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A robust gene signature predicting deficient homologous recombination DNA repair

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Homologous recombination-mediated DNA repair deficiency (HRD) predisposes to cancer development, but also provides therapeutic opportunities with poly (ADP ribose) polymerase (PARP) inhibitors being synthetically lethal with HRD. Here, we identified an HRD gene signature that robustly predicted HRD and sensitivity to PARP inhibitors. Unexpectedly, concurrent loss of *PTEN* in *BRCA1*-deficient cells may extensively rewire the HR repair network and confer resistance to PARP inhibitor, partially through over-expression of TTK. We used the HRD gene signature as a drug discovery tool and found several PARP-inhibitor-synergizing agents through the connectivity map. Thus gene expression profiling can be used to define the functional status of the HR repair network providing prognostic and therapeutic information.

Biography

Shiaw-Yih Lin has studied DNA damage response in cancer for more than 10 years, during which time he has authored more than 40 peer-reviewed reports. He has served on the editorial boards for the World Journal of Clinical Oncology, American Journal of Cancer Research, Frontiers in Molecular and Cellular Oncology, World Journal of Translational Medicine, and Experimental Hematology & Oncology. He is a member of the International Scientific Advisory Board for International Institute of Anticancer Research, and he has served on numerous review committees for the NIH, DOD and Susan G. Komen for the cure.

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