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Dissertation

Title *Mechanisms underlying control of anti-microbial immunity by acetylcholinesterase inhibitors.*

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Abstract

Inflammation is a crucial defense mechanism that protects the body from the devastating effects of invading pathogens. However, an unrestrained inflammatory reaction may result in systemic manifestations with dire consequences to the host. The extent of activation of the inflammatory response is tightly regulated through immunological and neural pathways. Previously, we demonstrated that cholinergic stimulation confers enhanced protection in experimental animals orally infected with a lethal dose of Salmonella typhymurium. In this study, we investigated the mechanism by which this enhanced protection takes place. We showed that cholinergic stimulation enhanced host survival following oral-route infection, which correlated with significantly reduced bacterial load in target organs, including livers and spleens. Enhanced protection was not due to increased gut motility or rapid bacterial clearance from the GI tract. Moreover, protection against bacterial infection was lost when the animals were infected systemically, suggesting that the acetylcholine-mediated protective effect was mostly confined to the gut mucosal tissue. In vivo imaging demonstrated more localized infection and delay in bacterial dissemination into systemic organs in mice pre-treated with acetylcholinesterase inhibitors. Morphological analysis of the small intestine (ileum) showed that acetylcholinesterase inhibition induced the degranulation of goblet cells and Paneth cells, two specialized secretory cells involved in innate immunity. Our findings demonstrate a crucial pathway between neural and immune systems that acts at the mucosal interface to protect the host against invading pathogens.

Keywords: cholinergic pathway, bacterial infection, innate immunity, intestinal mucosa.

Research Relevance and Potential Impact

The study demonstrates that cholinergic stimulation regulates immune response at the mucosal intestinal interface, thus highlighting the intricate link between nervous and immune systems. Our findings suggest the potential use of this pathway to control chronic inflammatory intestinal disorders. These results could provide a therapeutic advantage for the design of novel pharmacological anti-inflammatory strategies.

Relevant Publications

- R. Al-Barazie, G. Bashir, M.M. Qureshi, Y. Mohamed, B.K. al-Ramadi and M.J. Fernandez-Cabezudo. Acetylcholinesterase inhibition modulates the mucosal interphase by enhancing the gastrointestinal barrier defense mechanisms. (In preparation)

Career Aspirations

My aspiration is to be in a career that I enjoy and love as myself, be beneficial for people and help in the improvement of human lives. Also I would like to be in a position that offers me a contentious development and improvement of my experiences and knowledge, has a nice working atmosphere and cooperative colleges. I hope to achieve that through doing a research in health related matters as a post doctorate professional or through academic teaching position where I can provide the best educational outcomes and experience for the future generations.