



Cold
Spring
Harbor
Laboratory

Advanced Sequencing Technologies & Applications

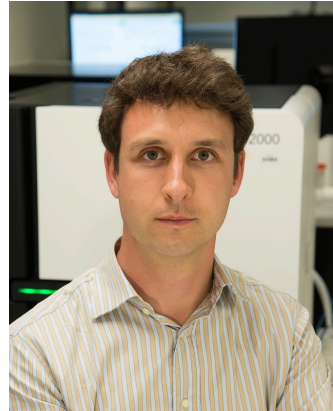
<http://meetings.cshl.edu/courses.html>

Introductions to MGI/WUSTL instructors



Malachi Griffith

Assistant Professor of Medicine
Assistant Professor of Genetics
Assistant Director, MGI



Obi Griffith, PhD

Assistant Professor of Medicine
Assistant Professor of Genetics
Assistant Director, MGI



Alex Wagner

Postdoc fellow



Jason Walker

Director of Informatics

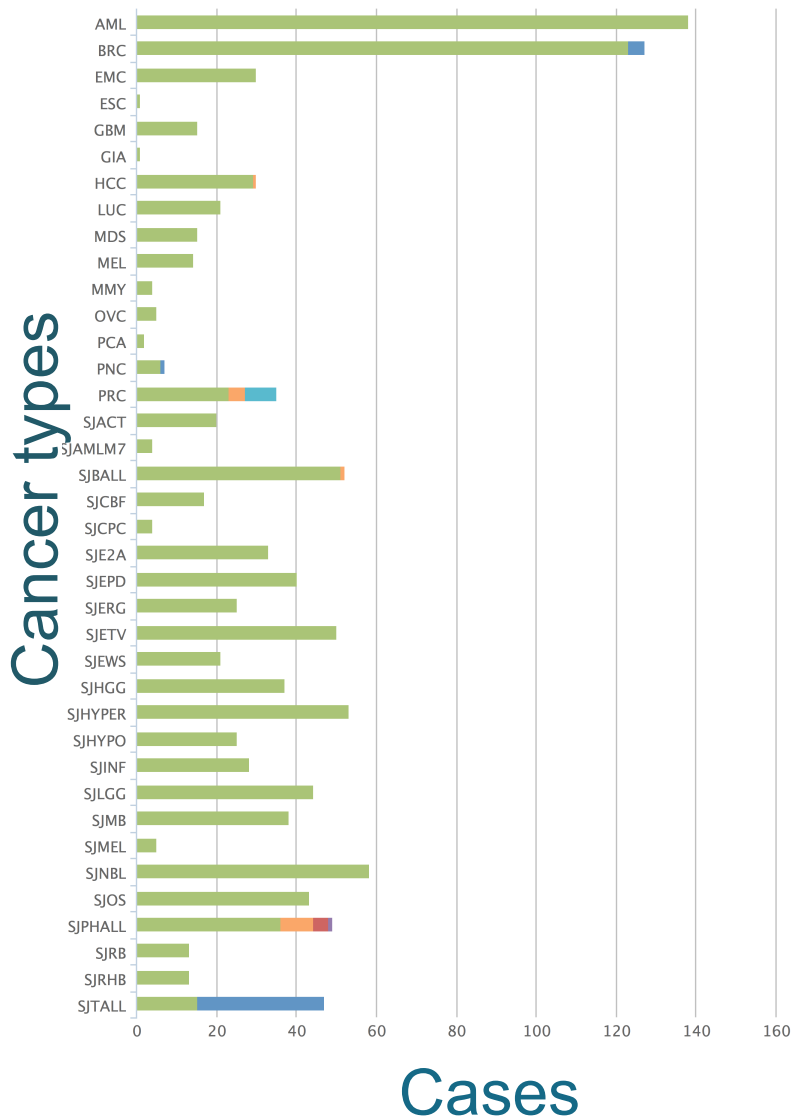


Kelsy Cotto

PhD candidate

McDonnell Genome Institute, Washington University School of Medicine

The McDonnell Genome Institute has pursued the field of genomics since inception: >1000 whole genomes, >5000 exomes, >1000 transcriptomes for dozens of tumor types



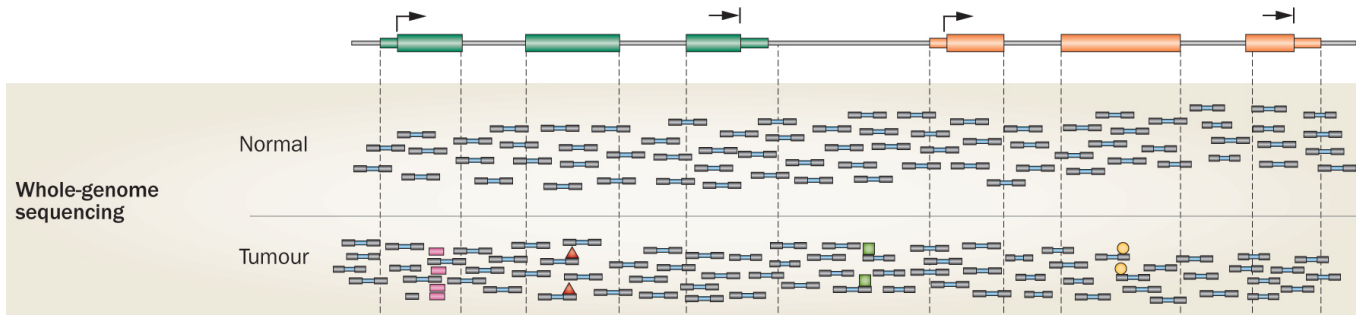
- Human Genome Project
- First to sequence and analyze a tumor whole genome sequence (Ley et al, 2008)
- Major contributor to TCGA, PCGP, etc.
- Most comprehensively sequenced single patient tumor ever published (Griffith et al, 2015)
- Early proof-of-principle for cancer precision medicine (Griffith et al, 2016)
- Analysis and tools for first personalized cancer vaccine design in humans (Carreno et al, 2015)
- Many other widely used tools

MGI – 1000+ tumor whole genomes, many more exomes, X10 & NovaSeq will accelerate this!

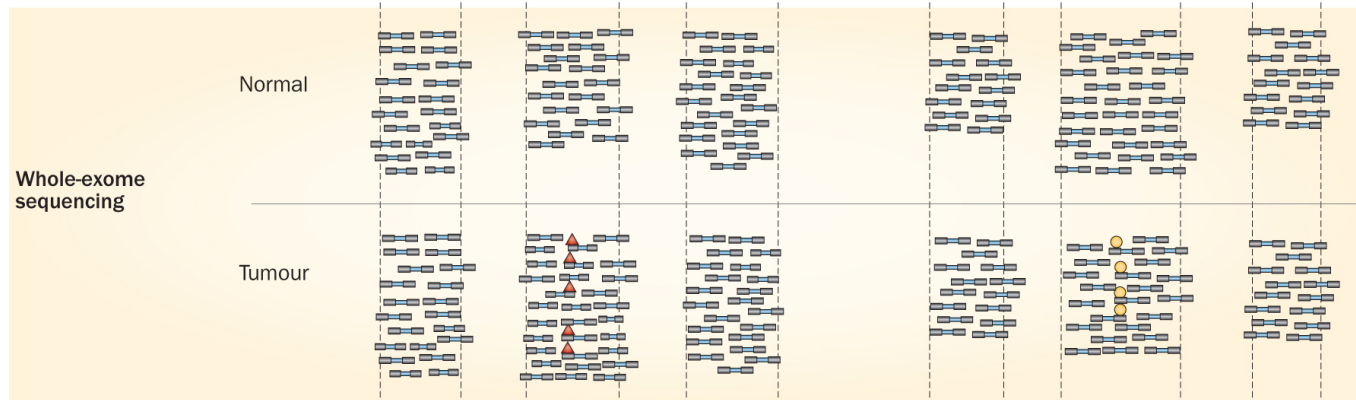
Whole genome, exome, transcriptome and other 'omic' sequencing allows us to detect and confirm many different variant types

Reference genome depicting two example genes

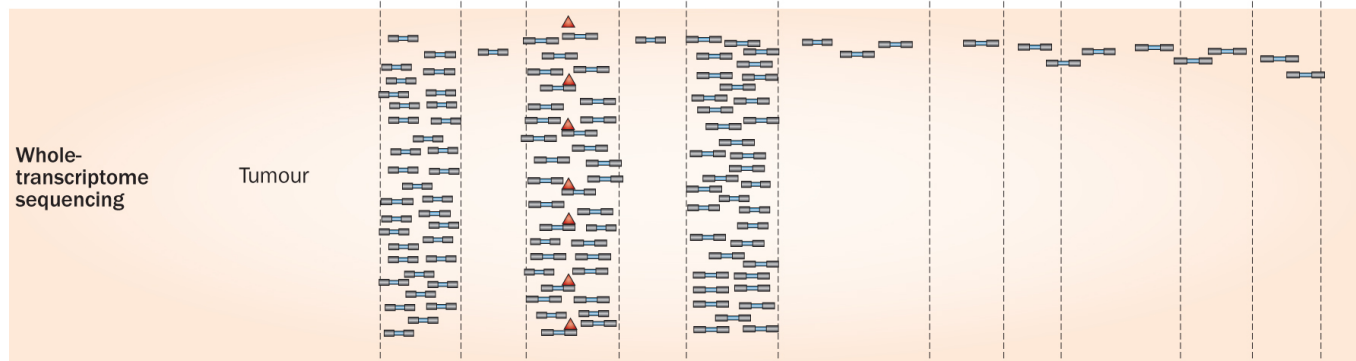
'WGS'



'Exome'

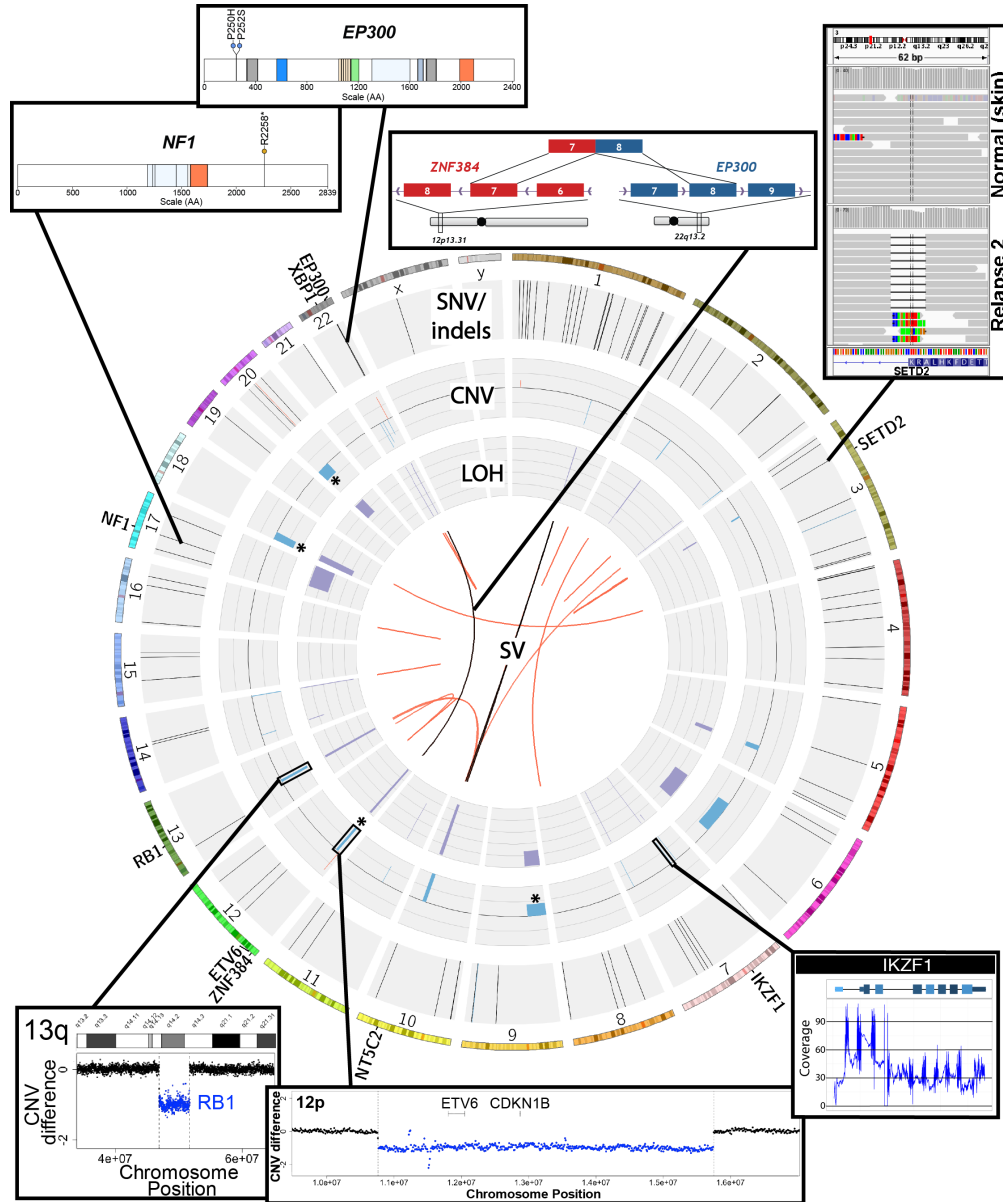


'RNA-seq'

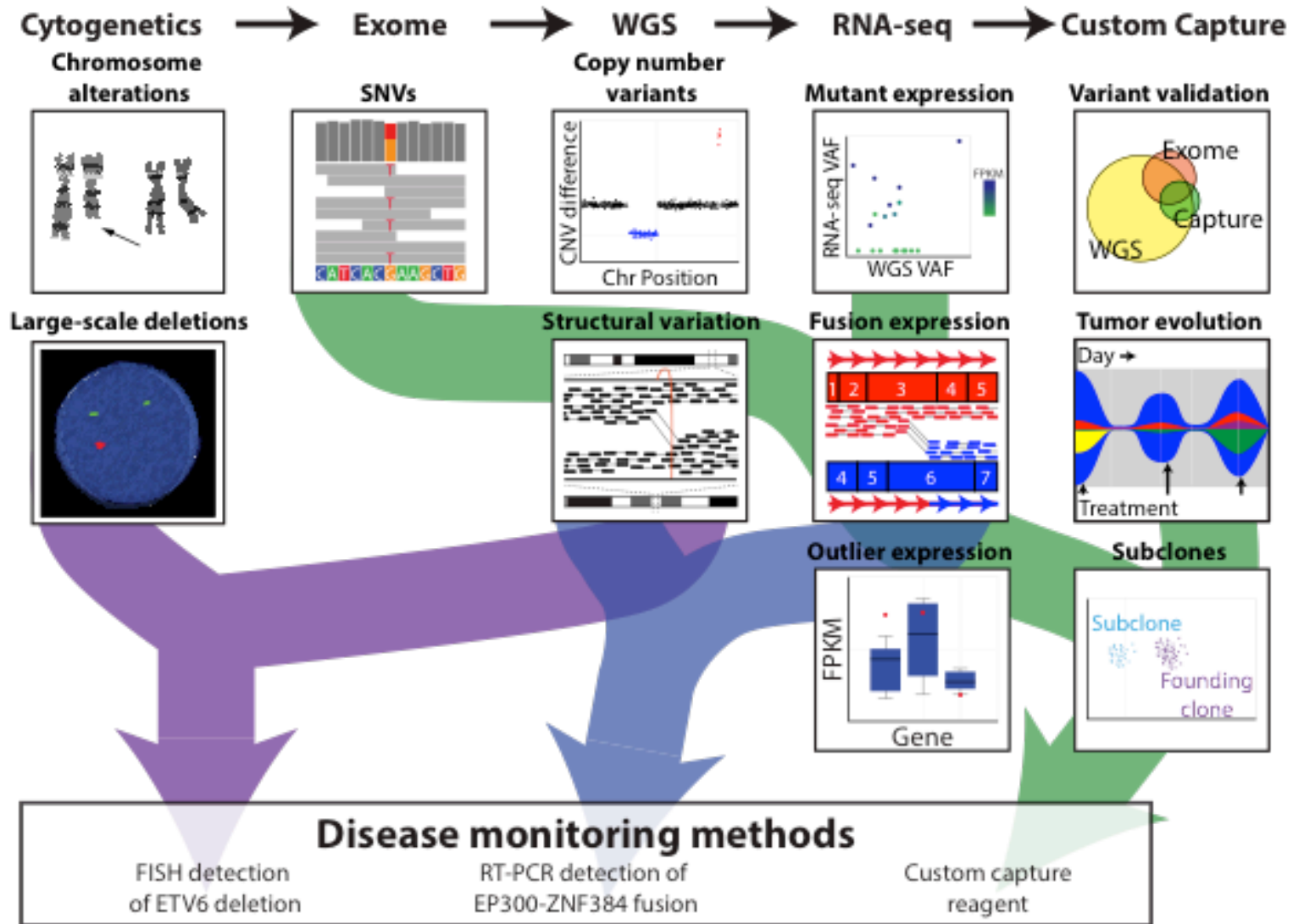


■ Discordant reads (structural variant) ▲ Variant base (coding) ■ Variant base (noncoding) ● Variant base (coding)

SNVs, Indels, CNVs, SVs, fusions, LOH, expression changes, methylation changes, and more

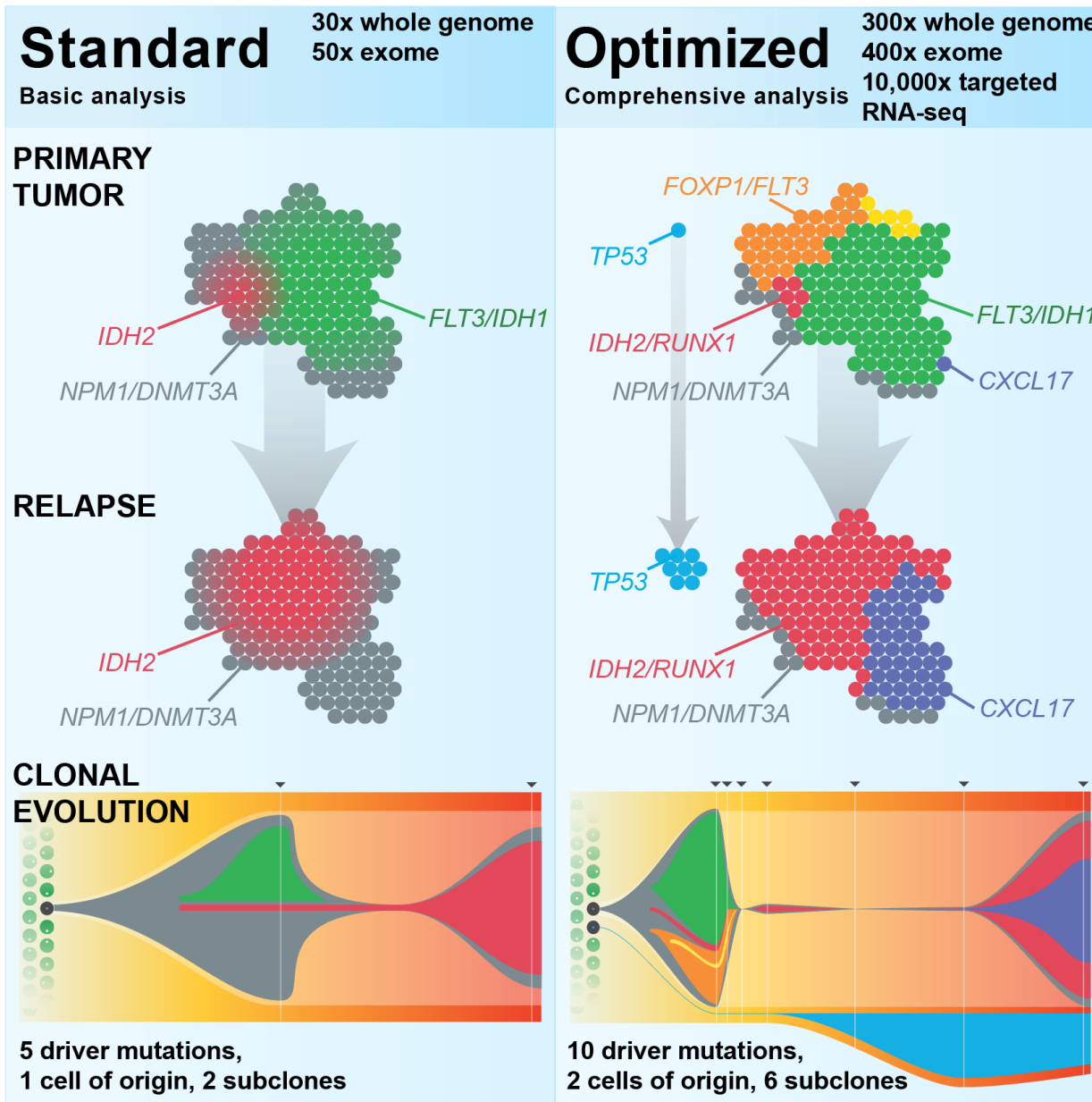


Comprehensive and integrative analysis methods are needed



Kilannin Krysiak

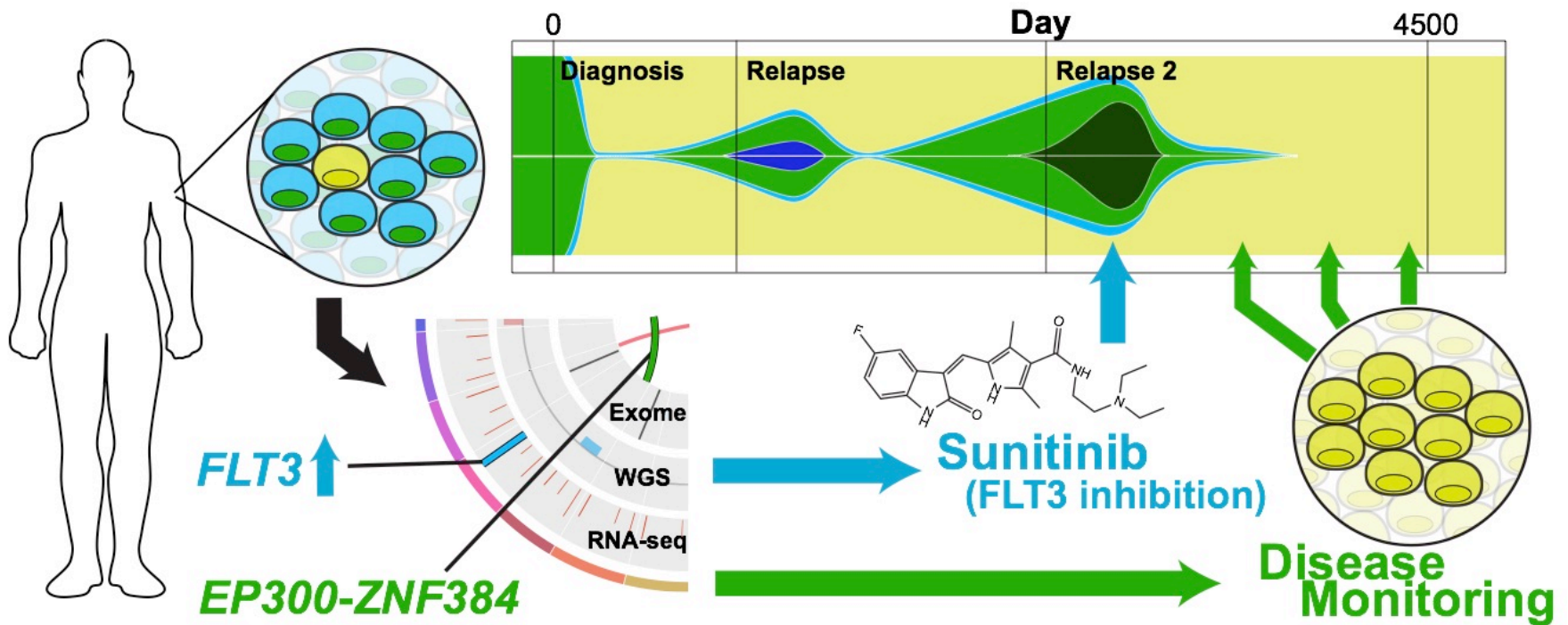
Each study often requires considerable customization



[Griffith et al. 2015](#)

Kilannin Krysiak

Personalized medicine requires personalized strategies



Experimental Hematology 2016;44:603–613

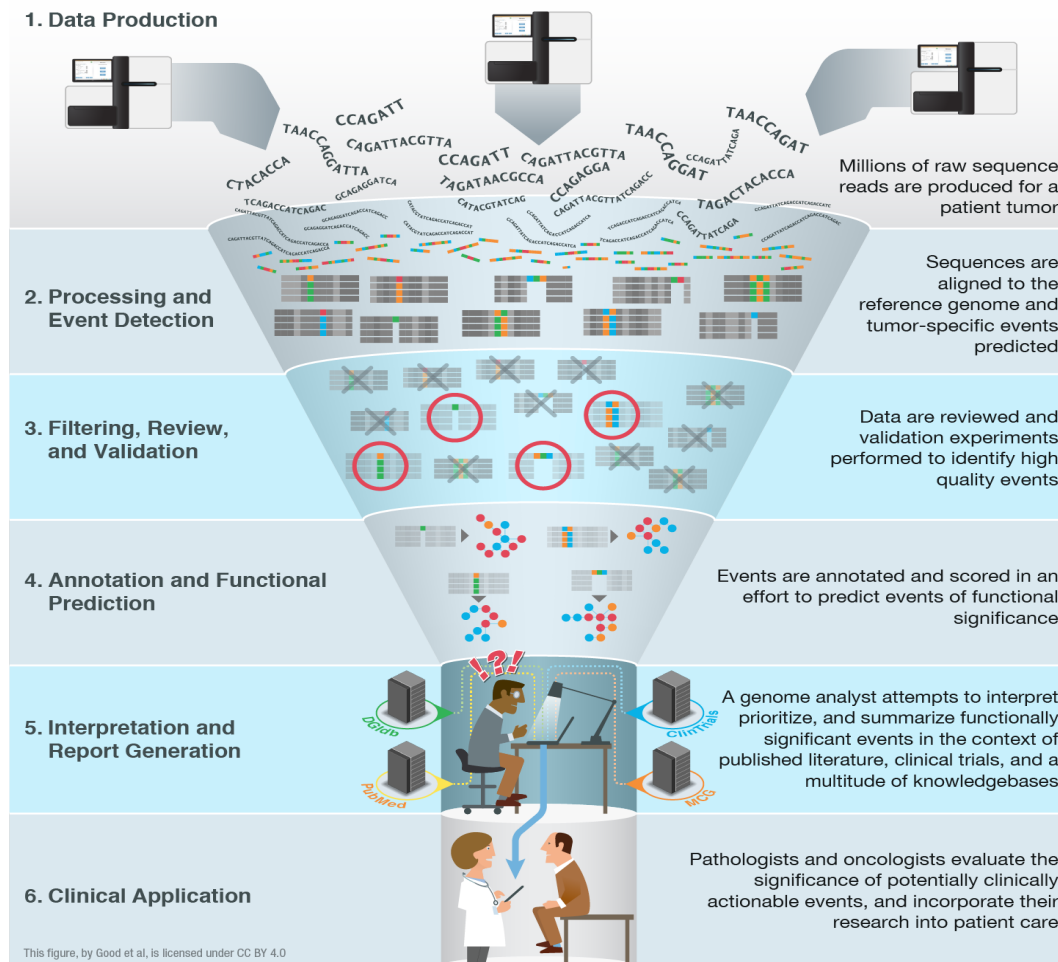
Experimental Hematology

Comprehensive genomic analysis reveals *FLT3* activation and a therapeutic strategy for a patient with relapsed adult B-lymphoblastic leukemia

Kilannin Krysiak

[Griffith et al. 2016](#)

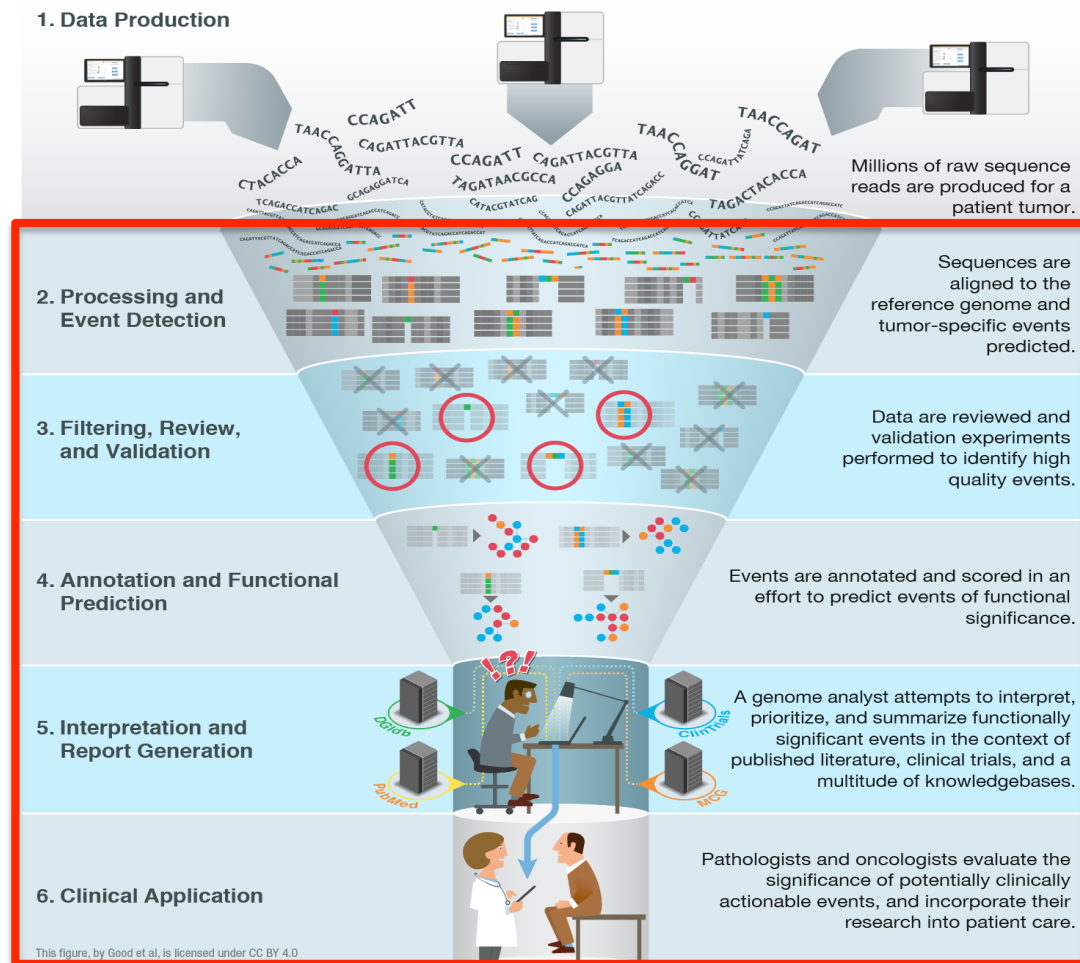
High-throughput sequencing has been largely automated



Good BM, Ainscough BJ, McMichael JF, Su AI, Griffith OL. 2014.
Genome Biology. 15(8):438.

Joshua McMichael

The rest of this workshop will focus on the methods and tools needed to take raw sequence data to interpretation and application – still the bottleneck!



Good BM, Ainscough BJ, McMichael JF, Su AI, Griffith OL. 2014.
Genome Biology. 15(8):438.

Joshua McMichael

The Griffith lab is focused on developing methods to address this bottleneck for precision medicine in cancer

- **Cancer genome analysis**
 - AML
 - [Optimizing cancer genome analysis](#)
 - Breast cancer
 - [Immunotherapy](#) (cancer vaccines)
 - STAT1^{-/-} mouse model
 - Targeted sequencing of 625 ER+ with long-term follow-up
 - Liver cancer
 - Small cell lung cancer
 - OSCC...
- **Precision Medicine for Cancer**
 - [Genomics Tumor Board](#)
 - [Case Reports](#) and [Clinical Trials](#)
- **Education projects**
 - [RNA-seq analysis and cloud computing](#)
 - [CSHL](#) and [CBW](#)
 - [Genomic Data Visualization/Interpretation](#)
- **Tool development**

Where tools/resources do not exist we build them



www.dgidb.org

Search genes for known and potentially druggable interactions



<https://github.com/griffithlab/pVAC-Seq>

Personalize vaccine design



www.docm.info

Filter against highly curated set of mutations known to cause cancer



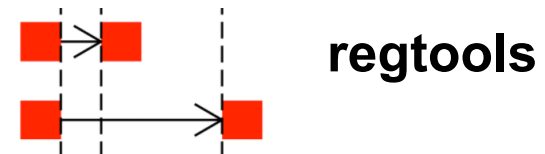
<https://github.com/griffithlab/GenVisR>

Create genomic visualizations



www.civicdb.org

Identify highly curated summaries of clinical interpretations for variants in cancer



regtools

<https://github.com/griffithlab/regtools>

Identify regulatory variants

Encourage best practices for software development

The screenshot shows the GitHub organization page for 'The Griffith Lab'. The header includes navigation links for 'Pull requests', 'Issues', and 'Gist'. The organization's profile picture and name are at the top, followed by a description: 'Academic Lab of Obi and Malachi Griffith' and the website 'http://www.griffithlab.org'. Below this, there are tabs for 'Repositories', 'People (25)', 'Teams (21)', 'Projects (0)', and 'Settings'. A search bar and filters for 'Type: All' and 'Language: All' are present. The main content area displays three repositories: 'dgi-db' (Ruby, 23 stars, 14 forks), 'pVAC-Seq' (Python, 37 stars, 33 forks), and 'GenVisR' (R, 95 stars, 37 forks). A 'Top languages' section shows R, Python, Ruby, Perl, and HTML. A 'People' section shows a grid of 25 team members.

- All code deposited in Github
 - 35 repos for different software/projects
 - Virtually all public and open-source
 - Test-driven, code review, pull requests, etc

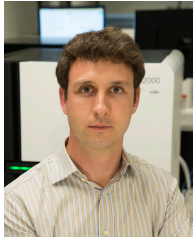
<https://github.com/griffithlab>

<https://github.com/genome>

WUSTL – MGI: Group members



**Malachi
Griffith**



**Obi
Griffith**



**Benjamin
Ainscough**



**Erica
Barnell**



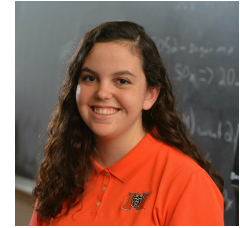
**Katie
Campbell**



**Kaitlin
Clark**



**Adam
Coffman**



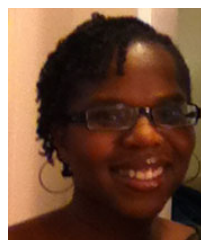
**Kelsy
Cotto**



**Arpad
Danos**



**Yang-Yang
Feng**



**Felicia
Gomez**



**Jasreet
Hundal**



**Susanna
Kiwala**



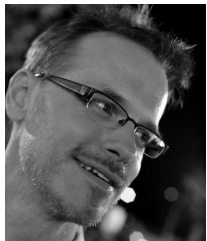
**Kilanin
Krysiak**



**Lynzey
Kujan**



**Jason
Kunisaki**



**Josh
McMichael**



**Cody
Ramirez**



**Zachary
Skidmore**



**Nick
Spies**



**Lee
Trani**



**Alex
Wagner**



**Jason
Walker**

Informatics background poll

- Student poll
 - Are you doing genomics research?
 - Do you consider yourself a bioinformatician?
 - What kind of NGS data are you working with?
 - WGS?
 - Exome?
 - RNAseq?
 - Epigenome?
 - Single cell?
 - Other?
 - What organism do you work with?
 - Did you bring data?

Student poll continued

Not counting the pre-requisites and materials for this course:

- Are you familiar with linux/command line?
 - Intermediate?
 - Expert?
- Do you sometimes write code?
 - What language?
- Are you familiar with R?
 - Intermediate?
 - Expert?
- Are you familiar with ggplot?
 - Intermediate?
 - Expert?
- Do you use git/github?