Targeting colon cancer tumor initiating cells

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Colorectal cancer (CRC) is the third most common malignancy and the second leading cause of cancer-related deaths in America. Nearly two thirds of newly diagnosed CRC cases include lymph node (LN) involvement, and LN metastasis is one of the strongest negative prognostic factors for CRC. It is thought that CRC tumors contain a small population of drug-resistant CRC tumor-initiating cells (Co-TICs) that may be responsible for cancer recurrence. To investigate the role for Co-TICs in tumor growth and define the influence of LN stromal cells on Co-TICs, we established experimental platforms for both in vitro and in vivo testing. We found that LN stromal cell line HK cells and HK cell–conditioned media enhanced CRC tumor formation, tumor angiogenesis, and distance metastasis in our unique xenoplant model using CRC cells isolated by enzymatic digestion from consented patient specimens, HT-29 cells, HCA-7 cells, and HK cells. Cells expressing CD133 and the stromal cell–derived factor 1α (SDF-1α) receptor CXCR4 were chemotherapeutic drug resistant and metastatic to liver and lung. CD133+CXCR4+ Co-TICs isolated from patient specimens were more tumorigenic than unsorted tumor cells. Furthermore, the inhibitors specific to HK cell–derived SDF-1α reduced tumor formation and tumor angiogenesis. In addition, the functional role of soluble factors produced by stromal cells including IL-6, IL-8 and CXCL1 were examined. Taken together, we have identified a major Co-TIC/LN microenvironment-specific mechanism for CRC resistance to chemotherapeutic agents. Our results indicate the stromal cell factors may be targets for eradicating Co-TIC.

Biography

Li Li received her MD and Master’s Degree in Immunology from the Shanghai Second Medical University, Ph.D from the Lübeck Medical University, and her postdoctoral studies at Ochsner Clinic Foundation in New Orleans. She is a Director of Laboratory of Translational Cancer Research and an Associate Director of Laboratory of Cellular Immunology, Ochsner Clinic Foundation. Li has authored more than 20 papers in peer reviewed journals and shares patent ownership. Her B cell lymphoma studies were supported by various research grants including an R01 NIH grant. Her research interests include cancer stem cells and tumor microenvironment in drug resistance and disease recurrence in colon cancer, bladder cancer, and B cell lymphoma.