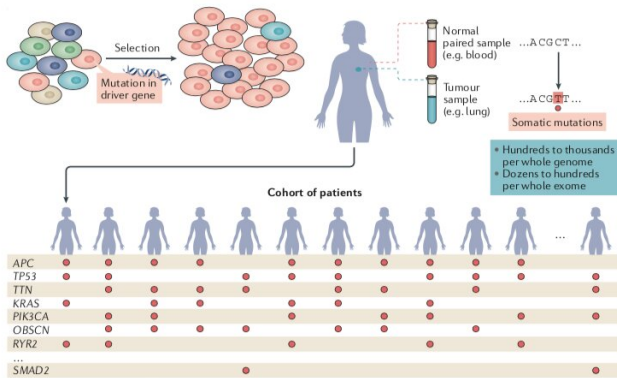


568 genes identified with the potential to trigger cancer

17 August 2020



Genomics Lab, led by ICREA researcher Núria López-Bigas, have performed an extensive computational analysis of around 28,000 tumors from 66 types of cancer and have identified 568 cancer driver genes. These pivotal genes play specific roles in the regulation of cell growth, the cell cycle and DNA replication, among others. Mutations in these genes, confer malignant cells the capacity to reproduce rapidly and endlessly, evade the [immune system](#) and other defense systems, spread and invade other tissues, and modify the environment to their benefit, among other capabilities.

Credit: Institute for Research in Biomedicine - IRB

Analysis of the genomes of 28,000 tumors from 66 types of cancer has led to the identification of 568 cancer driver genes

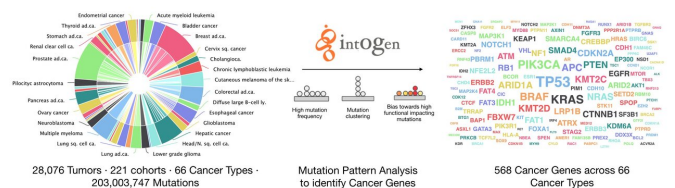
Performed by the Biomedical Genomics Lab at IRB Barcelona, the study has allowed a major update of the Integrative OncoGenomics (IntOGen) platform, aimed at identifying mutational [cancer](#) driver genes.

Published in *Nature Reviews Cancer*, the results provide the most complete snapshot of the compendium of cancer driver genes to date.

Cancer is a group of diseases characterized by uncontrolled cell growth caused by mutations, and other alterations in the genome of cells. A tumor can present from hundreds to thousands of mutations, but only a few are vital for its tumorigenic capacity. These key mutations affect the function of cancer driver genes. Finding the genes that harbor this cancer driver mutations is one of the main goals in [cancer research](#).

Researchers from IRB Barcelona's Biomedical

"The compendium of driver genes provides cancer researchers, both in the clinical and basic research setting, with crucial knowledge and it has an important impact on clinical decision-making," says López-Bigas. "For instance, if we know that the tumorigenic capacity of a tumor relies on a specific protein, an approved targeted therapy—i.e., antibodies or other inhibitors hindering its function—may be employed by oncologists to treat the patient," she adds.



Credit: Institute for Research in Biomedicine - IRB

Most cancer driver genes are highly specific

With the identification of the 568 cancer driver genes, the researchers have observed that most are highly specific and with their mutations capable

of triggering only a few tumor types. However, there is a small group, accounting for less than 2% of those identified, that is very versatile and can drive more than 20 different types of cancer. "Although it's been known that cancer driver genes have different degree of specificity since they were first identified, having this snapshot of the compendium has allowed us to address this question in an unbiased way," says Abel González Pérez, Research Associate in the Biomedical Genomics Lab, who also led the study.

Previous studies by other groups have shown that cancers are caused by an average of four key mutations in cancer driver genes. Some types of cancer, characterized by a low number of mutations, present only one mutation in these genes, while others that typically present many mutations, such as colorectal and uterus tumors, hold up to 10. Other genomic alterations, such as structural variants, changes in the number of copies of genes, and mutations affecting non-coding areas of the genome also contribute to tumorigenesis.

Positive selection as an indicator

Surprising mutational patterns in a gene, different from the expected under neutrality, constitute signals that they are under [positive selection](#) in tumorigenesis. IRB Barcelona researchers use these signals of positive selection to identify mutational driver genes. To compute these signals, the accumulation of mutations under neutrality needs to be accurately modeled for all genes, so that deviations of any gene from the expected pattern may be readily spotted.

Signals of positive selection that are exploited to identify mutational driver genes are, for example, the abnormally high number of mutations in a gene or an unexpected distribution of [mutations](#) along the sequence of a gene. In this latest article, published in the journal *Nature Reviews Cancer*, the researchers present an update of the open-access IntOGen platform, including the values computed for these signals across all mutational driver [genes](#). "The IntOGen platform provides the ideal infrastructure for the systematic update of the compendium, as more tumor sequencing data are released into the public domain," says first author

Francisco Martínez-Jiménez, postdoctoral researcher in the Biomedical Genomics Lab.

More information: Francisco Martínez-Jiménez et al. A compendium of mutational cancer driver genes, *Nature Reviews Cancer* (2020). [DOI: 10.1038/s41568-020-0290-x](https://doi.org/10.1038/s41568-020-0290-x)

Provided by Institute for Research in Biomedicine (IRB Barcelona)

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