中药调控MAPK信号通路干预慢传输型便秘的研究进展Δ

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摘　要　慢传输型便秘（STC）是一种因结肠传输功能减弱，导致排便次数减少、粪便干结及排便困难的常见功能性肠病。丝裂原活化蛋白激酶（MAPK）信号通路[主要包括胞外信号调节激酶（ERK）、c-Jun氨基端激酶（JNK）、p38亚型]在STC的发生发展中发挥了关键调控作用。本文系统梳理了MAPK信号通路在STC中的多重致病机制及中药干预的研究进展。在机制层面，MAPK信号通路可通过以下环节推动STC进展：（1）激活p38，上调结肠中水通道蛋白3（AQP3）/AQP4的表达，导致肠腔水分过度重吸收；（2）与核转录因子κB（NF-κB）形成正反馈环路，维持肠道低度炎症，释放肿瘤坏死因子α、白细胞介素1β等炎症因子，抑制平滑肌收缩；（3）过度激活p38，下调occludin、黏蛋白2的表达，上调claudin-2的表达，破坏黏膜屏障；（4）JNK/p38信号通路可激活胱天蛋白酶级联反应，诱导肠上皮细胞、神经元及Cajal间质细胞凋亡；（5）ERK信号异常及p38/JNK过度激活可抑制肠平滑肌收缩，减少5-羟色胺分泌，最终导致结肠传输功能减弱。在干预层面，中药复方及单味中药被证实可通过调控MAPK信号通路改善STC。其作用呈现证型依赖性：滋阴类复方（如增液承气汤、通便汤）多调控ERK/AQP轴，温阳类复方（如济川煎）兼顾ERK/JNK与抗凋亡，清热类复方（如三仁汤）侧重p38/NF-κB抗炎；同一药物可同时覆盖水分代谢、炎症、屏障、凋亡、肠道动力中的多个环节。现有相关研究仍存在机制多停留在相关性层面、缺乏病证结合研究模型等不足，未来应联合特异性抑制剂或基因敲除明确核心靶点，建立病证结合的STC模型，并结合网络药理学与分子对接技术深入解析“成分-靶点-表型”的精细机制，为中药精准调控MAPK信号通路干预STC提供高质量证据。

关键词　慢传输型便秘；MAPK信号通路；水通道蛋白；中药

Research progress on traditional Chinese medicine regulation of MAPK signaling pathway in intervening slow transit constipation

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ABSTRACT　Slow transit constipation (STC) is a common functional intestinal disorder caused by impaired colonic transit function, characterized by reduced bowel movement frequency, hard stools, and difficulty in defecation. The mitogen-activated protein kinase (MAPK) signaling pathway, which mainly includes extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), and p38 subtypes, plays a critical regulatory role in the occurrence and development of STC. This paper systematically reviews the multiple pathogenic mechanisms of the MAPK signaling pathway in STC and the research progress of traditional Chinese medicine (TCM) intervention. At the mechanistic level, the MAPK signaling pathway promotes the progression of STC through the following links: (1) Activation of p38 upregulates the expression of aquaporin 3 (AQP3)/AQP4 in the colon, leading to excessive reabsorption of water in the intestinal lumen; (2) It forms a positive feedback loop with nuclear factor-κB (NF-κB) to maintain low-grade intestinal inflammation, releases inflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), and inhibits smooth muscle contraction; (3) Overactivation of p38 downregulates the expression of occludin and mucin 2 while upregulates the expression of claudin-2, thereby disrupting the mucosal barrier; (4) The JNK/p38 signaling pathway activates the caspase cascade to induce apoptosis of intestinal epithelial cells, neurons, and interstitial cells of Cajal; (5) Abnormal ERK signaling and excessive activation of p38/JNK inhibit intestinal smooth muscle contraction and reduce 5-hydroxytryptamine secretion, ultimately resulting in impaired colonic transit function. At the

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