

Speakers at the CC BIO Annual Symposium 2017

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The cell response to anticancer drugs is defined by the p53 protein isoforms in mutant TP53 cells

Abstract:

All genetic models, experimental and clinical data indicate that TP53 gene play key roles in cancer formation, progression and treatment. For 30 years, it was thought that TP53 is a dedicated tumor-suppressor encoding a single transcription factor, p53, which protects cells from genotoxic stress. However, it is poorly understood how a single protein, p53, can be responsive to so many stress signals and orchestrates very diverse cell responses to maintain/restore cell/tissue functions.

The uncovering that TP53 gene physiologically expresses, in a tissue-dependent manner, not one p53 protein but twelve different p53 proteins with distinct biochemical activities (p53 isoforms) may prove fundamental to decipher the p53 pathway and improve cancer treatment. Over the last decade, all genetic animal models of p53 isoforms (zebrafish, drosophila and mouse), have consistently indicated that altering expression of a few p53 isoform, without affecting canonical p53 protein expression (ie. p53 α), promote different pathologies: premature ageing, (neuro-)degenerative diseases, inflammation, cancer, embryo malformation and altered responses to ionising irradiation or infectious diseases. The p53 isoforms are dynamically reforming in depth the p53 field.

I will summarise a decade of research on p53 isoforms and present our latest experimental and clinical studies in breast cancer that could be extended to predict response to treatment in other type of cancer.