ABSTRACT

Inflammation is considered as one of the main defence mechanisms of the immune system against threats that occur in the body. When present in its acute form, minimal or no detectable subsequent damage of original affected tissue exists. The more pathological form, chronic inflammation, is associated with permanent damage of the tissue and typically a hallmark of various diseases such as ulcerative colitis or colon carcinogenesis. These two pathologies are evolving in the unique colon microenvironment, where intensive interaction between the host cells and bacteria is present. The aim of our study was to investigate the immunological (ELISA, FACS, RT-PCR) and structural (histology, confocal microscopy) changes in the colon mucosa of Wistar-AVN rats induced by dextran sodium sulphate (DSS) to produce colon colitis and by azoxymethane (AOM) to produce colon carcinogenesis. Conventional (CV) and also germ-free (GF) reared animals were used to investigate the effects of the mucosal inflammation activated by the administered inducers as well as the role of colon microbiota - as promoters of a continuous immune activation - in the modulation of immunity and collagen scaffold remodelling. Our results showed that even in the early period after the induction, both inducers produced a smouldering inflammation, able to activate immunological and collagen structural changes in the colon mucosa. This can be indicated as a consequence of variation of what we can call “inflammatory threshold”, representing the limit of tolerance for not dangerous inflammation. Significant differences were found between CV and GF mucosa structure with higher complexity in the CV rats associated to a more activated immune environment. The cytokine production in CV rats was more balanced, regulated to achieve homeostatic levels present in GF rats. This project has achieved the main result attended, i.e., identification of a new marker (collagen scaffold modification) linked to the immunological environment in the colon mucosa, with predominance of IL-6, perspective to be used for very early detection of cancer risk and local immunological pathology.