

Effect of secretin on biliary epithelium growth by regulating expression of MicroRNA 125b and MicroRNA let7a in mice

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Proliferating cholangiocytes have the capacity to respond and secrete several hormones and neuropeptides, including secretin (Onori et al., 2010). We investigated whether secretin secreted by S cells and cholangiocytes increases biliary proliferation in mice. Cholestasis was induced in secretin knockout ($Sct^{-/-}$) and wild-type (control) mice by bile duct ligation (BDL) (Glaser et al., 2009). After 7 days of BDL, control and $Sct^{-/-}$ mice received tail-vein injections of morpholinos against microRNA 125b or let7a. One week later, liver tissues and cholangiocytes were collected and immunohistochemical, immunoblot, and real-time polymerase chain reaction assays were performed. Intrahepatic bile duct mass (IBDM) and proliferation were evaluated. Secretin secretion was measured in conditioned media from cholangiocytes and S cells. Secretin secretion was increased in supernatants from cholangiocytes and S cells after BDL in control mice. BDL $Sct^{-/-}$ mice had lower IBDM, reduced proliferation, and reduced production of VEGF and NGF compared with BDL control. BDL and control mice given morpholinos against microRNA 125b or let7a had increased IBDM, expression of VEGFA and NGF. Secretin regulated VEGF and NGF expression that negatively correlated with microRNA 125b and let7a levels in liver tissue. After liver injury, secretin produced by cholangiocytes and S cells reduces microRNA 125b and let7a levels, resulting in up-regulation of VEGF and NGF. Modulation of cholangiocyte expression of secretin could be a therapeutic approach for biliary diseases.

References

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Keywords

Biliary epithelium, secretin.