

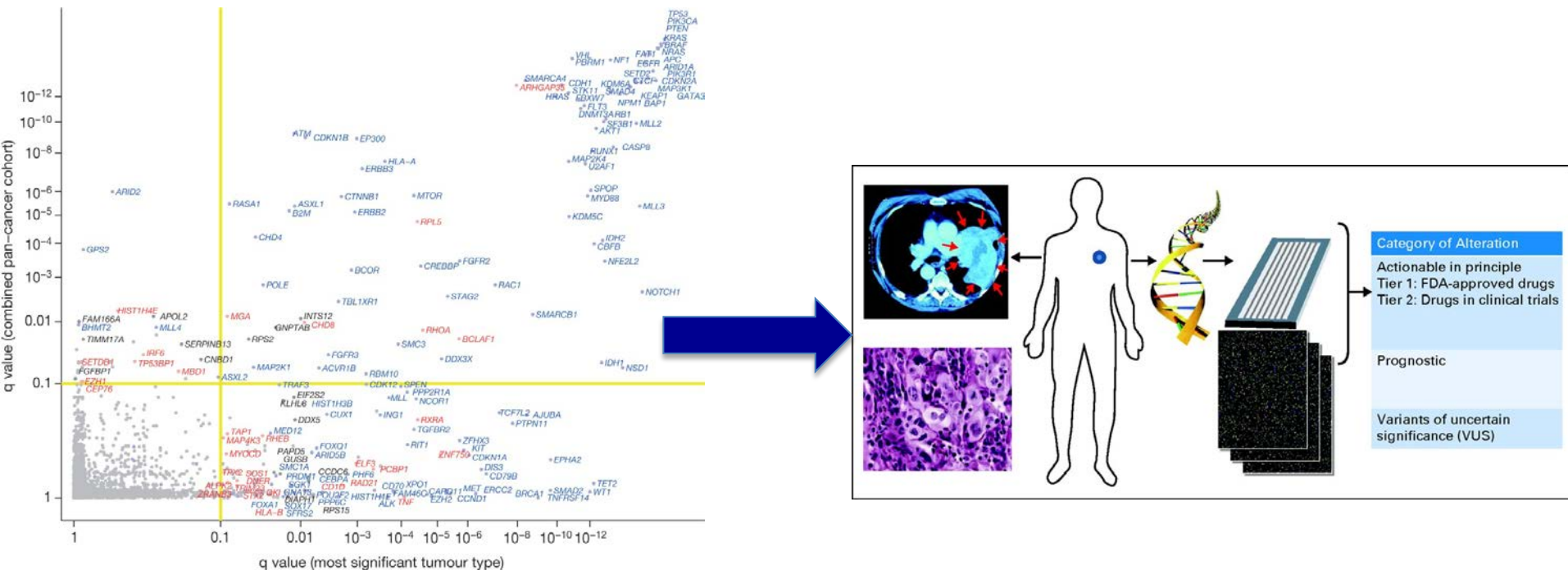
Somatic alterations in clinically relevant cancer genes among 12 TCGA tumor types

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Alterations in clinically relevant genes



- **Question: What is the spectrum of alterations in clinically relevant cancer genes across tumor types?**

Analysis approach

- Somatic mutations and indels called from exomes of $n = 3276$ TCGA cases

How can I contribute to the TARGET database?

If you would like to nominate a particular gene for inclusion as being clinically relevant, please [complete this survey](#).

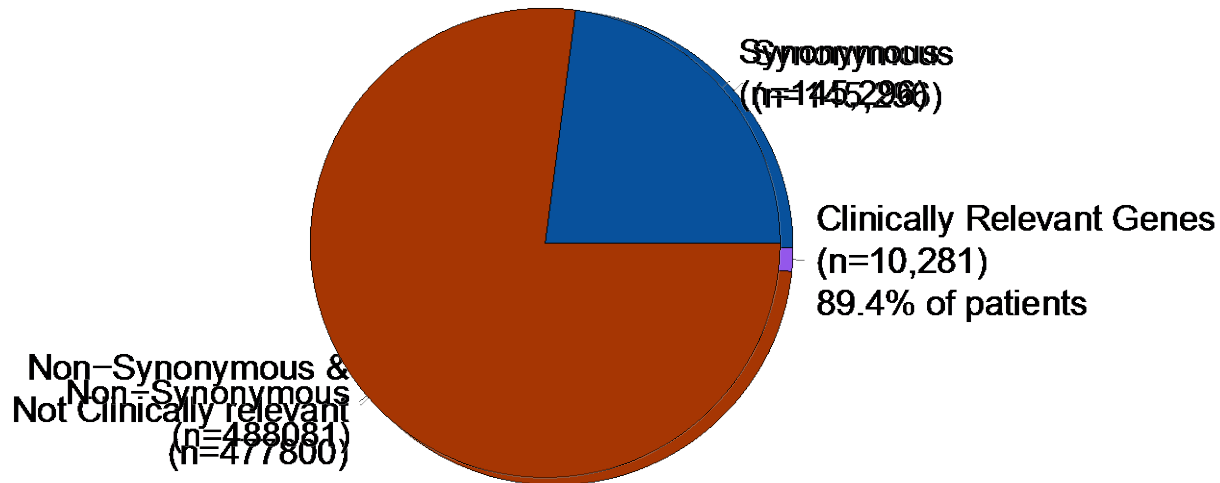
If your submission is selected for inclusion, you will be notified. Furthermore, if you would like to be acknowledged as the expert for that submission, you will be attributed in future editions of TARGET.

www.broadinstitute.org/cancer/cga/target

— PROGNOSTIC

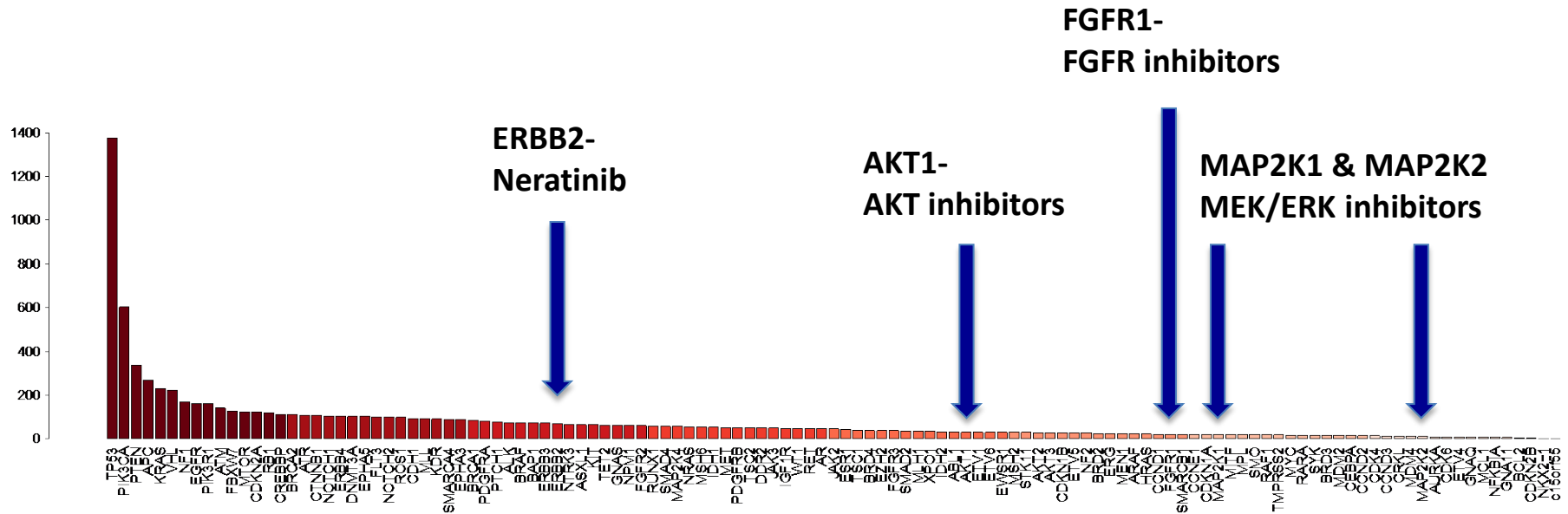
- *Open/crowd-source this list*

Global Results



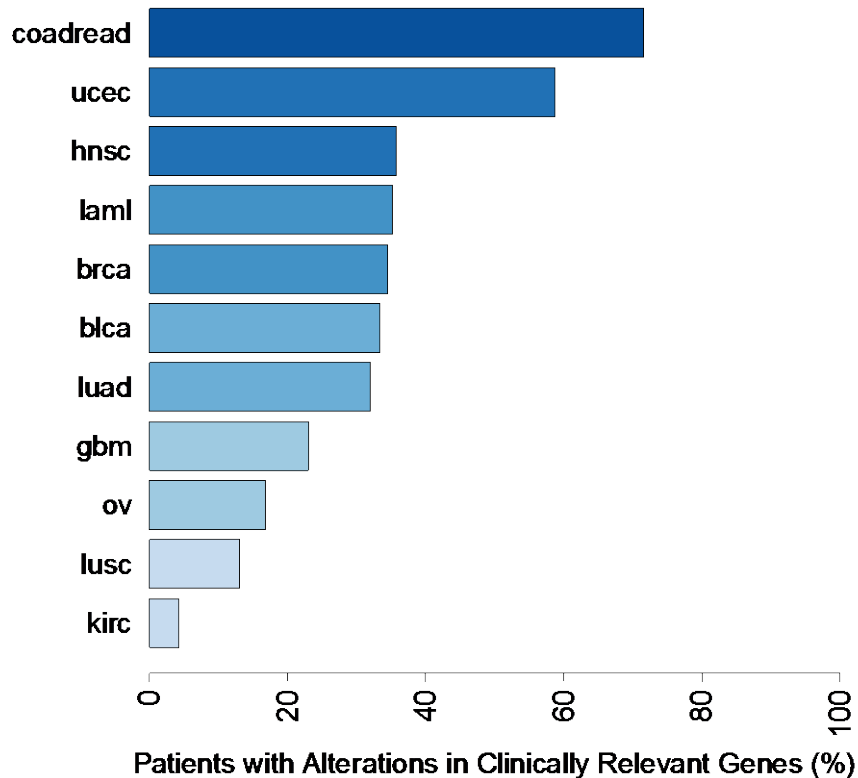
- *We recognize that not all alterations themselves are well-characterized and clinically relevant – working at a gene level.*

A “long tail” of alterations in clinically relevant genes

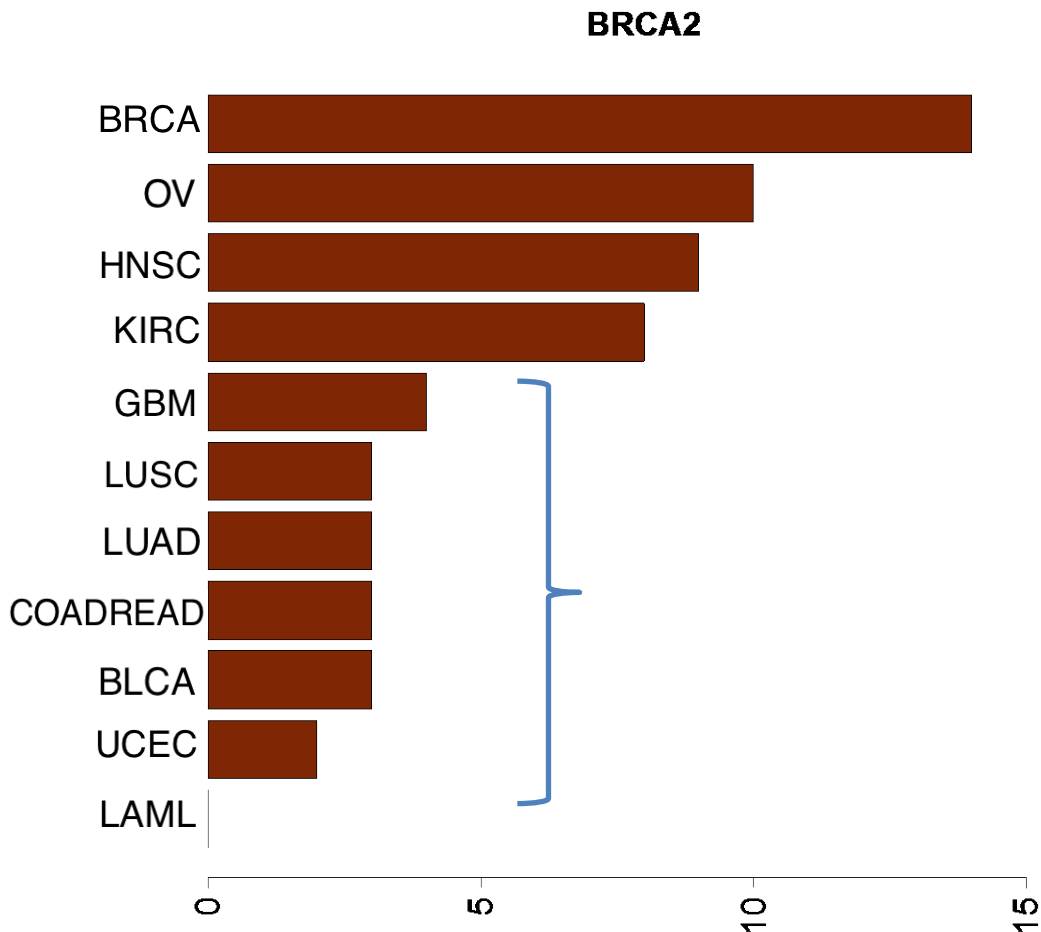


Theme 1: Shift from hotspot to exome sequencing across tumor types

Hotspot Profiling

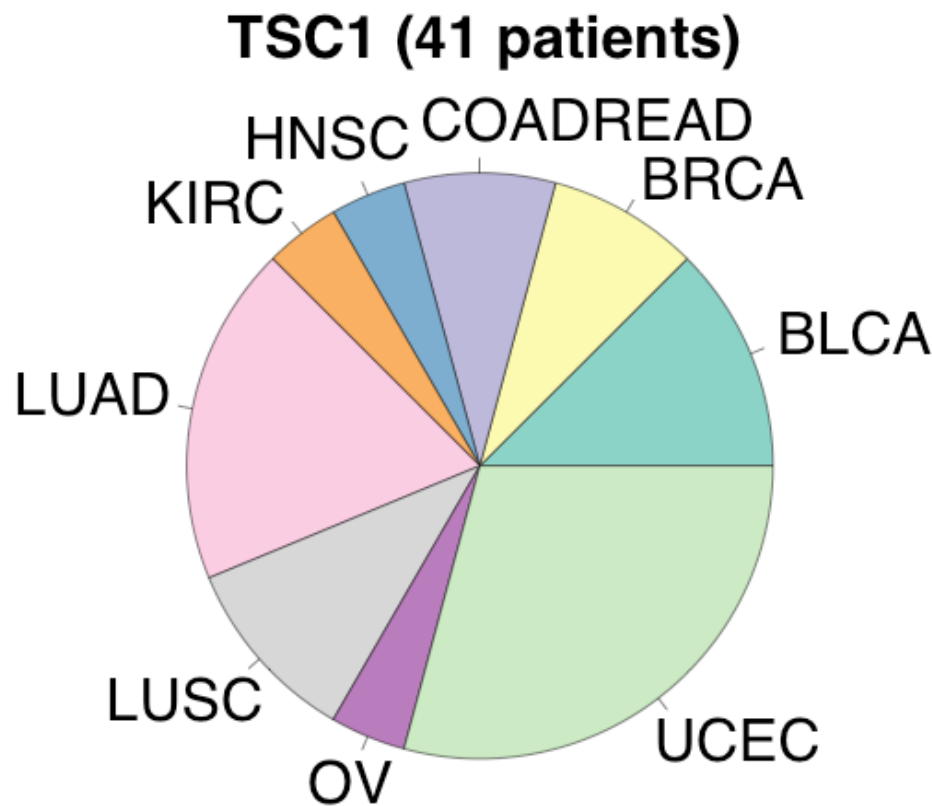


Theme 2: Well known clinically relevant genes may rarely be altered in unexpected tumor types



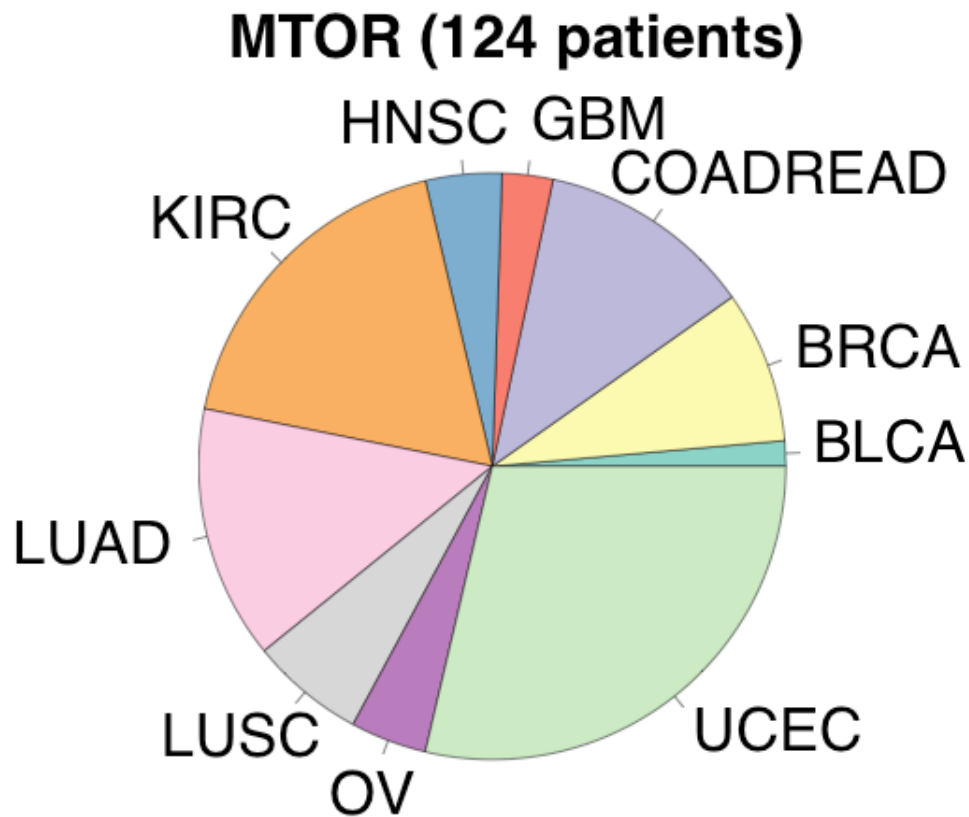
- Important for these rare (sometimes n-of-1) patients

Theme 3: Genes that are rarely mutated in one tumor type occur frequently across tumor types



- Alterations in TSC1 may predict sensitivity to everolimus [Iyer, et al. Science. 2012]
- Many variants are of unknown functional significance
- ***Need clinical annotations linked to these variants***

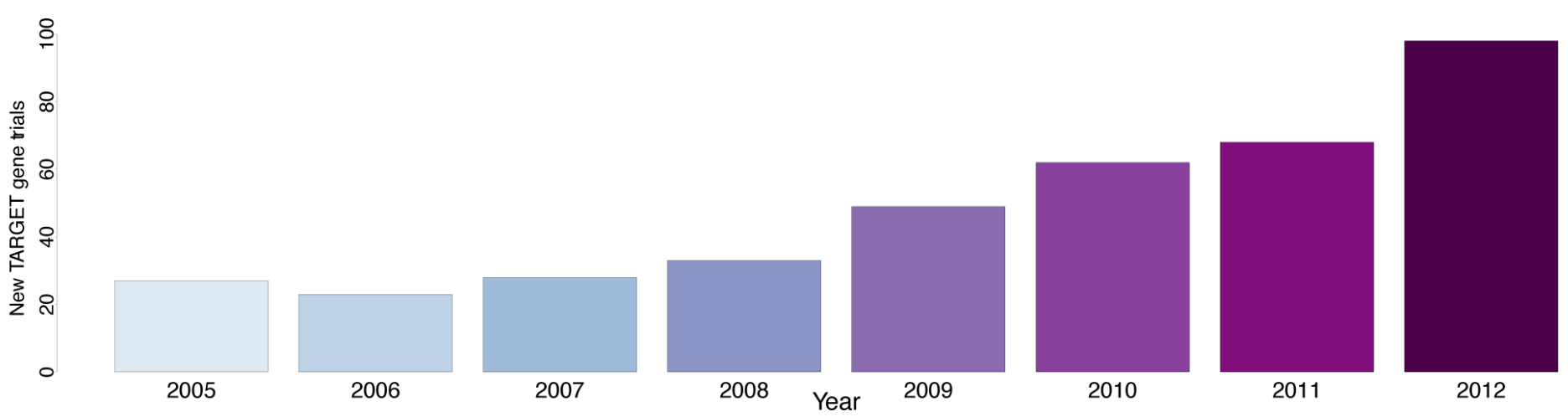
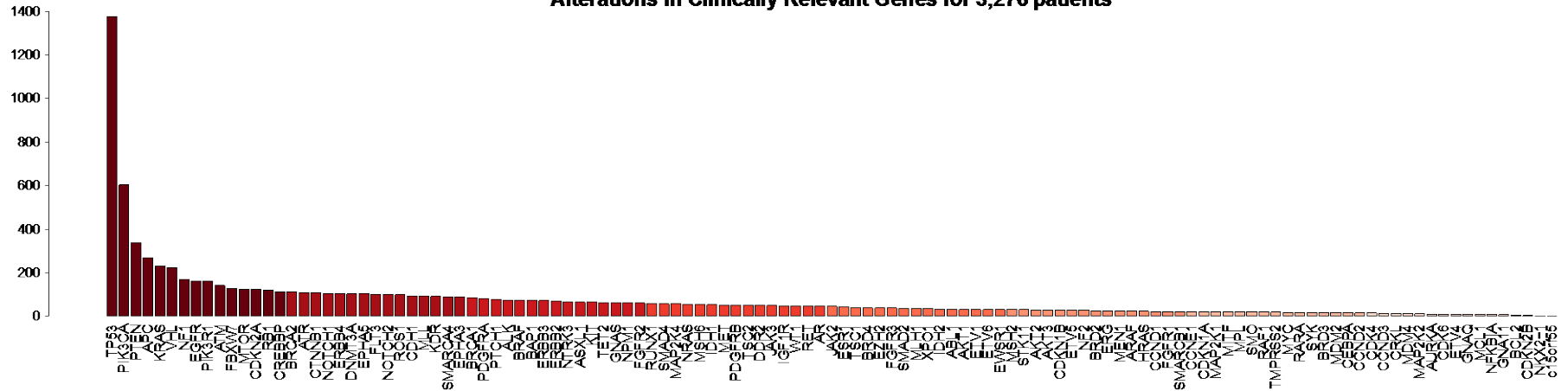
Theme 3: Genes that are rarely mutated in one tumor type occur frequently across tumor types



- Alterations in MTOR may also predict sensitivity to everolimus [Wagle et al. Cancer Discovery 2014]
- Low frequency alterations in aggregate and across pathways are even more powerful.

Longer tail and clinical trials

Alterations in Clinically Relevant Genes for 3,276 patients



Conclusion

- Long tail of alterations in clinically relevant genes
- Upgrading from hotspot profiling to exome sequencing will yield a more complete and clinically useful patient tumor profile
- Clinically relevant alterations in well-known genes occur rarely in unexpected tumor types
- Genes rarely mutated in any given tumor type are more regularly altered when considering aggregate studies

Acknowledgments

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