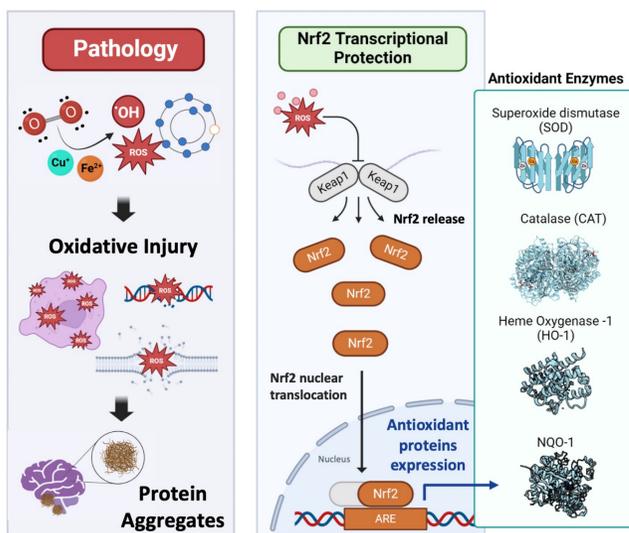
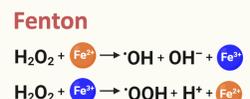
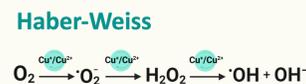


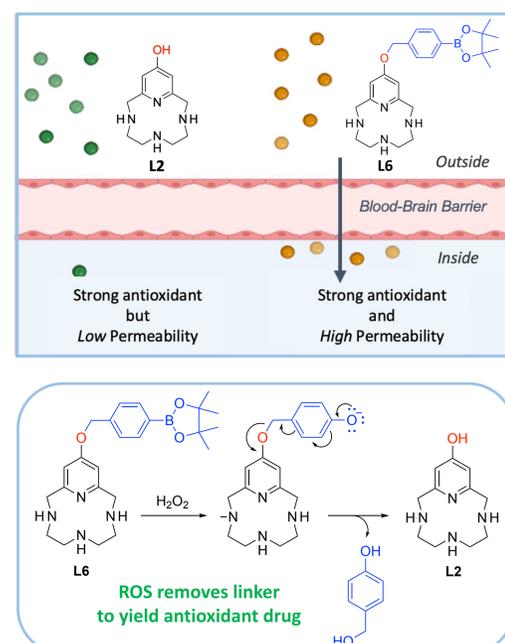
Saba Anjum, Shrikant Nilewar, David Mingle, Kayla N. Green
Green Research Group, Department of Chemistry & Biochemistry, Texas Christian University

Introduction

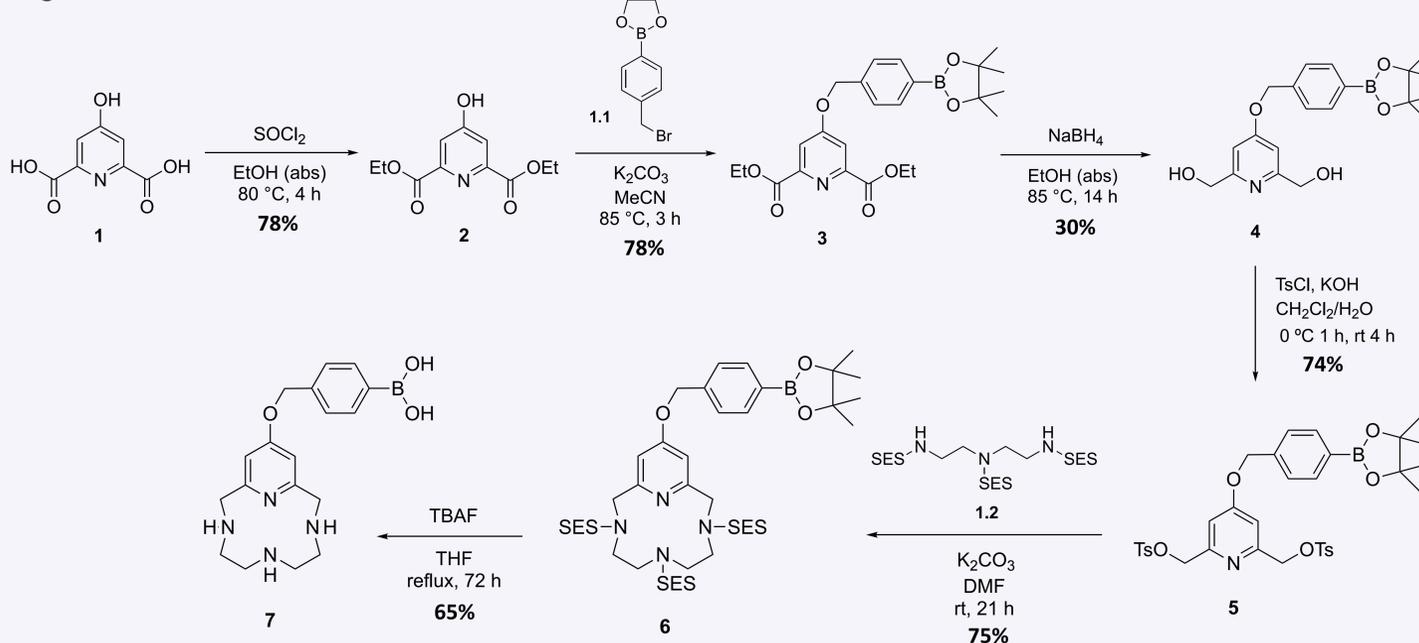
- 6+ million Americans live with Alzheimer's disease.
- Oxidative stress is a common feature of neurodegenerative conditions like Alzheimer's disease and Parkinson's disease.



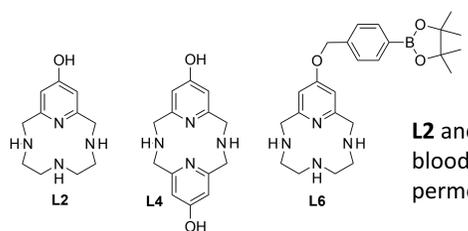
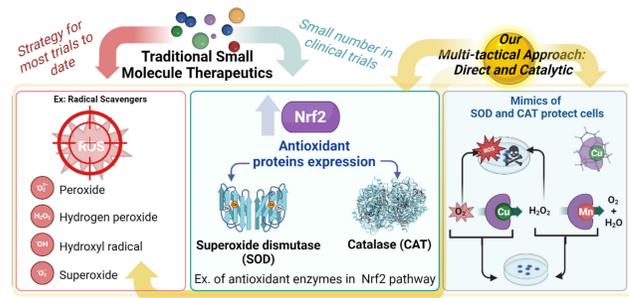
Prodrug Design



Synthetic Scheme



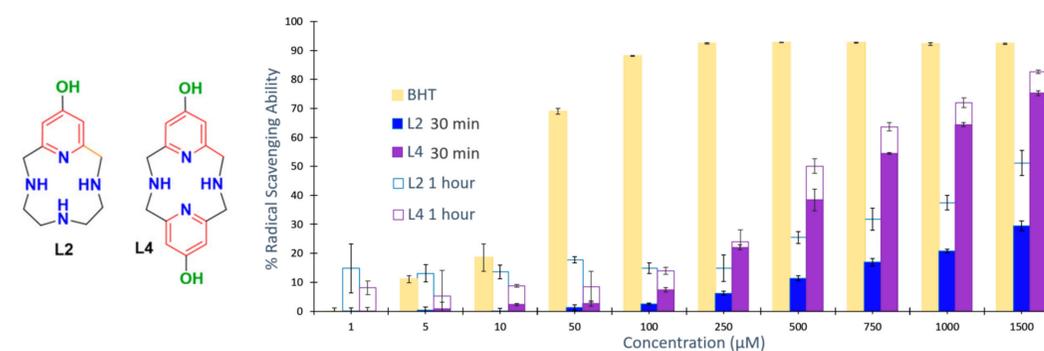
Small Molecule Therapeutics



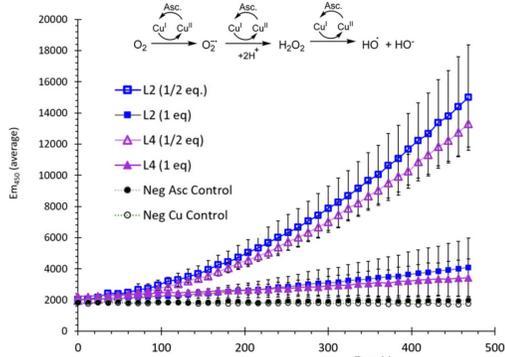
L2 and L4 have low blood-brain barrier permeability.

Compound	MW	c log P	HBA	HBD	TPSA (Å²)	log BB
L2	222	-0.38	5	4	69.21	-0.961
L4	272	1.12	6	4	89.24	-1.012
L6	438	0.90	7	3	76.67	-0.859
Target Values	≤ 450	≤ 5.0	≤ 10	≤ 5	≤ 90	> 3.0 (readily) < -1.0 (poorly)

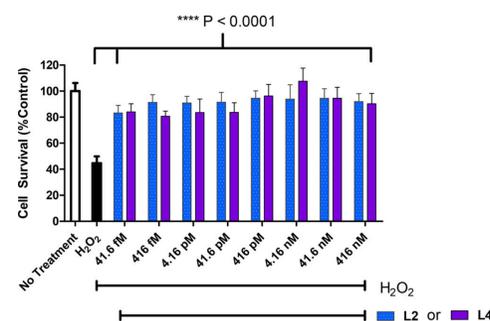
Multi-Target Antioxidant Activity



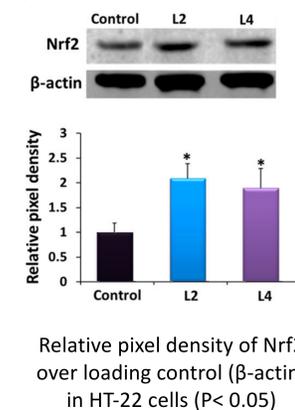
Radical scavenging ability measured using DPPH* versus L2 and L4 compared to the standard antioxidant BHT



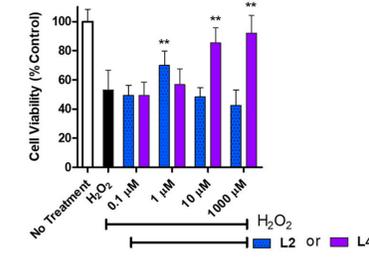
Fluorescence intensity of 7-hydroxy-CCA after incubation of CCA and ascorbate with copper(II)



Cytoprotective effects in BV2 microglial cells measured using MTT assay (P < 0.0001)



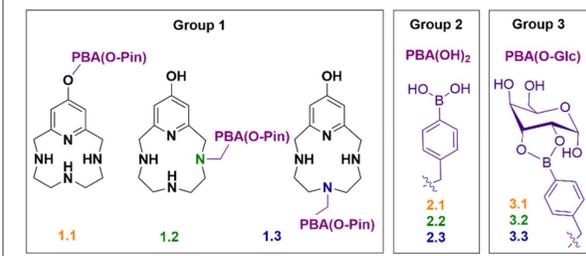
Relative pixel density of Nrf2 over loading control (β-actin) in HT-22 cells (P < 0.05)



Cytoprotective effects in HT-22 cells measured using WST-8 assay (P < 0.01)

Future Directions

We aim to utilize different moieties to enhance the blood-brain barrier permeability of macrocycles while maintaining antioxidant activity.



Acknowledgements

