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Obesity 2018: What roles do colon stem cells and gap junctions play in the left and right location of origin of colorectal cancers?- James E Trosko- Kermanshah University of Medical Sciences, Iran

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This "Comment" examines an important clinical observation that colorectal cancers on the right side appear less treatable than cancers on the left side. The concepts of (a) the "initiation / promotion / progression" process, (b) the stem cell hypothesis, (c) the role gap in intercellular binding communication, (d) cancer cells lacking GJIC due to non-expression of connexin genes or non-functional gap junction proteins, and (e) the role of the microbiome in promoting colon stem cells initiated to divide symmetrically or asymmetrically is examined for an explanation.

It has been speculated that "embryonic-type" lesions in the ascending colon are initiated stem cells, promoted by symmetric cell division, whereas 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 whether right-sided lesions could express the Oct4A and ABCG2 genes but not any connexin genes, while left-sided lesions could express a connexin gene, but not the Oct4A genes. or ABCG2. Treatment of right-sided lesions could include transcriptional regulators, while left-sided lesions would have to restore the post-translational state of connexin proteins.

With the important observation that the location of the origin of colorectal cancers seems to determine the lethality of the tumors, the importance of this observation tells us to look for some fundamental biological basis that can serve to provide guidelines for the prevention and treatment of both. colon cancers Metastatic colorectal cancers (CRC) can be defined based on the location of the primary tumor.

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Patients with RCC and CCL differ in their microbiome, clinical characteristics, molecular profile, clinical outcome, and response to treatment. However, embryology cannot explain these differences since the middle and posterior intestines are derived from the same origin, the endoderm and the rectum are derived from the cloacal membrane. The microbiome differs significantly between the right and left colon, which may explain the gradual changes in CRC Types MSI and CIMP throughout The gut . Regional differences in the physiological functioning of the right and left regions of the colon could expose these two types of initiated stem cells that could affect antimitogenic factors (niche extracellular matrices and soluble factors, low oxygen microenvironment) for non-expressing cells. connexin stem or contact inhibiting factors for non-GJIC-initiated stem cells expressing connexin. "LCCs are more chromosomally unstable and RCCs have a higher frequency of phenotypes with high MSI content and KRAS and BRAF mutations which may explain the worse prognosis of these patients. The location of the primary tumor is a known prognostic factor for patients with RCC. RCCs are associated with a worse prognosis than CCLs, but they can also be predictive of anti-EGFR therapies and antiangiogenic

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