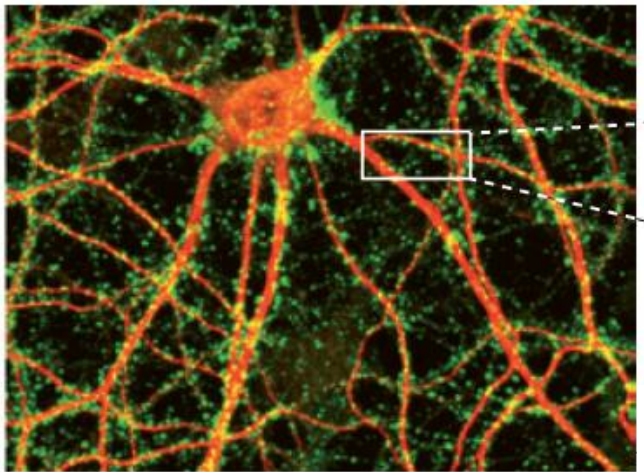
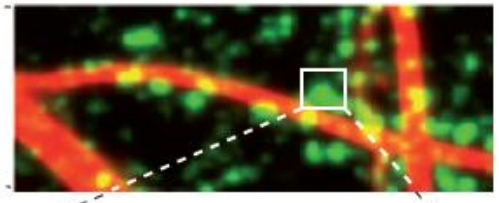
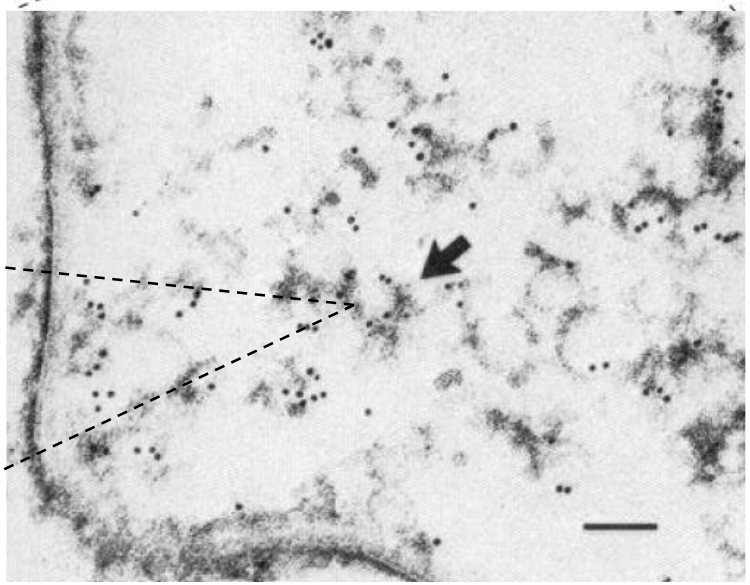
Molecular Determinants of α-Synuclein Toxicity

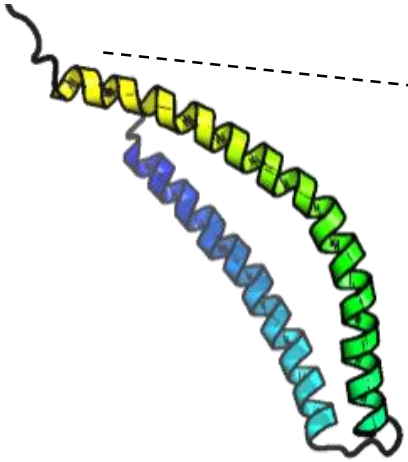
Biology of α-Synuclein



Dendrites α-Synuclein







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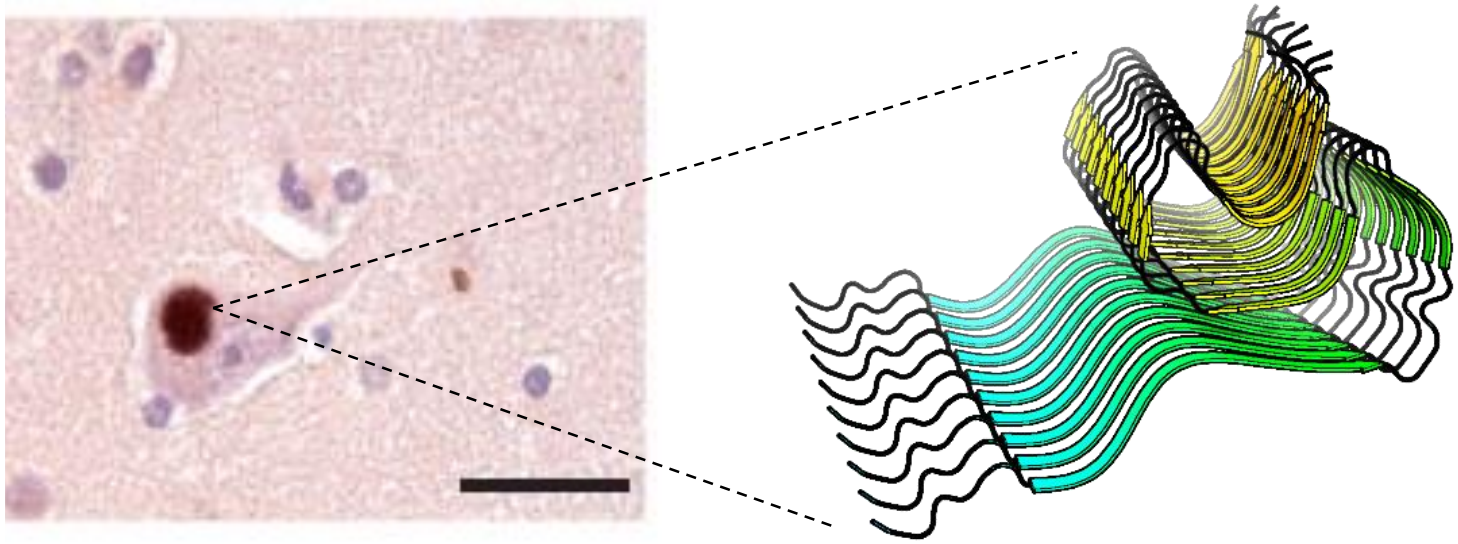
Pathology of α-Synuclein



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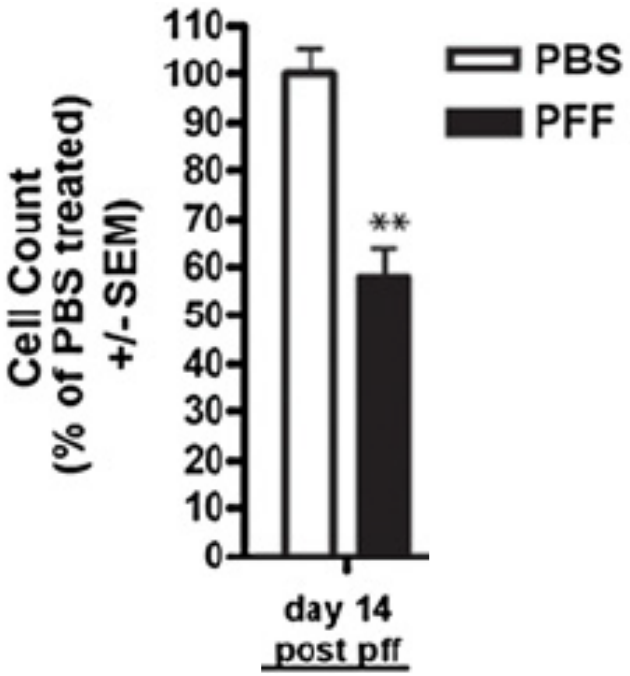
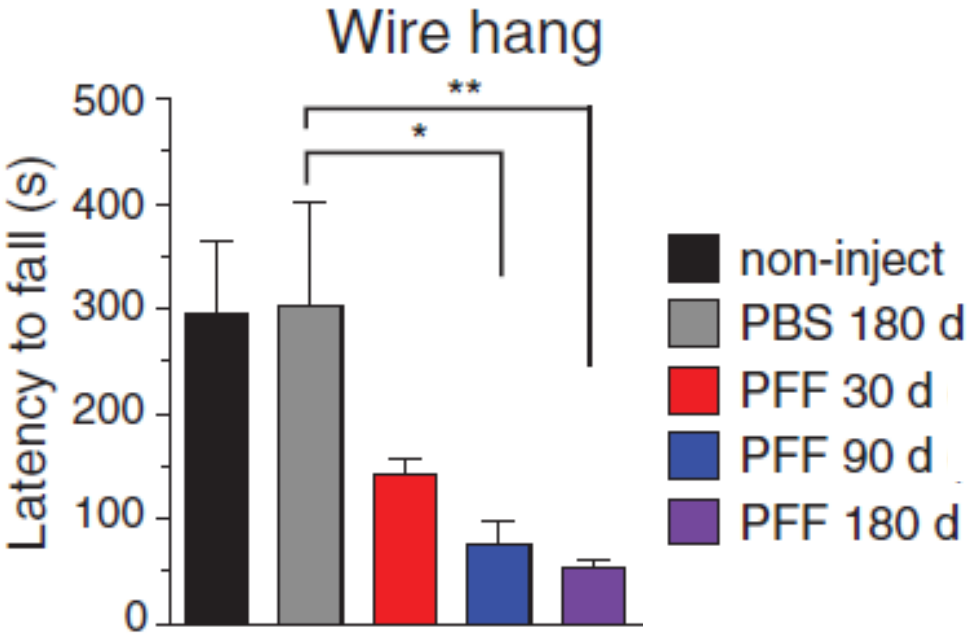
Pathology of α-Synuclein





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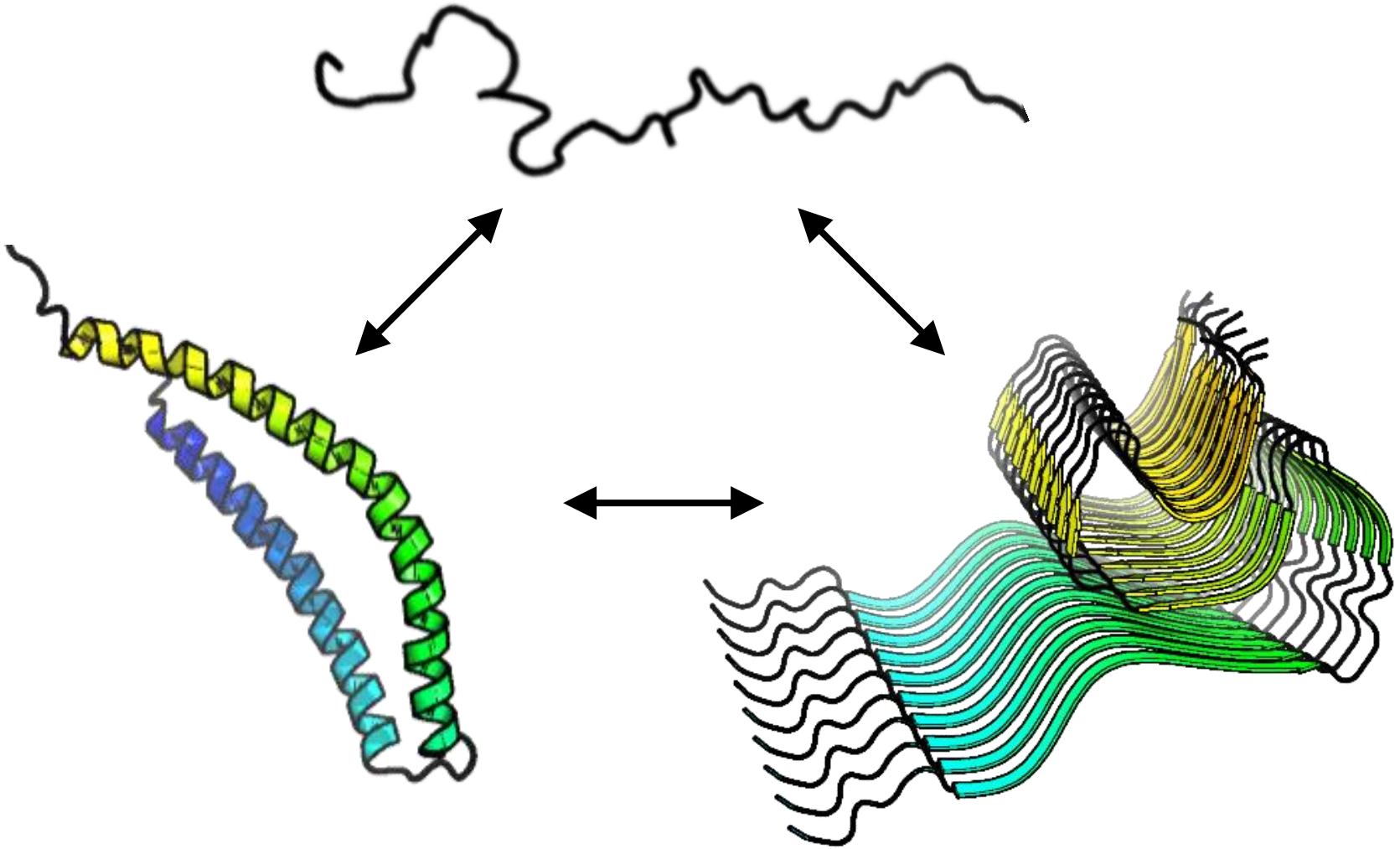
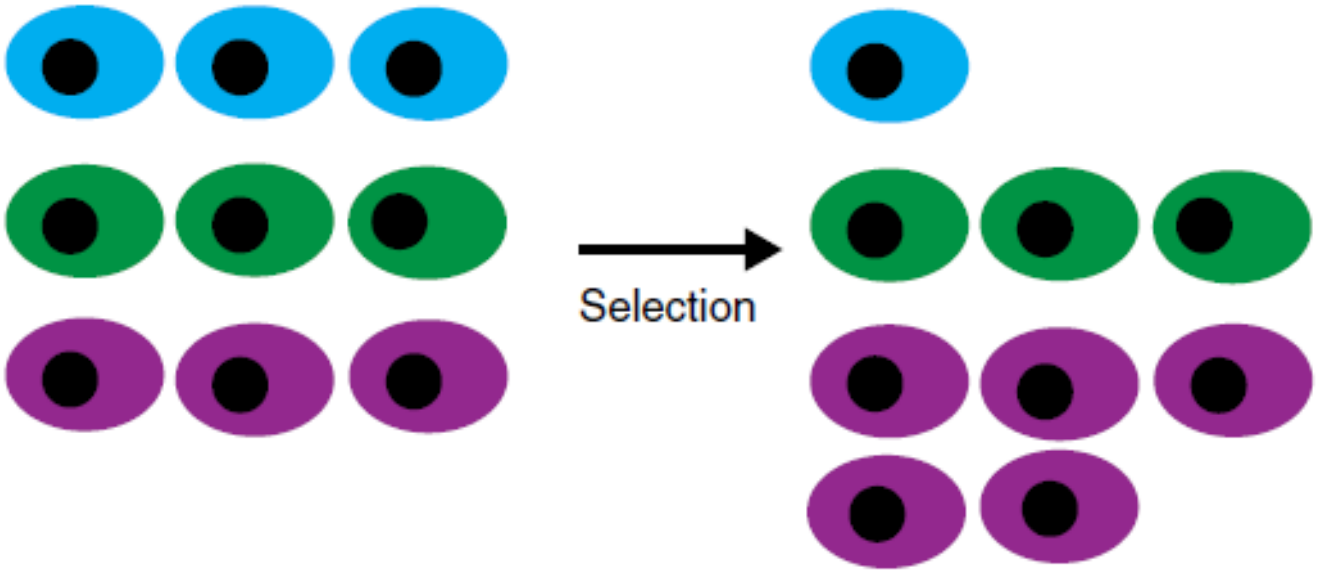
α-Synuclein (Mis)Folding



Deep Mutational Scanning



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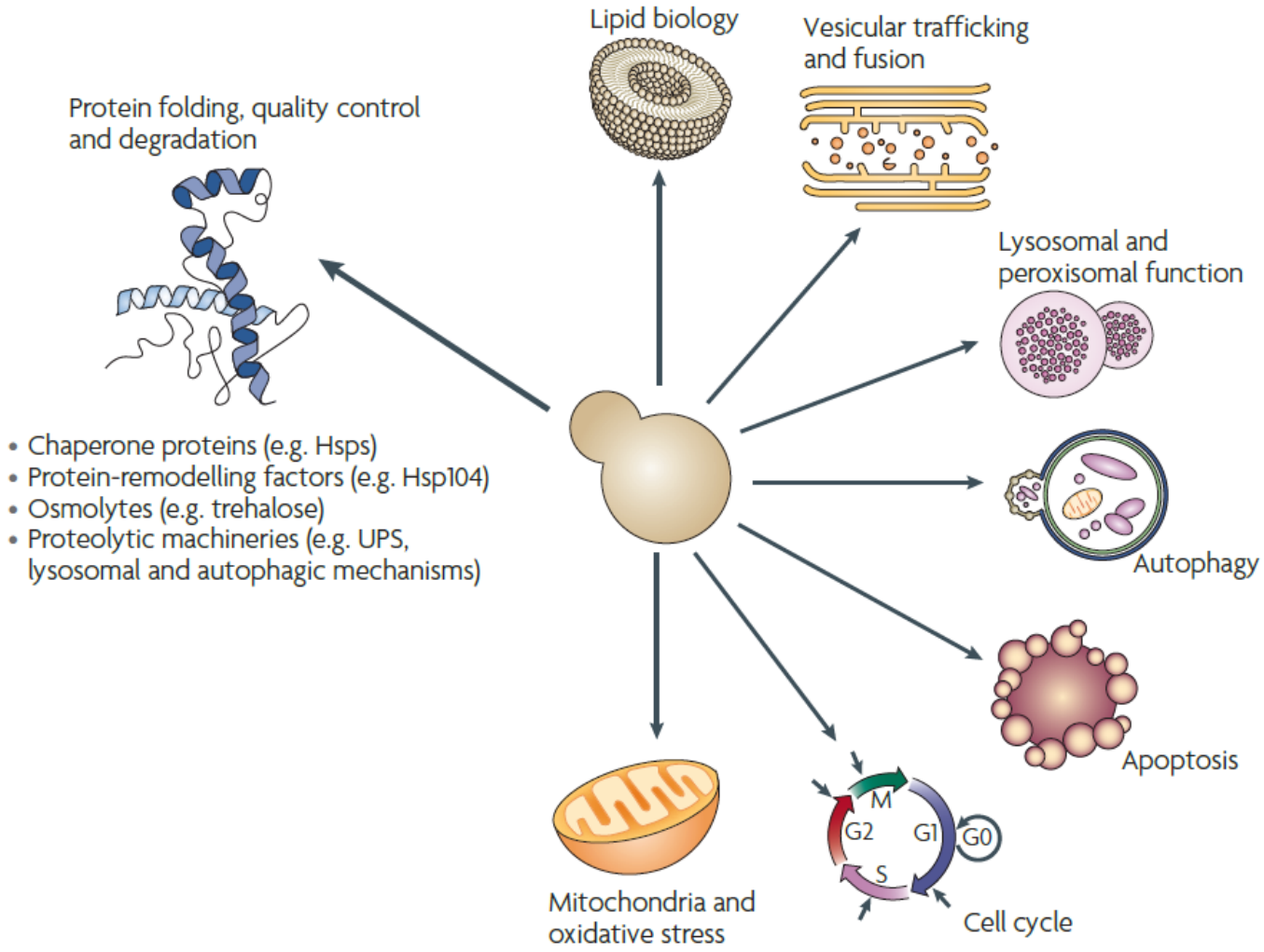
The Model: Yeast



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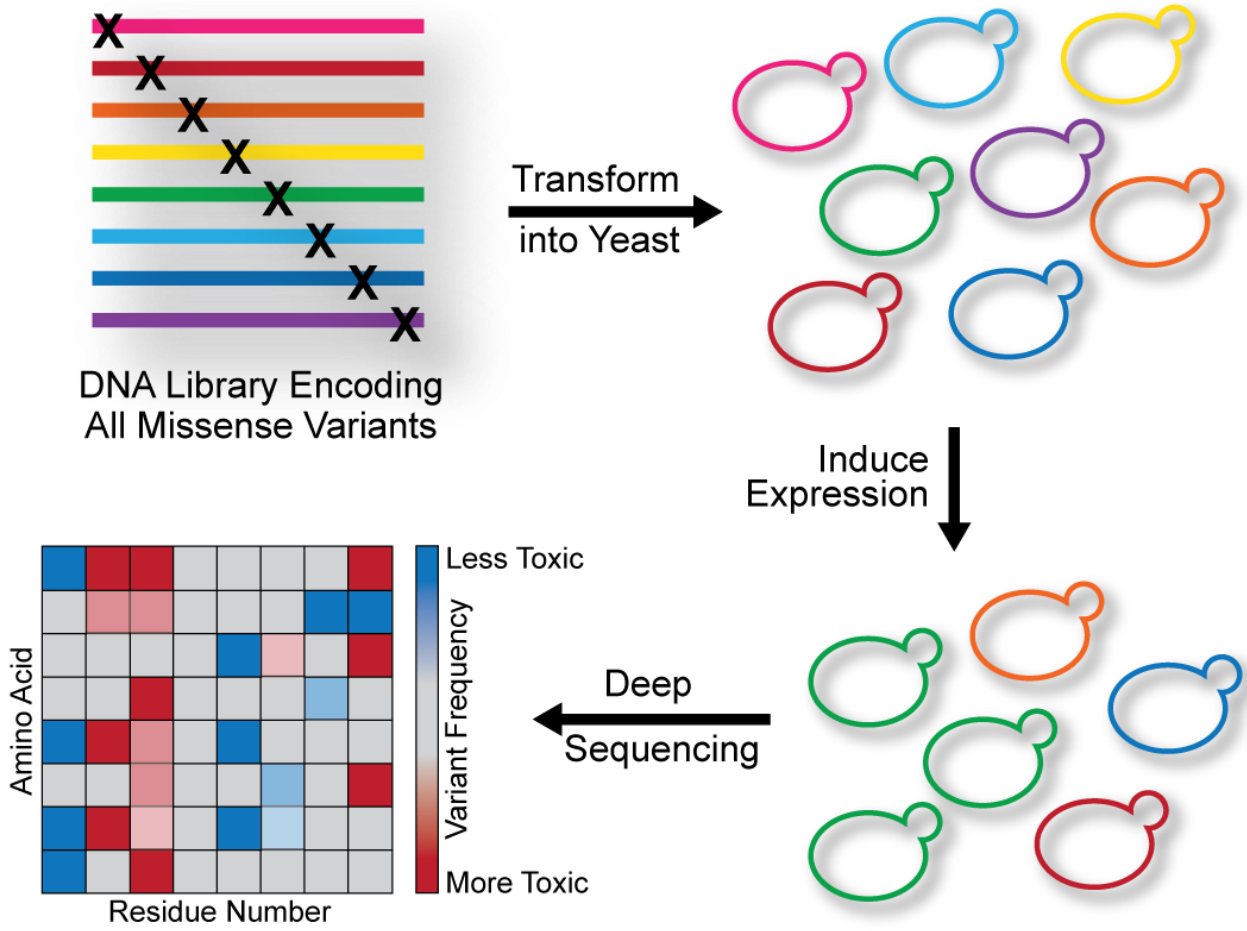
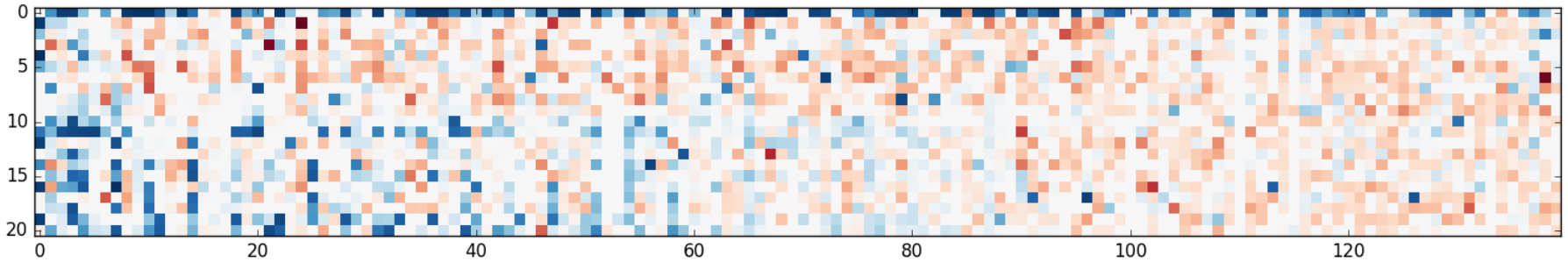
Deep Mutational Scanning

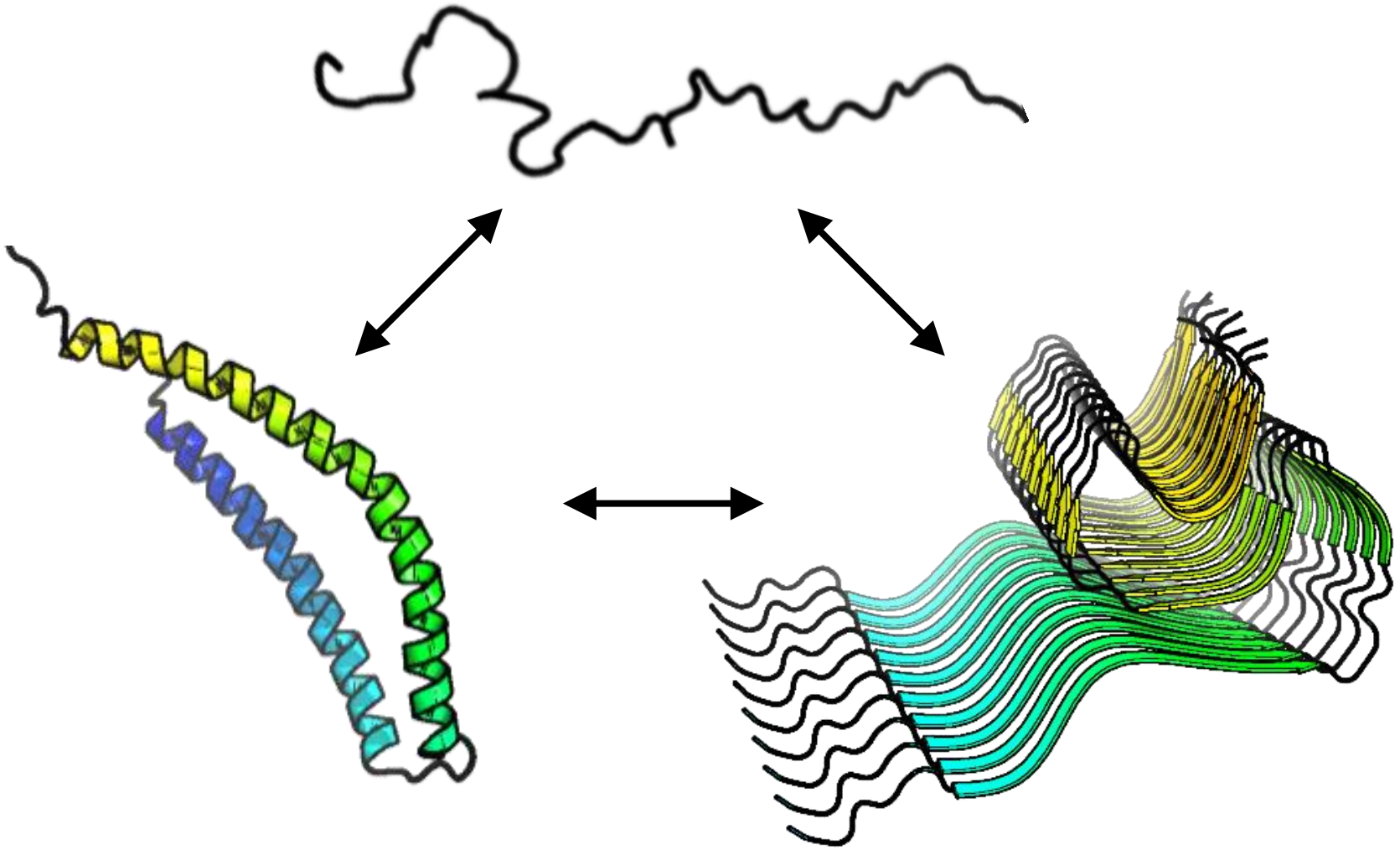


Fitness Scores



More Toxic WT Less Toxic

α-Synuclein (Mis)Folding



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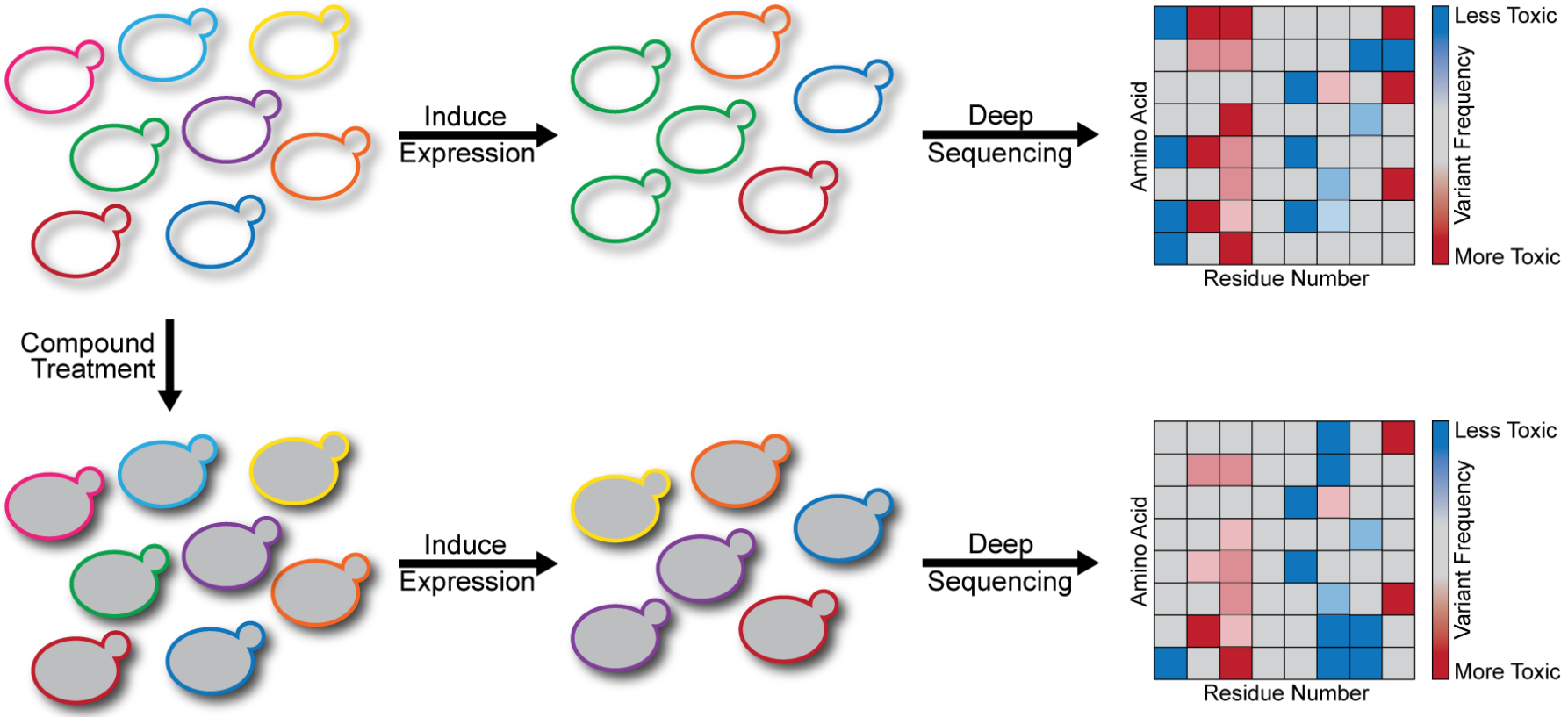
Open Questions

- 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?
- What features of the cell promote or deter α-synuclein misfolding?

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
- Set up cluster access
- Choose the compound for your experiment
- One minute presentation about your compound

Compound Choices

Brefeldin A

Rotenone

Miconazole

Dopamine

Rapamycin

Melatonin