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Stem Cell Differentiation Toward Secretory Progenitors after Intestinal Ischemia-Reperfusion in a Rat is Accompanied by Inhibited Notch Signaling Cascade

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Abstract : Objectives: Notch signaling is thought to act to drive cell versification in the lining of the small intestine. When Notch signaling is blocked, proliferation ceases, and epithelial cells become secretory. The purpose of the present study was to evaluate the role of Notch signaling pathway in stem cell differentiation in a rat model of intestinal ischemia-reperfusion (IR). Methods: Male Sprague-Dawley rats were randomly divided into four experimental groups: Sham-24 and Sham-48 rats underwent laparotomy and were killed 24 or 48 h later, respectively; IR-24 and IR-48 rats underwent occlusion of SMA and portal vein for 30 min followed by 24 or 48 h of reperfusion, respectively. Notch-related gene and protein expression were determined using Real Time PCR, Western blotting and immunohistochemistry. Wax histology and immunohistochemistry was used to determine cell differentiation toward absorptive (enterocytes) or secretory progenitors (goblet cells, enteroendocrine cells or Paneth cells). Results: IR-48 rats exhibited a significant decrease in Notch-1 protein expression (Western blot) that was coincided with a significant decrease in the number of Notch-1 positive cells (immunohistochemistry) in jejunum and ileum as well as Hes-1 positive cells in jejunum and ileum compared to Sham-48 rats. A significant down-regulation of Notch signaling related genes and proteins in IR animals was accompanied by a significant increase in the number of goblet and Paneth cells and decreased number of absorptive cells compared to control rats. Conclusions: Forty-eight hours following intestinal IR in rats, inhibited Notch signaling pathway was accompanied by intestinal stem cells differentiation toward secretory progenitors.

Keywords : Intestine, notch, ischemia-reperfusion, cell differentiation, secretory
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