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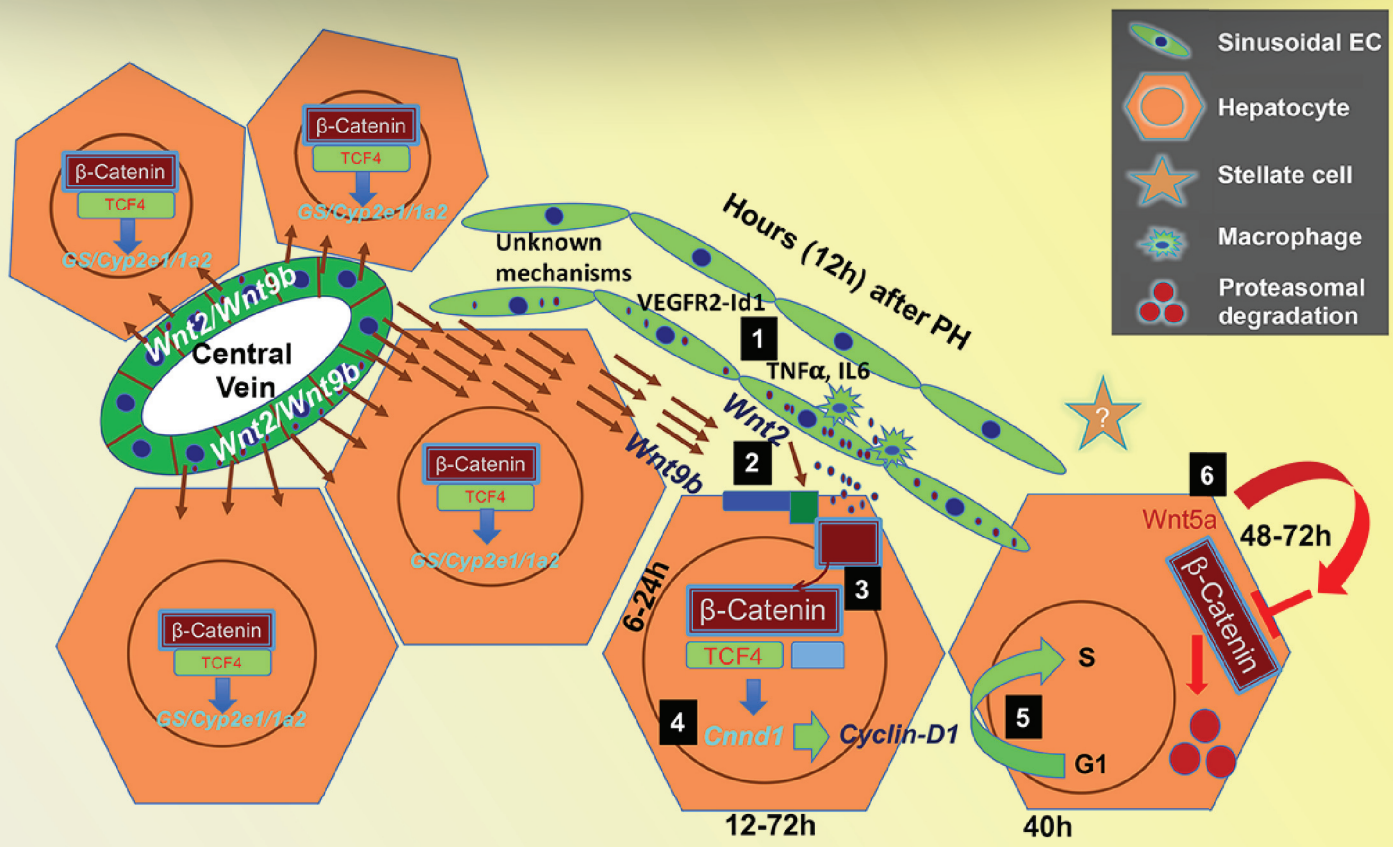

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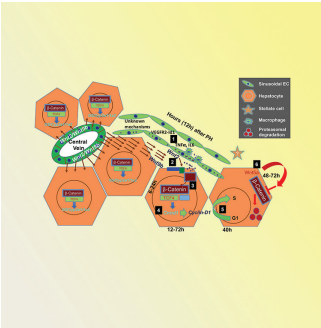

> **Cover Figure:** Cell-molecule circuitry of Wnt-β-catenin signaling during LR. Following PH, VEGFR2-Id1 axis, cytokines, such as TNFα and IL6, and as yet unidentified mechanisms appear to induce expression and secretion of Wnt2 from sinusoidal ECs, central venous ECs, and macrophages and secretion of Wnt9b from central venous ECs and macrophages (1). The secreted biologically active but hydrophobic Wnt2 and Wnt9b bind to as yet uncharacterized Frizzled and LRP5/6 coreceptors on hepatocytes in close proximity (2) to induce β-catenin stabilization, nuclear translocation, and formation of β-cateninTCF complex (3). The resulting increase in *ccnd1* expression and cyclin-D1 protein (along with other β-catenin targets, such as GS) (4) allows for hepatocytes to transition from the G1- to S-phase (5) and eventually undergo cell division to restore loss hepatic mass. Upon accomplishment of required hepatocyte proliferation, hepatocytes secrete Wnt5a (6), which induces β-catenin degradation to terminate Wnt/β-catenin signaling. The role of stellate cells in Wnt-β-catenin signaling in LR remains unknown. Abbreviations: IL6, interleukin-6; TNFα, tumor necrosis factor α; VEGFR2, vascular endothelial growth factor receptor 2.

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