PRINCIPE FELIPE
CENTRO DE INVESTIGACION

The Future of Biomedical Research Lecture Series

Tumor genomes shed light into somatic mutational processes and cancer vulnerabilities

Speaker: Dra. Nuria López-Bigas
ICREA and Institut for Research in Biomedicine (IRB), Barcelona, Spain
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Somatic mutations are the driving force of cancer genome evolution. The rate of somatic mutations appears to be greatly variable across the genome due to variations in chromatin organization, DNA accessibility and replication timing. However, other variables that may influence the mutation rate locally are unknown. We have recently demonstrated that DNA-bound proteins, such as transcription factors and histones, interfere with the Nucleotide Excision Repair machinery, which results in an increased rate of DNA mutations at the protein binding sites. This finding has important implications for our understanding of mutational and DNA repair processes and in the identification of cancer driver mutations. Given the evolutionary principles of cancer, one effective way to identify genomic elements involved in cancer is by tracing the signals left by the positive selection of driver mutations across tumours. We have identified 459 cancer genes with driver mutations by analyzing close to 7000 tumor exomes from 28 different cancer types, and we have search for their targeted therapeutic opportunities. Currently we are analyzing hundreds of tumor whole-genomes to identify non-coding elements, including promoters, enhances, 5' and 3' untranslated regions, microRNAs and lncRNAs, with cancer driver mutations.

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