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Gut microbiome: A potential regulator of cancer stem cells and colon carcinogenesis

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The concept that pluripotent cancer stem cells (CSCs) are involved in the development and progression of many types of malignancies, including colorectal cancer (CRC), is now well accepted. Earlier, we reported that patients with ≥ 3 adenomas (*High-risk for CRC*) exhibit a marked increase in CSCs in the colon than those without adenomas. Although the regulatory mechanisms for this increase in CSCs are poorly understood, we have suggested a role for secondary bile acids in the intestine, specifically deoxycholic (DCA) and lithocholic (LCA) acids, bio-transformed by gut microbiota, in regulating this process. Indeed, we observed a marked rise in *Fusobacterium nucleatum* and *Enterobacterium* (both are associated with CRC) in High-risk CRC patients. An opposite phenomenon was noted for the anti-inflammatory *Bifidobacteria* and also for the probiotic *Lactobacillus acidophilus*. Among the secondary bile acids, DCA and LCA are thought to be the most significant with respect to the development of CRC. Interestingly, we found the levels of DCA and LCA in the colon of High-risk CRC patients to be markedly higher than those at lower risk for CRC. We also found DCA and LCA to induce stemness in normal human colonic epithelial cells, as evidenced by increased colonosphere formation and elevated expression of several CSC markers as well as p-EGFR, c-myc and MMP-2, accompanied by a marked rise in lncRNAs, specifically CCAT2 and HOTAIR, which are known to be upregulated in CRC. Our observations suggest that alterations in specific gut micro-organisms resulting in increase in DCA and LCA that induce stemness in colon mucosal cells could partly be responsible for the development of sporadic CRC.

Biography:

Dr. Adhip PN Majumdar, received his MS and Ph.D. degrees from the University of London, England, and D.Sc (Doctor of Science) degree in Gastroenterology from the University of Aarhus, Denmark. Dr. Majumdar has been a Professor at Wayne State University since 1992. He also holds the post of Senior Research Career Scientist at the Detroit VA Medical Center. Over the past several years Dr. Majumdar's work has been streamlined to uncover the biochemical and physiological pathways governing the growth of gastrointestinal (GI) tract. He has published over 196 original scientific articles in peer-review journals and a multitude of book chapters and review articles. As reflected by the literature published from Dr. Majumdar's lab, he is particularly interested in elucidating the patho-physiology of age-related changes in the GI mucosa specifically those that lead to malignancy. To this end, Dr. Majumdar has begun to investigate the role of pluripotent, self-renewing CSCs in the development and progression of GI malignancies. Dr. Majumdar has been continually funded by the VA and NIH and is considered one of the nation's leading investigators in gastrointestinal aging and cancer.