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<td><strong>Author(s)</strong></td>
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Role of Chaperones in Selective Autophagy of Protein Inclusions

Introduction

Autophagy is a catabolic process that facilitates degradation of intracellular components in lysosomes\(^1\) (Fig. 1). Up-regulation of autophagy to clear protein inclusions has been shown to alleviate pathogenesis of various neurodegenerative diseases and represents an attractive therapeutic approach to slow down disease progression\(^2\). However, we have found that autophagic clearance of disease-linked inclusions is not a universal phenomenon and, instead, cells target the removal of these protein inclusions in a selective manner\(^3\) (Fig. 1). Currently, the factor(s) governing selection of protein inclusions for autophagic degradation is not well understood. Chaperones and co-chaperones, which modulate protein quality control, have recently been suggested to be critical in this selection process\(^4\). In this study, we seek to investigate whether the association of pertinent chaperone(s) with protein inclusions determines the susceptibility of protein inclusions toward autophagic degradation.

**AIM**

To investigate whether there are differences in the association of chaperones with protein inclusions of varying autophagic susceptibility.

**Results**

Cellular models of various protein inclusions were generated by overexpressing the respective GFP-tagged aggregation-prone proteins in HEK293 cells followed by proteasomal inhibition. The presence of the different chaperones in the protein inclusions was analyzed by immunocytochemistry and fluorescence microscopy. The representative fluorescent images and percentage colocalization (>20 protein inclusions analyzed/set) were shown below.

**Conclusion**

The level of co-chaperone Bag3 in a protein inclusion may determine its susceptibility toward autophagic clearance.

**Future Direction**

To examine the effects of ablating the endogenous level of Bag3 in cells on autophagic degradation of protein inclusions.

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### References


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**Project Title:** Role of chaperones in mediating selective autophagy of protein inclusions

**Supervisor:** Asst Prof Wong Siew Peng Esther