Tumor Suppressor Fbw7 Protein Aggregation: A Novel Tumorigenic Mechanism in Cancer?

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FBW7 is a substrate recognition component and a tumor suppressor in the E3 ligase complex. It plays a major role in combating oncoproteins and regulating different types of cancers, most notably colorectal cancer. Colorectal cancer is one of the most widespread cancers in the world. FBW7 gene mutations are often found in this type of cancer. Loss of function in FBW7 leads to the buildup of oncoproteins which leads to the spread of tumors. Our study aims to establish a deeper understanding of the ubiquitination of FBW7 and to certify if it undergoes aggregation, which might affect its function. We used different procedures and experiments to help us study FBW7. Our research included western blotting, protein aggregation assays and in-vitro ubiquitination assays. The results of our experiments indicated that FBW7 doesn't undergo aggregation as previously suspected. Rather the high molecular band (HMW) as judged by western blotting might be a result of the hyper-ubiquitination of FBW7. To elucidate this, we compared it with another protein in the same complex (CULL1) which strengthened our results. In conclusion, the hyper-ubiquitination of FBW7 results in the loss of stability which in turn leads to the formation of cancer. We hope with our research to lay the foundation and ground to create drugs to target pathways to enhance the function and stability of FBW7.

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