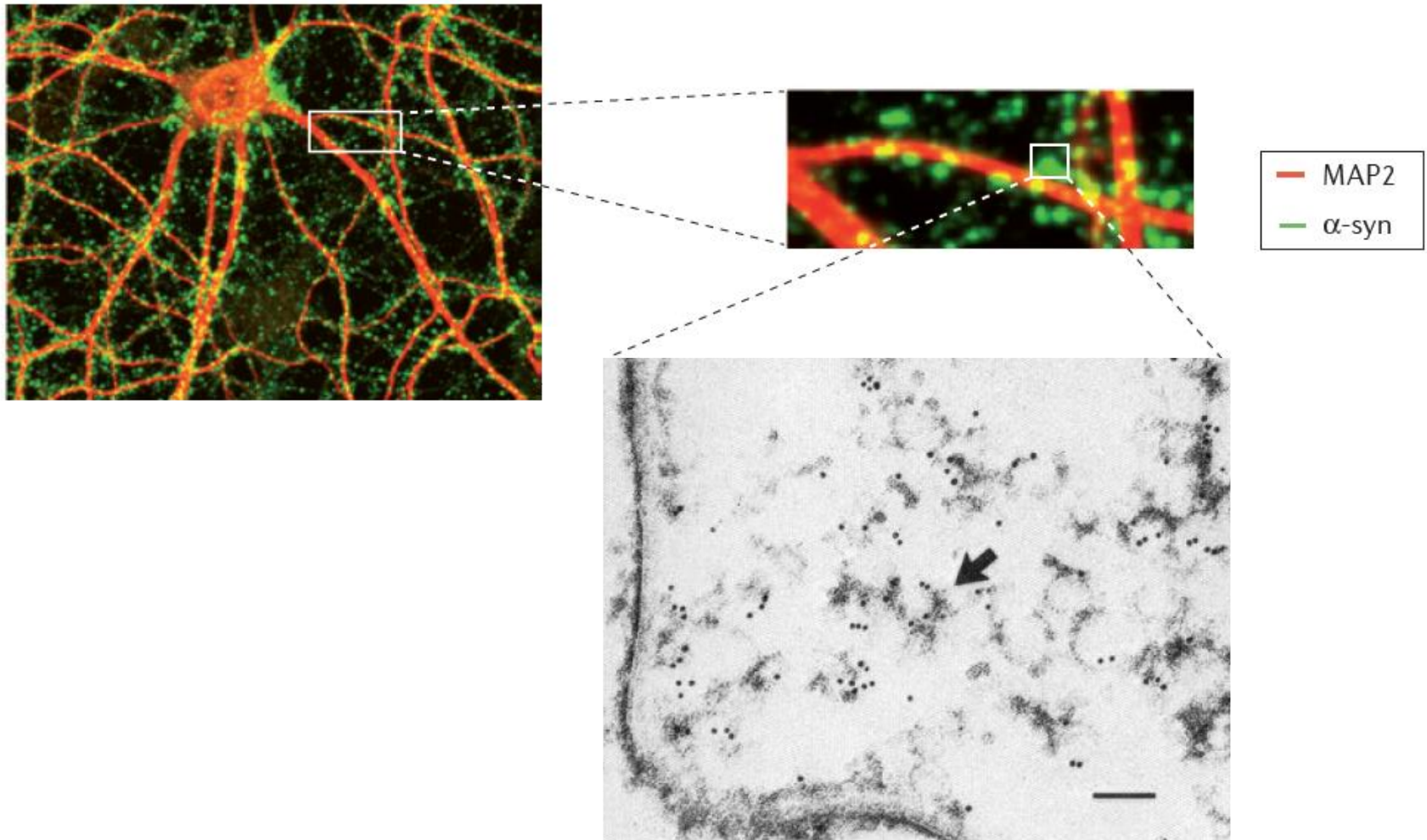
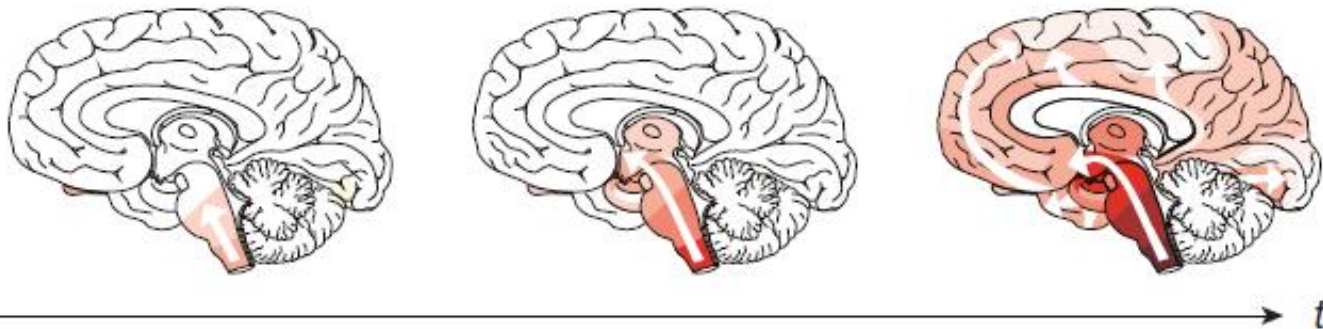
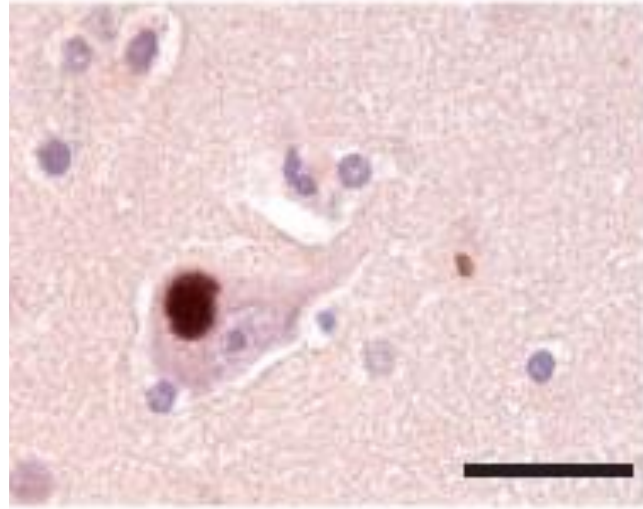

Determinants of α -Synuclein Toxicity

Biology of α -Synuclein

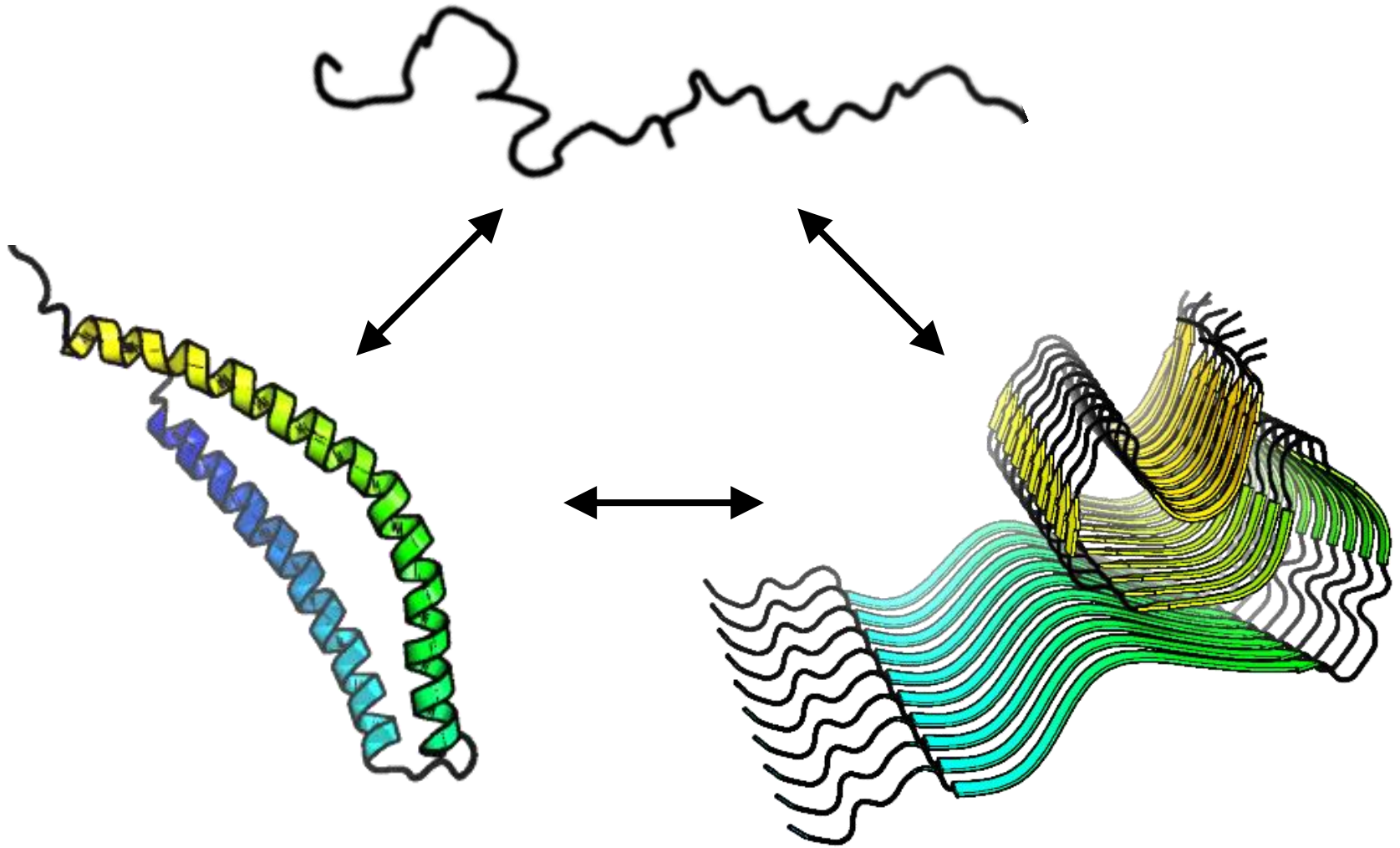


Maroteaux, et al. *J. Neurosci.* **1988**, 8, 2804
Lashuel, et al. *Nat. Rev. Neurosci.* **2013**, 14, 38

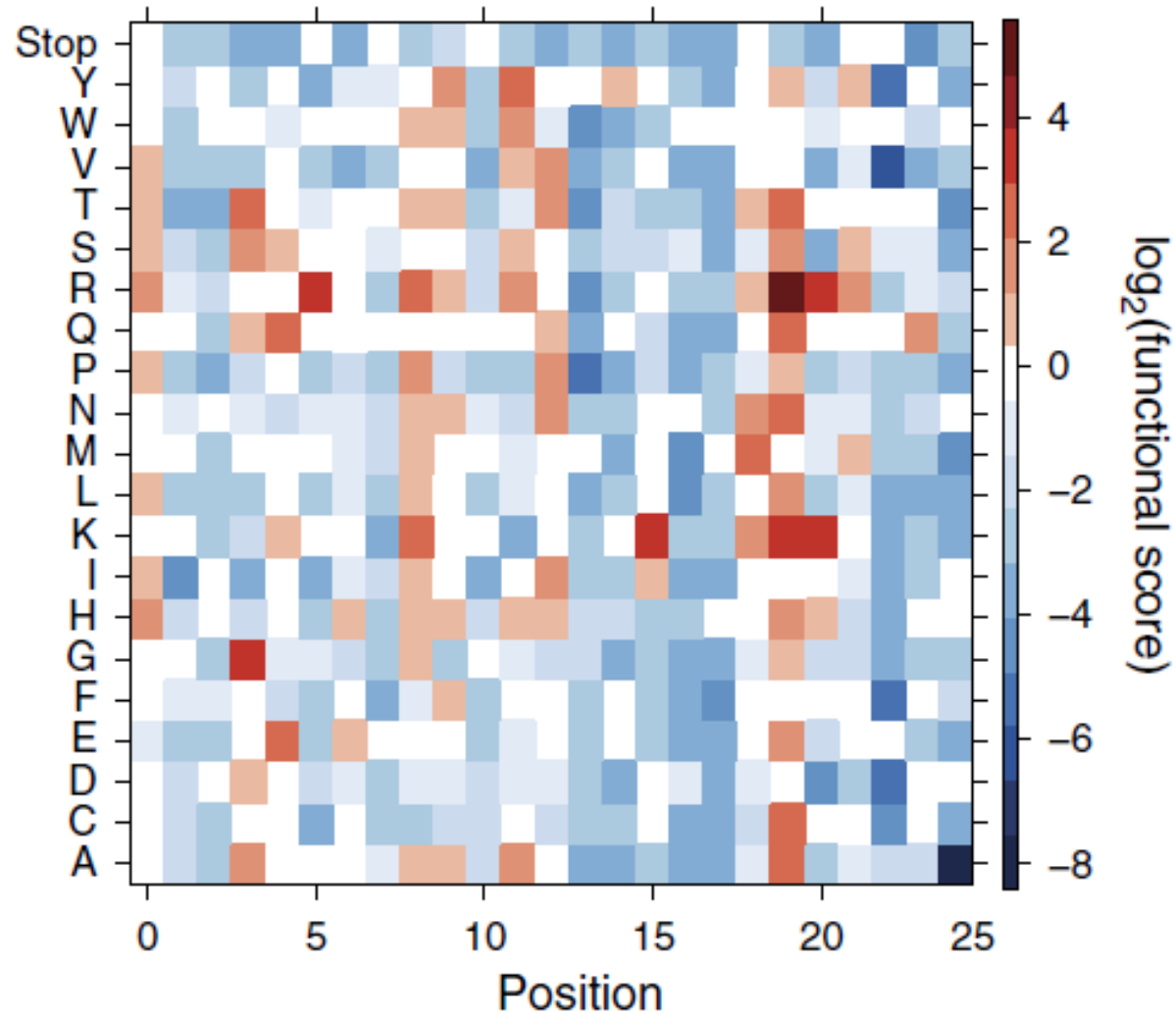
Pathology of α -Synuclein



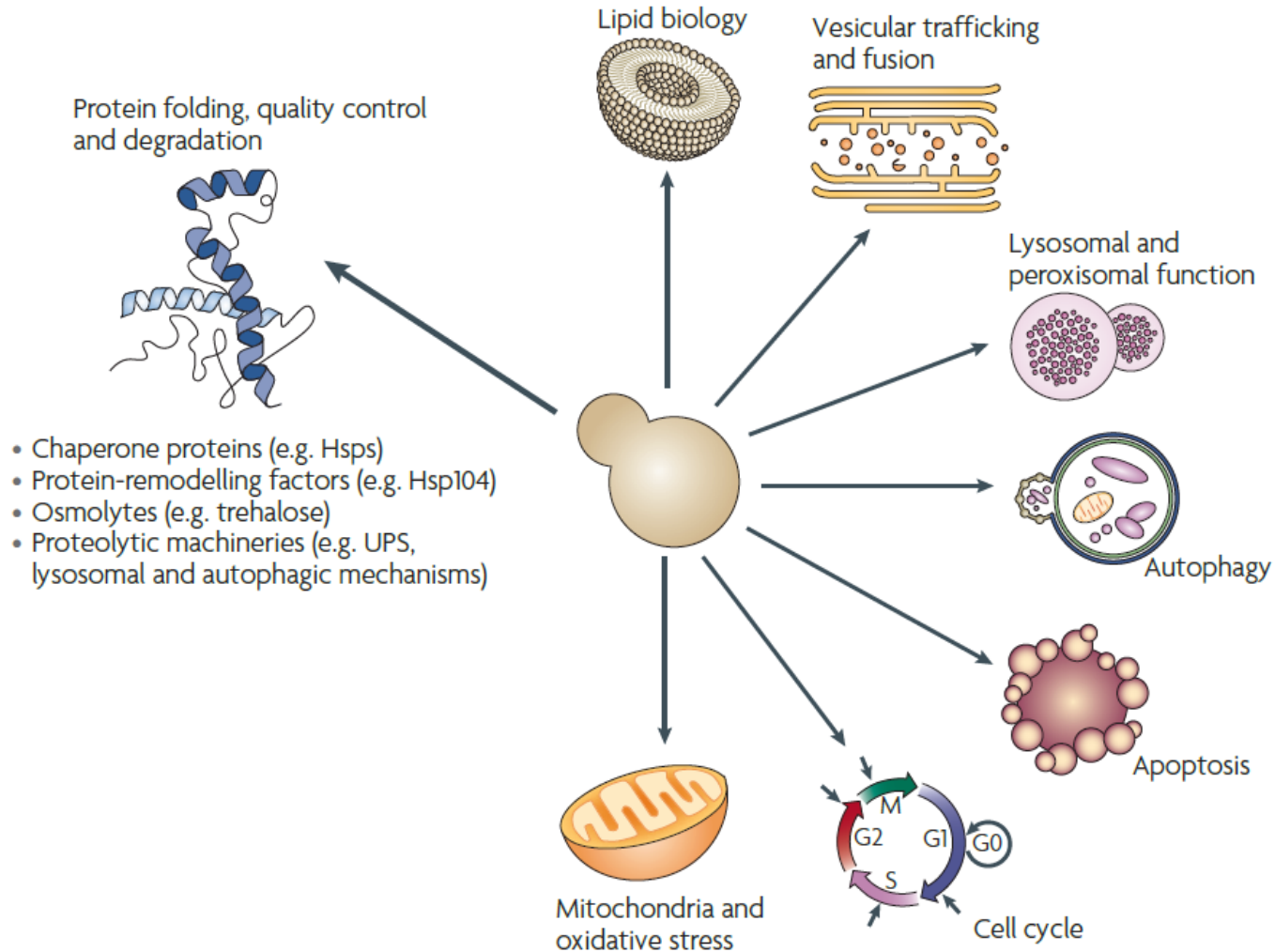
α -Synuclein (Mis)Folding



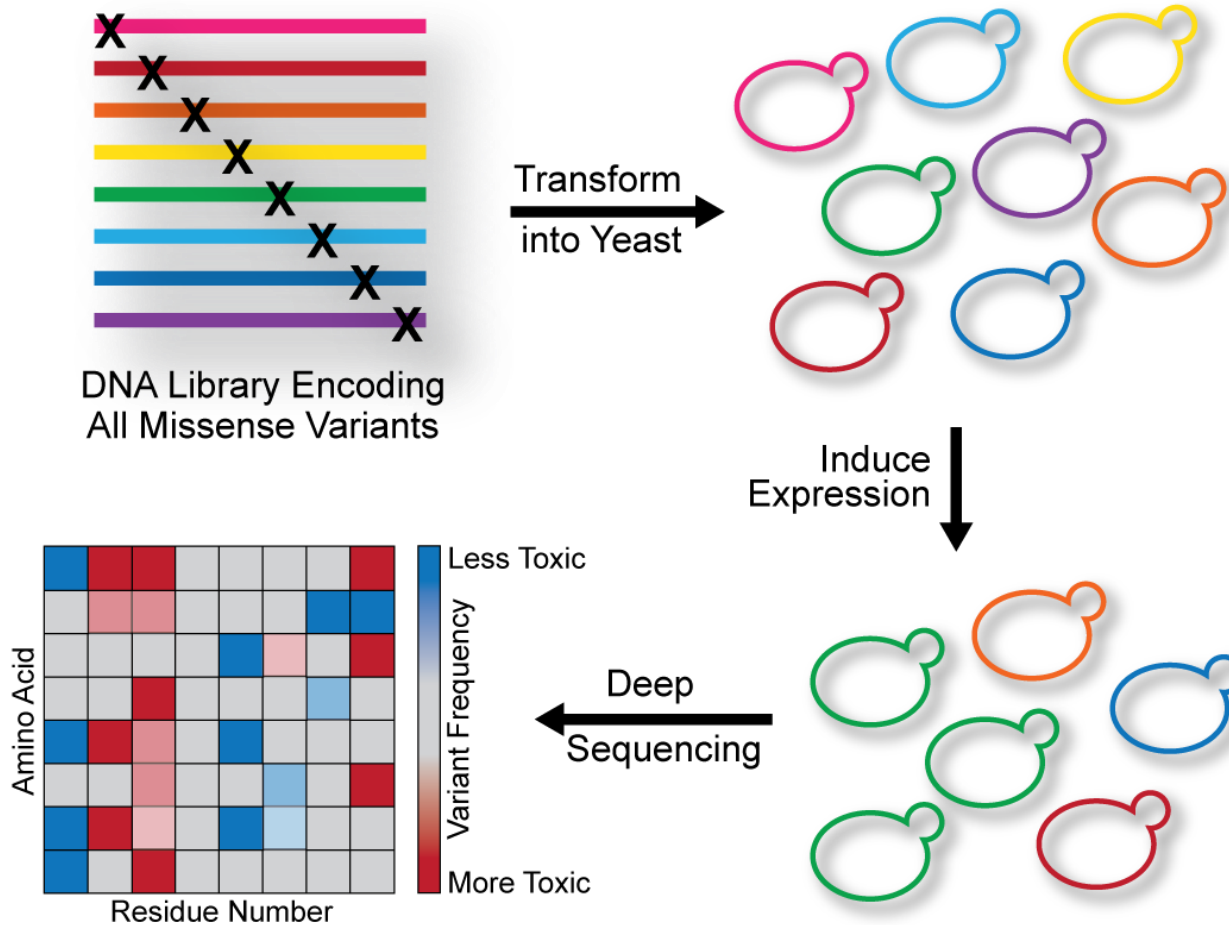
Deep Mutational Scanning



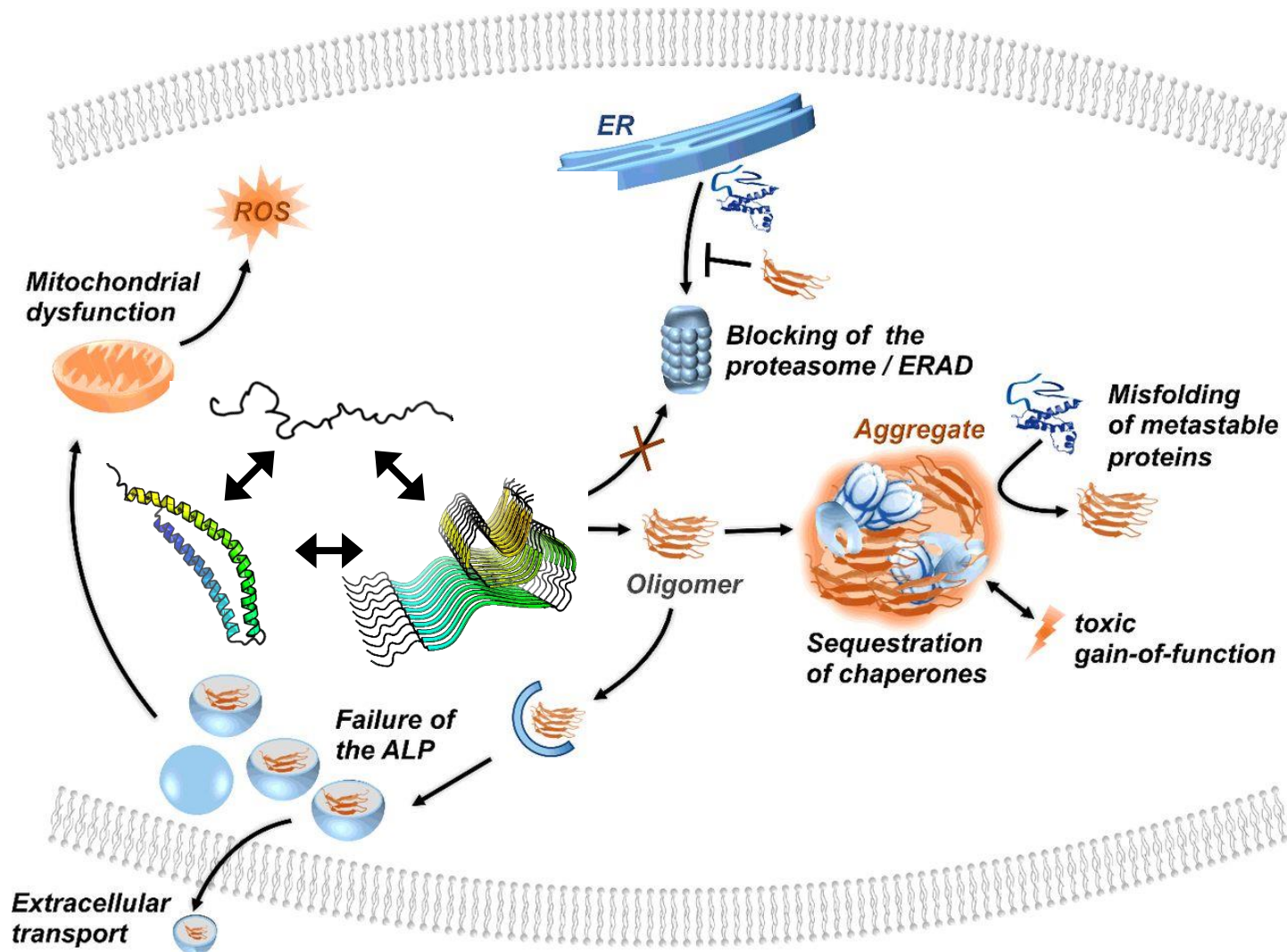
The Model: Yeast



Deep Mutational Scanning



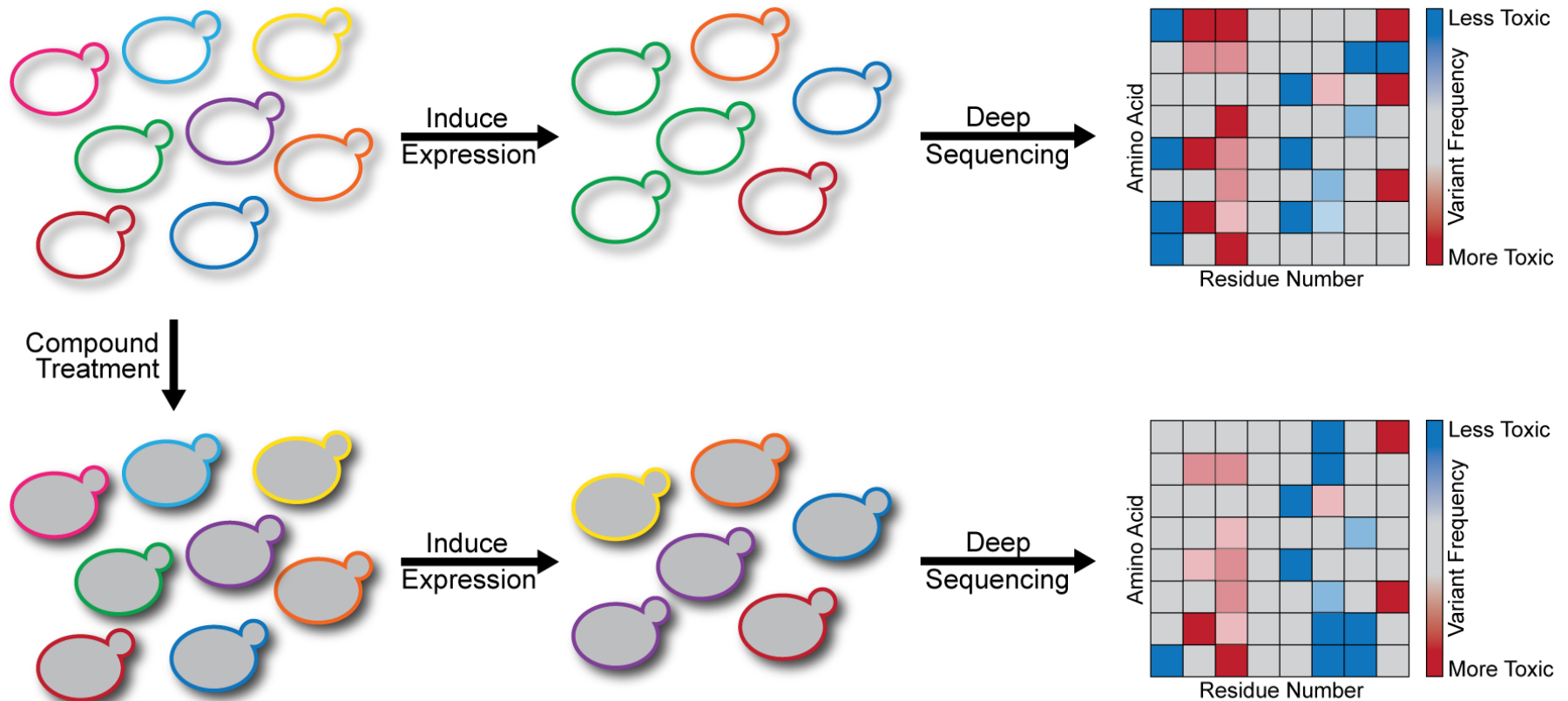
α -Synuclein (Mis)Folding



Open Questions

- What cellular stresses would make a cell more susceptible to α -synuclein toxicity?
- Is the toxicity of α -synuclein dependent on its ability to engage different cellular factors?
- What features or properties of α -synuclein enable those cellular interactions?
- Is the cell targeting particular structures or residues of α -synuclein to mitigate toxicity?

A Chemical Biology Approach



Authorship Criteria

- Intellectual Contribution
 - Conceive/revise/develop approaches
 - Analyze/interpret data
- Technical Execution
 - Do something to help the study be accomplished
- Dissemination
 - Describe your work and its implications
 - Certify the manuscript

Goals for Today

- Meet your groups
- Come up with a name
- Choose the compound for your experiment, give 1 minute presentation justifying the compound selection
- Set up cluster access

Compound Choices

- MG132
- Brefeldin A
- Tunicamycin
- Geldanamycin
- Miconazole
- Menadione
- Spermidine
- TPCK
- Dopamine
- L-Dopa