PARP & DDR Inhibitors Summit

SPEAKER INTERVIEW

AN EXCLUSIVE SPEAKER INTERVIEW WITH...

Timothy A. Yap
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Dr. Timothy Yap is a Medical Oncologist and Physician-Scientist based at the University of Texas MD Anderson Cancer Center. He is an Associate Professor in the Department for Investigational Cancer Therapeutics (Phase I Program), and the Department of Thoracic/Head and Neck Medical Oncology. Dr. Yap is the Medical Director of the Institute for Applied Cancer Science, a drug discovery biopharmaceutical unit where drug discovery and clinical translation are seamlessly integrated.

Dr. Yap's main research focuses on the first-in-human and combinatorial development of molecularly targeted agents and immunotherapies, and their acceleration through clinical studies using novel predictive and pharmacodynamic biomarkers. His main interests include the targeting of the DNA damage response (DDR) with novel therapeutics, such as ATR and PARP inhibitors, as well as the development of novel immunotherapeutics. His laboratory interests included the development of patient-derived xenografts (PDXs) and circulating plasma DNA as predictive biomarkers of response for novel targeted agents and immunotherapies in clinical trials.

What, in your opinion, are the 3 greatest challenges faced in the DDR therapy field today?

- Determining the specific mechanisms that underlie response and resistance to DDR therapies
- Establishing registration strategies for DDR therapies beyond PARP inhibitors, e.g. ATR, DNA-PK, ATM, WEE1 inhibitors
- Managing challenging overlapping toxicities observed with DDR combination therapies, e.g. myelosuppression

How do you envision these challenges being addressed? What interesting progress is being made to further the field?

- Translational studies undertaken on sequential tumor biopsies and ctDNA samples taken from patients on DDR therapies will provide greater insights into specific mechanisms that underlie response and resistance to DDR therapies
- Innovative early phase clinical trials that assess the respective roles of DDR therapies beyond PARP inhibitors are being undertaken with early promise being made.
- Innovative strategies, such as the creative scheduling of DDR combination therapies, as well as the use of drug conjugates with alphalex peptides to enable a more tumor-specific delivery of DDR agents are showing promise preclinically and are novel approaches about to enter the clinic soon.

What are the most important or promising DDR targets in your opinion and why?

The most important DDR targets are PARP, ATR, ATM, DNA-PK, WEE1, CHK1/2 and POLQ, as these are potentially druggable targets for the clinic.

Where do you see DDR therapy fitting in the universe of cancer therapy? ie combination approaches, maintenance therapy, which line of therapy, precision medicine...

I see DDR therapy as a platform therapy with multiple applications, as monotherapy using molecularly-driven approaches, as seen with BRCA1/2 mutant cancers, both in the maintenance and relapse settings, but also in different lines of therapy, and in combination approaches to deepen responses, reverse resistance and increase the proportion of patients who may respond to single agent strategies.

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