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Searching for Modulators of Cancer Therapeutic Resistance

Miquel Angel Pujana

Catalan Institute of Oncology, IDIBELL

Abstract

In the past recent years, there has been a substantial progress in the development of precise therapies against cancer. However, inference of the likelihood of cancer progression and/or therapeutic response based on data of a given cancer driver and/or therapeutic target is frequently incomplete. Too often cancer patients show insufficient benefit from an indicated therapy and this is in part likely due to incomplete knowledge of the molecular modifiers of current therapeutic approaches. Here, we have developed and applied an analytical framework to systematically identify the modulators of cancer drivers compiled through 15 human cancer types.



More than 30,000 gene pairs have been identified, and the predictions are robust when effects are assessed using protein expression or somatic mutation data. The modulators are classified in different biological processes and signaling pathways according to the type of gene expression association with the corresponding drivers and to the effect on risk (increasing or decreasing) of relapse. While some modulators represent synthetic lethal interactions with their corresponding drivers, integration of drug and small

compounds information reveals approximately 1,900 instances where cancer relapse could be modified. Experimental validations are ongoing. A data web portal will be open to the community to facilitate the discovery of new single or combined therapeutic approaches for improving cancer cure.

Short bio



Dr. Miquel Angel Pujana leads the “Resistance, Susceptibility and Tumor Progression” research group of the Catalan Institute of Oncology (ICO), IDIBELL (L’Hospitalet del Llobregat). The group generates and integrates experimental and bioinformatic data towards a better understanding on how cancer develops, progresses and responds to therapies. The team’s work is mainly focused on breast cancer, although novel approaches have been applied to different settings. In 2015, Dr. Pujana was designated Director of a new ICO

research program focused on “therapeutic resistance”; ProCURE. This program includes 10 independent research groups across three institutes and whose activity is centered on “fighting” cancer therapeutic resistance. Dr. Pujana is author of >100 peer-review publications, including studies of new cancer susceptibility genes, genetic interactions influencing risk, molecular mechanisms of resistance, and integrative-network analysis of biological and/or medical data. Dr. Pujana is also member of the Consortium of the Investigators of Modifiers of BRCA1/2 (CIMBA) and in this context leads studies on the genetic basis of breast cancer risk.