

Current study retains two sections; first section identified the molecular mechanisms associated with regulatory role of quality control E3 ubiquitin ligase Gp78 on cell cycle regulatory proteins. Whereas, the second section explained the functional roles of the small natural molecule Myricetin, a flavonoid, as modulator of another quality control E3 ubiquitin ligase E6-AP that facilitates elimination of aggregates formed by intracellular aberrant proteins.

5.1 SUMMARY

The complex molecular function of Gp78 in the regulation of Cyclin-dependent kinase inhibitor p27 (kip1) has been observed in the present study. It has been analyzed that the higher expression of Gp78 under stress conditions regulates both expression and functional activity of p27, which results in increase in the overall cellular proliferation. The model of overall observations obtained from these results is represented in Figure 5.1.

In previous studies, few natural molecules were identified for their critical functional roles as neuroprotectants. Here, Myricetin has been reported for its role in cytoprotection by modulating expressions of protein quality control components, like E3 ubiquitin ligase E6-AP, chaperone Hsp70, and transcription factor HSF1. Myricetin treatment was given to cells expressing various aggregate-forming proteins, linked with different neurodegenerative disorders. Interestingly reduced number of aggregates was found as compared to control, thus establishing the link between Myricetin mediated neuroprotection through UPS.

5.2 CONCLUSION

The study mentioned in this thesis reported few important roles of quality control E3 ubiquitin ligases in various complex diseases like cancer and neurodegeneration. In depth understanding of molecular mechanisms of these ubiquitin proteasome system's components and their modulation strategies may give a new hope for better therapeutics for these mortal protein conformational disorders.

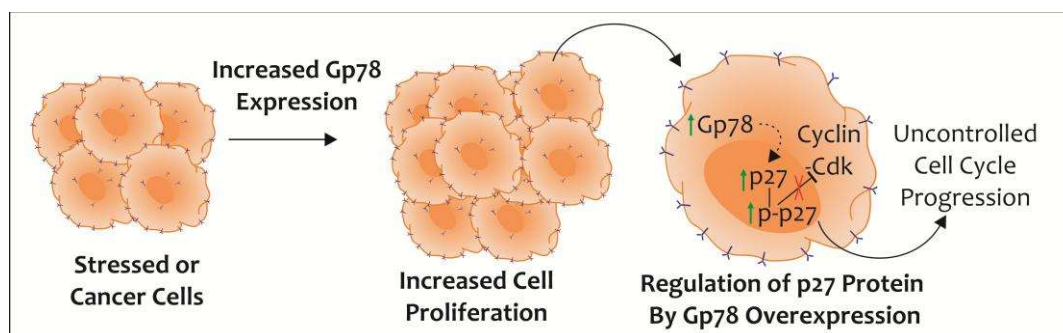


Figure 5.1: Model proposed for Gp78 mediated cell cycle regulation.

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