

Cx43, RhoA and c-kit in diverticular disease

Cristina Segnani¹, Barbara Battolla¹, Chiara Ippolito¹, Rocchina Colucci², Sauro Dini¹, Nunzia Bernardini¹, Letizia Mattii¹, Amelio Dolfi¹

¹Departments of Human Morphology and Applied Biology (Section of Histology), Faculty of Medicine and Surgery, Pisa University, Italy

²Internal Medicine (Div. of Pharmacology and Chemotherapy), Faculty of Medicine and Surgery, Pisa University, Italy

Diverticular disease (DD) is one of the most common diseases related to the gastrointestinal tract in Western countries. It has been postulated that abnormal colonic motility including increased overall motility, abnormal response to a physiologic stimulus and retropropagation of mass movement, predisposes to the formation of pulsion diverticula in the segments of the bowel containing the diverticula. Intestinal motility is regulated by complex interactions among smooth muscle cells (SMCs) of muscularis propria, enteric nerve endings and interstitial cells of Cajal (ICC). ICC are emerging as potential colonic pacemaker cells which modulate neuroenteric transmission by connecting SMC with varicosities of myenteric neuron axons. In colonic SMCs, transmembrane channels rich in connexin (Cx), in particular Cx43, contribute to intercellular gap junctions, which ensure coordinated motor responses to nerve inputs. There is evidence that SMCs motility and gap junction permeability are regulated by the GTPase RhoA, an emerging key modulator of SMCs phenotype.

The aim of the present study was to evaluate the Cx43 and RhoA expression in SMCs, as well as ICC density in colonic specimens from patients affected by diverticular disease (DD).

Immunohistochemistry for Cx43, RhoA and c-kit and image analysis were used to examine muscularis propria of surgical whole thickness colonic samples from DD patients.

Semiquantitative analysis of DD colonic specimens displayed a marked decrease in Cx43 and RhoA expression in SMCs. There was also a reduced ICC density in myenteric ganglia (ICC-MY), circular (ICC-CM) and longitudinal (ICC-LM) muscle, as compared to controls. Overall, it is suggested that abnormalities in gap junctions and RhoA expression in SMCs, together with a reduced density of muscular ICC, account for the colonic dysmotility occurring in DD.

Keywords: diverticular disease, Cx43, RhoA, ICC, SMC