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Role of Ubiquitination in lung cancer progression

Ubiquitin is a critical modifier that regulates the degradation and function of its target protein during post-translational modification. In this study, we found that USP24 is higher expressed in the cell lines with more malignancy and lung cancer clinical samples of late stage. Studying the single nucleotide polymorphism of USP24 using genomic DNA of lung cancer patients found an increase in the SNP at 7656C→T. Instead of genomic DNA, using RNA specimens of lung cancer patients to study the SNP of USP24 appeared that significant increase the ratio of the variant in the 930C→T and 7656T→C compared to the ratio found in the genomic DNA, suggesting that the variant at these two sites is not only found in genomic level but in the process of RNA editing. *USP24-930T* and *USP24-7656C* increases expressed level through increasing their RNA stability. Knocking down the level of USP24 increased SUV39h1 level through a decrease in the MDM2 level, thus increased lysine 9 methylation of histone-H3, resulted in preventing lung cancer malignancy. Finally, to study the SNP of USP24 using blood specimen of lung cancer patients also found a higher ratio variant compared to normal population, indicating that the SNP of USP24 at 930C→T and 7656T→C might be as a diagnostic marker for cancer detection. Recently we also found that several cancer-related proteins (Bax, p300, E2F4, TFDP1 and securin) have been proven to be substrates of USP24 and relevance has been shown between USP24 and its substrates in samples from clinical lung cancer patients. Silencing USP24 increases the cancer formation by inhibiting cellular apoptosis and increasing cellular proliferation. The molecular mechanism involves a decrease in the USP24 level, which reduces the expression of E2F4 and its partner TFDP1 and thus increases the G1/S transition. The decrease of USP24 in mitosis also reduces the securin level and promotes separase activation, thereby facilitating the metaphase-anaphase transition. In conclusion, the USP24 level was decreased during the early stage of cancer and the mitotic stage of the cell cycle to regulate its substrates p300, Bax, E2F4, and securin, resulting in decreased cell apoptosis and increased cell cycle progression and thus, cancer formation.

Biography

Jan-Jong Hung has completed his PhD in Life Sciences from National Tsing Hua University, Hsinchu and Post-doctoral studies from Academia Sinica in Taiwan during 1999-2003. At 2009, as a visiting scholar, he came to NIH to do the research with the Dr. Chung-Pin Su. He is the Director of precision instrument of Cheng-Kung University in Taiwan. He has published more than 40 papers related to the lung cancer progression including the initiation and metastasis of lung cancer in reputed journals. Recently he is also to be one of the editors in the ROS Journal.

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