What can we contribute to breast cancer in Taiwan?

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Our goal is to develop effective treatments for cancer patients. To this end, we showed the important role of ubiquitination and glycosylation pathways in regulating the immunosuppressive activity of PD-L1 (***Nature Comm*** 2016; ***Cancer Cell*** 2016). We have engineered monoclonal antibodies against glycosylation-specific PD-L1 with impressive therapeutic effect (***Cancer Cell*** 2018a). To select the proper cohort to be treated with the right drugs, we developed a method to accurately detect PD-L1 expression in tumors by removing the glycan moieties from PD-L1 (***Cancer Cell*** 2019). This method prevents at least 50% false-negative PD-L1 detection in human tumors. It can be used to select PD-L1 positive tumors for effective treatment. In collaboration with KMU, the CMU/KMU team recently showed that nine TNBC patients excluded for Atezolizumab treatment based on the criteria from the IMpassion131 trial for PD-L1 staining in the immune cells exhibited a close correlation between clinical response and the levels of de-glycosylated PD-L1 in tumor cells (***AJCR*** 2022).

In addition, we demonstrated the therapeutic efficacy of metformin-anti-CTLA4 combination in different mouse models (***Mol Cell*** 2018); etoposide suppressing signaling of PD-L1 to sensitize cancer cells to anti-Tim 3 therapy (***Nature Comm*** 2018); the role of Tyro 3 in resistance to anti-PD-1 therapy (***JCI***, 2021). Through vigorous studies, we identified additional potential targets to develop effective immune-combinational therapy, including c-MET inhibitors (***Gastroenterology*** 2019), IL-6/JAK1 pathway (***JCI*** 2019), and Galectin-9 (***Nature Comm*** 2021). We also reported a novel PD-L1 function that is independent of its role in immune checkpoint, namely PD-L1 in the nucleus harbors a nuclear transcriptional activity and promotes tumor pyroptosis downstream of TNFα (***Nat. Cell Biol*** 2020; ***Mol Cell*** 2021). More recently, resistant mechanism was identified to the PARP inhibitors and effective combination therapy was developed (***Nature Cancer*** 2022). In this talk, I will also summarize multiple new advances of anti-PD-L1/ PD-1 that have recently been developed in the literature, if time allows (***Nature Reviews Clinical Oncology***, 2022).