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What roles do colon stem cells and gap junctions play in the left and right location of origin of colorectal cancers?

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This Commentary examines an important clinical observation that right-sided colorectal cancers appear less treatable than the left-sided cancers. The concepts of the initiation/promotion/progression/process, the stem cell hypothesis, the role gap junctional intercellular communication, cancer cells lacking GJIC either because of the non-expression of connexin genes or of non-functional gap junction proteins and the role of the microbiome in promoting initiated colon stem cells to divide symmetrically or asymmetrically are examined to find an explanation. It has been speculated that embryonic-like lesions in the ascending colon are initiated stem cells, promoted via

symmetrical cell division, while the polyp-type lesions in the descending colon are initiated stem cells stimulated to divide asymmetrically. To test this hypothesis, experiments could be designed to examine if right-sided lesions might express *Oct4A* and *ABCG2* genes but not any connexin genes, whereas the left-sided lesions might express a connexin gene, but not *Oct4A* or the *ABCG2* genes. Treatment of the right sided lesions might include transcriptional regulators, whereas the left-sided lesions would need to restore the posttranslational status of the connexin proteins.

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