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Tumor associated mesenchymal stem cells promote tumor development through CCR2-dependent recruitment of macrophages

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Mesenchymal stem cells (MSCs) tend to infiltrate into tumors and form a major component of the tumor microenvironment. Yet, the mechanisms through which these tumor-resident MSCs may affect tumor growth are largely unknown. We found that MSCs isolated from spontaneous mouse lymphomas (L-MSCs) could strikingly enhance lymphoma growth, whereas bone marrow MSCs (BM-MSCs) did not. Surprisingly, tumor promotion by L-MSCs was not related to immunosuppression by these cells, while they recruited abundant CD11b+Gr-1+ myeloid suppressor cells and F4/80+ macrophages to the tumor. Depletion of macrophages but not myeloid suppressor cells completely abolished the tumor-promoting effect by L-MSCs. Furthermore, L-MSCs expressed high levels of CCR2 ligands-CCL2, CCL-7 and CCL-12, and macrophage accumulation and tumor-promotion by L-MSCs were absent in CCR2-/- mice. Interestingly, inflammatory cytokine-treated BM-MSCs acted similarly with L-MSCs, indicating the importance of the inflammatory cytokines in remodeling the tumor stroma. Finally, these findings were found nonspecific to lymphomas, but also applicable to other tumor types, such as mouse melanoma. Therefore, our findings demonstrate that tumor-associated MSCs contribute to tumor development through CCR2-dependent recruitment of macrophages to the tumor, a novel mechanism through which tumor-resident MSCs function in the tumor microenvironment. This study also bears important information for current MSC-based therapies.

Biography

Guangwen Ren completed his Ph.D from UMDNJ-Rutgers University and postdoctoral studies from Robert Wood Johnson Medical School. He is currently a research teaching specialist of Child Health Institute of New Jersey. His studies are focusing on the immunoregulation of mesenchymal stem cells, which have been published in Cell Stem Cell, Journal of Experimental Medicine, Stem Cells, Journal of Immunology and Cell Research, with him as the leading author. He served as peer-reviewers for over 25 scientific journals and editorial board members of World Journal of Stem Cells, Journal of Medical Science and The Open Autoimmunity Journal.