OSCILLATIONS OF THE DEUBIQUITASE 28 LEVELS IN CELL CYCLE OF THE HUMAN ADENOCARCINOMA Cell LINE HCT116 SUGGEST ITS FUNCTINAL ROLE IN REGULATION OF THE G_1/S TRANSITION

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Usp28 is a deubiquitylating enzyme which removes ubiquitin from ubiquitin conjugates with substrates and prevents them from degradation in proteasomes. Recent investigations discovered that Usp28 and Fbw7 E3 ubiquitin ligase makes a functional pair of proteins that controls the ubiquitin-mediated degradation of several key regulators of cell functions, including Myc, Jun, Nicd, and Hif1α. In this pair, Usp28 counteracts Fbw7's destructive activity and plays the role of a tumor-promoting factor. Because the Myc and Jun, associated with cell cycle, are the Usp28 targets, we suggested that Usp28 may regulate cell division and its level is cell cycle associated. The goal of this work was to evaluate the cell cycle associated Usp28 oscillations in cells of human adenocarcinoma HCT116. The HCT116 cells were cell cycle synchronized using their 72 hour cell culture in the growth medium with 0.15% of FCS. In asynchronously growing cells the Usp28 level was low and the protein was distributed between nucleus and cytoplasm. The total level of Usp28 increased in and the protein translocated from cytoplasm to nucleus in late G1 phase, while showed back distribution after S phase. The immunoblotting results registrating the level and distribution of the Usp28 corresponded to the immunofluorescence data. Our results suggest that Usp28 may regulate the levels and functional activity of the Cdc25A which controls the G_1/S transition.

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