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Targeting casein kinase II (CK2) for treatment of high risk leukemia

Acute lymphoblastic leukemia (ALL) is the most common cancer in children and accounts for highest death rate among children aged 10-19 years. Current treatment for relapsed high risk ALL involves augmented chemotherapy, hematopoietic stem cell transplant and radiation therapy which adds to the morbidity of already sick children. Recent genome-wide studies of leukemic blasts have detected genetic lesions such as deletions or mutations in *IKZF1*. Alterations in *IKZF1* have proven to be an indicator of inferior outcome in patients with high-risk ALL. Ikaros (*IKZF1*) functions as a master regulator of hematopoiesis and a tumor suppressor in ALL. Ikaros binds to the upstream regulatory elements of its target genes and regulates their transcription via chromatin remodeling. Casein kinase II (CK2) is a pro-oncogenic protein which is overexpressed in various cancers including leukemia. Functional experiments showed that CK2-mediated phosphorylation of Ikaros, regulates Ikaros' DNA binding affinity, subcellular localization, and protein stability. Dysregulation of several biological pathways in children with high-risk B-ALL results from CK2 overexpression and impaired Ikaros function. Targeted inhibition of CK2 restores Ikaros tumor suppressor function in high-risk B-ALL even in cases with single allele Ikaros deletion. Treatment with the selective CK2 inhibitor, CX4945 exhibits an anti-leukemic effect in primary xenograft models of high-risk B-ALL. Further studies use precision medicine approaches (targeting specific pathways and/or functional defects) to develop novel drug combinations to target these dysregulated pathways by inhibiting CK2 and restoring Ikaros tumor suppressor function as well as using a specific inhibitor of the signaling pathway.

Biography

Chandrika Gowda is a Board Certified Pediatric Hematologist-Oncologist and Physician Scientist at Penn State Children's Hospital and Penn State college of Medicine in United States. After completing her training in 2013, she continued at PSU as an Assistant Professor. Her research focus for the past seven years has been in pediatric leukemia, specifically to determine the mechanisms of tumor suppression by *IKZF1* gene and development of novel targeted therapies for treatment of high risk pediatric leukemia and neuroblastoma. She has authored several publications and presented her work in various national and international scientific forums. She leads a well-funded research program at PSU.

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