

Dietary indoles serve as novel therapeutic agents by targeting inflammation through epigenetic modulation and miRNA expression in T cells and there by suppressing inflammatory diseases

Mitzi Nagarkatti and Prakash Nagarkatti
University of South Carolina, USA

Dietary indoles, such as 3,3'-diindolylmethane (DIM) and its precursor, indole-3-carbinol (I3C), found in high amounts in cruciferous vegetables, have been demonstrated to exert beneficial effects against cancer. However, whether they can modulate the immune cell functions has not been well-established. In the current study, we investigated the effect of I3C and DIM on autoimmune and inflammatory diseases such as colitis and experimental Multiple Sclerosis. We found that these compounds suppressed the clinical course of these diseases with significant decrease in infiltrating inflammatory cells in the colon and central nervous system, respectively. Also, I3C and DIM promoted the differentiation of CD4⁺ T cell subsets into Regulatory T cells (T-regs) while suppressing Th17. To understand the role of miRNA in the regulation of immune response, we performed miRNA arrays and found that both I3C and DIM had a profound effect on miRNA profile in activated T cells. Both the indoles (I3C and DIM) significantly up- or down-regulated several miRNAs that regulated Th17 and Treg differentiation. We also tested if the I3C and DIM mediated epigenetic changes such as DNA methylation in activated T cells leading to altered T cell differentiation. We observed significant decrease in methylation and significant increase in demethylation of FoxP3 promoter in the presence of indoles compared to vehicle. These data demonstrate that both I3C and DIM may play important role in regulation of Foxp3 and IL-17 genes by causing epigenetic changes in their promoters as well as modulation of miRNAs, which in turn alter their expression. (This work was supported in part by National Institute of Health Grants R01 AT006888, R01 ES019313, R01 MH094755, P01 AT003961, P20 RR032684 and VA Merit Award BX001357).

Biography

Mitzi Nagarkatti is the Chair of the Department of Pathology, Microbiology and Immunology (PMI) at USC SOM as well as Deputy Director, Basic and Translational Research at the USC Cancer Center. She has been the recipient of 5 R01 grants from the National Institutes of Health (NIH) as P.I. and on 4 as Co-P.I. She is also a Co-P.I. on a Center Grant from National Center for Complementary and Alternative Medicine (NIH) for \$6 million and an NIH COBRE grant for \$10million. She has published >150 scientific papers in high impact journals. She has also been the recipient of a number of awards such as the Pfizer Research Award. She has served on several national and international grant review committees.

Mitzi.Nagarkatti@uscmcd.sc.edu