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Exploring Open Scientific Questions Through Publicly Available Resources

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Exploring Open Scientific Questions Through Publicly Available Resources

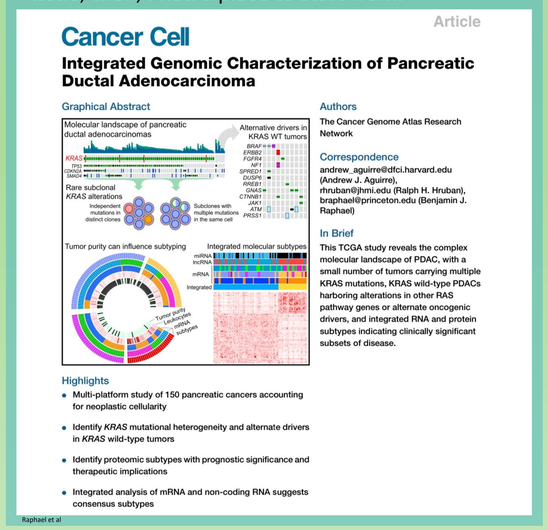
By Luke Seeman and Dr. Sarah Justice

Introduction

At countless points during any sort of scientific pursuit, there are many interesting questions that are raised that might pique the interest of those with curious minds. Questions aren't hard to come by, then, but the task becomes this: how might a scientist begin to explore a brand new question that they don't really know anything about? As it turns out, there are many ways to explore scientific data through public and open-source research tools. Over the course of the summer, I found one question in particular that grabbed me: pancreatic cancer—as of today, one of the deadliest, least-understood, and most hopeless cancers that exists—is tied astonishingly tightly to mutations in one particular gene called KRAS. Why pancreatic cancer and that gene? KRAS is expressed more in other types of tissue in the body, but cancers in those tissues are less commonly tied to KRAS mutations. For some reason, despite not seeming to rely heavily on expression of the KRAS gene, mutations in KRAS contribute to over 90% of pancreatic cancers. Why? That's what I set out to understand, and this was the path I followed to explore a question with the whole world of science in front of me.

Materials, Methods, and Results

The first place to start with any question in the sciences is an exploration of the current literature on and around the subject. Maybe the question of interest has already been answered! If not, it's always a great idea to get familiar with the current state of research and to get an idea of where to start pursuing the question. PubMed and the NCBI websites are great places to do both broad and advanced literature searches. I was able to find a number of informative articles about KRAS and its significance to pancreatic cancer, but no concrete answers. Armed with a better understanding of the issue, then, I had a place to start from.



Article

Cancer Cell

Integrated Genomic Characterization of Pancreatic Ductal Adenocarcinoma

Graphical Abstract

Highlights

- Multi-platform study of 150 pancreatic cancers accounting for neoplastic cellularity
- Identify *KRAS* mutational heterogeneity and alternate drivers in *KRAS* wild-type tumors
- Identify proteomic subtypes with prognostic significance and therapeutic implications
- Integrated analysis of mRNA and non-coding RNA suggests consensus subtypes

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In Brief

This TCGA study reveals the complex molecular landscape of PDAC, with a small number of tumors carrying multiple KRAS mutations, KRAS wild-type PDACs harboring alterations in other RAS pathway genes or alternate oncogenic drivers, and integrated RNA and protein subtypes indicating clinically significant subsets of disease.

Raphael et al

References and Links

1. Raphael, B. J., *et al*. (2017). Integrated genomic characterization of pancreatic ductal adenocarcinoma. *Cancer Cell*, *32*(2). https://doi.org/10.1016/j.ccell.2017.07.007
2. https://portal.gdc.cancer.gov/
3. https://www.proteinatlas.org/
4. https://www.cbioportal.org/

The Cancer Genome Atlas | The Human Protein Atlas | cBioPortal

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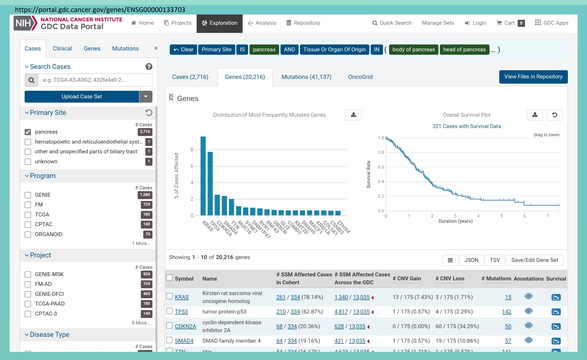
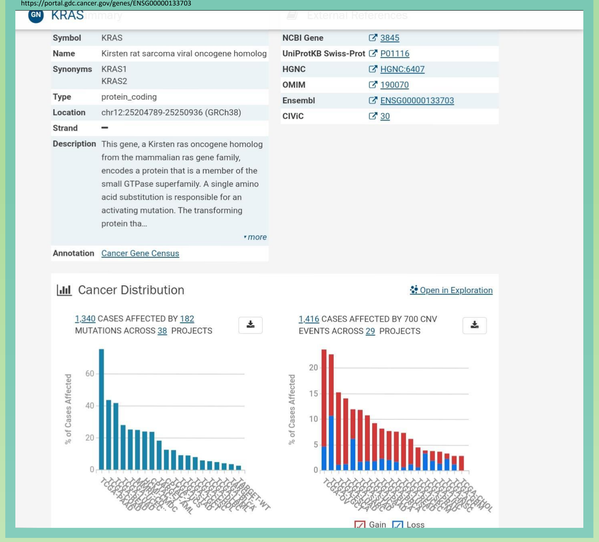
All Glory to God.

https://portal.gdc.cancer.gov/genes/ENSG00000133703

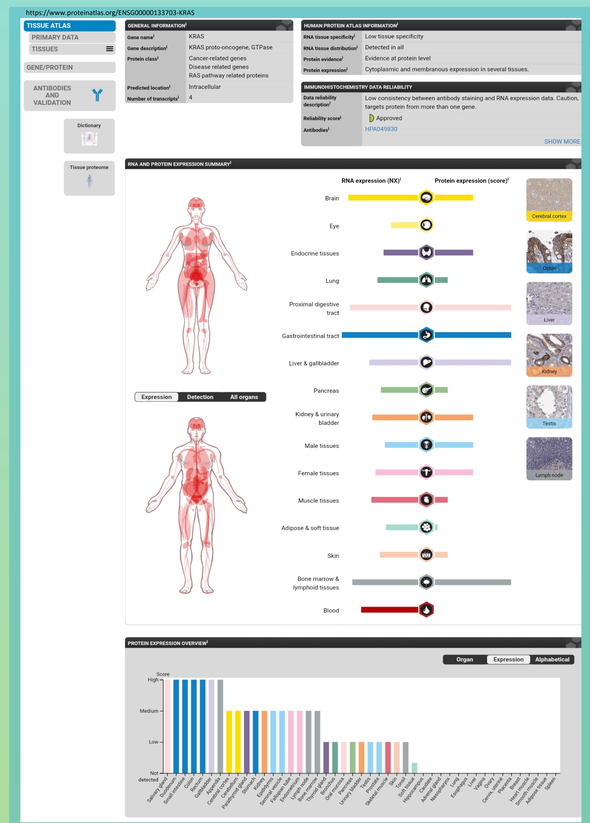


There are so many useful, public online tools to use in scientific research. Given that my question was about genomics and cancer, I decided to start with a resource tailored to my needs: The Cancer Genome Atlas. TCGA is a massive collection of data and analysis from hundreds of sources and studies, all compiled into a publicly accessible, free website. I focused in on two particular subjects using this tool: pancreatic cancer and the KRAS gene.

https://portal.gdc.cancer.gov/genes/ENSG00000133703

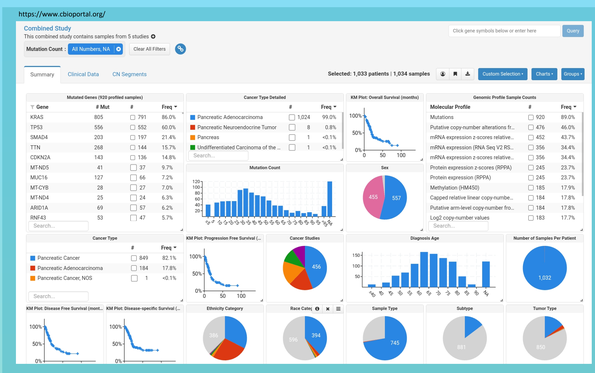


https://www.proteinatlas.org/ENSG00000133703-KRAS



I wanted to know exactly what the KRAS gene does and why mutations in it so often lead to cancer, especially in the pancreas. This led me from The Cancer Genome Atlas to another online atlas: The Human Protein Atlas. I, of course, was interested in KRAS, specifically its function and its significance to the pancreas. What I found surprised me. The KRAS gene is expressed at much higher levels in tissue other than the pancreas, especially in the gastrointestinal tract. Despite that, KRAS mutations are tied to significantly *less* cancer in the intestines than in the pancreas. Why? I had found out important information, but my question seemed to be getting stranger.

https://www.cbioportal.org/



The last of the unique online resources I used to pursue this question is called cBioPortal. This tool helped provide visualizations of data from hundreds of pancreatic cancer cases, including demographic statistics, survivability rates, and, most relevant to me and my research, the number and significance of the various mutations found across the cases. A combination of KRAS and TP53 (a tumor-suppressing gene) were far and away the most prevalent mutations. A further dive into the cBioPortal website allowed me to examine in detail each mutation, including multiple different mutations within the KRAS gene, and their specific effects and results.

https://www.cbioportal.org/

Conclusion

With the new information I'd gathered, I was no closer to being able to answer my question. In fact, the more I had found out about KRAS, the more perplexing it seemed that it should have such a strong tie to pancreatic cancer. After another literature search, my rather inconclusive conclusions had been confirmed. A number of articles looked at similar things, and the consensus is that nobody knows yet quite why KRAS mutations are so crucial to pancreatic cancer. What is undeniable is that there is a connection, and a shockingly strong one, between the two. The mystery makes the question all the more compelling, and it continues to be the focus of research, study, and experimentation from scientists all over the world. Though my research did not unlock all the secrets of cancer to me, I was able to gain invaluable experience in freely exploring a specific scientific question using resources freely available to anyone. The tools are out there waiting for you, and all you need to use them is a question and a curious mind.