Cheng-Yen Chang
Predoctoral Student
Translational Biology and Molecular Medicine Graduate Program

Irreversible Mitochondrial Metabolic Reprogramming in Alveolar Macrophages Accelerates Lung Cancer Progression

Cheng-Yen had her bachelor's degree at National Tsing Hua University in Taiwan. She further trained herself and had her master's degree in microbiology at National Taiwan University. She came to the US for graduate training in The Translational Biology and Molecular Medicine Program at Baylor College of Medicine. In 2017, she joined Dr. Farrah Kheradmand's lab. During her time at Baylor, she attained meetings and obtained awards, including the NIOSH T41 training grant and CPRIT fellowships.

Abstract: Small airborne pollutants from incomplete combustion of tobacco and other organic matter drive inflammation and have been associated with chronic lung diseases. We have discovered that nano-sized (<50 nm) particulate matter (e.g., elemental nano-carbon black; nCB) is formed in cigarette smoke and accumulates in lung macrophages. Mice exposed to nCB develop pulmonary emphysema, supporting the clinical significance of nCB in causing lung inflammation. However, little is known about the role of nCB in lung cancer initiation and progression. Using two murine models of non-small cell lung cancer (NSCLC), we found nCB accelerates NSCLC progression. nCB-exposed lungs had increased lactate, an immunosuppressive metabolite, resulting in PD-1+ T lymphocytes, PD-L1+ myeloid cells, and FOXP3+ Tregs recruitment and tumor growth. The source of increased lactate is from alveolar macrophages, which condense nCB particles in their cytoplasm and mitochondria, impairing mitochondria energy homeostasis and promoting glycolysis. Due to the hydrophobic nature of nCB, this metabolic reprogramming is irreversible, permanently activating the mTOCR1-HIF1 pathway to drive glycolysis. Furthermore, nCB-induced expression of PD-L1, IL-10, Il4i1, and Arg1 expression in lung macrophages leads to impaired anti-tumor immunity. Our findings demonstrate that nCB metabolically reprograms lung macrophages and fosters immunosuppression to promote lung cancer.

Reference: You, R., et al. Nanoparticulate carbon black in cigarette smoke induces DNA cleavage and Th17-mediated emphysema. Elife (2015).