Blockade of integrin alpha4 by natalizumab sensitizes T-ALL cells to chemotherapy

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Acute lymphoblastic leukemia (ALL) occurs in both children and adults with peak incidence between 2 and 5 years of age. Over the last decades, survival in pediatric ALL has improved to 85%~90% and around 40% in adults. Still the relapse remains major obstacle for the cure of ALL. In our previous study, we demonstrated that integrin alpha4 blockade using natalizumab, a humanized monoclonal antibody against integrin alpha4, reduced adhesion of pre-B ALL cells to bone marrow (BM) stroma and with combination of conventional chemotherapy eliminated resistant pre-B-ALL clones in a MRD mouse model. The present study explored the potential of Natalizumab as a novel T-ALL treatment modality. Natalizumab inhibited adhesion of patient-derived T-ALL cells to BM stroma and attenuated leukemia progression, resulting in prolonged survival of recipient NOD/SCID IL2R gamma-/- mice of patient-derived T-ALL. Integrin alpha4 blockade interferes with adhesion of T-All cells to its ligand VCAM-1 and might be considered as a novel adjuvant strategy against T-ALL. Further study is needed to investigate at the molecular level to elucidate the effect of alpha4 blockade in T-ALL.

Biography

Enzi Jiang received her MD from Norman Bethune College of Medicine, Jilin University, formerly Norman Bethune University of Medical Science, Changchun, China in 1987. She completed her PhD from Harbin Medical University in 1999 and Postdoctoral research from University of Texas Southwestern Medical Center at Dallas in 2007. She is working as a Senior Scientist at Division of Hematology and Oncology, Children’s Hospital Los Angeles University of Southern California Keck School of Medicine, Los Angeles, USA. She has published more than 15 papers in reputed journals related to mesenchymal stem cells and leukemia and contributed to a book chapter (Chapter 4: Molecular Pathogenesis of ALL, Contemporary Management of Acute Lymphoblastic Leukemia, In Press 2014). She has been serving as an Editorial Board Member for the Journal of Blood Disorders and Transfusion since February, 2013. Her research interests include overcoming drug resistance in ALL and related mechanisms.

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