

smmart g2p

G2P – genotype to phenotype

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For **researchers**, who need to investigate genotype phenotype associations, smmart-g2p is a **search tool that aggregates evidence** from several knowledge bases unlike ad-hoc searches, the product allows the researcher to **focus on the evidence, not on the search.**

Current workflow

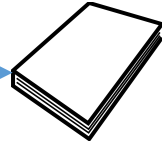
(simplified)



Patient
Sample



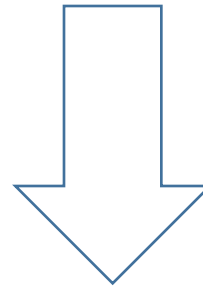
Pipeline
Annotations



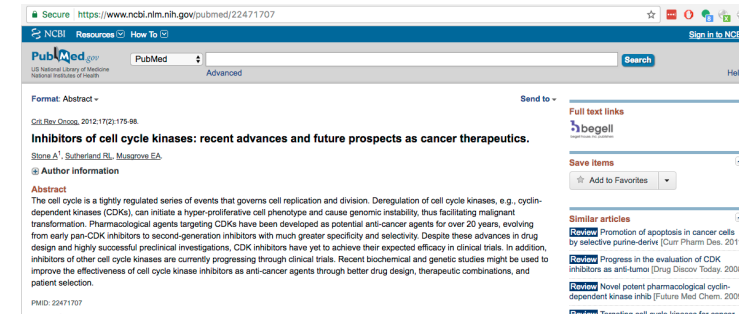
Gene Trails
Report



Lots of reading
google, pubmed, ...



recommendations



Where g2p fits in

(simplified)

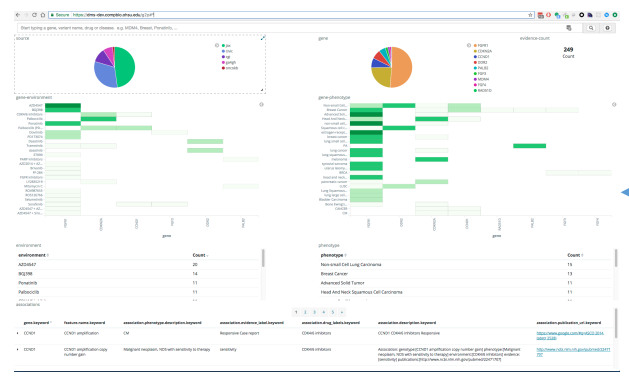


Patient Sample

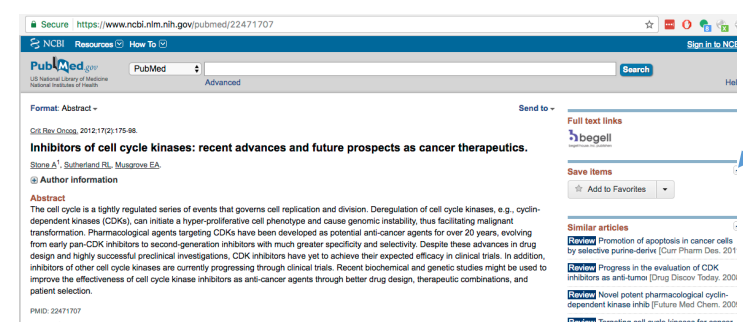
Pipeline and annotations

Gene Trails Report

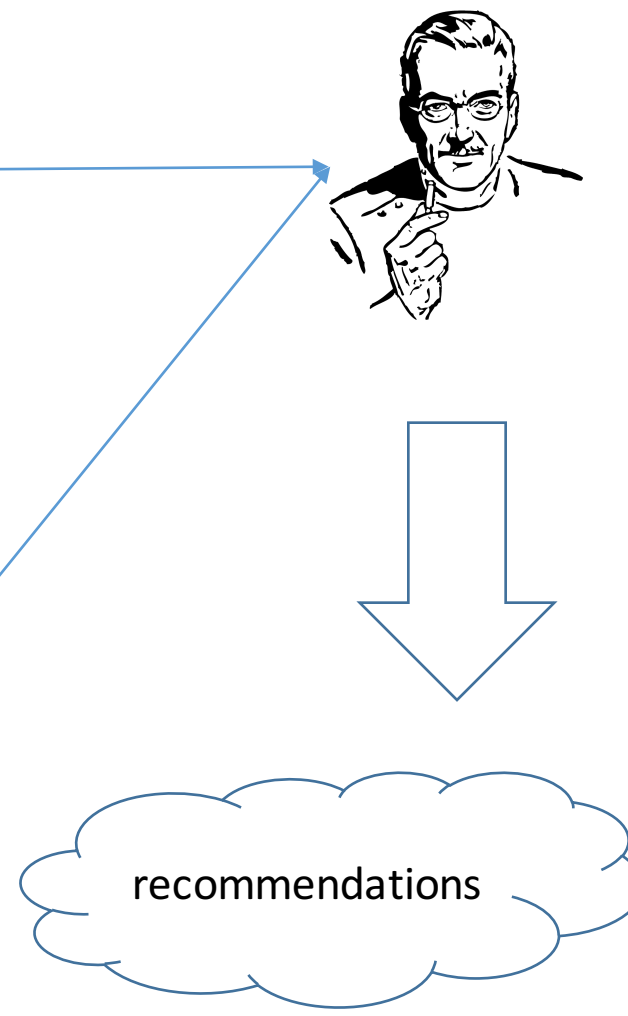
- oncokb
- civic
- ga4gh (rodrigo)
- jax.org
- Cancer Genome Interpreter
- Molecular match



Search assistant



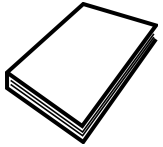
Focused research



The details

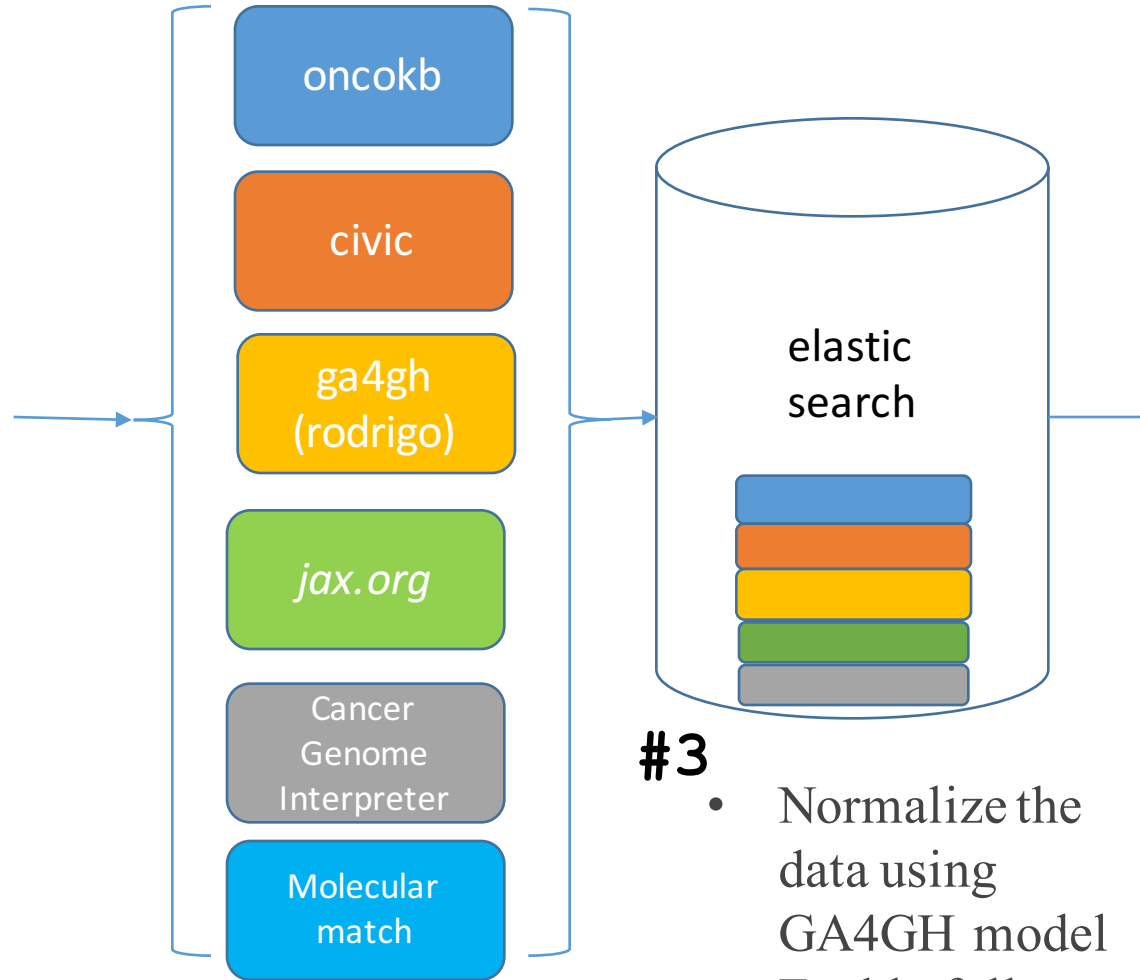
(simplified)

['CCND1', 'CDKN2A', 'CHEK1', 'DDR2',
'FGF19', 'FGF3', 'FGF4', 'FGFR1', 'IDO1',
'IDO2', 'MDM4', 'RAD51D']



#1

List of genes
from
GeneTrails,
Pathways or
other annotation
source



Knowledge Bases

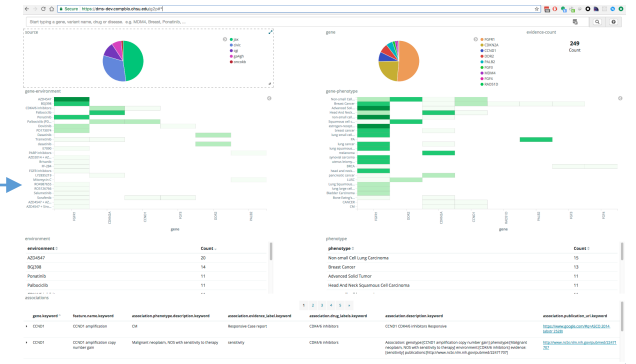
#2 Harvest the
evidence from
trusted sources

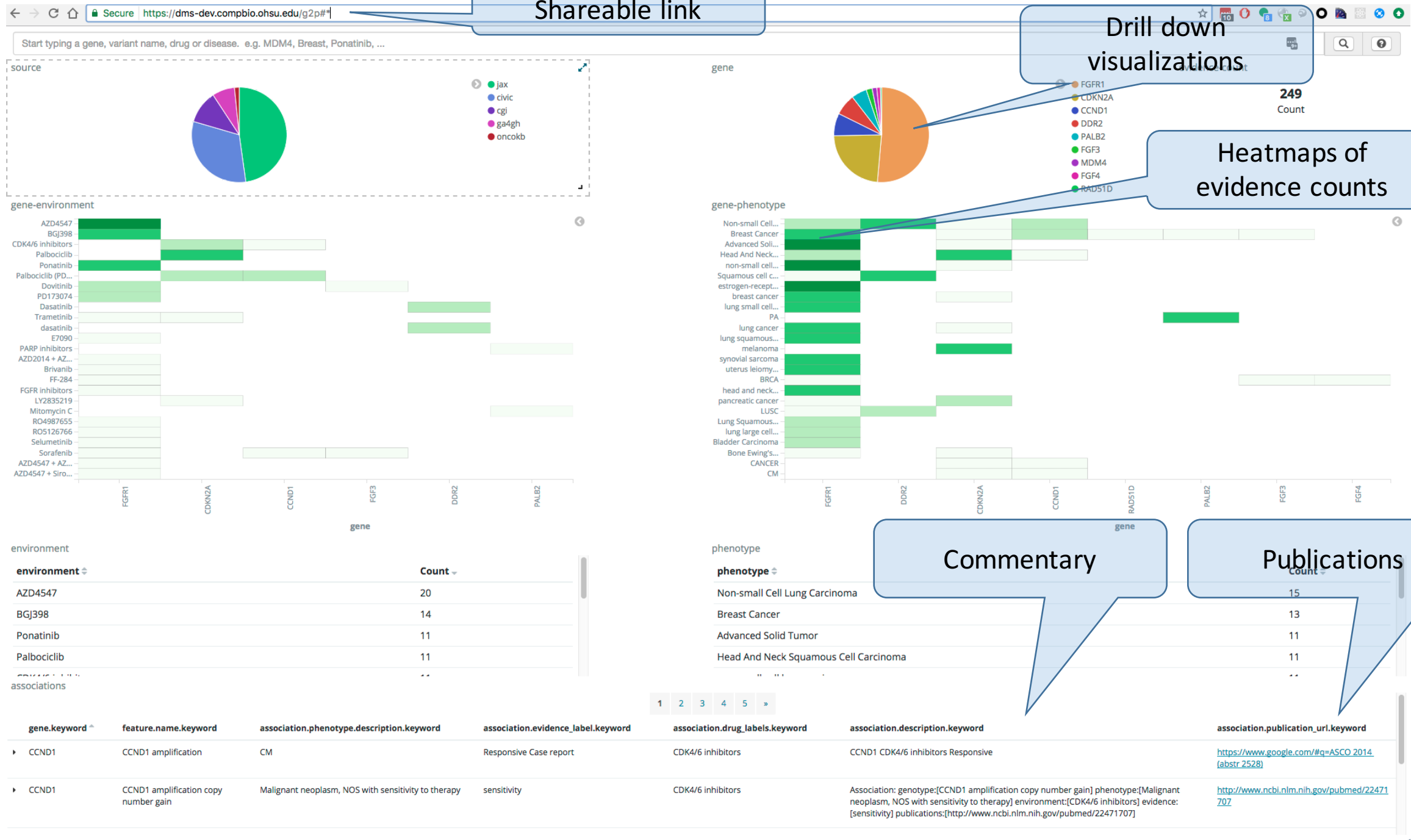
#3

- Normalize the
data using
GA4GH model
- Enable full text
search
- Populate other
consumers
(kafka)

#4

Visualize and
query



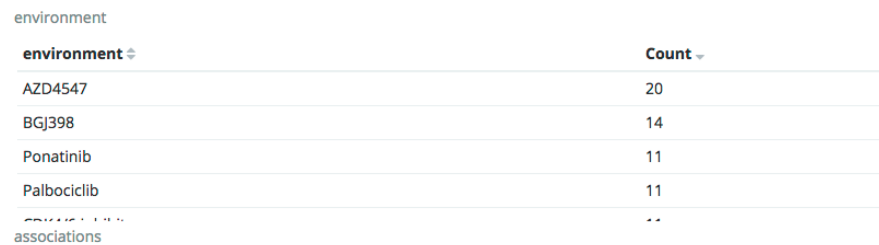


Worked Examples

Show me all evidence for a
patient

“Default”

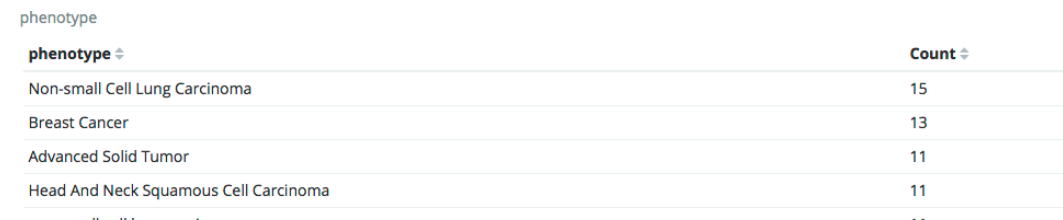
Source	Percentage
jax	~55%
civic	~25%
cgi	~10%
ga4gh	~5%
oncokb	~2%



associations

A pie chart illustrating the distribution of 10 genes. The largest segment is FGFR1 (orange), followed by CDKN2A (olive green) and CCND1 (blue). Other genes include DDR2 (red), PALB2 (teal), MDM4 (purple), FGF4 (pink), FGF3 (green), and RAD51D (light green).

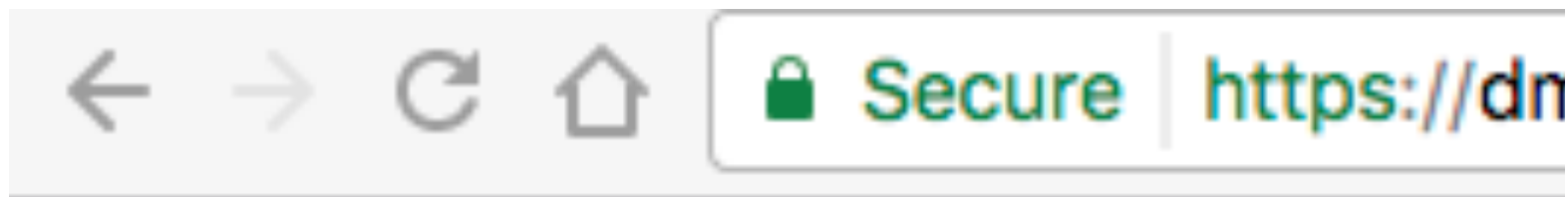
Gene	Color
FGFR1	Orange
CDKN2A	Olive Green
CCND1	Blue
DDR2	Red
PALB2	Teal
MDM4	Purple
FGF4	Pink
FGF3	Green
RAD51D	Light Green



Click on any field to constrain further

I'm just interested in CCND1 or
FGFR1

Just "Google" it



CCND1 OR FGFR1

Constrain using terms and ['AND', 'OR', 'NOT']

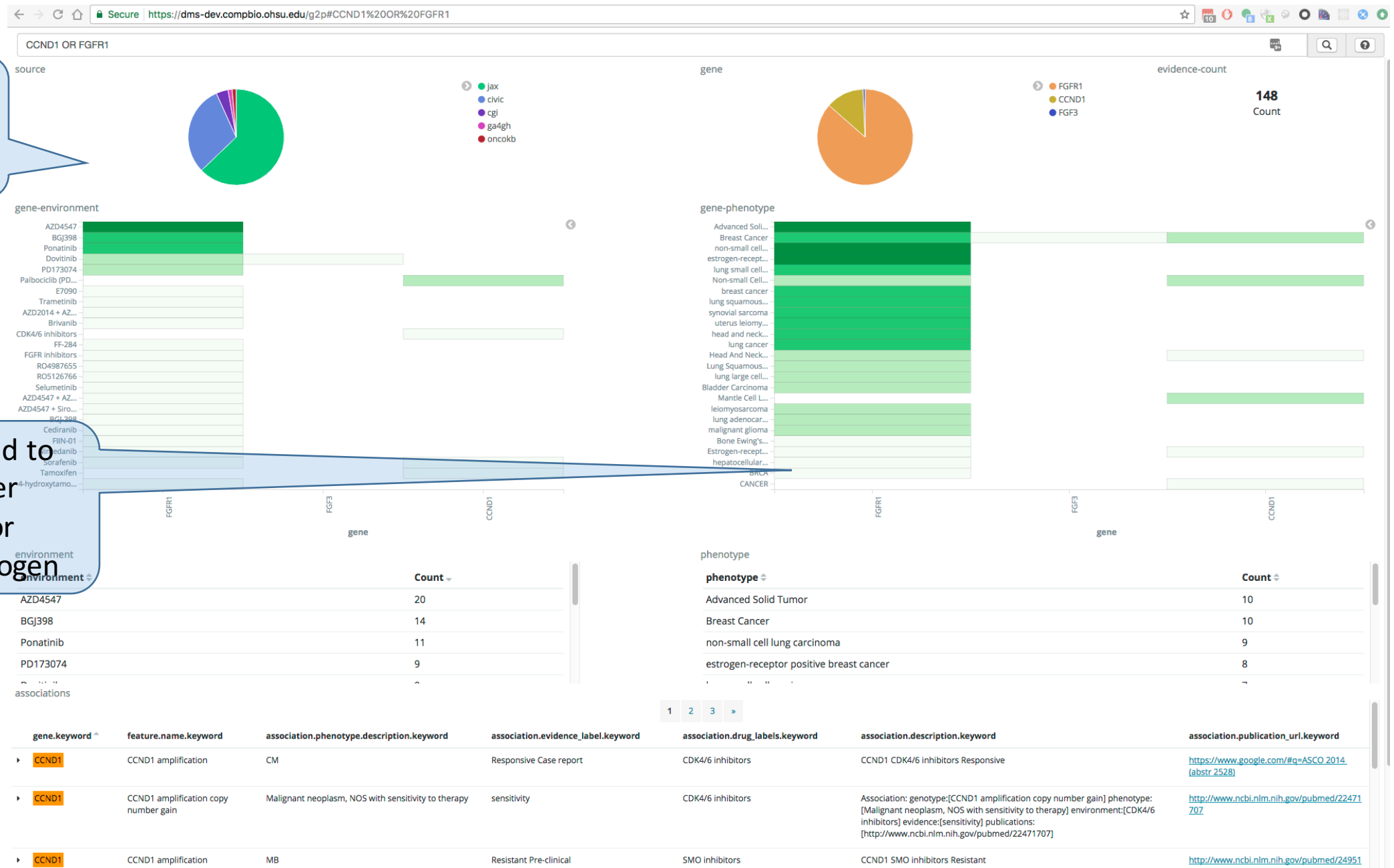
FGFR1

FGFR1 AND head

+FGFR1 +HEAD -LUNG

(+FGFR1 +HEAD -LUNG) OR Gefitinib

A full complement of user query phrases are available



Visualizations reflect results

Click on any field to constrain further e.g. Evidence for FGFR1 and estrogen

Drill down

Short list of evidence

phenotype

phenotype ▾

Count ▾

estrogen-receptor positive breast cancer

8

Sortable list of evidence

association.evidence_label.keyword

association.drug_labels.keyword ▾

association.description.keyword

association.publication_url.keyword

sensitive

Nintedanib

In a preclinical study, Ofev (nintedanib) inhibited the growth of ER-positive breast cancer cells harboring FGFR1 amplification in culture (PMID: 22238366).

<http://www.ncbi.nlm.nih.gov/pubmed/22238366>

sensitive

Lucitanib

In a preclinical study, an estrogen-receptor positive breast cancer cell line harboring FGFR1 amplification demonstrated sensitivity to treatment with Lucitanib (E-3810) in culture (PMID: 27126994).

<http://www.ncbi.nlm.nih.gov/pubmed/27126994>

sensitive

E7090

In a preclinical study, an estrogen-receptor positive breast cancer cell line harboring FGFR1 amplification (PMID: 7506125) demonstrated sensitivity to E7090 in culture, resulting in decreased cell viability (PMID: 27535969).

<http://www.ncbi.nlm.nih.gov/pubmed/7506125>

sensitive

Dovitinib

In a preclinical study, Dovitinib (TKI258) inhibited cell proliferation in estrogen receptor (ER)-positive breast cancer cells harboring FGFR1 amplification in culture (PMID: 22238366).

<http://www.ncbi.nlm.nih.gov/pubmed/22238366>

sensitive

Cediranib

In a preclinical study, Cediranib (AZD-2171) inhibited growth of estrogen receptor (ER)-positive breast cancer cells with FGFR1 amplification in culture (PMID: 22238366).

<http://www.ncbi.nlm.nih.gov/pubmed/22238366>

no benefit

Brivanib

In a preclinical study, Brivanib (BMS-540215) did not inhibit growth of estrogen receptor (ER)-positive breast cancer cells with FGFR2 amplification in culture (PMID: 22238366).

<http://www.ncbi.nlm.nih.gov/pubmed/22238366>

resistant

BYL719

In a preclinical study, an estrogen-receptor positive breast cancer cell line harboring an FGFR1 amplification demonstrated resistance to Alpelisib (BYL719) in culture (PMID: 27126994).

<http://www.ncbi.nlm.nih.gov/pubmed/27126994>

sensitive

Alpelisib + Lucitanib

In a preclinical study, an estrogen-receptor positive breast cancer cell line over expressing FGFR1 and expressing a PIK3CA mutation demonstrated sensitivity to

<http://www.ncbi.nlm.nih.gov/pubmed/27126994>

Next steps

- Work with users, gather feedback
- Load alternative data sources [literome, ensemble]
- Load smmart drugs [Olaparib, Folfox, Pembrolizumab, ...]
- Integrate with bmeg (machine learning evidence)
- Improve data normalization
 - Variant naming (HGVS)
 - Ontologies (diseases, drugs, variants)
- Add GA4GH::G2P api (or successor)
- Harden prototype:
 - python notebook
 - web app (deprecate kibana UI)