

Colorectal Cancer

Major finding: Colon cancer stem cells are comprised of 3 distinct functional subtypes.

Impact: One particular subtype of TICs exclusively drives metastasis formation.

Clinical relevance: Self-renewing, long-term TICs may represent therapeutic targets.

CLONAL HETEROGENEITY WITHIN THE COLON CANCER STEM CELL COMPARTMENT

Tumor-initiating cells (TICs) are cancer cells that possess stem cell-like qualities and are capable of both self-renewal and differentiation. In solid tumors, including colon cancer, TICs have been thought to consist of a homogenous population of cancer stem cells. However, Dieter and colleagues recently demonstrated that, in human colon cancer, the TIC compartment contains 3 subtypes of TICs that play distinct roles in tumor initiation, self-renewal, and metastasis formation. To assess their functional contribution, individual TICs were isolated from primary colon cancer specimens, genetically marked, and serially transplanted into primary, secondary, and tertiary recipient mice. This strategy allowed the authors to track TIC clones through the various stages of tumor initiation, tumor maintenance, and metastasis. Two types of TICs were found to contribute to the formation of primary tumors: T-TACs (tumor transient-amplifying cells) and LT-TICs (long-term tumor-initiating cells). Whereas T-TACs showed no self-renewal potential and contributed only to the generation of primary tumors, LT-TICs were self-renewing and contributed to serial tumor development. Significantly, LT-TICs were also the predominant source of metastases. The third subtype, DC-TICs (delayed contributing tumor-initiating cells), were not detectable in primary tumors, but contributed to tumor formation in subsequent transplants. Overall, the identification of 3 distinct functional groups of TICs establishes the presence of clonal heterogeneity within the stem cell compartment and delineates a cancer stem cell hierarchy that will provide insight into the regulation of tumorigenesis and inform the identification of novel therapeutic targets in colon cancer.

Dieter SM, Ball CR, Hoffmann CM, Nowrouzi A, Herbst F, Zavidij O, et al. Distinct types of tumor-initiating cells form human colon cancer tumors and metastases. Cell Stem Cell 2011;9:357–65.

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