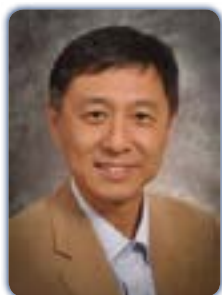


PEDIATRIC ONCOLOGY AND PEDIATRIC MEDICINE

October 05-06, 2017 Las Vegas, USA



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Lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) is a therapeutic target of sickle cell disease vasculopathy

Sickle cell disease (SCD) is a recessively inherited disorder that affects hemoglobin structure, function and stability. Although the principal manifestation of SCD is anemia, the significant morbidity and mortality of SCD is due to vaso-occlusive complications. Strokes in children and adults with SCD continue to be a major cause of morbidity and mortality, <50% of the children with SCD will have either an overt or silent cerebral infarct before their 18th birthday. Lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) has been identified as a major receptor for oxidized low-density lipoprotein (ox-LDL) as well as phosphatidylserine of aged RBC cells in endothelial cells. We have recently reported increased expression of LOX-1 in human vascular endothelial cells exposed to sickle erythrocytes, as well as in the vessels of SCD patients with vaso-occlusive damage, suggesting a possible causative link between the increased expression of LOX-1 and SCD vasculopathy. The sickle erythrocyte/LOX-1 axis plays a key role in initiating the vicious cycle of SCD that results in vaso-occlusion. The mechanism involves LOX-1 serving as a tether that attaches sickle red blood cells to vascular endothelial cells. This in turn causes signaling amplification that involves upregulation of LOX-1 expression, oxidative stress, and the release of thromboxane A2 that results in further platelet activation/aggregation and vasoconstriction, ultimately leading to vaso-occlusive events and the clinical manifestations of SCD. We anticipate the findings could also lead to the identification of useful therapeutic strategies for the effective clinical management of this debilitating inherited disease.

Biography

Mingyi Chen is currently an Associate Professor at UTSW Medical center since 2016. Formerly, He was an Associate Professor at the UC Davis Health System in California (since 2010). He is a board certified in Hematology and Pathology (Anatomic and Clinical Pathology). His areas of clinical interest include: hematopathology - lymphoma, leukemia, flow cytometry, bone marrow transplant, diagnostic molecular pathology by NGS mutational analysis, pulmonary pathology and GI-liver pathology. My research interests include atherosclerosis, thrombosis, vascular biology, lipid metabolism, GVHD, molecular pathogenesis of lymphoma and leukemia, tumor immunology, viral infections and carcinogenesis. His current research focuses on the genetic and epigenetic alterations of endothelial cells and hematopoietic cells. The primary diseases against which advancements in his laboratory are targeted are malignant lymphoma, leukemia and other hematological problems. He received MD from Peking University Health Science Center and PhD in Pharmacology from Kyoto University. He has completed residency training at UCSD and Loma Linda University Medical Center and Fellowship in Hematopathology at City of Hope National Medical Center. He published over 90 peer reviewed papers and 120 abstracts, 11 book chapters, and delivered many speeches and education courses in scientific meeting in ASH, USCAP, CSP, ASCP, ISH etc.

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