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Does intestinal inflammation impact the lung response to bacterial endotoxin?

Lung inflammation leading to airway hyperresponsiveness causes illnesses for more than ten percent of the population in USA. Recent research had indicated that patients with inflammatory bowel disease have higher incidence of airway hyperresponsiveness compared to the general population. We investigated this observation in mice with intestinal inflammation.

We used Rag1 mice of the C57Bl/6 background, lacking functional T and B lymphocytes to generate the model of intestinal inflammation. We reconstituted the mice with T cells from genetically compatible splenocytes and induced colitis by administration of non-steroid anti-inflammatory drug (NSAID) mixed with powdered food.

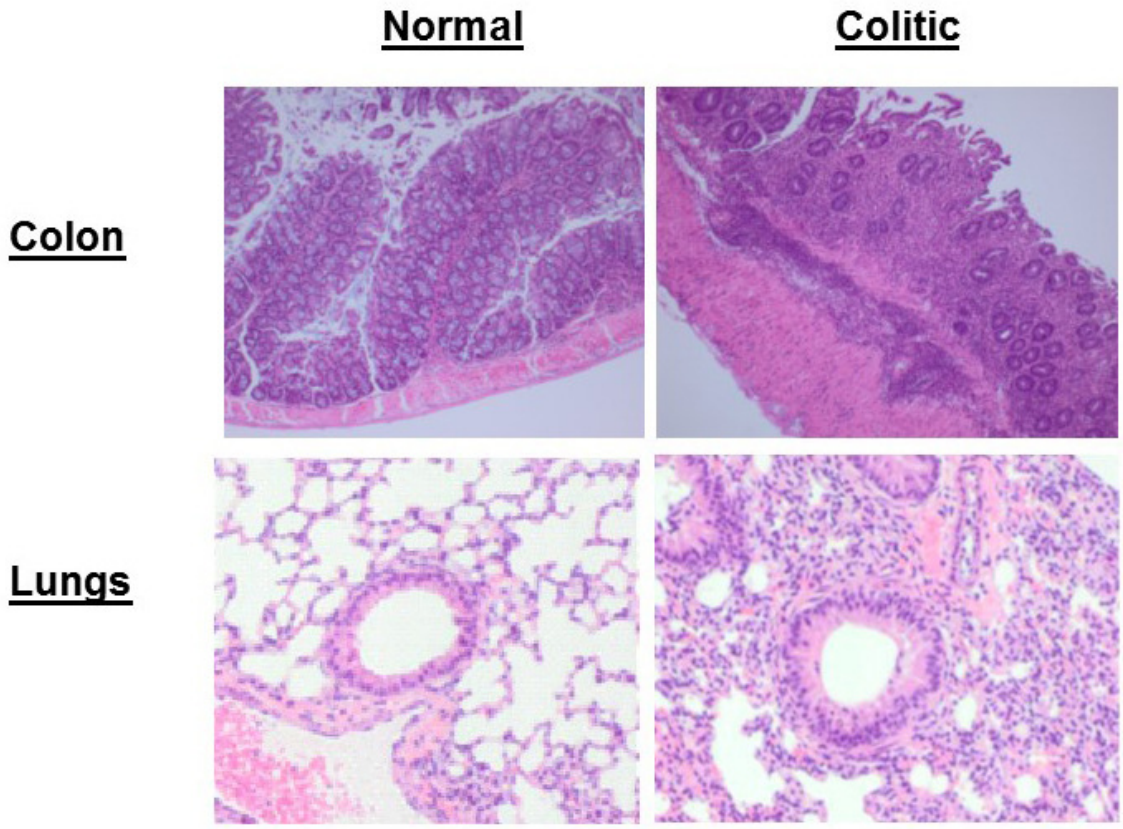

Fig. 1. Histology sections from normal and inflamed colons and lungs documenting lymphocytes infiltration in lung inflammation of colitic mice exposed to bacterial endotoxin.

Mice developed colon transmural inflammation with massive lymphocyte infiltration and disrupted epithelium allowing a direct contact between the gut immunocytes and intestinal contents. Exposure of colitic mice to

bacterial endotoxin after development of colitis intensified the lung inflammation as compared to non-colitic mice with the same treatment. Lymphocytes infiltrated the lung tissue associated with fibrosis around the bronchioles are evident in histology slides (Fig. 1).

We extracted inflammatory lymphocytes from the lamina propria of inflamed colons and transferred them to normal untreated Rag1 mice. We documented the presence of these inflammatory cells in the lungs of the reconstituted mice proving that primed migratory effector lymphocytes from the inflamed gut may home in the lungs (Fig. 2).

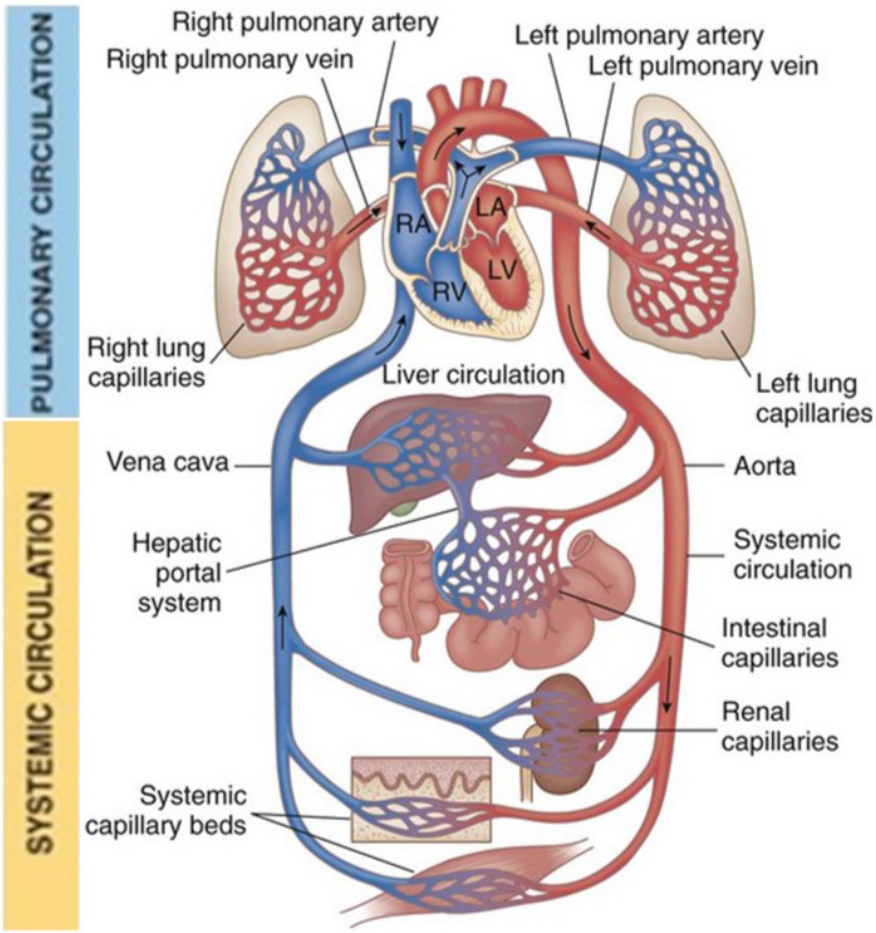

Figure from: Quizlet.com

Fig. 2. Leukocytes (lymphocytes and monocytes) originating in the gastrointestinal tract under normal conditions, expose to luminal antigens in the lymphoid aggregates and secondary lymphoid organs like Peyer's patches and mesenteric lymph nodes. They leave the intestinal tissue to enter systemic circulation through the thoracic duct. Altered expression of homing receptors on lymphocytes may occur in intestinal inflammation resulting in mis-homing of lymphocytes pre-sensitized to gut antigens into the lungs. Allergens enter the lungs with the inhaled air. Pre-sensitized leukocytes exposed to recall gut antigens generate exacerbated hypersensitivity reaction in the lungs of colitic subjects.

Pulmonary $CD4^+$ lymphocytes from colitic mice displayed proinflammatory cytokine profile manifested by high IFN-γ inflammatory cytokine and low IL10 regulatory cytokine. They expressed high ICAM1 proinflammatory receptor and had low content of $CD4^+$, $FoxP3^+$ regulatory lymphocytes. $CD11c^+$ dendritic cells bind antigens from gut-localized microbiota and had higher expression of TLR4 indicating enhanced capabilities of adaptive as well as innate responses set to respond to breathed air-born recall antigens from the environment.

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Publication

Recirculating Immunocompetent Cells in Colitic Mice Intensify Their Lung Response to Bacterial Endotoxin.
Metwali A, Thorne PS, Ince MN, Metwali N, Winckler S, Guan X, Beyatli S, Truscott J, Urban JF Jr, Elliott DE
Dig Dis Sci. 2018 Nov