Adhip P N Majumdar, J Clin Exp Oncol 2017, 6:6
DOI: 10.4172/2324-9110-C1-005

MicroRNAs in regulation of cancer stem cells and colon carcinogenesis

Adhip P N Majumdar
Wayne State University, USA

Accumulating evidence supports the contention that many malignancies, including sporadic colorectal cancer (CRC), the incidence of which increases with aging, are diseases driven by self-renewing cancer stem cells (CSCs). We have reported that CSC population in the colonic mucosa increases with advancing age, accompanied by a concomitant rise in microRNA-21 (miR-21) and reduction in miR-145 in the colon. Likewise, similar changes in miR-21 and miR-145 were also noted in the colonic mucosa of patients with CRC. These observations prompted us to speculate a role for miR-21 and miR-145 in regulating CSCs. Indeed, we found overexpression of miR-21 in colon cancer cells greatly increases CSCs and induces tumor growth. An opposite phenomenon was noted in colon cancer cells where miR-145 was upregulated. In addition, administration of either antagomir-21 (anti-sense miR-21) or excess miR-145 greatly decreases the growth of xenograft of colon cancer cells in SCID mice. Cell culture studies have further demonstrated miR-21 to regulate miR-145 and vice versa. Although the precise mechanism(s) by which miR-21 or miR-145 regulates CSCs in the colonic mucosa during the progression of CRC is unknown, our studies suggest that they induce differentiation of colon CSCs, as evidenced by the increased expression of CK-20 in colon cancer cells following downregulation of miR-21 and upregulation of miR-145. In contrast, Sox-2 expression is decreased following overexpression of miR-145. Our recent studies further suggest that both miR-21 and miR-145 are regulated by the long non-coding RNA (lncRNA) CCAT2 (Colon Cancer Associated Transcript 2), which is known to be upregulated in CRC. This inference comes from the observation that downregulation of CCAT2 in colon cancer cells, which produces a marked 50% reduction in miR-21 expression, causes a 7-fold increase in miR-145 expression. In conclusion, our current observations suggest that miR-21 and miR-145, that are upregulated and downregulated, respectively, in the colonic mucosa during aging and CRC, play critical roles in regulating stemness in colon cancer cells. Both miR-21 and miR-145 are regulated by CCAT2.

Biography

Adhip P N Majumdar received his MS and PhD degrees from the University of London, England, and DSc (Doctor of Science) degree in Gastroenterology from the University of Aarhus, Denmark. He 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 his work has been streamlined to uncover the biochemical and physiological pathways governing the growth of gastrointestinal (GI) tract. He has published 200 original scientific articles in peer-reviewed journals and a multitude of book chapters and review articles. 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, he has begun to investigate the role of pluripotent, self-renewing CSCs in the development and progression of GI malignancies. He has been continually funded by the VA and NIH and is considered one of the nation's leading investigators in gastrointestinal aging and cancer.

a.majumdar@wayne.edu

Notes: