GRANT RECIPIENT: Haizhen (Jen) Wang, Ph.D. (Profile)

HOLLINGS CANCER CENTER (MEDICAL UNIVERSITY OF SOUTH CAROLINA)

PROJECT: CDK6 in T-cell Leukemia Immune Evasion

Project Details: Relapse is the most common cause of treatment failure in acute lymphoblastic leukemia (ALL). It is not clear how leukemia cells escape the immune system to infiltrate and relapse. Upregulation of PD-L1 on cancer cells is one of the important mechanisms to initiate their immune evasion. Recent studies showed that high PD-L1 expression levels are associated with relapse and worse overall survival rates in leukemia. Understanding the regulatory mechanism of PD-L1 expression in leukemia cells will help to develop therapeutic strategies to prevent immune evasion, infiltration and relapse of leukemia. My previous work showed that cyclin-dependent kinase 6 (CDK6) has pro-survival functions in T acute lymphoblastic leukemia (T-ALL) by regulating glycolysis and cellular reactive oxygen species. Recent work by my laboratory found CDK6 facilitates PFKP nuclear translocation to promote leukemia infiltration. Importantly, we found CDK6 dependent phosphomimic PFKP-S679E upregulates PD-L1 expression in T-ALL. This study will elucidate the molecular functions of CDK6 in regulating PD-L1 expression and immune evasion of leukemia cells, and provide fundamental theory about therapeutic effect of CDK6 inhibition on T-ALL relapse. The overarching hypothesis is: CDK6 drives T-ALL immune evasion through the phosphorylation of PFKP and PD-L1 expression.

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