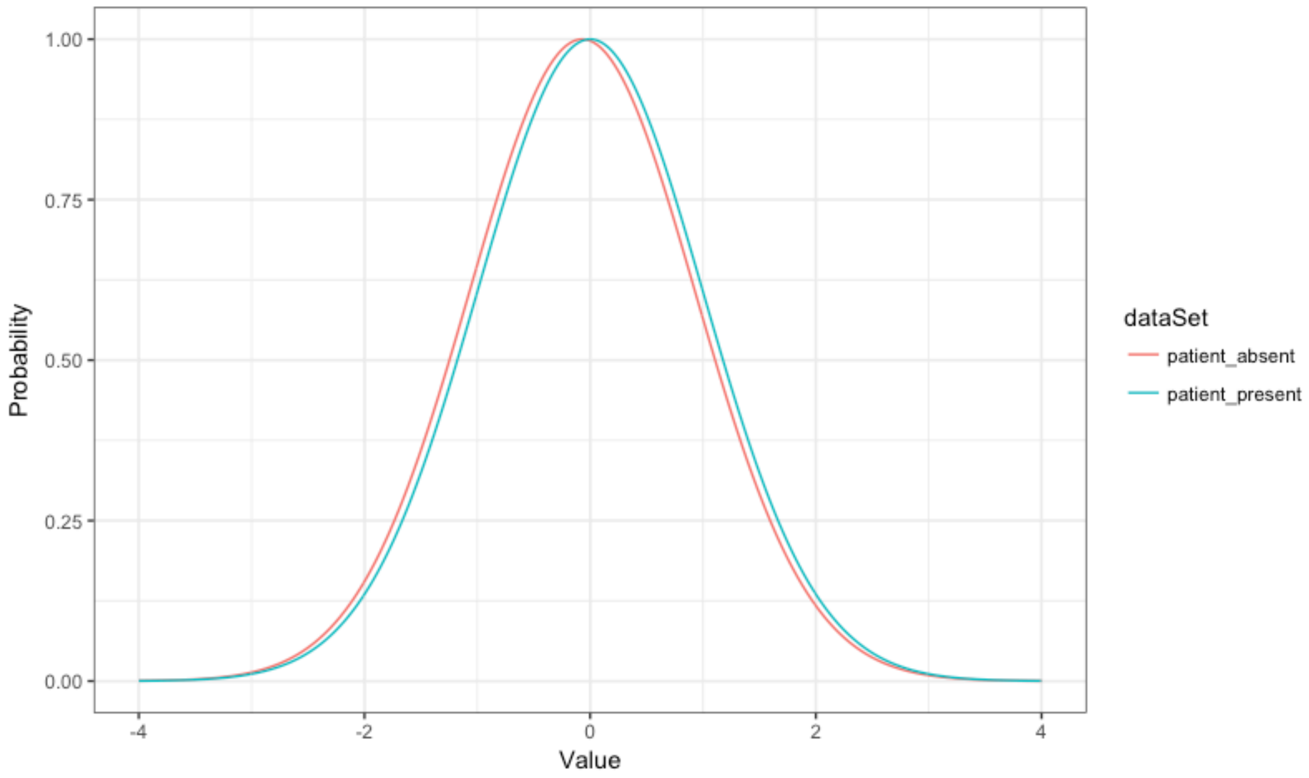


Differential Privacy

- Patient: “There is a quantifiable, minimal, cost to my privacy by participating in this database”.
- Researcher: “I would get an essentially equal distribution of answers from this query if any one row had been absent from the database”.

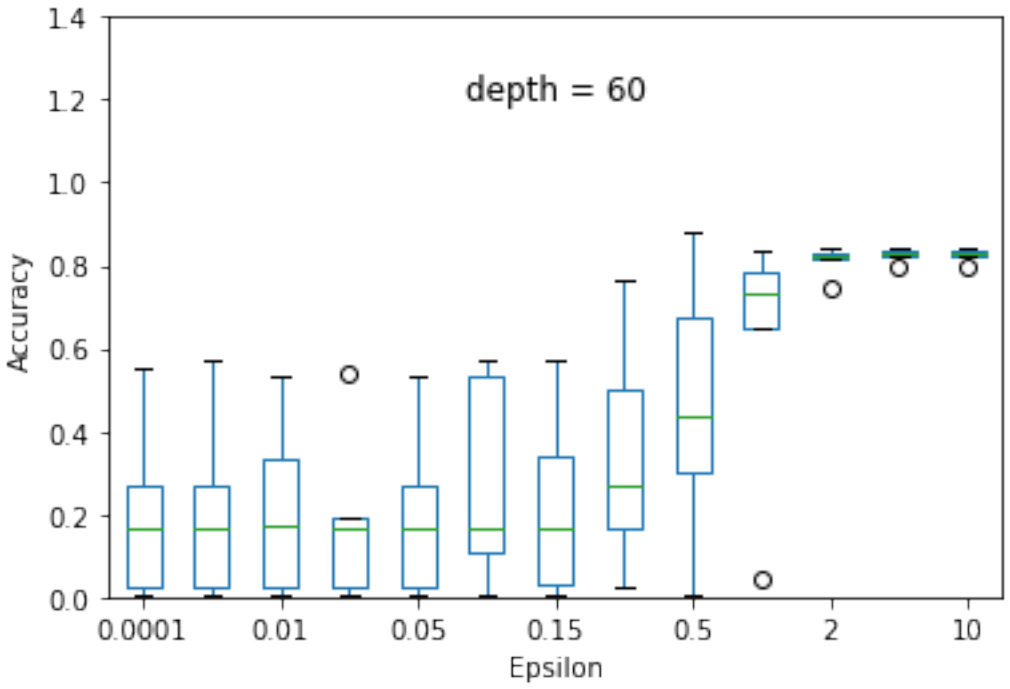
Differential Privacy

- Typical way of implementing: keep *inputs* unperturbed, add noise to *outputs*.
- For any query, add enough random noise that contribution of any one row can't be ascertained



Differential Privacy

- Work by Neelam Memon and Justin Foong: differentially private calculation of classifiers trained on federated thousand genomes data
- Can you perform complex analyses while keeping data private? (Yes!)
- Built with counting queries.
- Informing:
    - How we'll build our differential privacy layer
    - What should go in user queries and what should go in server/API



Federated Analysis of Data

- First task - demonstrate that we can successfully analyze federated data over API.
- Thousand Genome Project - now-classic (2010-2015) sequencing of 2,504 individuals across the world; public data.
- Attempt to reproduce several important population genetics results using simple queries.

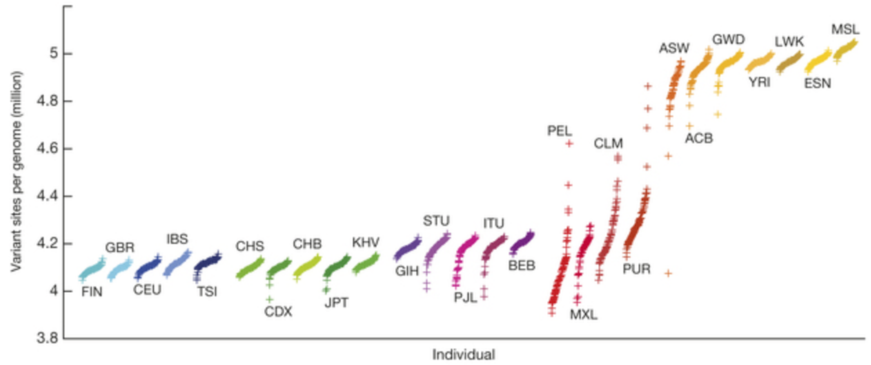


Figure 2: Population structure and demography.

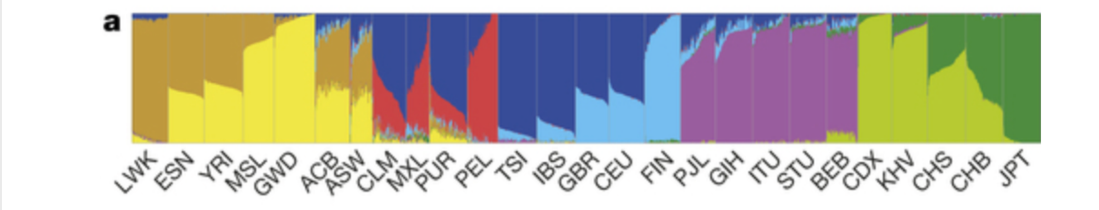
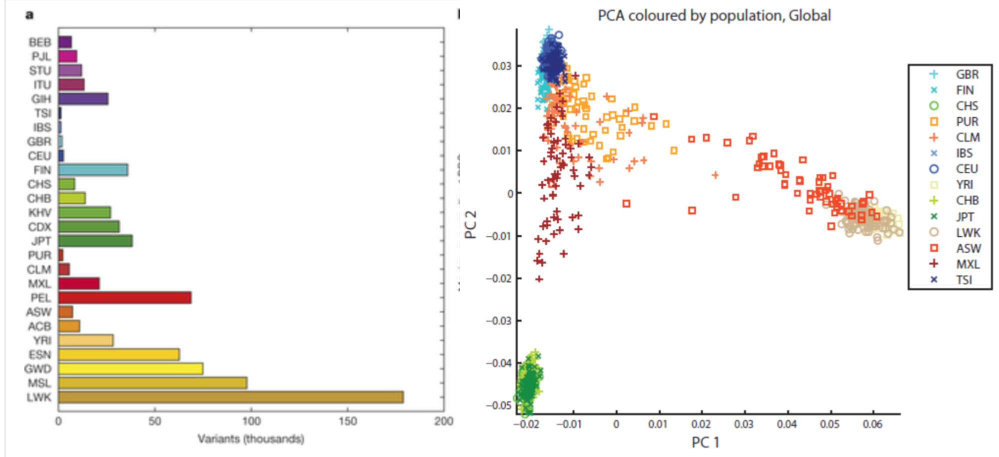
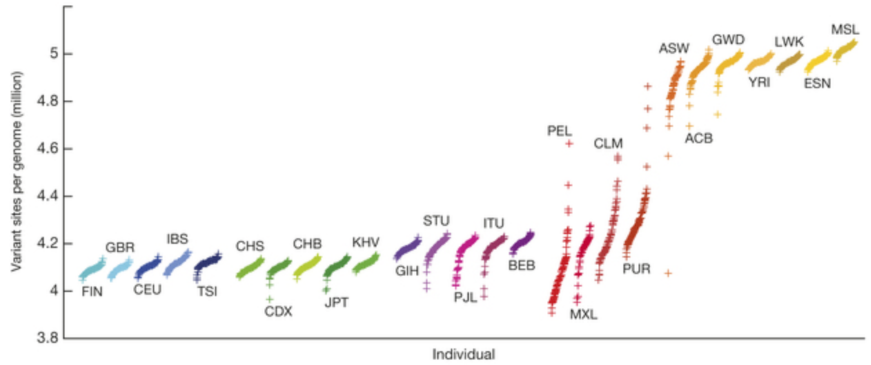


Figure 3: Population differentiation.



Federated Analysis of Data

- Work done by Neelem Memon (BCGSC), Jason Foong (HSC)
- Several of the analyses are straightforward; one is more complicated
- All come down to being able to readily access genotype matrix (does individual *i* have variant *j*)



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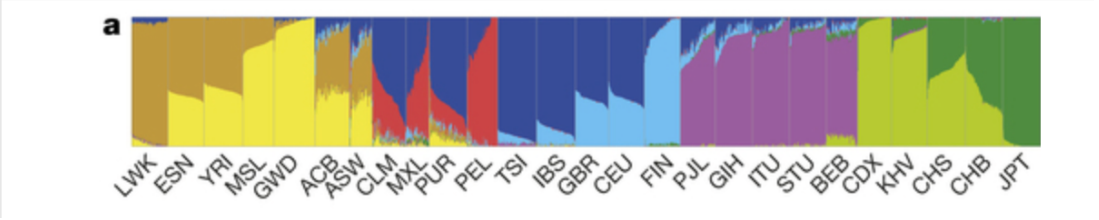

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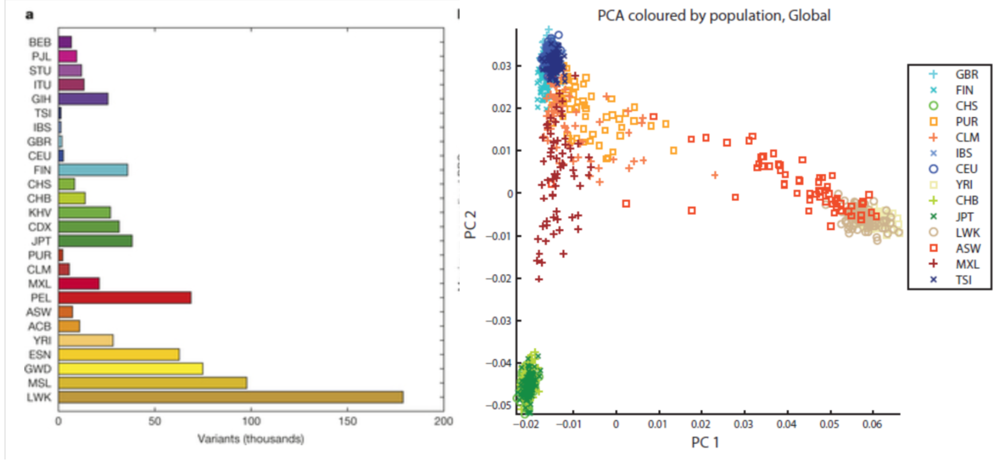

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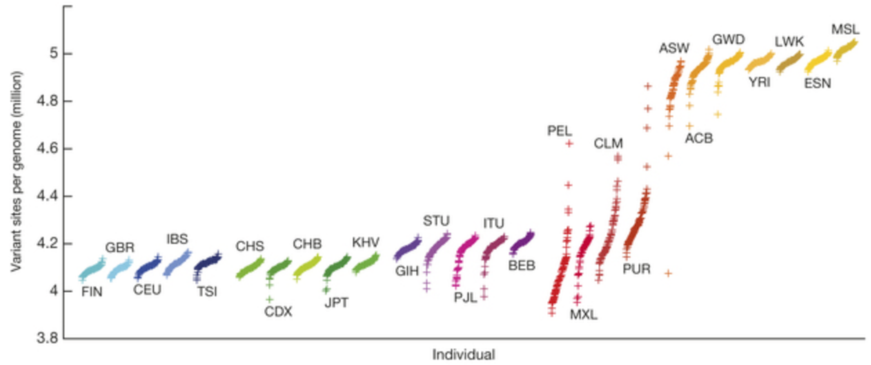
Federated Analysis of Data

- Existing API too slow!
  - Made 4x speed improvements, contributed back to GA4GH
  - Added specific genotype API. (15x)
  - Developed process distributing updated servers across the network
- Analysis now being completed (code already in place)



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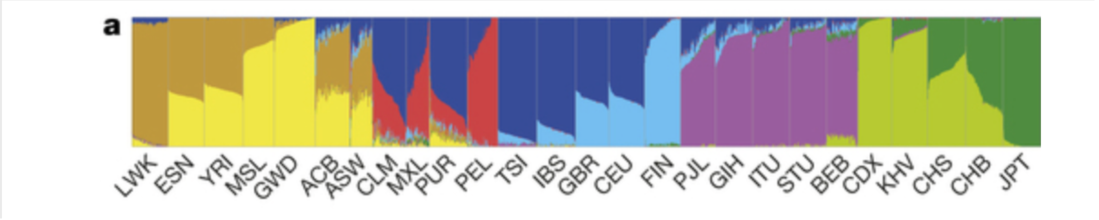

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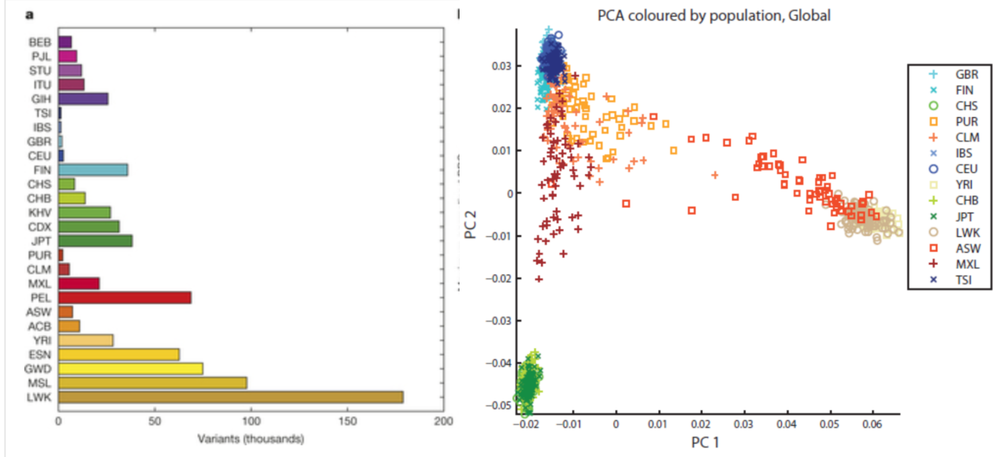
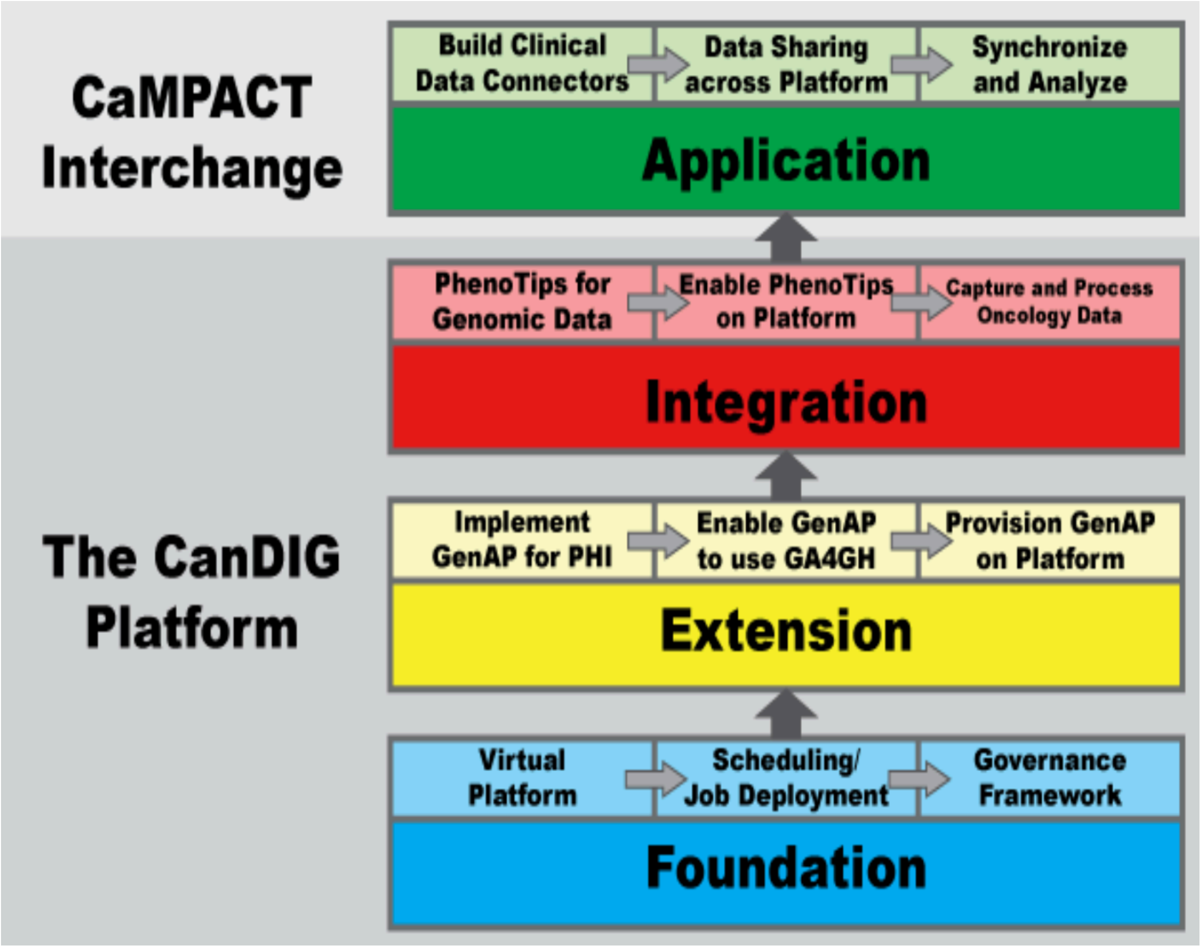


Layered Design

- GA4GH (++) layers provide foundational data movement/ access layer



CaMPACT Interchange

Build Clinical Data Connectors → Data Sharing across Platform → Synchronize and Analyze

Application

PhenoTips for Genomic Data → Enable PhenoTips on Platform → Capture and Process Oncology Data

Integration

The CanDIG Platform

Implement GenAP for PHI → Enable GenAP to use GA4GH → Provision GenAP on Platform

Extension

Virtual Platform → Scheduling/ Job Deployment → Governance Framework

Foundation

Foundation TODOs:

- Support the PROFYLE project (Precision Oncology For Young peopLE)
  - Dynamic data directory
  - David Bujold, McGill
- Full authentication:
  - Dustin Hu, Kevin Chan, UHN
  - GENIE data
- Portal:
  - Carol Gauthier, Sherbrooke

TERRY FOX PROFYLE PRECISION ONCOLOGY FOR YOUNG PEOPLE

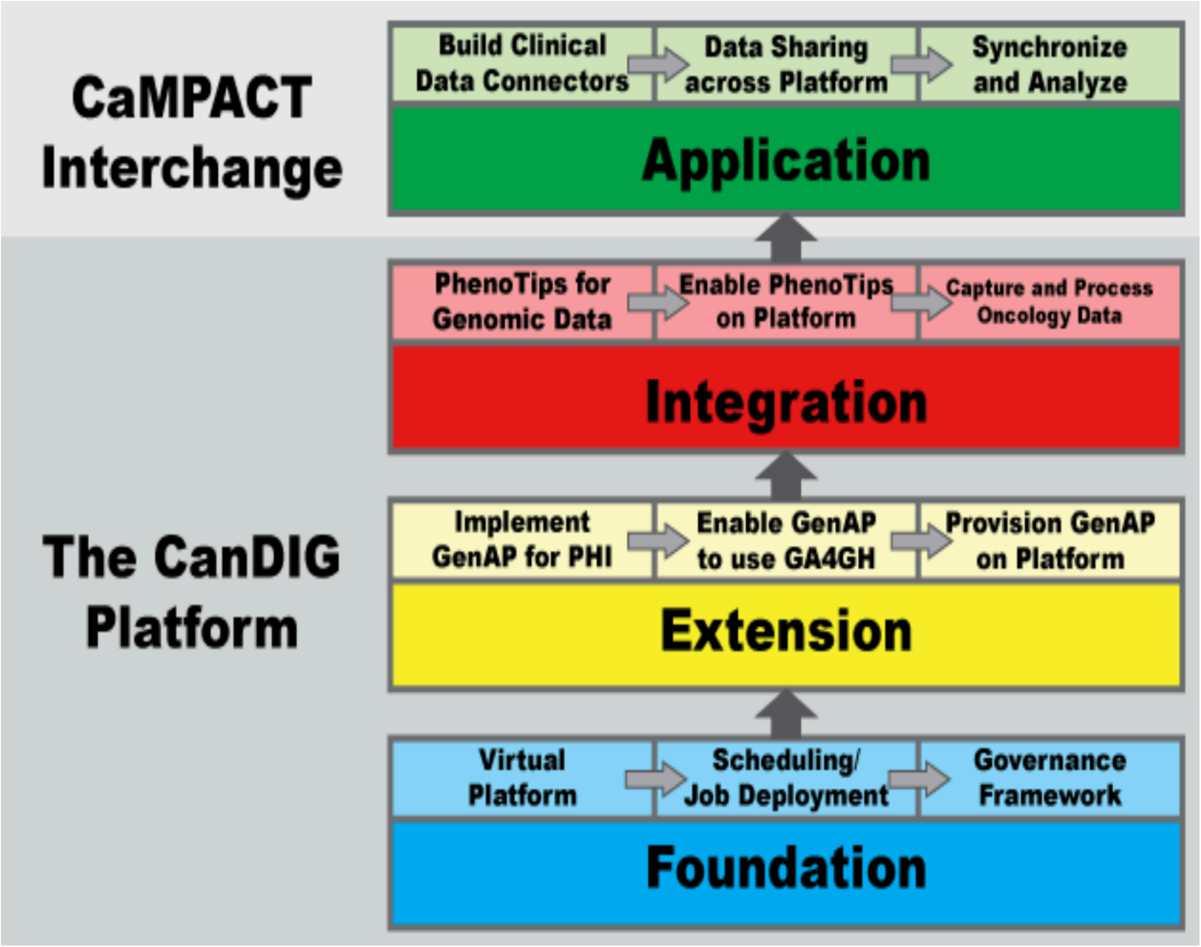
OpenID Connect

AACR American Association for Cancer Research FINDING CURES TOGETHER™

PROJECTGENIE Genomics Evidence Neoplasia Information Exchange

Layered Design

- Then CanDIG-enable existing bioinformatics pipelines
- GA4GH (++) layers provide foundational data movement/ access layer



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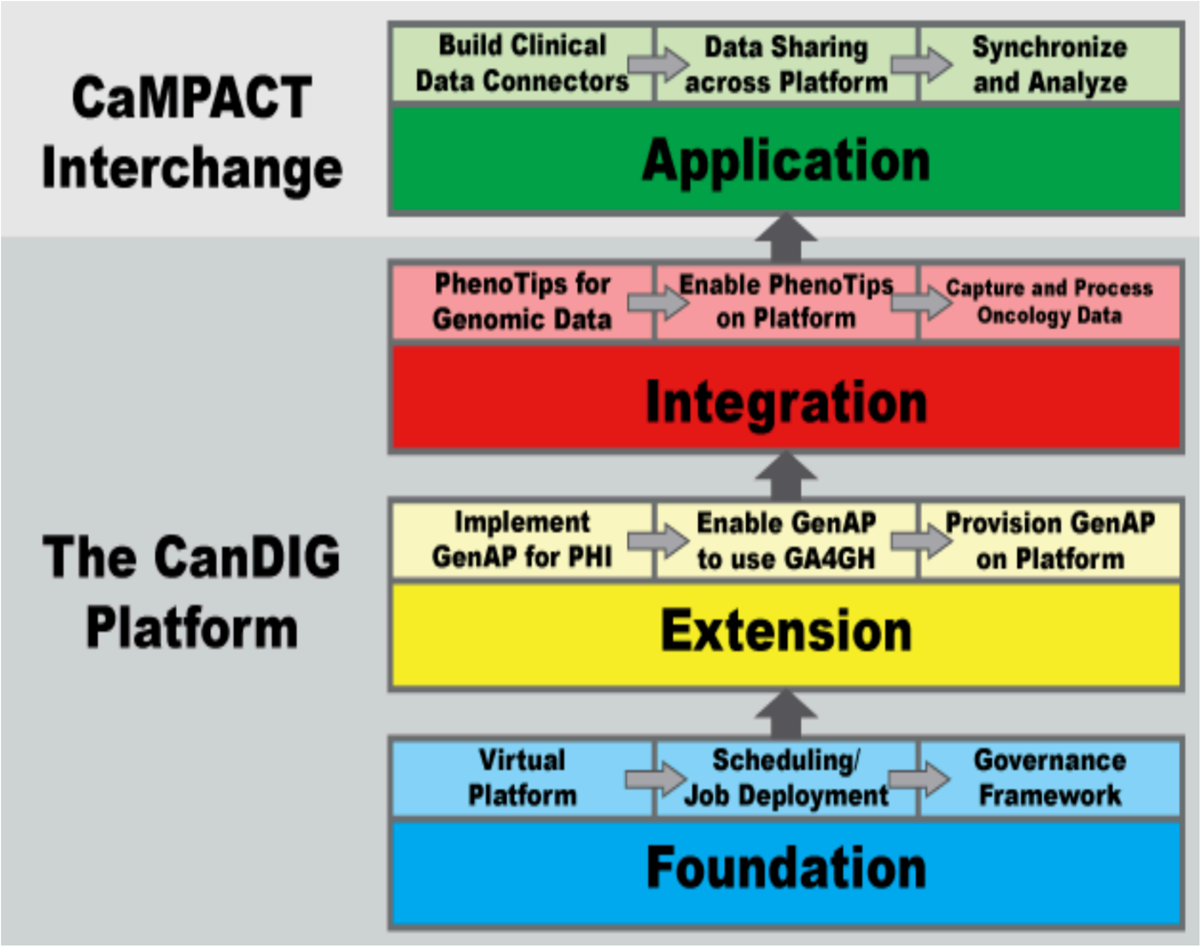
Layered Design

- Support PhenoTips (allow integration of phenotypic data)
- Then CanDIG-enable existing bioinformatics pipelines
- GA4GH (++) layers provide foundational data movement/ access layer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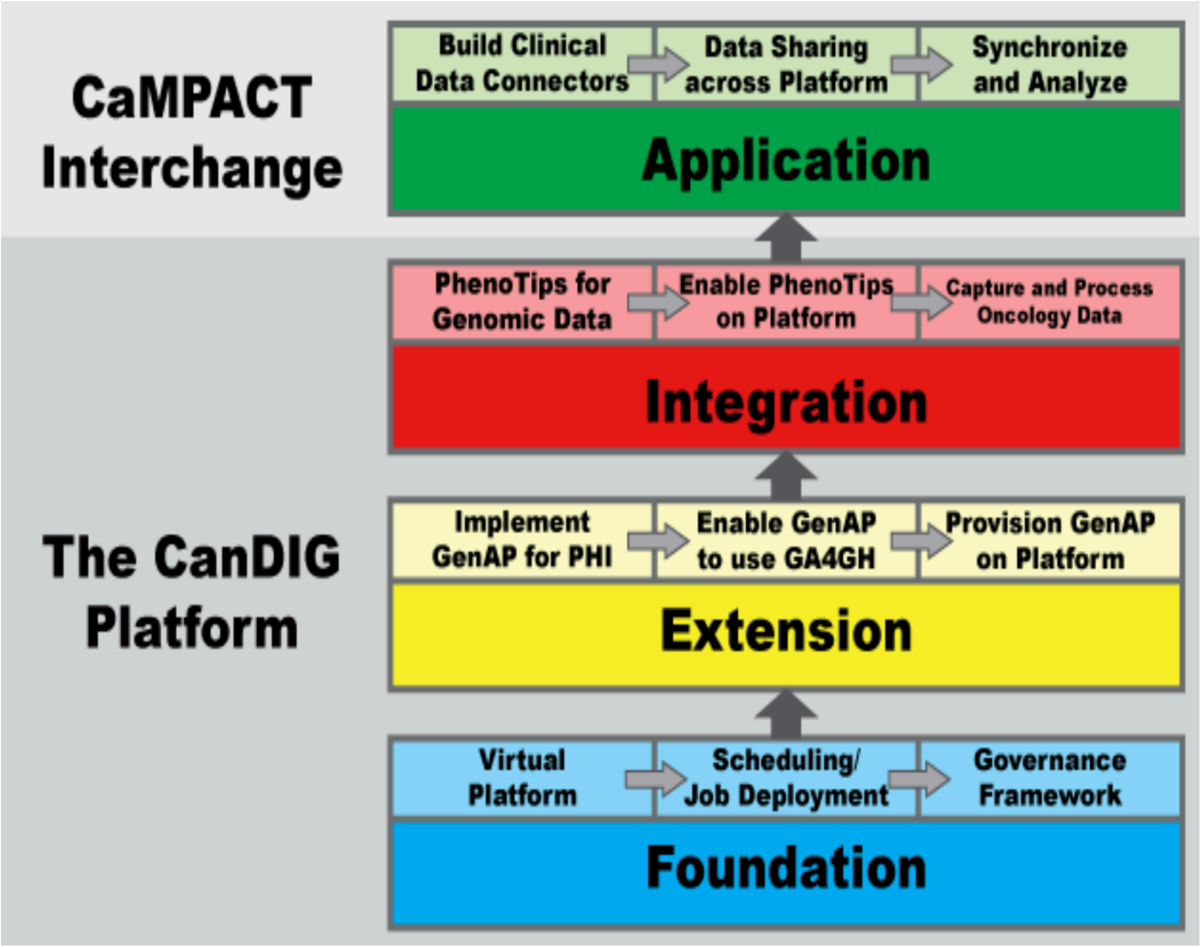
Foundation

Layered Design

- Enable clinical studies atop the platform
- Support PhenoTips (allow integration of phenotypic data)
- Then CanDIG-enable existing bioinformatics pipelines
- GA4GH (++) layers provide foundational data movement/ access layer



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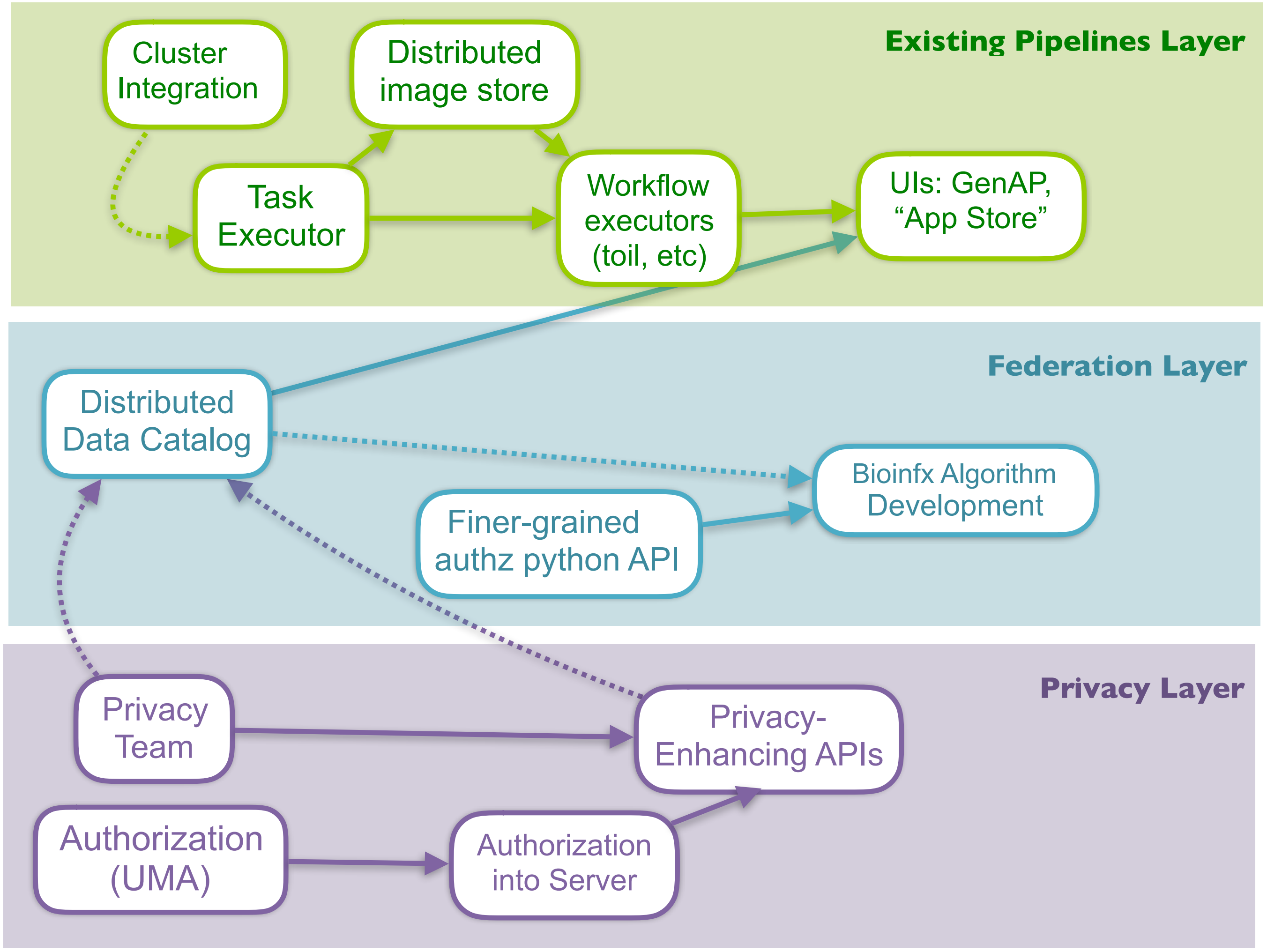
Future Plans

- Lots of cool, important, hard problems ahead:
  - Bioinformatics algorithms (joint calling?) on distributed data
  - Federated Authorization (UMA)
  - Orchestrating workflows across independent sites



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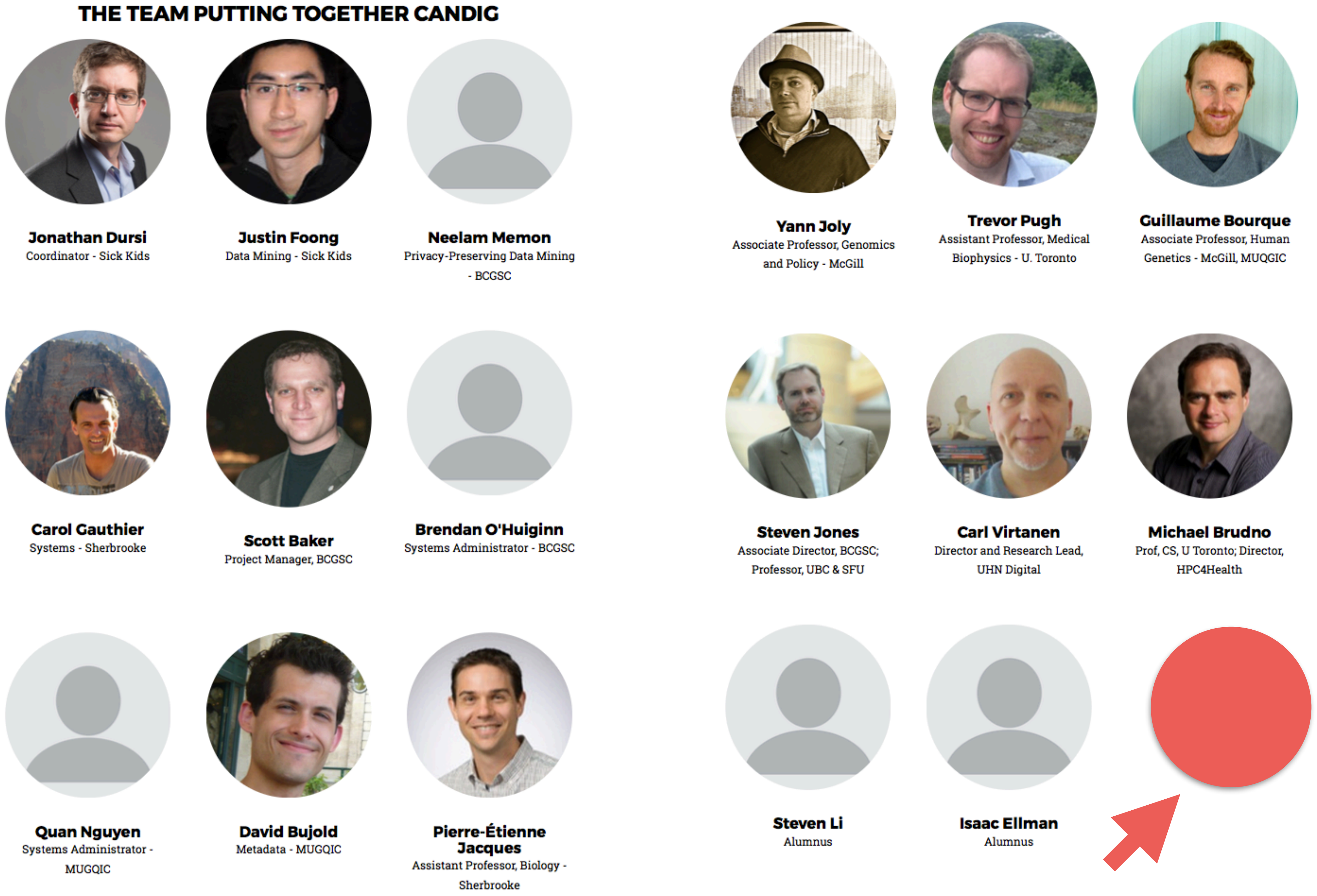
Come Work With Us!



THE TEAM PUTTING TOGETHER CANDIG

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Data Mining - Sick Kids

Neelam Memon
Privacy-Preserving Data Mining - BCGSC

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Systems - Sherbrooke

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Project Manager, BCGSC

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Systems Administrator - BCGSC

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Trevor Pugh
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Carl Virtanen
Director and Research Lead, UHN Digital

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Steven Li
Alumnus

Isaac Ellman
Alumnus

You (could be) here

CanDIG

National Analysis of Distributed Private Genomic Data

Come Work With Us!

- **CanDIG**: CanDIG
  - Keep an eye on https://CanDIG.github.io
- **C3G:** Canadian Centre for Computational Genomics
  - Jr/Sr Bioinformatician
  - Postdoc/RA
  - https://ccm.sickkids.ca; ccm.admin@sickkids.ca