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The effect of surface glycans on leukemia susceptibility to NK-mediated cytotoxicity

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The aberrant glycosylation on proteins and lipids has been implicated in malignant transformations through promoting the tumorigenesis, metastasis and the evasion from the host immunity. The I-branching β-1,6-N-acetylglucosaminyltransferase, responsible for the straight I conversion to branched I histo-blood group antigens, has been reported for its important effects on the migration, invasion and metastasis of solid tumors. First, we demonstrated that SHP-2-ERK2 signaling regulates the phosphorylation status of C/EBPα by altering its binding affinity onto the IGnTC promoter region, thereby activating the synthesis of cell-surface I antigen formation during erythropoiesis. Second, we addressed how the branched I antigens on the leukemia impacted the host immuno-surveillance mediated by Natural Killer (NK) cells. The levels of I antigen presented on leukemia cells showed a positive correlation with the susceptibility to NK-mediated lysis. Third, by the conjugation assay, elevating the expression of the I antigens on the leukemia cells that can only display low level of cell surface I antigens greatly increased the sensitivity to NK cytotoxicity. Our findings suggested that branched I of the leukemia cells not only is important for NK targeting but also could serve as a potentially evaluation maker for NK-cell based leukemia treatment.

Biography

Yuh-Ching Twu is an Associate Professor at Department of Biotechnology and Laboratory Science in Medicine, National Yang-Ming University, Taiwan. She received her BS and Master degrees in Biotechnology & Laboratory Science from National Yang-Ming University and PhD degree in Biochemistry Science from National Taiwan University. She has done Post-doctoral programs in Department of Microbiology and Immunology, University of British Columbia and Terry Fox Laboratory, BC Cancer agency. She works on the molecular genetics of human blood group I locus, the regulatory mechanism of branched I formation and the correlation with immune-surveillance.

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