"Targeted Inefficient Autophagy: Using the Trash Man to Enhance Cancer Treatment"

VCU #12-085

Applications

- Novel chemotherapy agent
- Treatment of multiple human malignancies
- Potential adjunct to current chemotherapy agents

Advantages

- Novel autophagy targeted therapeutic strategy
- May improve efficacy of current and novel chemotherapy agents
- May over-come drug resistance

Inventors

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Market Need

Many cancer patients do not respond to chemotherapy, while virtually all cancer patients who initially respond relapse due to drug resistance. While one of the most important mechanisms underlying drug resistance is inhibition of apoptosis, recent studies have also highlighted the role of "autophagy" in the development of resistance. Apoptosis and autophagy often occur together in response to many current standard chemotherapies. The bulk of evidence suggests that inhibition of autophagy can lead to enhanced efficacy of chemotherapeutic agents and may reduce the development of drug resistance.

Technology Summary

VCU researchers have identified a new approach to autophagy modulation involving the novel adaptor protein SQSTM1/p62, referred to as the "Trash Man" because it plays a critical role in loading unwanted cellular proteins into autophagic vacuoles for degradation. They have found that disrupting the function of this protein can prevent autophagy from protecting cancer cells from certain cytotoxic agents. Their concept represents an alternative and fundamentally different approach to autophagy-based therapy. This new approach could potentially overcome the disadvantage of using either autophagy inhibitors or inducers, because it interrupts autophagic cargo loading, a step essential for autophagy to selectively clean up the harmful malfolded proteins or damaged organelles, by targeting the adaptor protein, SQSTM1/p62. As a result, failure of cargo loading turns the "self-cleaning" and apoptosis into an "inefficient form of autophagy", which then triggers apoptosis by induction of NBK/Bik leading to tumor cell death.
This novel protein target and its method have the potential advantages of disabling an efficient, cytoprotective autophagic response, and simultaneously converting it into a pro-apoptotic one in transformed cells.

Technology Status

In vitro data with plans to progress into appropriate animal model
Patent pending: U.S. and foreign rights are available
This technology is available for licensing to industry for further development and commercialization.