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Cancer Center™

Reflections on Cancer Moonshots

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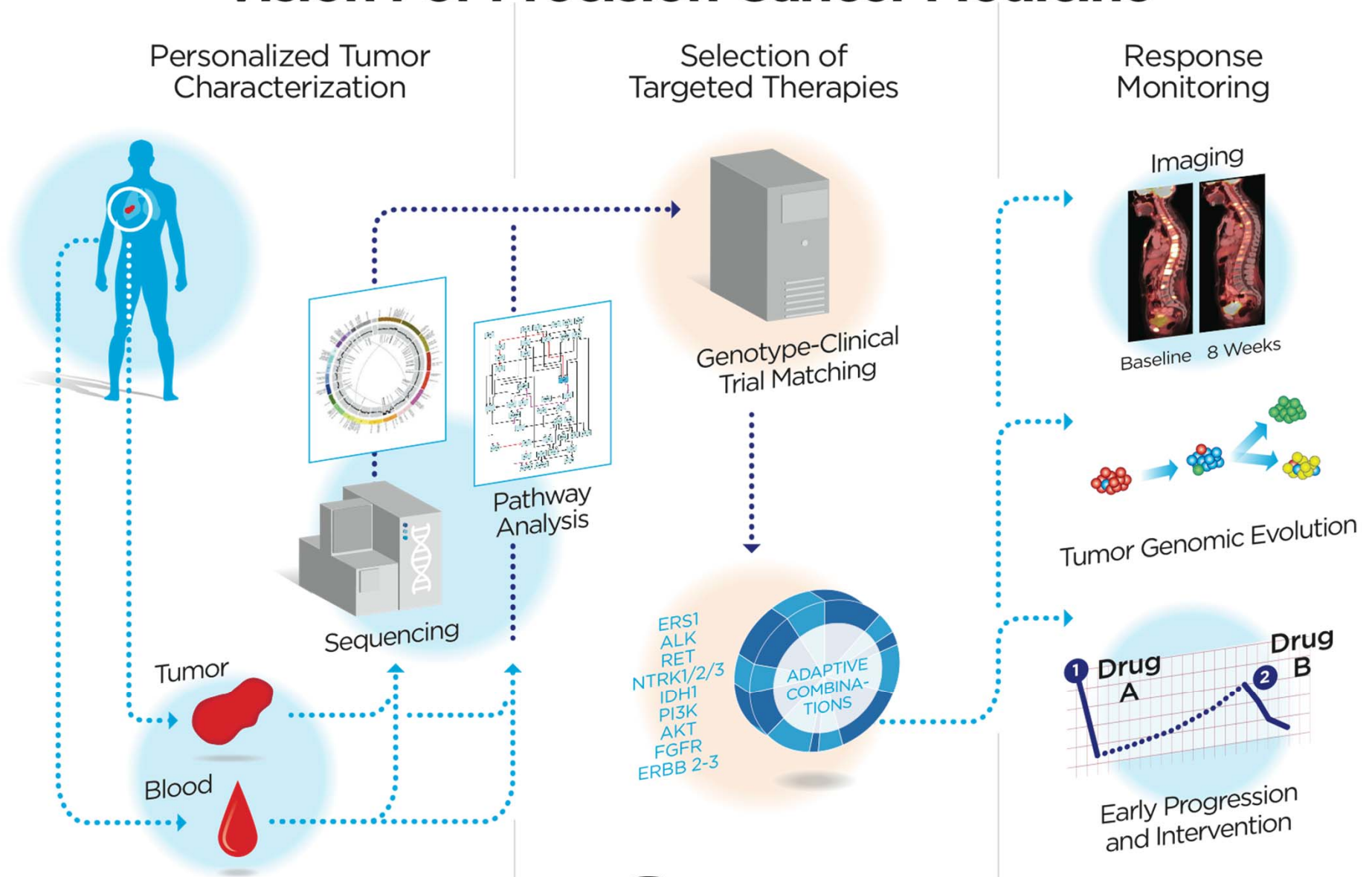
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Vision For Precision Cancer Medicine



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Cancer is a disease of mutations

- wrong location (cancer gene)
- wrong cell (stem/progenitor cell)
- wrong timing (too young)

....and bad luck

Cancer's Random Assault

By DEN

publication date: Jan 16, 2015

How the "Bad Luck" Cancer Paper was Misread by the Press

R *By Matthew Bin Han Ong*

George Johnson

RAW DATA JAN. 19, 2015



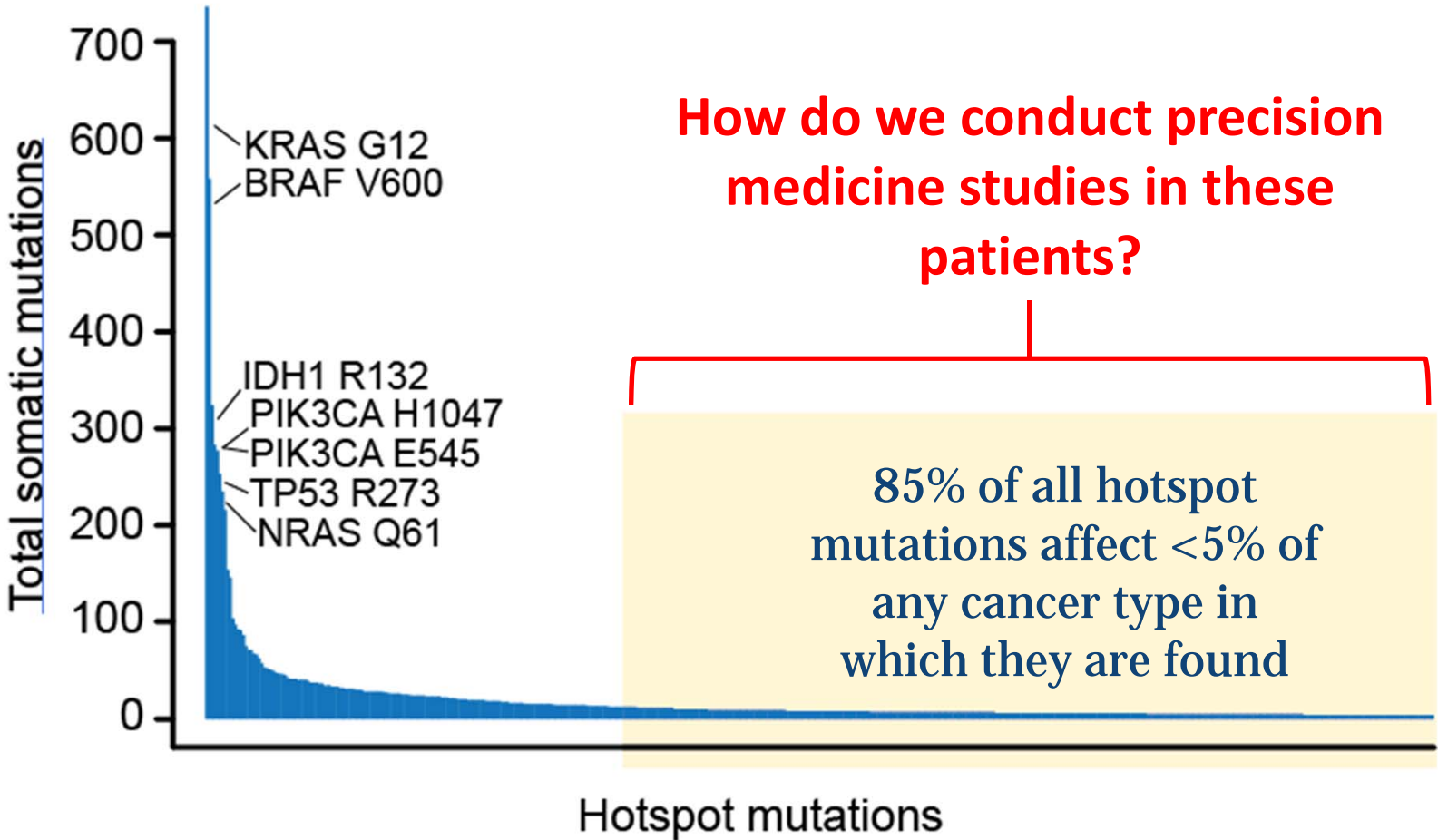


We know the genomic landscape of cancer

- large scale sequencing projects (TCGA, ICGC) have completed exomes (all coding regions) from ~10,000 cancers
- all common cancer drivers are defined (“common” means present at >5% frequency per tumor type)

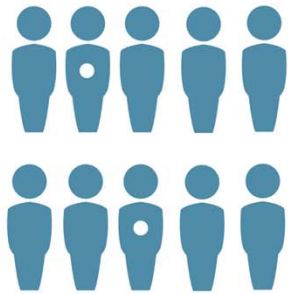


The 'Long Tail' of Hotspot Mutations Across Cancer

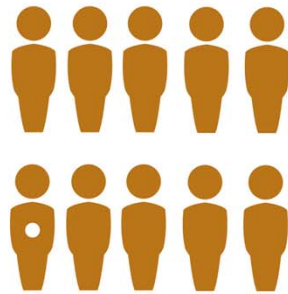


'Basket' Study Approach – Treating by Mutation not Tumor Location

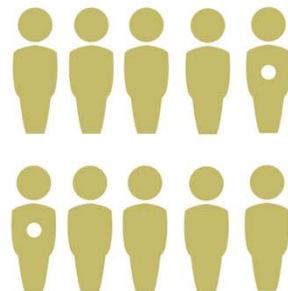
Lung Cancer



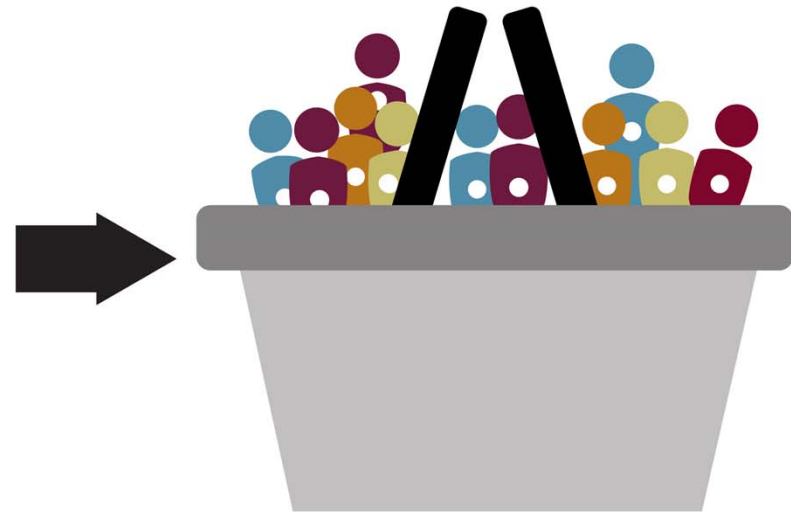
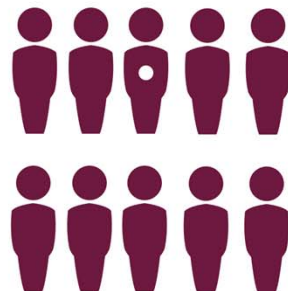
Colorectal Cancer



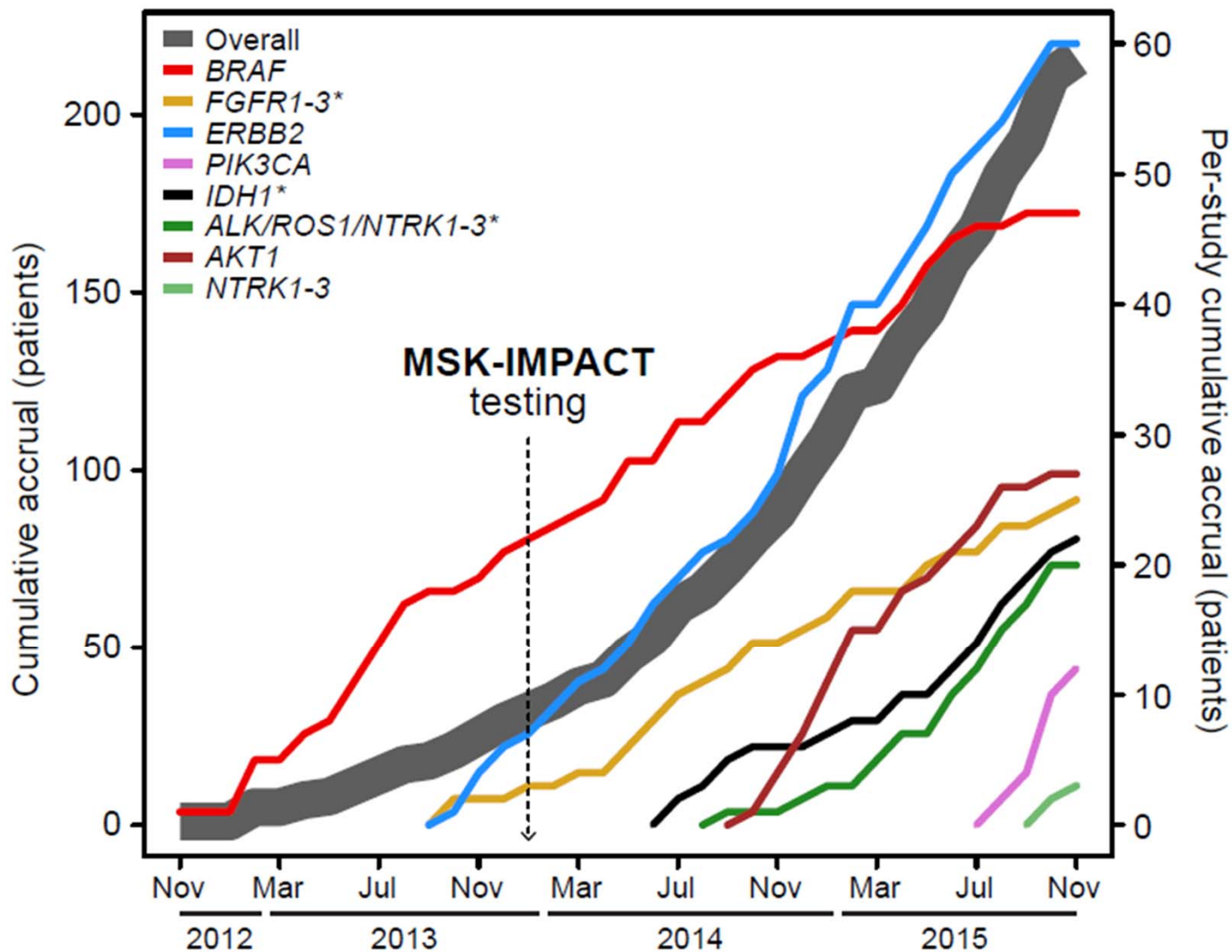
Breast Cancer



Various Rare Cancers



MSK-IMPACT Enables Study Accrual

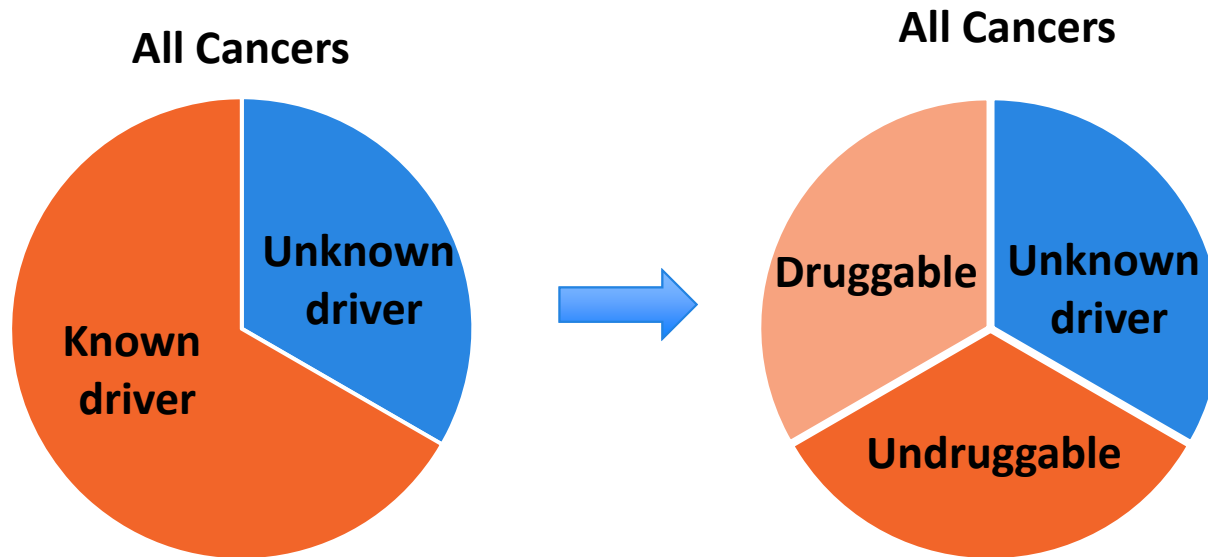


*-Indicates studies in dose escalation (enrollment limited by spots not patients)



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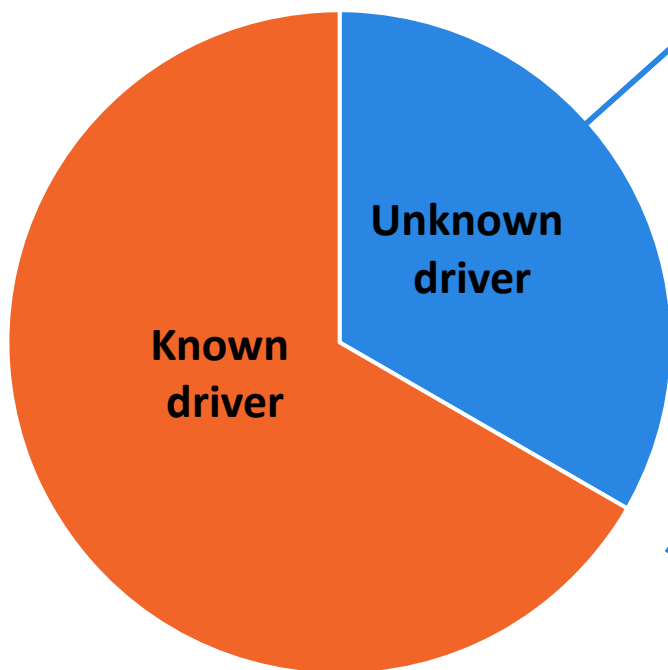
What fraction of cancer patients are benefiting?



- 2/3 of cancers have known drivers
- 1/2 of those with known drivers have therapies, but the other 1/2 are currently undruggable

How do we unravel the unknowns?

Cancers



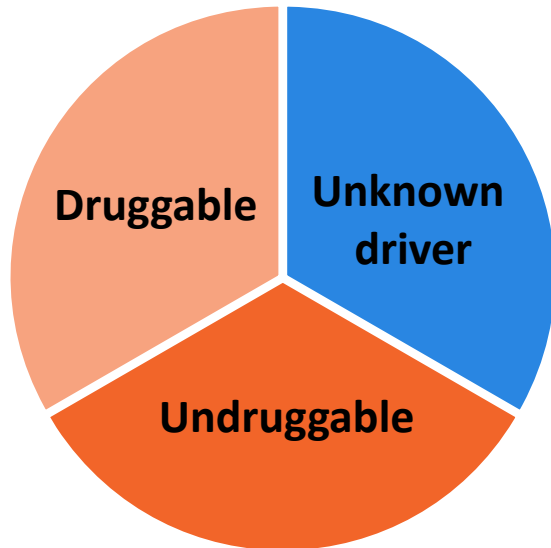
-more exome sequencing
(to discover all mutations at >1% frequency)
-whole genome sequencing
(to discover mutations in non-coding regions, e.g. enhancers)



How do we address undruggable drivers?



All Cancers



- 1) new chemistry/pharmacology
 - disrupt protein-protein interaction
 - oncoprotein degradation
- 2) Generate a comprehensive map of cancer vulnerabilities (synthetic lethal screens, etc)
- 3) crack the challenge of delivering genetic drugs (siRNA)
 - nanoparticles, etc

Note: druggable \neq cure (we need rational combinations)





Recommendations

1. Leverage the explosive growth of clinical sequencing
 - comprehensive clinical annotation of all mutations (registries)
 - encourage and support data sharing consortia (GENIE, CancerLinQ, ORIEN, etc)
2. Define all cancer vulnerabilities
 - fill in the gaps of existing cell line encyclopedias
 - conduct comprehensive genetic screens (CRISPR/shRNA)
3. Invest in new approaches to drug the undruggable
 - new chemistry, new drug delivery
4. Leverage the huge commercial investment in immuno-oncology
 - support basic cancer immunology (syngeneic models, etc)



Data sharing discussions with the VP



Davos, Jan 19, 2016

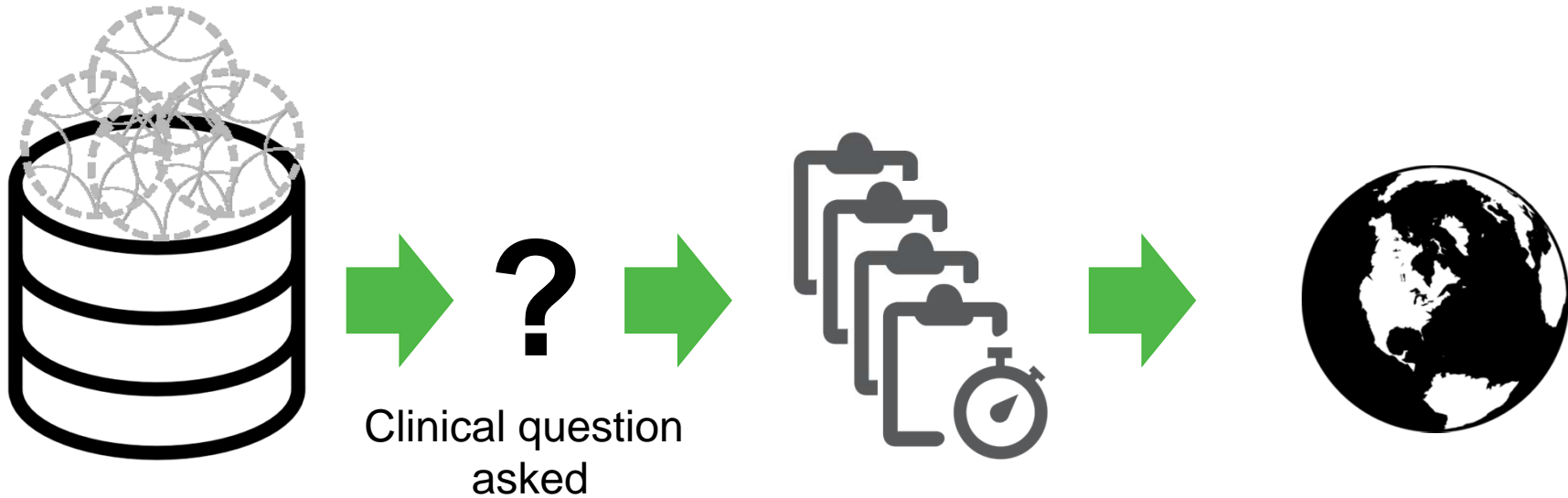


Wash DC, Feb 19, 2016



Goal: link genomics with clinical phenotypes

How Does It Work?



Aggregate tumor-only NGS data and limited clinical data from project participants into registry

Necessary clinical data Linked to data within the registry

Data made publicly available after defined periods.