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Tight Junction Integrity: Need for Non-Invasive Markers

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Editorial

Tight junctions (TJs) have attracted reasonable interest since the identification of their first protein "zonula occludens (ZO-1)" in 1986. Twenty eight years later, google search for TJs returns with more than two million hits while pubmed search retrieve more than 10,000 research articles about the TJs. TJ complex is made by approximately 35 different proteins and the number is still growing. TJ complex proteins are divided into two groups; integral membrane proteins and peripheral membranes proteins. Physiologically TJs perform "Barrier" and "Fence" function with barrier function involving the regulation of paracellular movement of solutes and nutrients across the epithelia between two adjacent cells. While fence function controls the mixing of apical components with basal components within the cell. Disturbances in TJ assembly results into hereditary diseases, (hypomagnesemia, deafness, neonatal sclerosing cholangitis with ichthyosis, familial hypercholanemia), gastrointestinal tract diseases (bacterial gastritis, pseudomembranous colitis, Crohn's disease, ulcerative colitis, celiac disease, collagenous colitis), bacterial and viral infections (for detail see review article [1]). List is not even near to complete as new epigenetic and proteomics techniques are shedding new light on the TJ complex structure and regulatory pathways implicated in different diseases. Ironically, the cytotoxic or chemotherapeutic agents (such as 5-fluorouracil (5-FU), methotrexate) prescribed to treat different types of cancers adversely influence the TJs, resulting an increased intestinal permeability and leaving intestinal epithelial monolayer open to infections [2]. Al-Refai proposed that the co-medication with TJ protective agents / additive can significantly reduce the 5-fluorouracil induced intestinal mucositis in albino rats. The study showed that the chamomile extract decreased the 5-FU-induced epithelial cells cytotoxicity and improved the TJ integrity [3].

Numerous TJ proteins are implicated in different disorders e.g., regulation of claudin-1, -2, -3, -4, -5, -7, -8, -10, -18, -23 and ZO-1, -2, -3 have been reported in biliary tract, breast, cervical, colon, colorectal, esophagus, gastric, head and neck, liver, ovary, prostate, thyroid, uterus, and pulmonary large and small cells carcinomas (for detail see review article [4]). Patients with inflammatory diseases (Crohn's disease, collagenous colitis, multiple sclerosis) shows an altered expression of TJ proteins claudin-2, -3, -4, -5, -8, occludin and ZO-1 [5,6]. Mutation in claudin-14 and -16 genes are reported in hereditary deafness and familial hypomagnesemia [7,8]. So far the breakdown of TJ can be detected after invasive intestinal biopsies and therefore search for noninvasive markers is essential. Increased urinary claudin-3 levels have shown a strong relation to the intestinal TJ loss. Urinary claudin-3 level is shown to be significantly increased in rat hemorrhagic shock model as compared to control and in patient with inflammatory bowel disease (IBD) relapsed as compared to IBD remission suggesting that the measurement of urinary claudin-3 can be useful as a non-invasive marker for intestinal TJ loss [9]. Such non-invasive marker could be a valuable tool for early diagnosis and/or to check the severity of the disease and for therapy efficacy.

References

1. Sawada N (2013) Tight junction-related human diseases. Pathol Int 63: 1-12.

2. Chang CT, Ho TY, Lin H, Liang JA, Huang HC, et al. (2012) 5-Fluorouracil induced intestinal mucositis via nuclear factor-κB activation by transcriptomic analysis and in vivo bioluminescence imaging. PLoS One 7: e31808.

3. Al-Refai AS. (2014) Immunohistochemical Study of the Effect of Chamomile Extract on 5-Fluorouracil Induced Intestinal Mucositis in Albino Rats. J Clin Cell Immunol 5: 232.

4. González-Mariscal L, Lechuga S, Garay E (2007) Role of tight junctions in cell proliferation and cancer. Prog Histochem Cytochem 42: 1-57.

5. Zeissig S, Bürgel N, Günzel D, Richter J, Mankertz J, et al. (2007) Changes in expression and distribution of claudin 2, 5 and 8 lead to discontinuous tight junctions and barrier dysfunction in active Crohn's disease. Gut 56: 61-72.

6. Förster C, Mäkela S, Wärri A, Kietz S, Becker D, et al. (2002) Involvement of estrogen receptor beta in terminal differentiation of mammary gland epithelium. Proc Natl Acad Sci U S A 99: 15578-15583.

7. Ben-Yosef T, Belyantseva IA, Saunders TL, Hughes ED, Kawamoto K, et al. (2003) Claudin 14 knockout mice, a model for autosomal recessive deafness DFNB29, are deaf due to cochlear hair cell degeneration. Hum Mol Genet 12: 2049-2061.

8. Simon DB, Lu Y, Choate KA, Velazquez H, Al-Sabban E, et al. (1999) Paracellin-1, a renal tight junction protein required for paracellular Mg2+ resorption. Science 285: 103-106.

9. Thuijls G, Derikx JP, de Haan JJ, Grootjans J, de Bruïne A, et al. (2010) Urine-based detection of intestinal tight junction loss. J Clin Gastroenterol 44: e14-19.