THE INNOVATION CENTER FOR BIOMEDICAL INFORMATICS

G-DOC *Plus*
Population genetics use case

Innovation Center for Biomedical Informatics

Georgetown University

Georgetown | Lombardi

Background

- Common variants in the CYP family cause modified drug function
- These variants differ greatly by ethnicity.
- Drug metabolizer status/Phenotype can be:

Drug metabolizer status	Copies of variant	Response to drug
Ultra rapid metabolizer (UM)	5-6 copies (due to gene amplification)	High
Extensive Metabolizers (EM)	2 copies	Normal
Intermediate Metabolizers (IM)	1 copy	Medium
Poor metabolizer (PM)	Both copies deleted	Low response/ Adverse effect

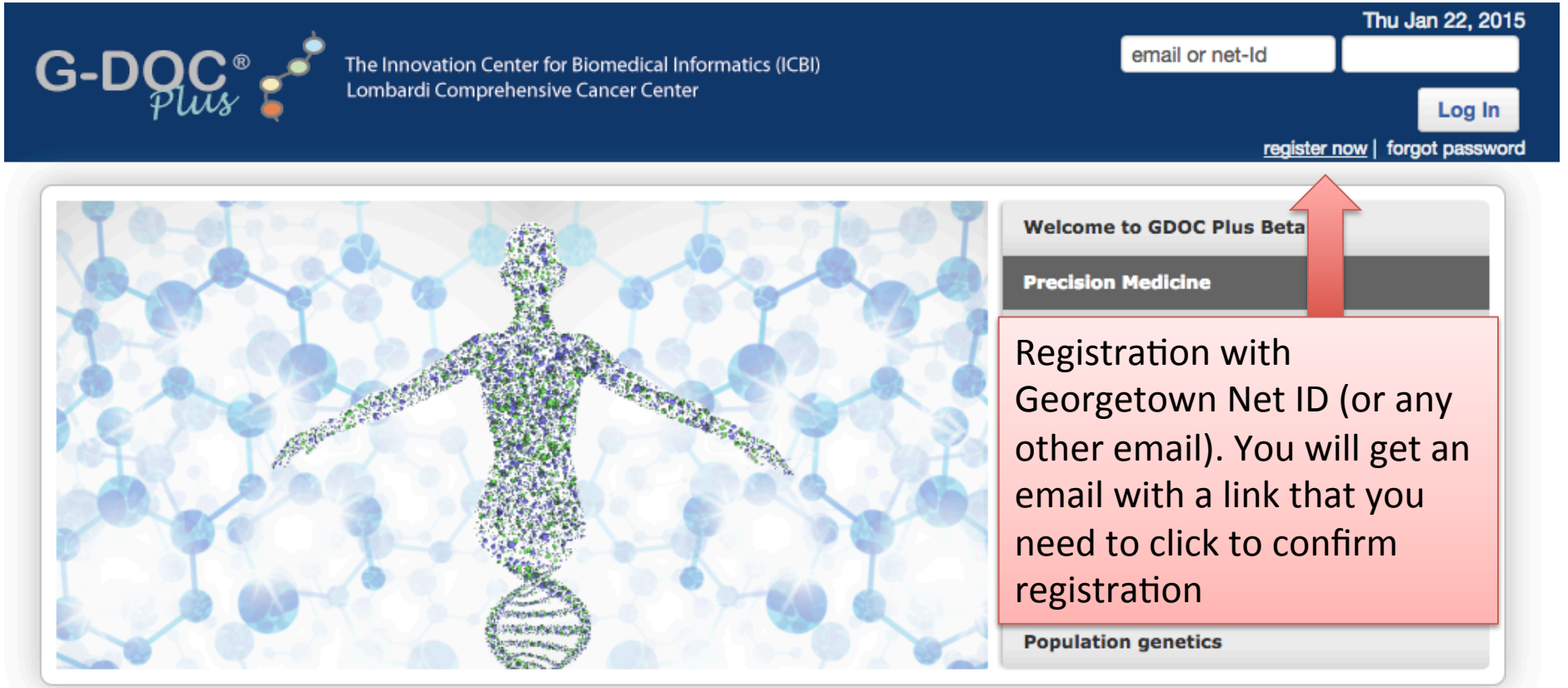
Case study: Drug metabolizer status search

- CYP2C19 is known to be involved in clopidogrel (Plavix) metabolism, and the activity of the drug depends on the active metabolite.
- Example query: ***How common is the "poor metabolizer" phenotype in CYP2C19 in the 1000 genomes dataset?***

Overview

- Register
- Login
- Navigation
- Population genetics use case

First time user



Understanding Data in G-DOC Plus

It all begins with a study...

All data in G-DOC Plus derives from studies on topics such as breast cancer, wound healing, or even 1,000 Genomes. Each study may contain clinical and/or biospecimen data. Below is an overview of studies by topic.
*

* private studies, ones which are uploaded and marked private, are not counted here

News

October 02, 2014: ICBI Symposium 2014 [read]

May 02, 2014: Featured in Frontiers' Top 10 2013 Most viewed Genetics Research articles [read]

March 12, 2014: AAAS Big Data Blog [read]

Login

G-DOC® Plus

The Innovation Center for Biomedical Informatics (ICBI)
Lombardi Comprehensive Cancer Center

Thu Jan 22, 2015

kb472 ••••••••••••••

Log In

register now | forgot password

Welcome to GDOC Plus Beta!

The Georgetown Database of Cancer Plus other diseases (G-DOC Plus) is a precision medicine platform containing molecular and clinical data from thousands of patients and cell lines, along with tools for analysis and data visualization. The platform enables the integrative analysis of multiple data types to understand disease

Precision Medicine

Translational research

Population genetics

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G-DOC Plus | Home | Studies | Lists | Analyses | Groups | Notifications | Study Options | Help | kb472

G-DOC Plus Launch Pad!

Welcome! The G-DOC Plus Launch Pad is your one-stop resource for learning more about G-DOC and getting started on the platform.

Studies

Lists

Groups

Notifications 0

It All Starts Here!

G-DOC has over seventy studies, We know this can be overwhelming! Let us guide you to choose the study that is relevant for your research.

Let's Go! ›

Select area of interest

What's your area of interest?

G-DOC Plus has three overlapping entry points for the user based on their interests. Choose your area of interest to launch the workflow.

Precision Medicine

Patients' molecular diagnostics and clinical data.

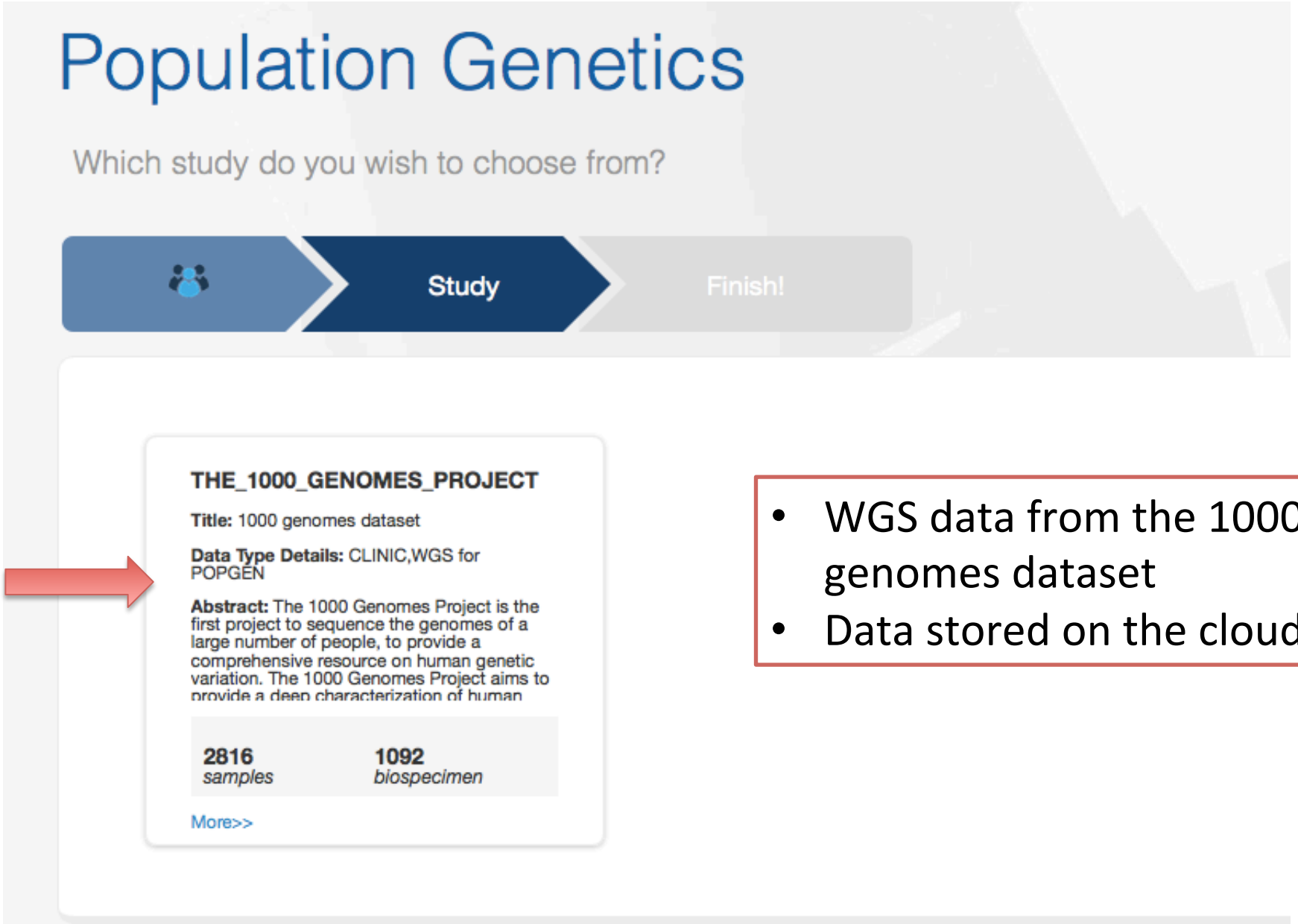
Translational Research

Analytic tools and workflows to enable discovery.

Population Genetics

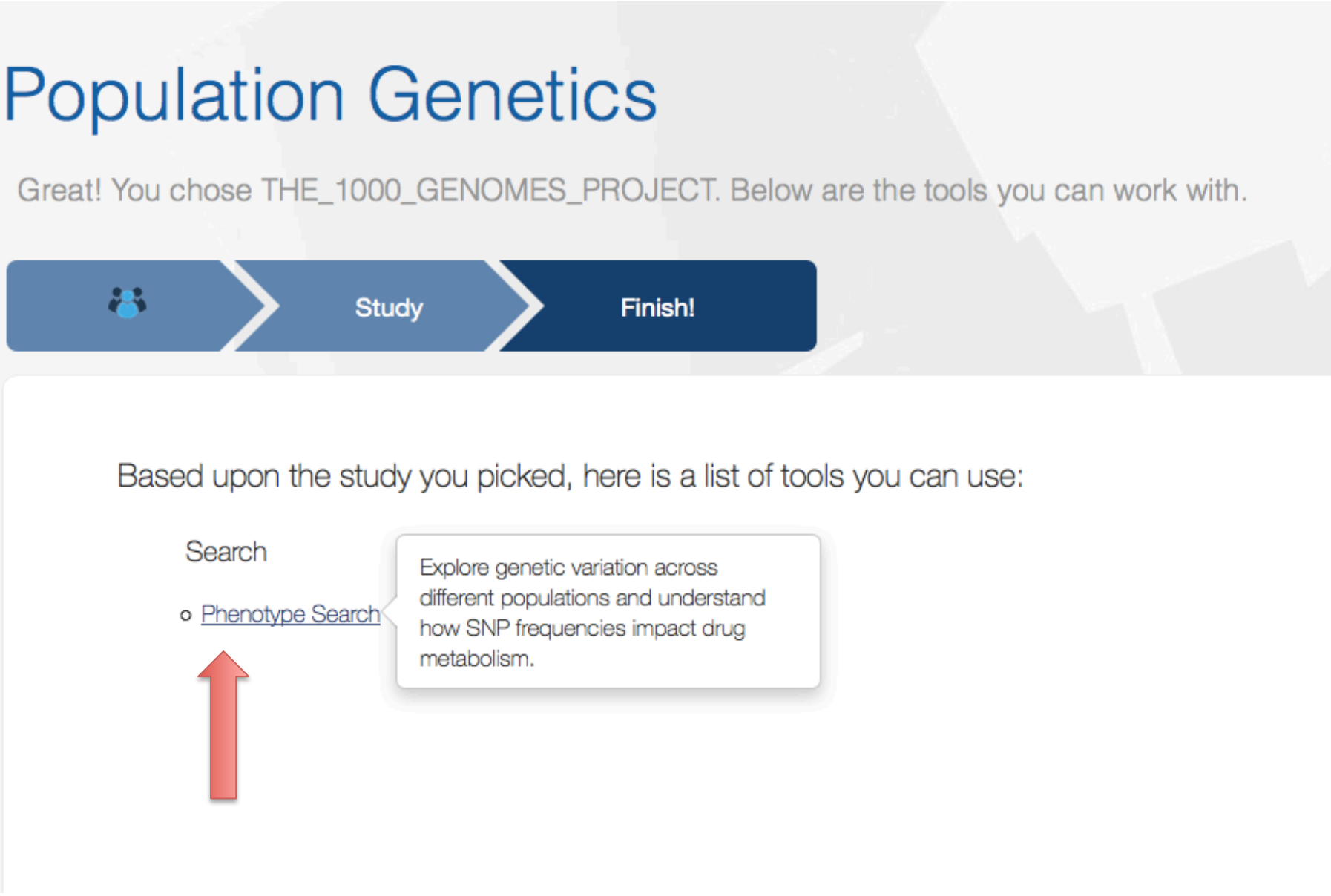
Race-based, genomic reporting and comparison.

Select study



- WGS data from the 1000 genomes dataset
- Data stored on the cloud

Pick tool


Population Genetics
Great! You chose THE_1000_GENOMES_PROJECT. Below are the tools you can work with.
Study
Finish!
Based upon the study you picked, here is a list of tools you can use:
Search
Phenotype Search
Explore genetic variation across different populations and understand how SNP frequencies impact drug metabolism.

Phenotype Frequency Search

Current Study: THE_1000_GENOMES_PROJECT change study?

Total ~ 62%

Genes

CYP2C19 ×

Phenotype

PM × IM ×

Defining SNP(s)

Enter RSID ID

Phenotypes by Gene

Druggabl	Diplotype	Activity1	Activity2	Phenotype	Defining SNP(s)	AMR	AFR	ASN	EUR	SAN
⊟ CYP2C19										
NO	*3/*1	normal	none	IM	*3=4986893	0.0	0.41	5.24	0.0	0.0
NO	*4/*1	normal	none	IM	*4=28399504	1.1	0.0	0.35	0.0	0.0
NO	*3/*2A	none	none	PM	*3=4986893*2A=42442	0.0	0.0	3.85	0.0	0.0
NO	*1/*2A	normal	none	IM	*2A=4244285	19.89	19.92	48.25	12.93	0.0
NO	*8/*1	normal	none	IM	*8=41291556	0.0	0.81	0.0	0.26	0.0
NO	*3/*3	none	none	PM	*3=4986893	0.0	0.0	0.35	0.0	0.0
NO	*13/*2A	normal	none	IM	*2A=4244285*13=1787	0.0	0.41	0.0	0.0	0.0
NO	*2A/*2A	none	none	PM	*2A=4244285	1.1	2.85	6.64	0.26	0.0
NO	*2B/*2A	none	none	PM	*2B=17878459*2A=424	0.0	0.0	0.0	1.32	0.0
NO	*1/*2B	normal	none	IM	*2B=17878459	1.66	0.0	0.0	6.07	0.0

50 View 1 - 10 of 10

What does this mean ?

- Majority of PMs and IMs (~62%) are East Asians
- Only ~ 20% of PMs are AMR (Ad-mixed American)
- ~ 20% are AFR (Africans)
- ~ 20% are EUR (Europeans)

Total numbers for each drug metabolizer status

Phenotype (Drug metabolizer status)	Ad-mixed American (AMR) %	African (AFR) %	East Asian (ASN) %	European (EUR) %
UM (*17/*17)	2	6	0	5
UM or EM (*1/*17)	16	23	2	29
EM	55	35	31	38
IM	23	22	54	19
PM (*2/*2, *2/*3, *3/*3)	1	3	11	1
Not PM	3	9	2	8
IM or PM	0	1	0	0
Unknown/NA	0	1	0	0
TOTAL %	100	100	100	100

- 11% of the East Asians were PMs, ~ 3% Africans, and ~ 1 % Ad mixed Americans were PMs
- We can see the opposite trend for UM where ~ 5% Europeans, ~ 6% of Africans, ~ 2 % of Ad-mixed Americans were UMs, none of East Asians were UMs

How can this info be used ?

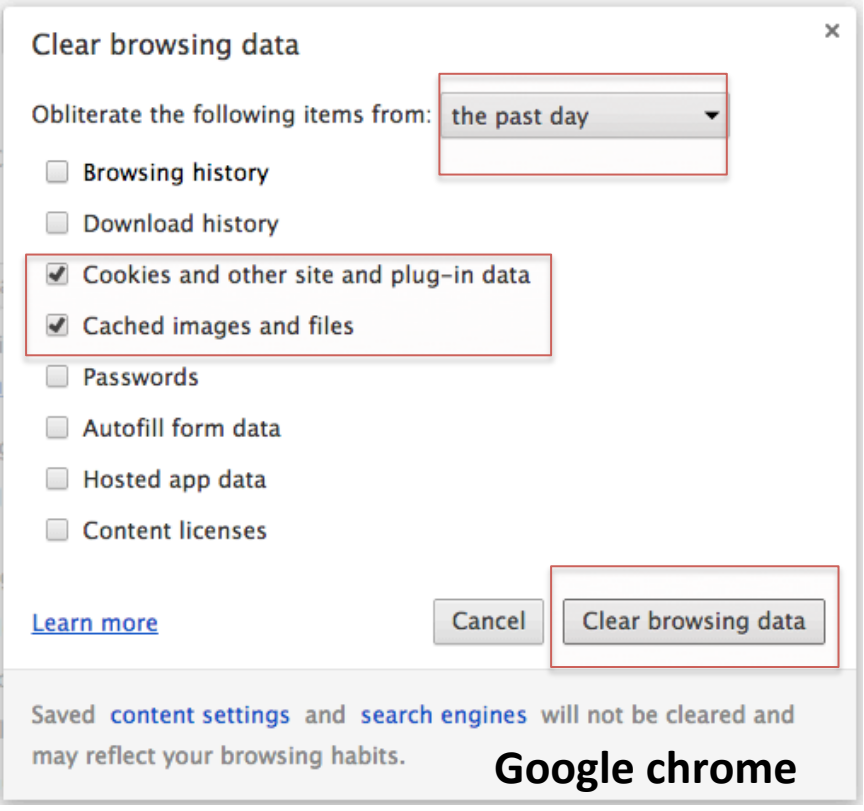
- Assess whether an individual with a SNP of interest will have efficacy to a drug or not
- Help understand SNP population frequencies for specific drug targets in new drug applications,
  - help inform broad applicability of a drug to different populations.
  - A new drug's sponsor can evaluate all relevant target variants in various subpopulations
- Adjust drug dosage,
  - UMs may need a smaller dose to get required efficacy compared to EMs;
  - an alternative drug treatment may be recommended for PMs

General tips

- G-DOC *Plus* works best is you don't use the **back** button in the web browser repeatedly.
- Once you select a study, most tools will be easily available from the the top menu bar inside G-DOC *Plus*.

Clearing cache

- If the G-DOC web page does not respond after several seconds, try:
  - refreshing the page.
  - Log out and log back in, and try again
  - If the above two do not work, its possible that your web browser cache may need to be cleared
    - For Google chrome, go to Settings -> Show Advanced Settings -> Under “Privacy”, select Clear Browsing data
    - For Mozilla Firefox, go to Preferences -> Advanced -> Network -> Under “Cached Web Content” -> Clear now



Google chrome

Mozilla Firefox