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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?

James E Trosko and Heinz-Josef Lenz
Kermanshah University of Medical Sciences, Iran

This "Commentary" examines an important clinical observation that right-sided colorectal cancers appear less treatable than the left-sided cancers. The concepts of (a) the "initiation/promotion/progression" process, (b) the stem cell hypothesis, (c) the role gap junctional intercellular communication, (d) cancer cells lacking GJIC either because of the non-expression of connexin genes or of non-functional gap junction pro-teins, and (e) 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 stimu-lated to divide asymmetrically. To test this hypothesis, experiments could be designed to examine if right-sided lesions might express Oct*4A* 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.

james_Trosko@hotmail.com