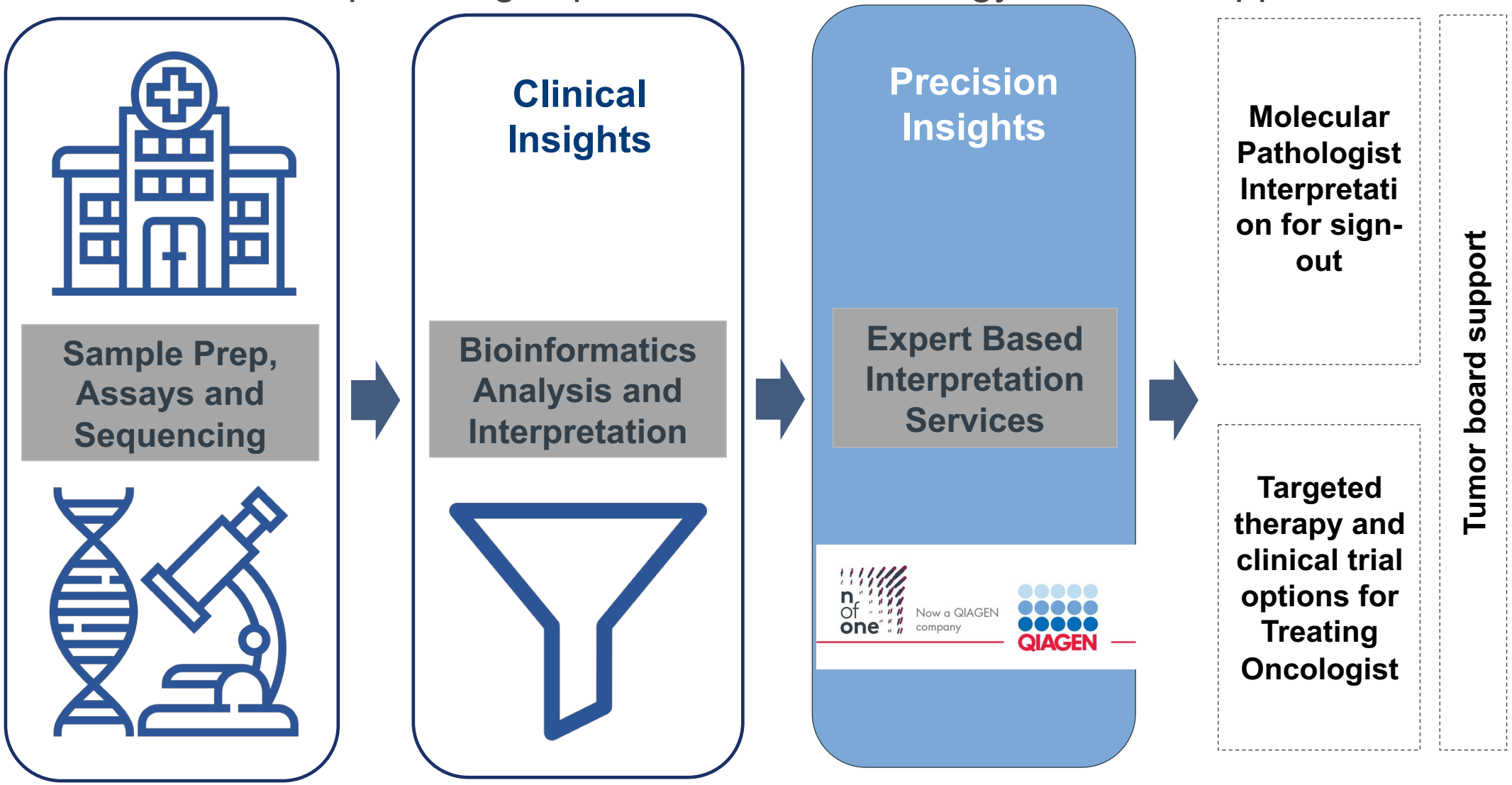
QIAGEN Genomic Insights: Insights from cancer genomic data

The potential to use OmicSoft to visualize N-of-One's genomic data

Kelly Sullivan, PhD.

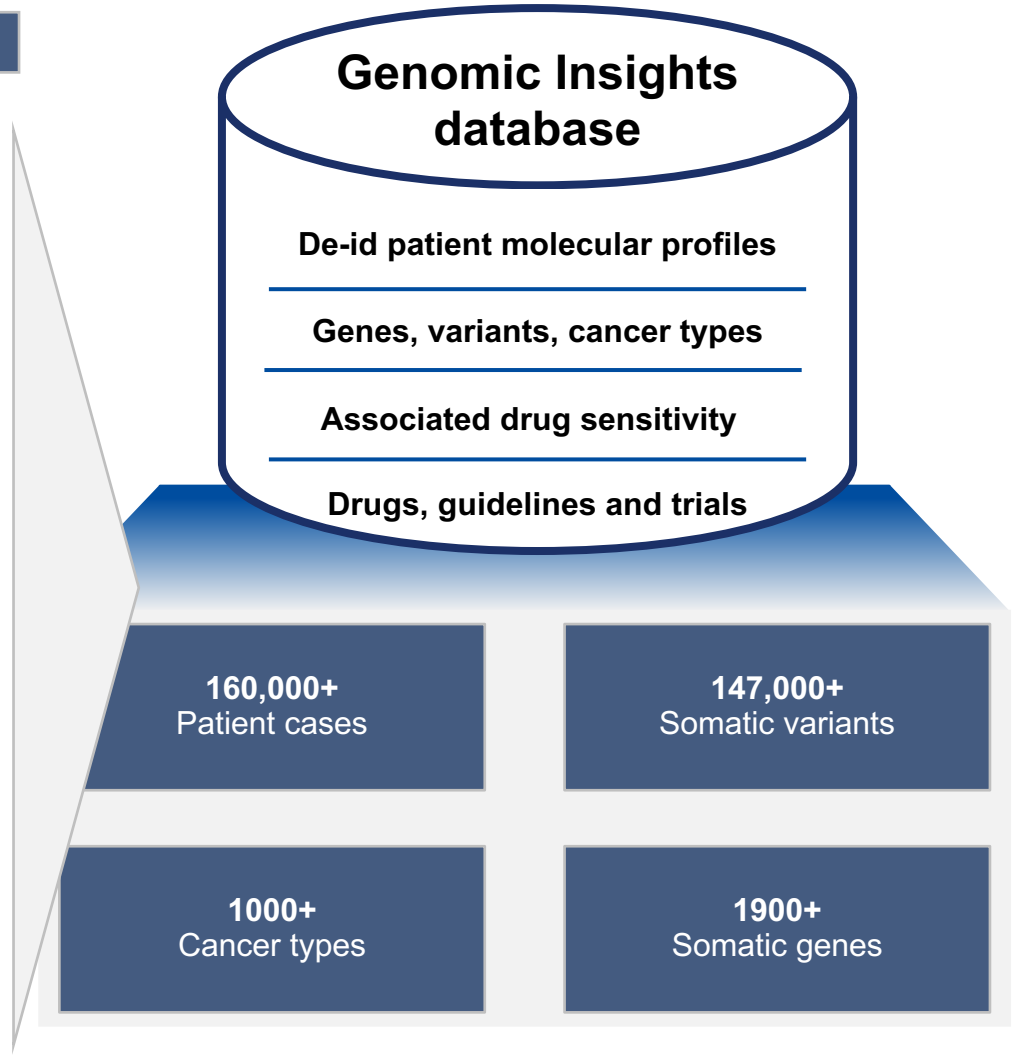
N-of-One is known for providing expert molecular oncology decision support



Genomic Insights database derived from de-identified patient cases

Industry Leading Database

- Derived from **>40 clinical testing labs, >100 different panels for solid and heme cancers**
- **Real-world data** including location, diagnosis, demographics, prevalence of cancer types
- **Manual expert clinical interpretation** including co-occurring variants and other factors
- SNVs, Indels, Fusions, CNVs alteration and **MSI and TMB marker support**
- Derived from both **ctDNA (est. 60%) and non-ctDNA (est. 40%)** sample types
- Rigorous **QMS process** for the development and maintenance of structured, curated database
- Additional **>60,000 new cases interpreted annually** with growing global network of labs



Genomic Insights: offerings and analyses for pharma as a service model

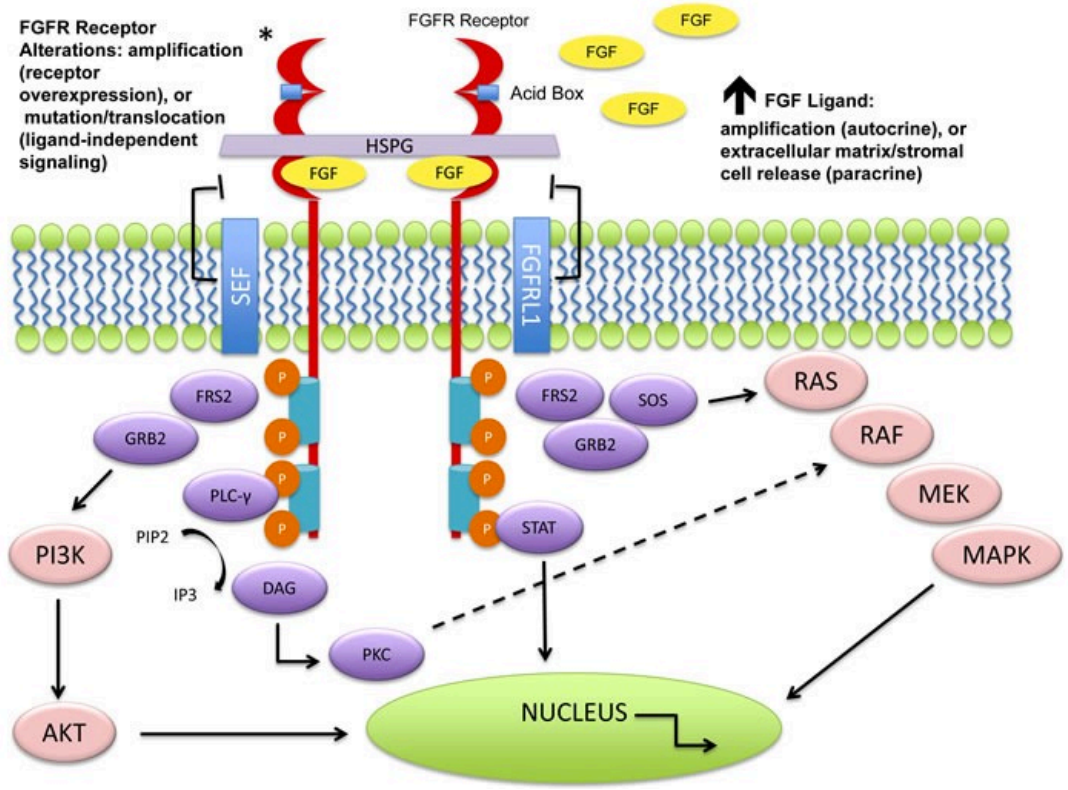
Biomarker and indication selection
gene alteration prevalence / real-world cancer type distribution

Trial cohort stratification & cdx design
variant info / co-occurring variant analysis / assay design considerations

Molecular profiling
clinical trial screening / treatment response analysis

Clinical trial accrual and drug market plans
real-world patient population reporting / clinical trial competitor analysis

Data that is relevant to drug development for precision oncology

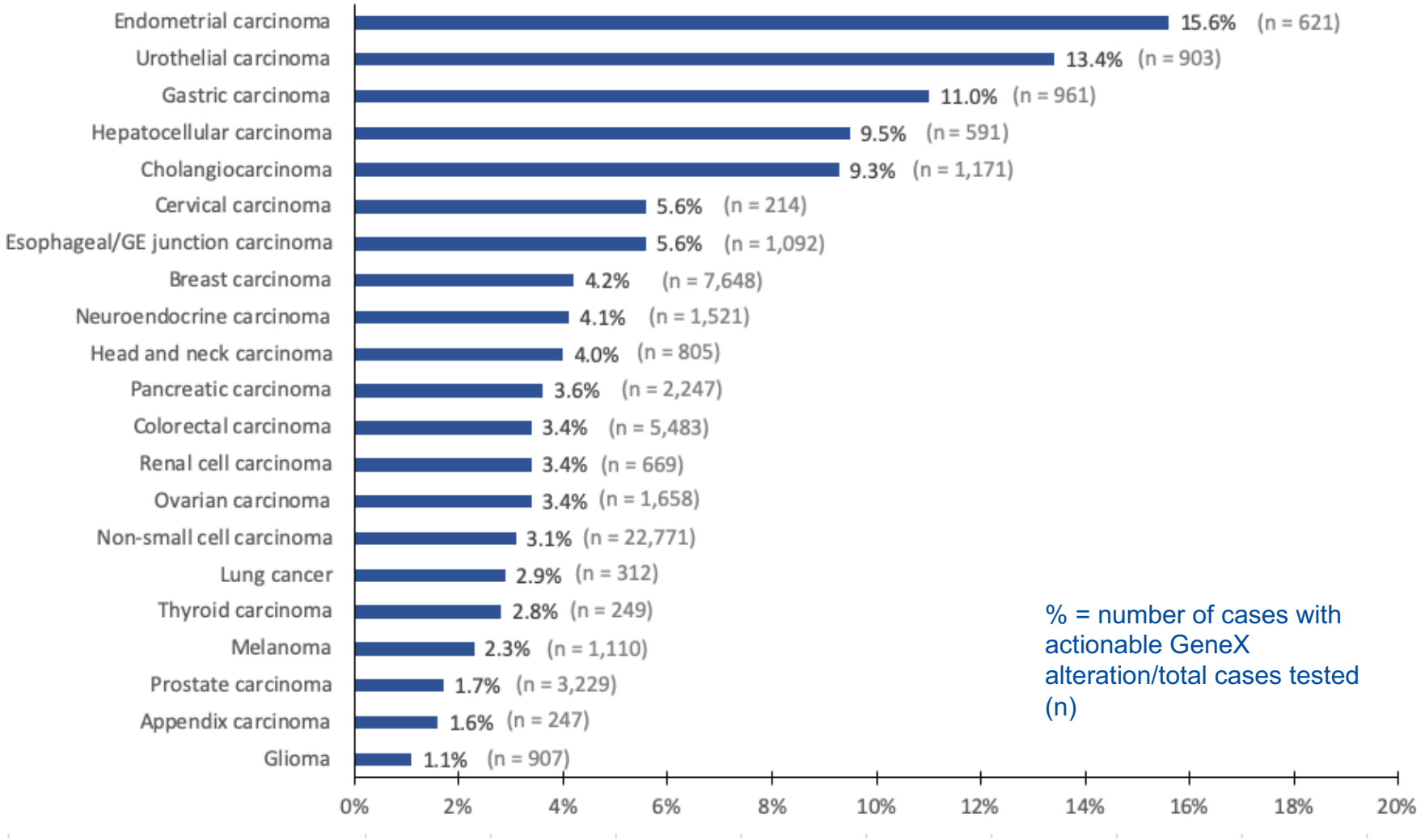


Molecular aberrations leading to FGFR pathway activation. The FGFRs dimerize upon ligand binding and trigger a downstream cascade of signaling pathways. The FGFR receptors (1-4) can become activated by mutation, translocation, or gene amplification. An increase in circulating FGF ligands can also cause activation. Downstream signaling can trigger the mitogen activated protein kinase (MAPK) pathway, the phosphoinositide-3-kinase (PI3K/Akt) pathway, the phosphorylation of the signal transducer and activator of transcription (STAT), and the PLCγ activation of the DAG-PKC and IP3-Ca^{2+}cascade resulting in DNA transcription. Negative feedback loops can attenuate the signaling cascade at varying levels. As seen above, the "similar expression to FGF" (SEF) family members can interact with the cytoplasmic domain of FGFRs and inhibit downstream signaling. It is hypothesized that FGFRL1 (atypical receptor/FGFR5) may serve as a ligand trap, may dimerize with other transmembrane FGFRs and inhibit autophosphorylation, or may increase turnover rates of other FGFRs [16]. No evidence exists for these mechanisms.

Oncotarget. 2017 Feb 28; 8(9): 16052–16074.

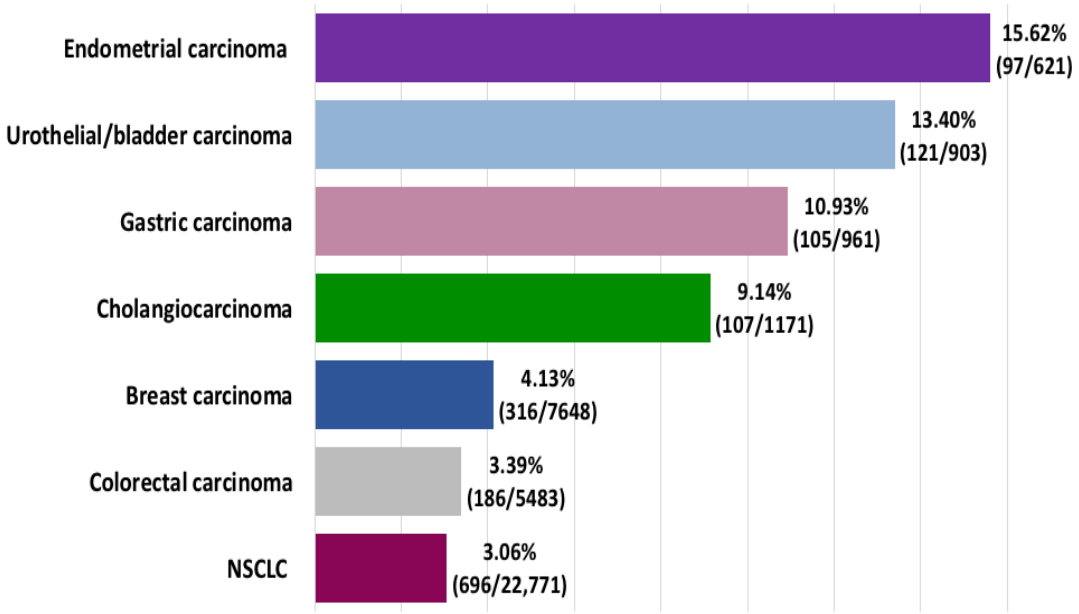
Gene	Total cases tested
FGFR1	118,180
FGFR2	119,223
FGFR3	119,281
FGFR4	19,188
PIK3CA	120,275
KRAS	124,993
HRAS	121,386
NRAS	124,270

Prevalence of actionable GeneX variants



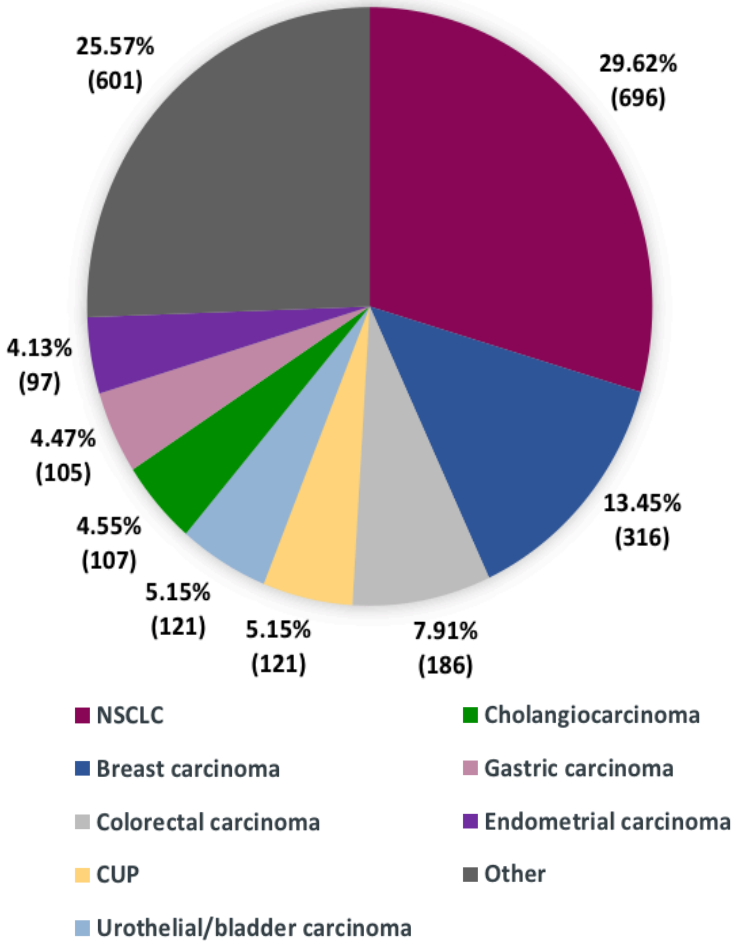
Alteration prevalence may differ from the distribution of cancer types

Prevalence



Prevalence:
(Cases with GeneX alteration/Total cases tested)

Distribution



Distribution:
(Cases by cancer type/Total GeneX-altered cases)

Variant data

Disease category	Gene	ctDNA	Variant	Variant type	Activation type	Molecular function
Breast carcinoma	Gene 3	ctDNA	Xxx-Gene3	fusion	activating	"…." (PMID xxxx)
	Gene 3	non-ctDNA	TxxxxM	SNV	VUS	"…." (PMID xxxx)
	Gene 1	ctDNA	Amplification	CNV	activating	"…." (PMID xxxx)
	Gene 2	ctDNA	GxxxD	SNV	VUS	"…." (PMID xxxx)
	Gene 2	ctDNA	GxxxD	SNV	VUS	"…." (PMID xxxx)
	Gene 1	non-ctDNA	Amplification	CNV	activating	"…." (PMID xxxx)
	Gene 2	ctDNA	GxxxD	SNV	VUS	"…." (PMID xxxx)
	Gene 1	ctDNA	Amplification	CNV	activating	"…." (PMID xxxx)
Cholangiocarcinoma	Gene 3	ctDNA	TxxxxM	SNV	VUS	"…." (PMID xxxx)
Neuroendocrine carcinoma	Gene 1	ctDNA	Amplification	CNV	activating	"…." (PMID xxxx)
NSCLC	Gene 2	ctDNA	GxxxD	SNV	VUS	"…." (PMID xxxx)
	Gene 2	ctDNA	GxxxD	SNV	VUS	"…." (PMID xxxx)
	Gene 1	non-ctDNA	Amplification	CNV	activating	"…." (PMID xxxx)
Pancreatic carcinoma	Gene 1	ctDNA	VxxxxE	SNV	VUS	"…." (PMID xxxx)
	Gene 1	ctDNA	Amplification	CNV	activating	"…." (PMID xxxx)
	Gene 2	ctDNA	Amplification	CNV	activating	"…." (PMID xxxx)
Urothelial carcinoma	Gene 3	ctDNA	Xxx-Gene3	fusion	activating	"…." (PMID xxxx)
	Gene 3	ctDNA	TxxxxM	SNV	VUS	"…." (PMID xxxx)

Visualizing N-of-One Genomic Insights Data using OmicSoft

Why provide it in this platform?

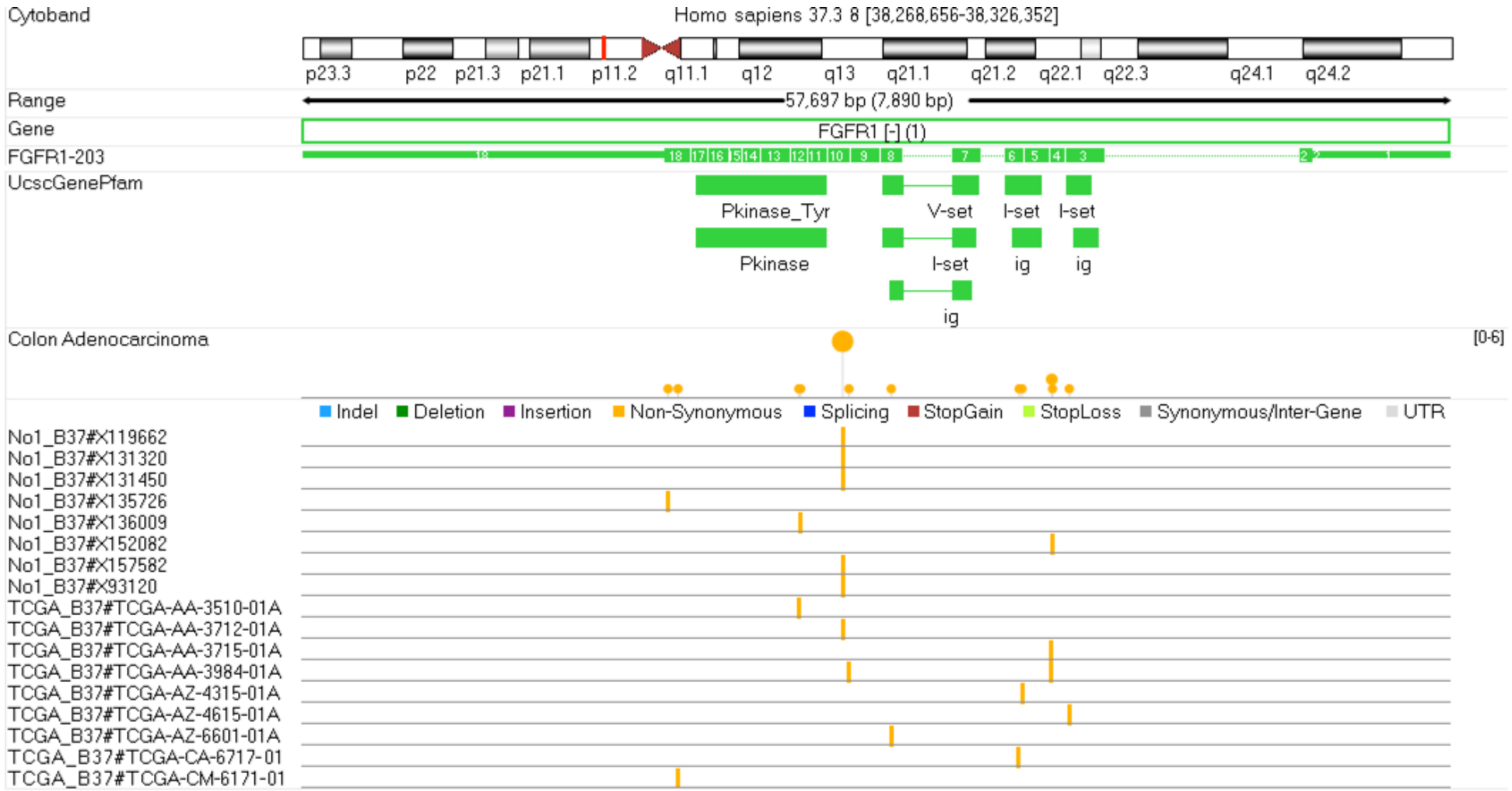
- Test “biomarker discovery” hypotheses
- Perform early analyses for design of a comprehensive Genomic Insights project
- Follow-up on questions that have come out of Genomic Insight projects

Examples of data requests – do they align with your needs?

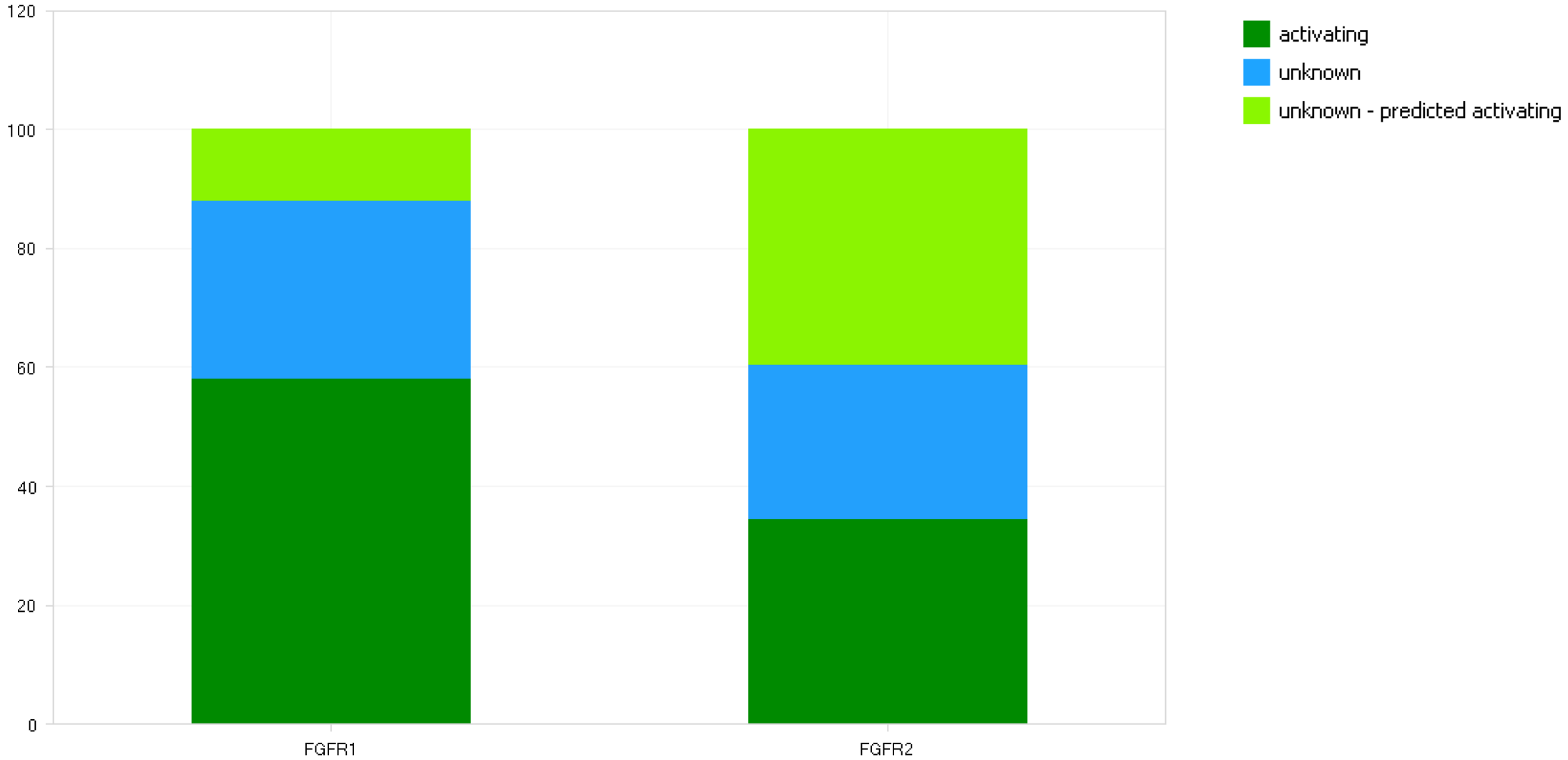
- Access data on genes related to your program
- Determine prevalence of alterations in your gene of interest for oncology cases tested in the real-world
- Compare to prevalence for cases from TCGA
- Review variant classification, annotations and frequency

Compare Genomic Insight data with TCGA data

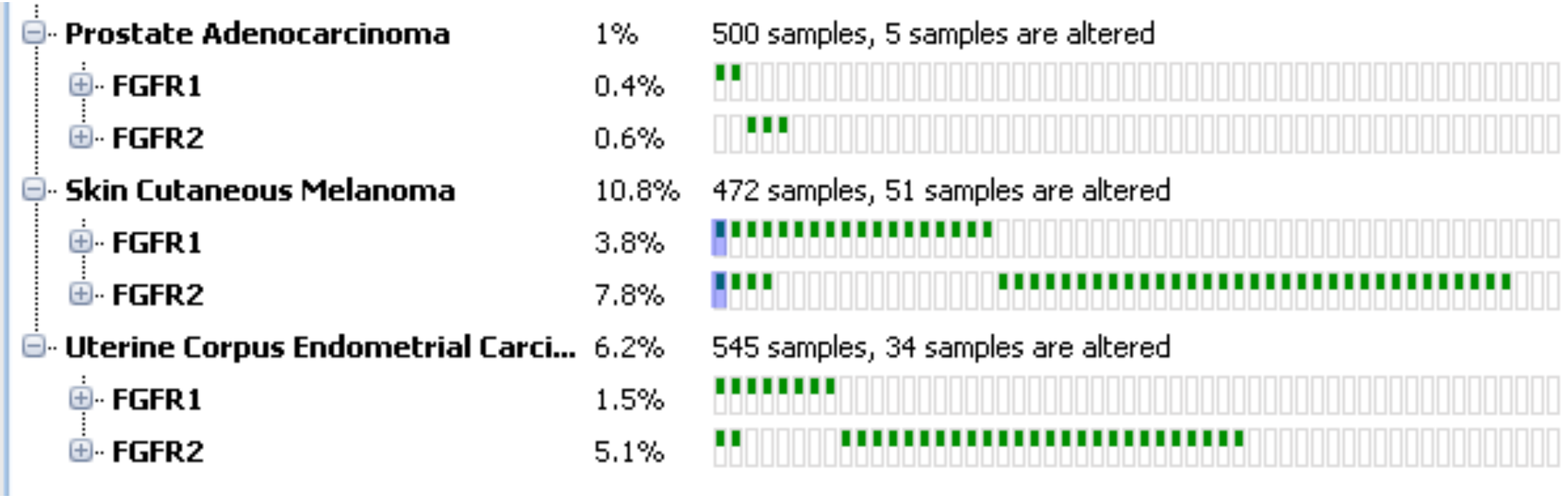
Explore variant frequency using lollipop mutation plots



Review the variant classifications determined for Genomic Insights



Identify alterations that co-occur between genes of interest



Thank you!

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Let's talk!

Meet today during break or lunch?

Set up a call to review the database and the prototype?

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