

Mechanism of mesenchymal stem cells-involved vascular repair/ remodeling

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Transforming growth factor (TGF) β is maintained in a sequestered state in extracellular matrix as a latent form, which is considered as a molecular sensor that releases active TGF β in response to the perturbations of the extracellular matrix. The biological implication of the temporal discontinuity of TGF β storage in the matrix and its activation is obscure. We show that active TGF β controls the mobilization and recruitment of (mesenchymal stem cells) MSCs to participate in tissue repair and remodeling. MSCs were mobilized into the peripheral blood in response to vascular injury and recruited to the injured sites where they gave rise to both endothelial cells for reendothelialization and myofibroblastic cells to form thick neointima. Intravenously injection of recombinant active TGF β 1 in uninjured mice rapidly mobilized MSCs into circulation. Further, inhibitor of TGF β type I receptor blocked the mobilization and recruitment of MSCs to the injured arteries. Thus, TGF β is an injury-activated messenger essential for the mobilization and recruitment of MSCs to participate in tissue repair/remodeling.

Biography

Mei Wan, M.D., Ph.D. is an Associate Professor of the Center for Musculoskeletal Research, Department of Orthopaedic Surgery at Johns Hopkins University School of Medicine. She got her M.D. at Hebei Medical University in 1991. She obtained her Ph.D. in Pathophysiology at the same school in 1997. In 1998, she came to University of Alabama at Birmingham (UAB) as a postdoctoral fellow. In a series of highly cited papers, she demonstrated that the importance of this proteasome degradation pathway and control of TGF β signaling. She got the Young Investigator Award at the American Society for Bone and Mineral Research Annual Meeting in 2000. She then took an Assistant Professor position in 2004 at UAB where she identified the central mechanism through which parathyroid hormone stimulates bone formation, which had been the major unresolved question in the bone field. She took an Associate Professor position at Johns Hopkins University in 2009. Her research focuses on understanding how TGF β /Smads signaling regulates the behavior of mesenchymal stem cells (MSCs) in tissue homeostasis, repair and remodeling. In particular, she found that active TGF β can be released from tissue in response to perturbations to the local environment such as bone remodeling (*Nat. Med.* 2009, *Cell Stem Cell* 2011) and arterial injury (*Stem Cells* 2012). The released active TGF β stimulates the migration of MSCs to participate in tissue repair or remodeling. Currently, she is an editorial board member for *Journal of Bone and Mineral Research* and *Bone Research*.

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