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The zinc-finger transcription factor SNAH down-regulates proliferating cell nuclear antigen (PCNA) expression in colorectal carcinoma cells

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The Snail family of zinc-finger transcription factors has previously been implicated in the differentiation of epithelial cells into mesenchymal cells (epithelial-mesenchymal transitions) and central nervous system (CNS) during embryonic development. Expression of Snail protein is also determinants of the progression of carcinomas, occurring concomitantly with the cellular acquisition of migratory properties following down-regulation of expression of the adhesion protein E-cadherin. But its target genes remain unknown. In this study, we found several potential SNAH binding sequences in the 5-flanking region of human PCNA gene. Cotransfection experiments, using human PCNA reporter plasmid and SNAH expression plasmid, showed that SNAH reduces human PCNA gene promoter activity in colorectal carcinoma cell lines (HCT116 and Colo320HSR). SNAH-reduced PCNA expression was also detected in immunoblot and immunohistochemistry experiments. In BrdU incorporation experiments, SNAH over-expression inhibited the BrdU incorporation. Taken together, our results suggest that SNAH inhibits cell proliferation through down-regulation of PCNA promoter activity.