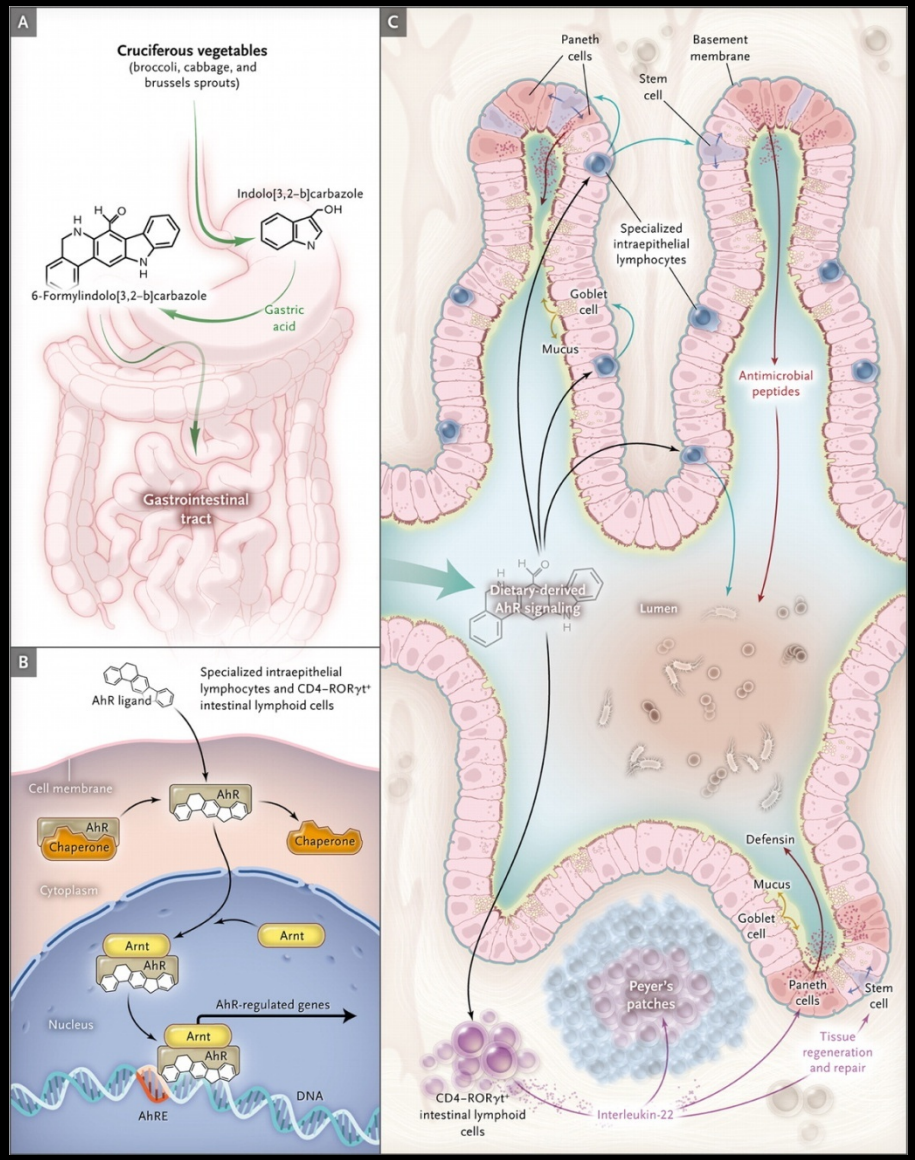
Dissecting Diet and Intestinal Immunity.



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Kiss et al.1 and Li et al.2 recently reported that intestinal immune functions are dependent on dietary aryl hydrocarbon receptor (AhR) ligands. Indole-3-carbinol is an AhR ligand found in cruciferous vegetables, such as broccoli and brussels sprouts. After oral consumption, indole-3-carbinol is converted in the presence of gastric acid to high-affinity ligands such as indolo[3,2-b]carbazole or 6-formylindolo[3,2-b]carbazole (Panel A). AhR ligands activate chaperone-bound AhRs that dimerize with the AhR nuclear translocator (Arnt) and regulate gene expression (Panel B). The studies showed that two cell types are critically dependent on dietary-derived AhR signals: specialized intraepithelial lymphocytes (e.g., intraepithelial T-cell receptor γδ cells) and CD4−RORγt+ intestinal lymphoid cells with lymphoid tissue–inducing function (e.g., Peyer's patches) (Panel C). Mice lacking AhR signals (obtained genetically or through dietary deprivation) lack specialized intraepithelial lymphocytes and intestinal lymphoid cells, which results in reduced epithelial turnover, reduced expression of antimicrobial peptides, an altered microbiota, and increased susceptibility to intestinal inflammation (induced by dextran sulfate sodium or in response to Citrobacter rodentium infection) (Panel C). The pathogenesis of enhanced inflammation in the mutant mice is incompletely understood and probably involves defective interleukin-22 production. (Interleukin-22 is a cytokine that controls intestinal