OC06 & P03 - **UVB light promotes intestinal homeostasis through Ahr activation**

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Introduction: The benefits of Ultra Violet B (UVB) phototherapy for the treatment of skin diseases such as psoriasis have been extensively studied. In contrast, little is known about the potential application of phototherapy to treat chronic inflammatory diseases at sites distant from the skin, such as Inflammatory Bowel Disease (IBD). In particular, the potential effects of narrow band UVB light on intestinal immunity and the gastrointestinal environment have been unexplored. This study examined how narrow band UVB light exposure on the skin promotes intestinal homeostasis.
Methods/Results: The dorsal skin of wild type C57BL/6 mice was shaved, and then exposed to UVB light. The effects of the UVB exposure on the gut microbiome and mucosal immunity were studied after a single UVB exposure (acute) or after multiple exposures (chronic). Microbiota sequencing of bacterial 16S genes showed a shift in the microbiota composition that was noticeable after acute exposure and was drastically increased after chronic UVB exposure. The relative abundance of Bacteroidetes increased in the UVB exposed mice where the relative abundance of Firmicutes and Proteobacteria decreased. The metabolic potential of the microbiota to metabolize tryptophan was found to increase, with a significant elevation identified in the levels of Aryl hydrocarbon receptor (Ahr) ligands. Correspondingly, the ability of the contents of the cecum to activate the AhR was significantly increased post-UVB, with metabolic analysis of the serum and cecum contents of UVB treated mice showing overt increases in the levels of the Ahr ligands tryptamine and indole-3-acetic acid. Since Ahr metabolism is well described as promoting intestinal homeostasis and maintaining the intestinal barrier, mucosal immune and antimicrobial responses were assessed. UVB treated mice were shown to undergo an increase in levels of IL-22 protein and the expression of the antimicrobial C-type lectins RegIIIβ/γ in the small intestine. To determine if the changes in the microbiota in response to the UVB light exposure were beneficial for intestinal health, mice were challenged with dextran sodium sulfate (DSS) colitis (3%) after chronic UVB exposure. The UVB exposed mice showed decreased pathology and inflammation in comparison to control mice. In contrast, when AhR deficient mice were exposed to UVB light and then challenged with DSS colitis, they showed no protection, indicating that the protective effect of UVB light exposures is likely mediated through Ahr activation.
Conclusions: Taken together, this report is the first to demonstrate that UVB skin exposure can alter the structure and function of the gut microbiota, and that such treatment increases AhR signaling that protects against experimental colitis. Using UVB light to modulate the gut microbiota could provide an important adjunct therapy to reduce the inflammation, tissue damage and microbial dysbiosis seen in IBD patients.