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## SIRT1 and Chk1 inhibition as novel therapeutic strategies in melanoma

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Melanoma is the deadliest form of skin cancer. Mutational activation of the protein kinase BRAF accompanied by loss of the tumor suppressor PTEN is the most common cause of melanomagenesis. Targeted therapy against BRAF mutation represents one of the most significant advances in the treatment of melanoma. However, response to BRAF inhibitor (BRAFi) PLX4032 (vemurafenib) is not durable because many patients acquire drug resistance. Thus, therapies that can overcome resistance to the drug are urgently needed. We have demonstrated that a specific inhibitor of protein deacetylase SIRT1 (SIRT1i) and BRAFi synergistically reduces the viability of melanoma cells and SIRT1i slows melanoma tumor growth in mouse xenografts. Cell cycle checkpoints are very promising targets for anticancer therapies because they control cancer cell responses to chemotherapy and radiation. Currently, Chk1 inhibitors (Chk1i) are being tested clinically for several cancers. Our novel findings show that a specific Chk1i significantly decrease cell proliferation, but even more impressively, triggers PLX4032-resistant melanoma cells regaining the sensitivity to the drug. We hypothesize that SIRT1i and Chk1i will augment the potency of BRAFi against melanoma. The use of combinatorial therapies will improve the outcomes and curtail the resistance to BRAFi in melanoma. Our work holds promise for finding novel targets for anti-cancer therapies and will provide new therapy options for melanoma patients.

### Biography

A-Lien Lu-Chang has completed her PhD from the University of North Carolina at Chapel Hill and has done her Post-doctoral studies from Duke University, School of Medicine with Paul Modrich (Nobel laureate in Chemistry in 2015). She is working as the Professor of Biochemistry and Molecular Biology at University of Maryland Medical School and a Member of University of Maryland Greenebaum Comprehensive Cancer Center. She has published more than 63 peer-reviewed papers in reputed journals, holds a patent, and has been serving as an Eeditorial Board Member for four journals. Her laboratory is currently studying the interplays among DNA repair, DNA replication, cell cycle checkpoint, transcription and chromatin remodeling. She investigates the impact of their co-ordination on telomere integrity and carcinogensis. Her team's work highlights potential targets that can be exploited clinically for cancer therapies.

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