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Analyzing cancer genomes

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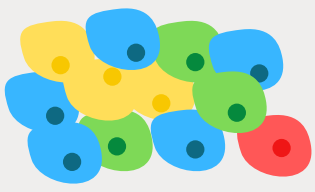
Cancer is a group of diseases characterized by **uncontrolled proliferation** of abnormal cells having the ability to spread throughout the body (**metastasis**)

Tumorigenesis follows a Darwinian evolutionary process

The formation of a tumour involves the action of two mechanisms: **variation** and **selection**.

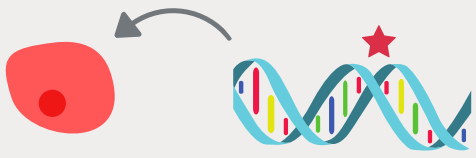
Variation

Introduces genetic differences between somatic cells



Driver mutations

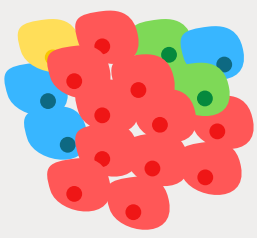
Genomic alterations that confer cells with the selective advantage to proliferate



Higher capacity to proliferate, survive, invade or hide from immune system

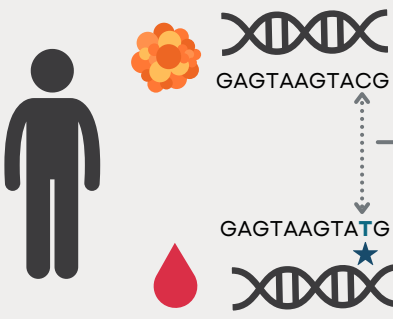
Selection

Cells which have higher fitness are positively selected



Identifying driver mutations is like looking for a needle in a haystack

Cancer cells accumulate thousands of somatic mutations, most of these are **passenger mutations** (not involved in oncogenesis). Thus, finding drivers and distinguishing them from passenger mutations is very challenging.



Identification of **somatic mutations** in the tumour by comparing the sequences from a tumour biopsy and blood sample

Somatic mutations
Are these cancer drivers?

Drivers can be detected by searching for signals of positive selection using bioinformatical tools

OncodriveFML
OncodriveCLUSTL
MutSig

Tools developed by BBGLab

BBGLab is a computational genomics laboratory led by Dr. Núria López-Bigas. BBGLab focuses on the study of cancer from a genomics perspective.

Intogen

A pipeline that analyses somatic mutations to identify cancer driver genes. It integrates seven different mutation-calling methods that detect signals of positive selection.

Cancer Genome Interpreter

A platform that interprets tumour variants. Identifies those mutations of a tumour that are more likely to be drivers and informs about the anti-cancer therapies that can target these genomic alterations.

BoostDM

A method to score all possible point mutations in cancer genes for their potential to be involved in tumorigenesis

References

Martínez-Jiménez, F., Muiños, F., Sentís, I., Deu-Pons, J., Reyes-Salazar, I., Arnedo-Pac, C., Mularoni, L., Pich, O., Bonet, J., Kranas, H., Gonzalez-Perez, A., & Lopez-Bigas, N. (2020). A compendium of mutational cancer driver genes. In Nature Reviews Cancer (Vol. 20, Issue 10, pp. 555–572). Nature Research. https://doi.org/10.1038/s41568-020-0290-x

https://bbglab.irbbarcelona.org/tools/