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Neuroimmunomodulation by Cholinergic Anti-Inflammatory Pathway in Gastrointestinal System Diseases

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The cholinergic anti-inflammatory pathway is a neural mechanism, which inhibits pro-inflammatory cytokine release via α7 nicotinic acetylcholine receptors (α7 nAChR). It has been established that vagus nerve signaling inhibits cytokine activities and improves disease endpoints in experimental models of sepsis, ischemia/reperfusion, hemorrhagic shock, myocardial ischemia, ileus, experimental arthritis and pancreatitis.

It is accepted that the vagus nerve and cholinergic. The mechanism for inhibition of cytokine synthesis is attributable to acetylcholine (ACh), the major vagus nerve neurotransmitter. Macrophages and other inflammatory cells releasing cytokines express ACh receptors, which transduce an intracellular signal to suppress cytokine synthesis and release. The mechanism of signal transduction probably involves ligand-receptor interaction on cytokine-expressing cells to decrease nuclear translocation of nuclear factor (NF)-κB as well as activation of the transcription factor signal transducer and activator of transcription (STAT)-3 via phosphorylation by janus kinase (JAK)2, which is recruited to the α7 nAChR agonists activate the sympathetic noradrenergic splenic nerve to control systemic inflammation. Splenic nerve stimulation mimics vagal and cholinergic induction of norepinephrine and re-establishes neuromodulation in α7nAChR-deficient animals. Thus, vagus nerve and cholinergic agonists inhibit systemic inflammation by activating the noradrenergic splenic nerve via the a7nAChR nicotinic receptors.

In contrast to the spleen, a direct vagal communication between the gut wall and the central nervous system has been experimentally proven in the gastrointestinal tract recently. Using anterograde tracers injected into the dorsal motor nucleus of the vagus, efferent vagal nerve terminals were shown to directly synapse with postganglionic neurons located in the enteric nervous system. These researches opened a new debate on the action mechanism of cholinergic anti-inflammatory pathway on gastrointestinal system. Some researchers have claimed that interaction between gastrointestinal system and cholinergic anti-inflammatory system is different and unique. So we investigated interaction and action mechanism of cholinergic anti-inflammatory pathway on different gastrointestinal inflammation models. Ulcerative colitis, acute panrceatitis, endotoxemia induced gastroenteritis models have been investigated by our group. In this speech some results of our researches will be discussed to elucidate the effects of cholinergic pathway on gastrointestinal inflammation.

Biography:

Meltem Kolgazi is working as an Assistant professor in Acibadem Mehmet Ali Aydinlar University, Department of Physiology (2014--…) and he worked as an Instructor – Eastern Mediterranean University with Dr. FazılKüçük Faculty of Medicine (2013-2014). He is a Research Assistant in Physiology Department, Marmara University School of Medicine (2009-2013). He is also a member of the Turkish Society of Physiological Sciences.