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Probiotics, inflammasomes and colorectal cancer: an evidence based approach.

Statement of the problem:

Colorectal cancer remains among the leading causes of cancer death across the globe and its management following the standard chemotherapy is not completely promising and alternative therapeutic approaches are being explored to arrest or delay the process of carcinogenesis by using alternate biotherapeutic agents such as probiotics.

Methodology and Theoretical Orientation:

The purpose of this study is to evaluate the therapeutic potential of indigenous probiotic *Lactobacillus plantarum* (CRD7) on the cell proliferation, activation of inflammasomes (NLRP3, NLRC4, NAIP5) and mediators of inflammation (IL-18, IL-1 β , NF-kB, Ik-B, caspase-1, TLR9 and cGAS) in three differently graded human colon cancer cell lines (namely HT-29, HCT-116, and SW-480) using MTT test and Real-time PCR at 24 h, 48 h and 72 h of treatment with live and heat-killed bacteria.

Findings:

Our results shows that CRD7 has the therapeutic potential in the activation of host derived factors such as inflammasomes and suppressing mediators of inflammation in HT-29, HCT-116 and SW480 cell lines of colorectal cancer. Treatment with CRD7 activates the NLRP3 inflammasome. NLRP3 activation leads to the production of IL-18 and IL-1 β , which may participate in the regulation of intestinal inflammation and colorectal carcinogenesis. As evident from our results that treatment of live probiotic bacteria significantly upregulated the mRNA expression of TLR9 and cGAS at all the time points of experimental set up which could also leading to the activation of NF-kB, inflammasome, and interferon signaling pathways, respectively. Based on our results, TLR-9 mediated recognition of probiotic bacteria and its components in the human colon cancer cells exerts a protective effect against inflammation. Furthermore, the therapeutic effects of the CRD7 totally diminished with the heat-killed treatment at all-time points in three human graded HT-29, HCT-116 and SW480 cell lines.

Conclusion & Significance:

Our study shows that indigenous probiotic *L. plantarum* CRD7 from a therapeutic point of view could be used in a future personalized functional food strategy for chemoprevention and cancer growth inhibition as evident from enhanced anti-proliferative efficacy in three human graded cell lines of colorectal cancer.

BIOGRAPHY:

Dheeraj Mohania, PhD, is presently working as Scientist in Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences (AIIMS), Ansari Nagar, New Delhi, India. He worked as Assistant professor and Associate Scientist Consultant, in Department of Research, Sir Ganga Ram Hospital, Rajinder Nagar, New Delhi, India (2010-2016). He received a PhD. in Biochemistry from National Dairy Research Institute, Karnal, Haryana, India (2011). He has completed his M.Sc. in Biochemistry, Jamia Hamdard, New Delhi, India (2004) and B.Sc. in Microbiology, University of Delhi, India (2002). He has guided 16 M.Sc. thesis and 2 Ph.D thesis at Sir Ganga Ram Hospital and AIIMS, New Delhi, India. He is the editor and board member of 2 PubMed-listed journals. He has co-edited a successful book on book entitled, "Microbes in the Service of Mankind: Tiny Bugs with Huge Impact", as a reference book and several book chapters on probiotics and vitamins. He has published 34 papers, 7 book chapters, and presented more than 30 research communications.

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