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Geoffrey Pawlak, Julia Puig, Aurélien Dispot, Wajdi Dhifli, Mohamed Elati

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BLCA-RegMap portal: a co-regulatory influence network view of bladder cancer heterogeneity and plasticity

Pawlak G., Puig J., Dispot A., Dhifli W., [Elati M.](#)

CANTHER, University of Lille, CNRS UMR 1277, Inserm U9020, 59045 Lille cedex, FRANCE

Introduction: Bladder cancer studies performed in a variety of laboratories and by a number of large-scale projects have given an unparalleled amount of information on tumors and in vitro models. Consolidating these data into an easily accessible and comprehensive system-level format is crucial to accelerate systems oncology model development.

Methods: We combined network biology with machine learning and visualization techniques to execute a cycle of systems oncology model development: inference of the co-regulatory networks (from transformed cells in vitro), interrogation of the tumors in vivo using the inferred networks, and intervention with the network (feeding back to the in vitro tumor models). First, analysis of the in vitro gene expression profiles of 36 bladder cancer cell lines of the CCLE with CoRegNet yields to the reconstruction of the first co-regulatory influence network (BLCA-CoRegNet) that contains 359 TFs/co-TFs linked by 508 significant co-operativity interactions and regulating 6,374 target genes. Second, BLCA-CoRegNet based influence map (BLCA-RegMap), is built using a meta-cohorts of > 2500 tumours and >100 cell lines transcriptome profiles.

Results: We introduce BLCA-RegMap a powerful web-based tool to help researchers to rapidly access a co-regulatory influence network view of bladder cancer heterogeneity and plasticity. BLCA-RegMap allow user to: explore the similarities and differences between cancer subtypes and identify their possible core regulators; identify rare subtypes; align tumor and cell line transcriptional profiles; and define new targets related to the different states and plasticity of the tumours (undifferentiated vs differentiated, therapy sensitive vs resistant cells, etc.). BLCA-RegMap has a very intuitive interface, and no bioinformatics skills are required. For all the networks and plots that are generated, the user can run different annotation (classification, genomic alteration and clinical), add new transcriptome data, and the raw data to reproduce the plots can be downloaded for future analysis or publications.

Conclusions: The identification of regulatory networks and the study of their plasticity should allow to identify efficient therapeutic strategies and will pave the way for precision oncology.