Cancer Core Europe Lecture

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SPEAKER

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Dissecting the function of copy number alterations in cancer

April 10, 2025 | 15:00 CEST

Link to Zoom

Chromosomal deletions are prevalent in cancer, yet their function remains ill-defined. One of the most frequent losses affects chromosome 9p21.3, which disables the CDKN2A/B tumor suppressor genes. Intriguingly, half of 9p21.3 deletions encompass a cluster of 16 type I interferons (IFNs) whose co-deletions have not been functionally characterized. To dissect this biology we developed MACHETE (Molecular Alteration of Chromosomes with Engineered Tandem Elements), a genome engineering strategy to create megabase-sized deletions. 9p21.3-syntenic deletions in a mouse model of pancreatic cancer revealed that concomitant loss of Cdkn2a/b and IFNs led to immune evasion and metastasis. Mechanistically, IFN co-deletion disrupted antigen-presenting cells and facilitated escape from CD8+ T cell surveillance in a cell extrinsic manner.

Our results establish co-deletions of the IFN cluster as a pervasive route to tumor immune evasion and metastasis. This study establishes a framework to dissect the functions of genomic deletions in cancer and beyond.

Francisco Barriga got his biochemistry degree in the Pontificia Universidad Católica de Chile. For his PhD, he joined the Batlle lab at IRB Barcelona to work on intestinal stem cell heterogeneity. For his postdoc joined the Lowe lab at MSKCC, where he focused on studying copy number alterations in cancer. He developed new genome engineering approaches and studied how chromosome 9p21.3 drives tumor suppression. He now leads the Cancer Genome Engineering lab at VHIO, where his group studies cancer genetics as a driver of immunity, tumor heterogeneity, and therapy response.

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