SÉMINAIRES ET CONFÉRENCES



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Head of Operations & Biology of ChemoGenix: the pooled CRISPR/Cas9 screening platform of IRIC, Université de Montréal

"Large scale genome-wide CRISPR/Cas9 chemogenomic KO screens reveal drug mechanisms of action and identify novel gene functions."

Genetic screens are one of the most potent unbiased tools to identify gene functions. Following pioneering studies of whole genome gene deletion studies in yeast, CRISPR/Cas9 pooled genome-wide KO screens now allow similar screens to interrogate directly the genetics of human cell lines. When made in the presence of bioactive compounds affecting growth (chemogenomic screens), the genes whose knockout are deleterious to growth (sensitizers or synthetic lethals) or favor growth (rescues or suppressors) can be used to infer Mechanism of Action (MOA) for compounds with unknown MOA and associate gene functions to gene hits for a given specific chemical perturbation. We have now screened a single human cell line (NALM-6 pre-B lymphocytes) with 710+ different compounds with various activities in 1000+ independent genome-wide screens. The resulting dataset is the single largest repertoire of isogenic human chemogenomic screens generated to date. We uncovered genetic signaling networks implicated in many aspects of cell biology among which are cell cycle control, apoptosis, mitosis, cytokinesis, oxidative phosphorylation, nucleotide biosynthesis, MTOR and RAS signaling. As our screening efforts continue, identifying MOA for compounds from cross-screen comparisons is anticipated to become easier, ChemoGenix, the IRIC-based pooled CRISPR/Cas9 screening platform we are launching, plans to share its expertise providing human chemogenomic CRISPR screening capacities to all academic institutions with access to comparison to the largest set of chemogenomic signatures. This endeavor has the potential to rapidly elucidate a large portion of the "chemical space" capable of affecting human cell growth while also democratizing access to low-cost genome-wide CRISPR screening capacities to all labs.

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