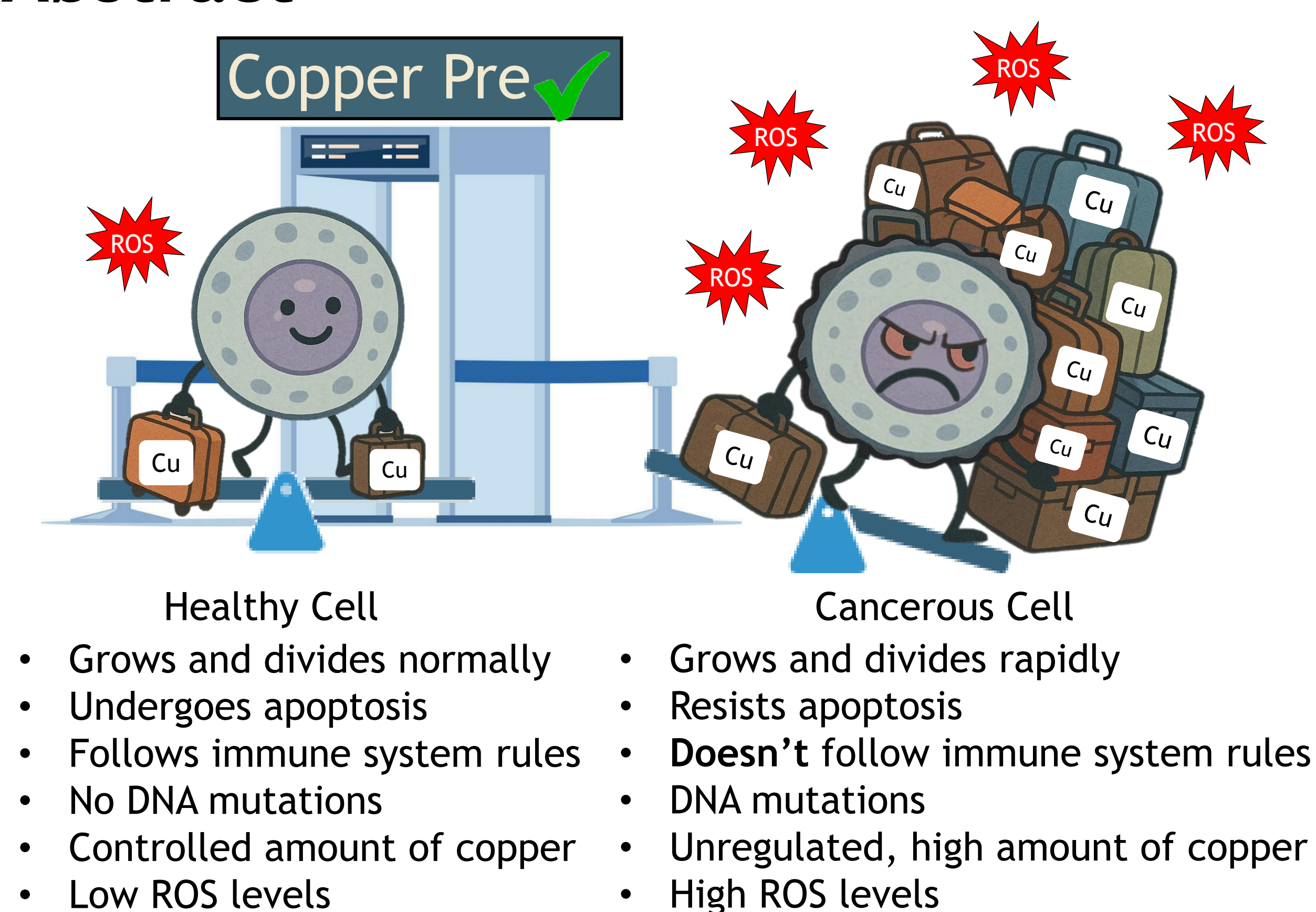


Development and Comparison of Novel Tetra-aza Pyridinophanes with Quinoline Moieties as Anticancer Therapeutics

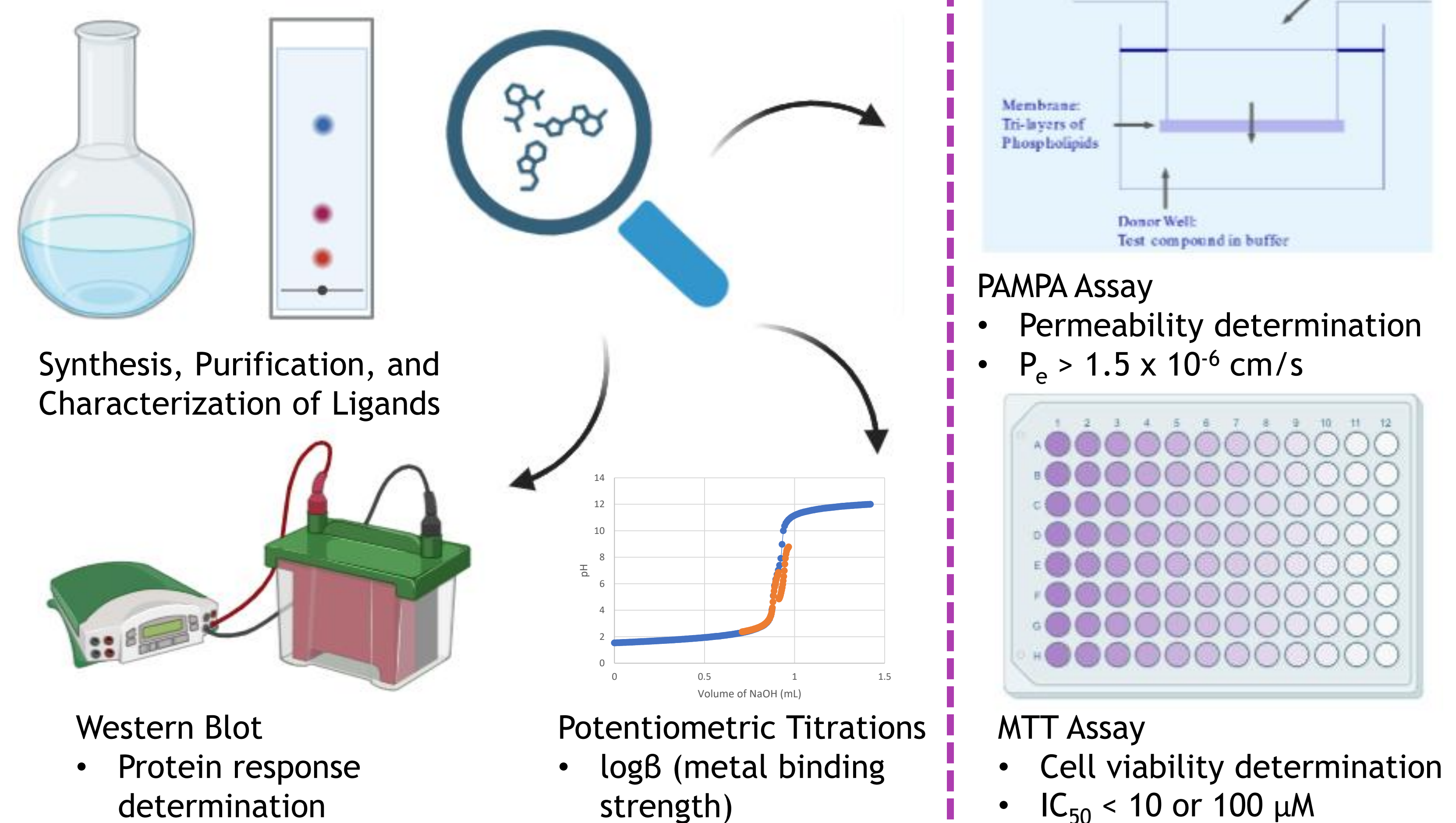
Sarah Dunn, Benito Morales, Natalie Plascencia, Giridhar Akkaraju, Ph.D., Kayla N. Green, Ph.D., Department of Chemistry and Biochemistry

Abstract

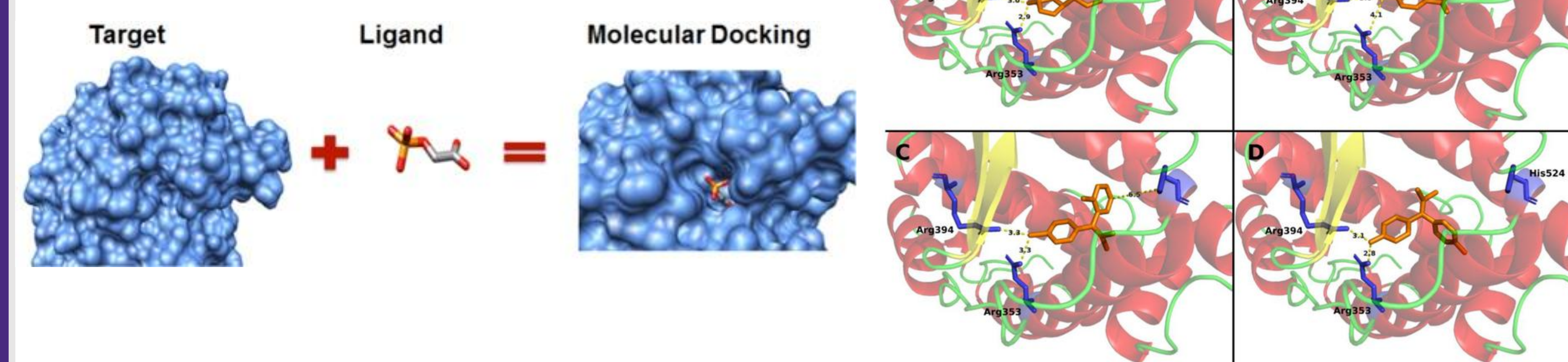


Objective: Synthesizing Multi-Function Ligands for Addressing Elevated Copper and ROS Levels in Diseased Cells

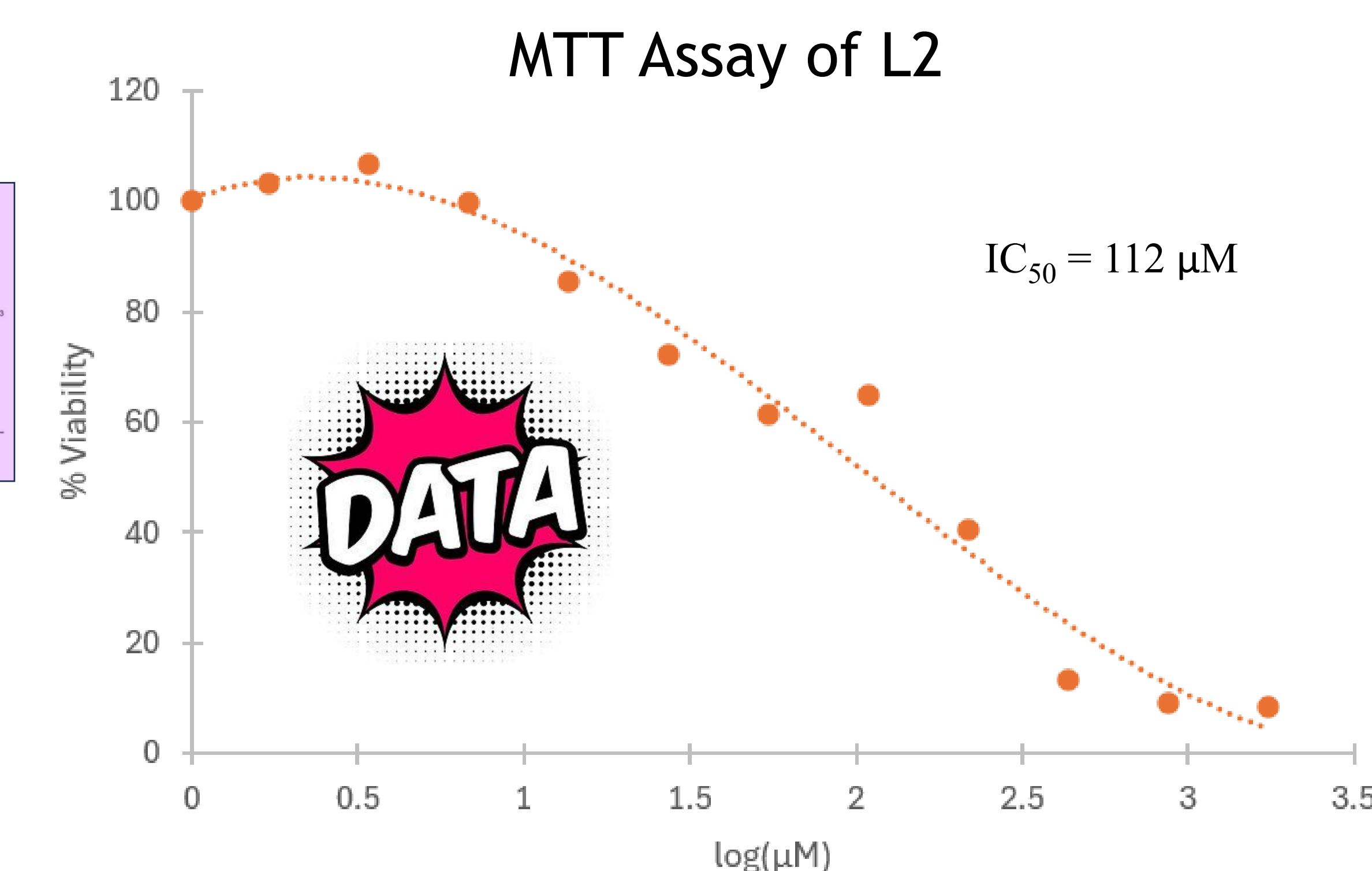
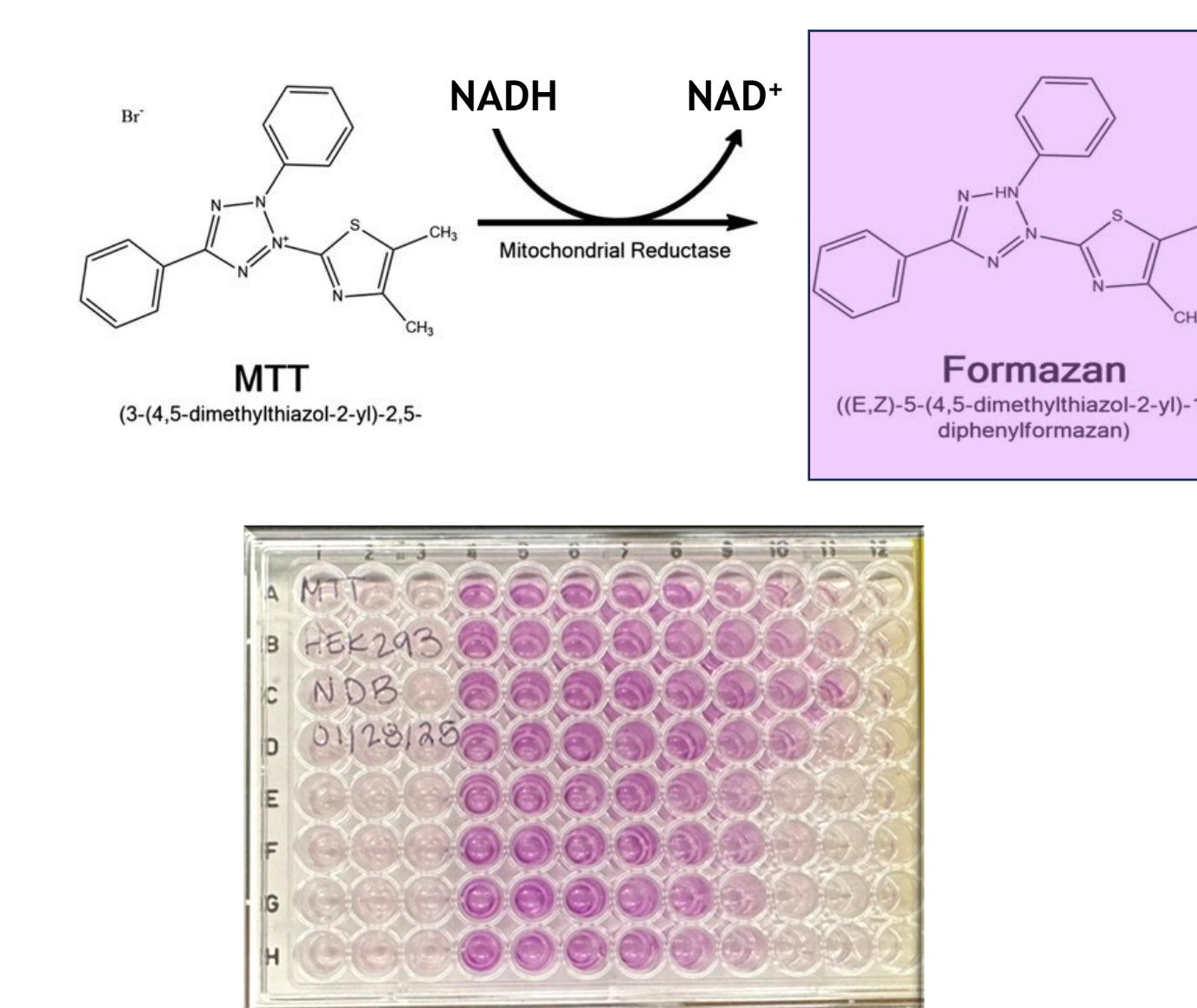
Workflow



Docking

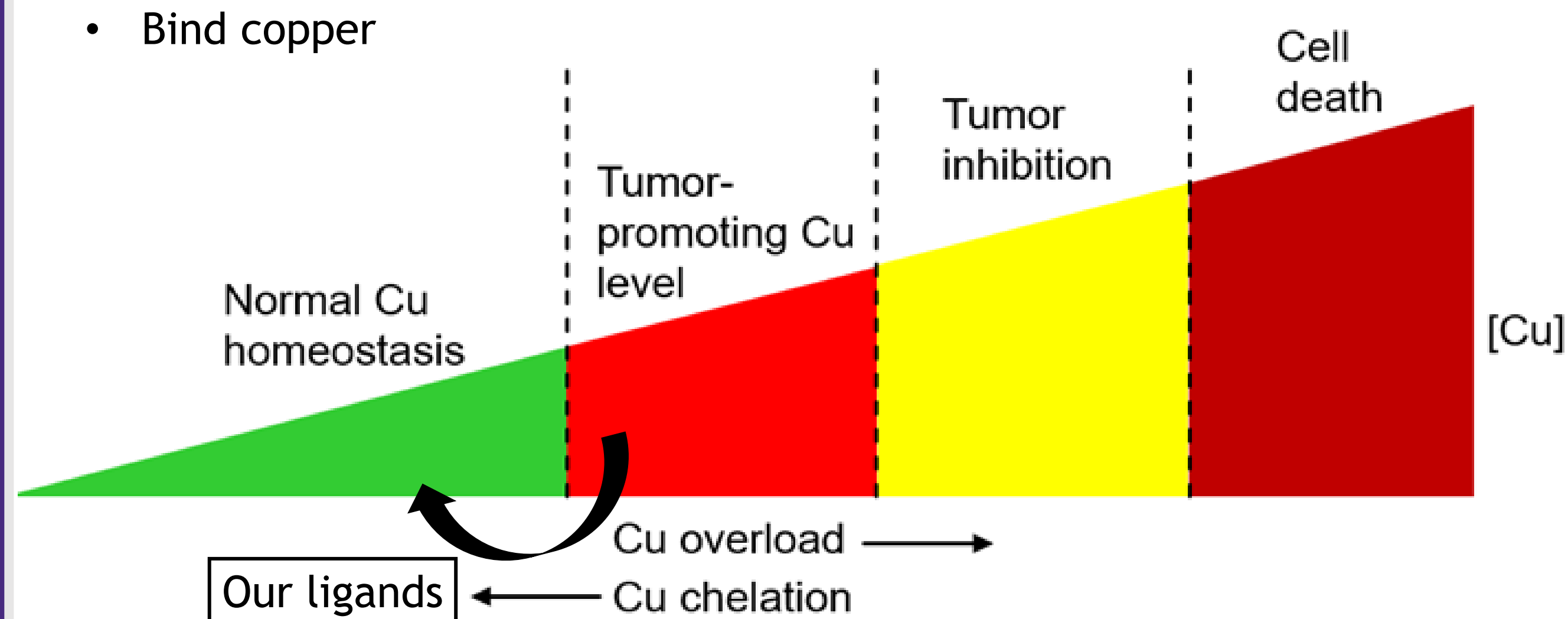


MTT Assay

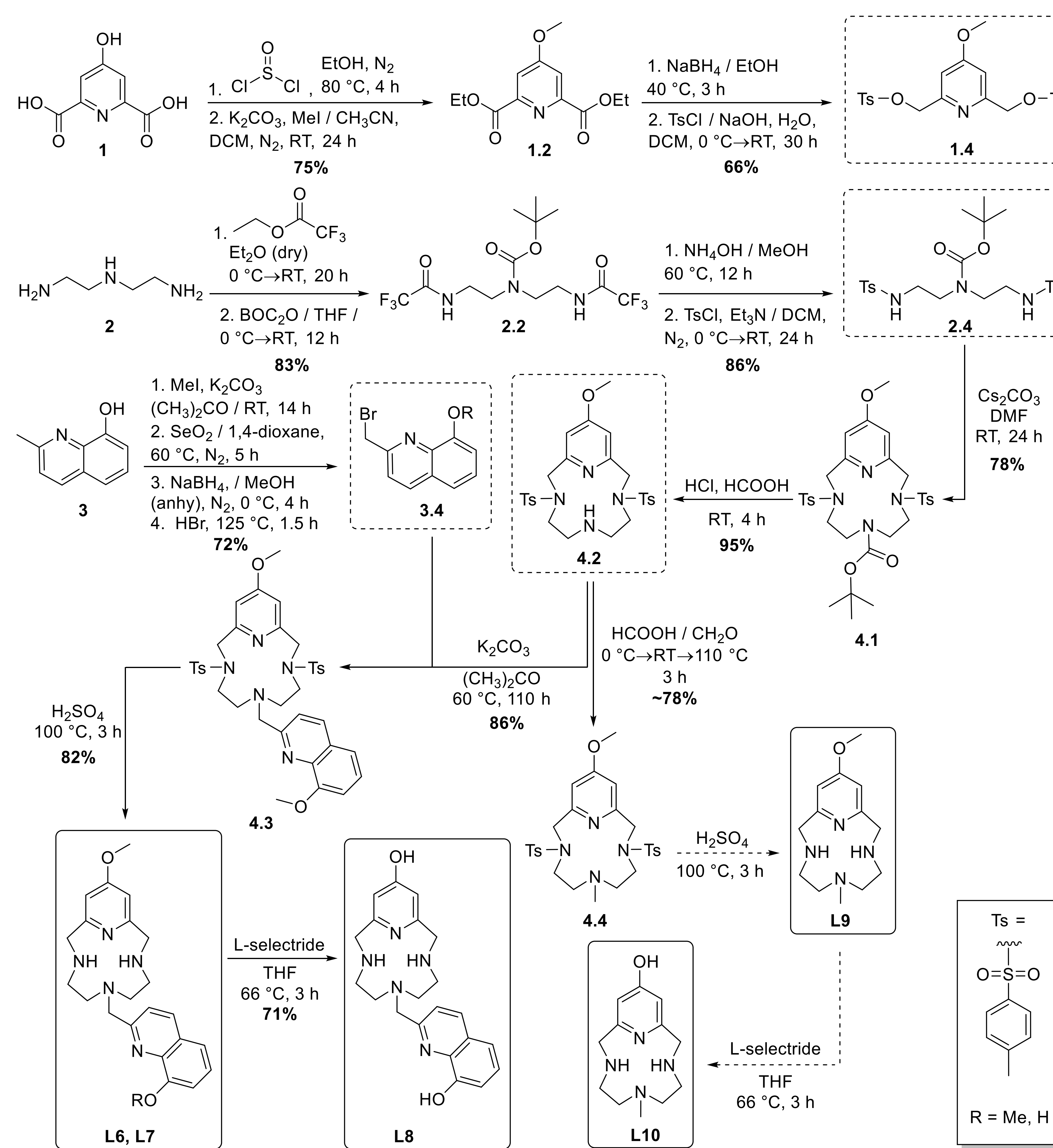


ROS, Copper, and Cancer

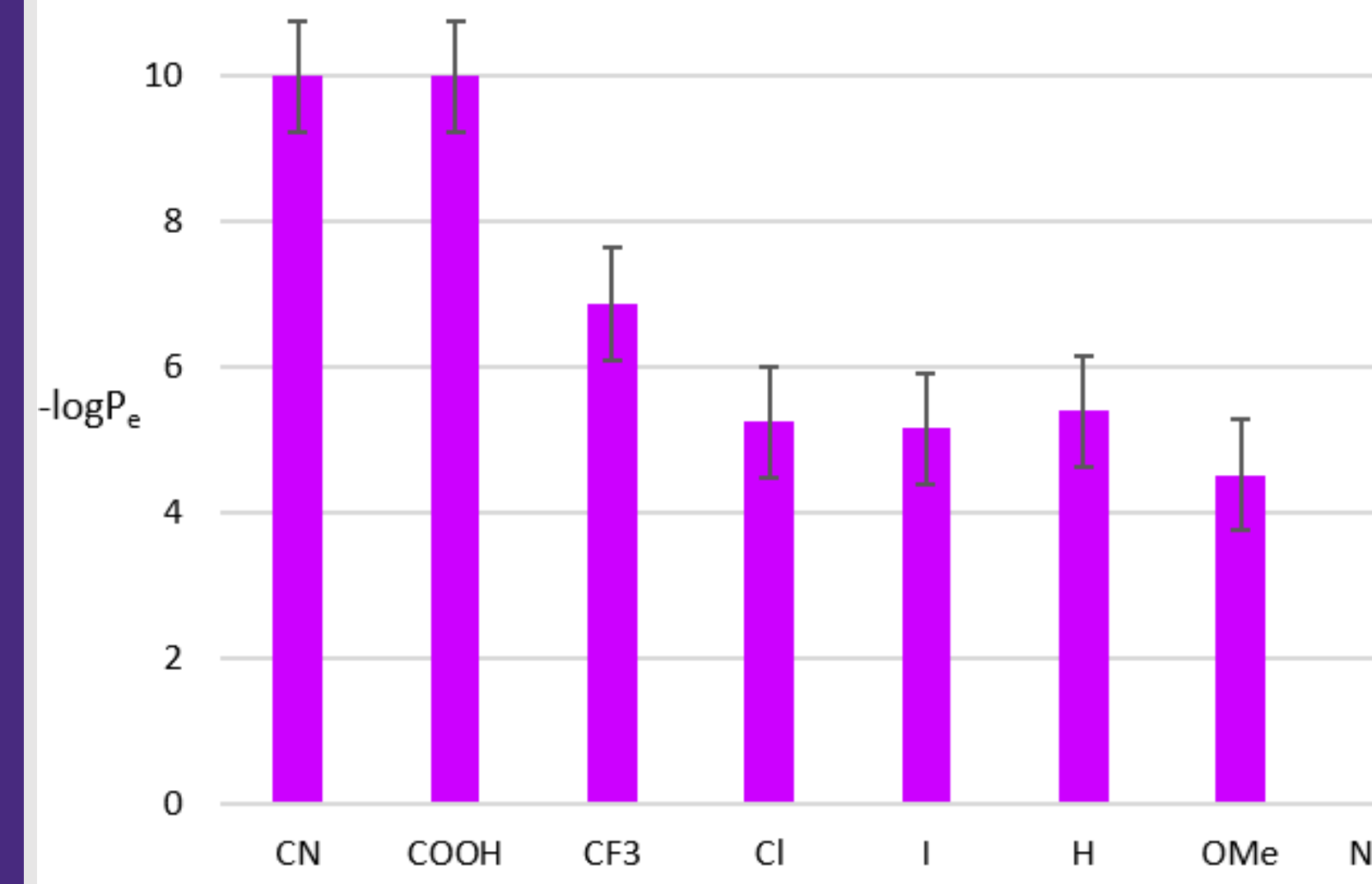
- Current Therapeutics:**
- Quench ROS
 - Stabilize radicals
 - Bind copper
- Proposed Therapeutics:**
- Combined effects



Synthetic Scheme for Novel ^RPyN₃-R' Ligands



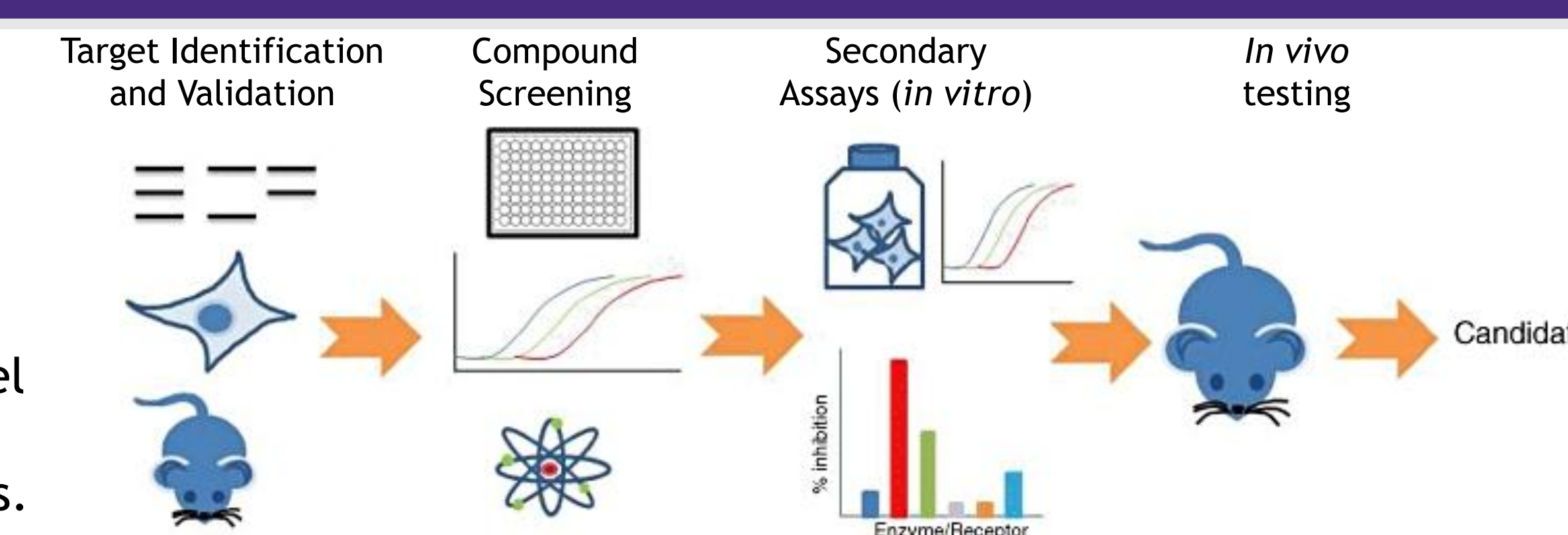
PAMPA Assay



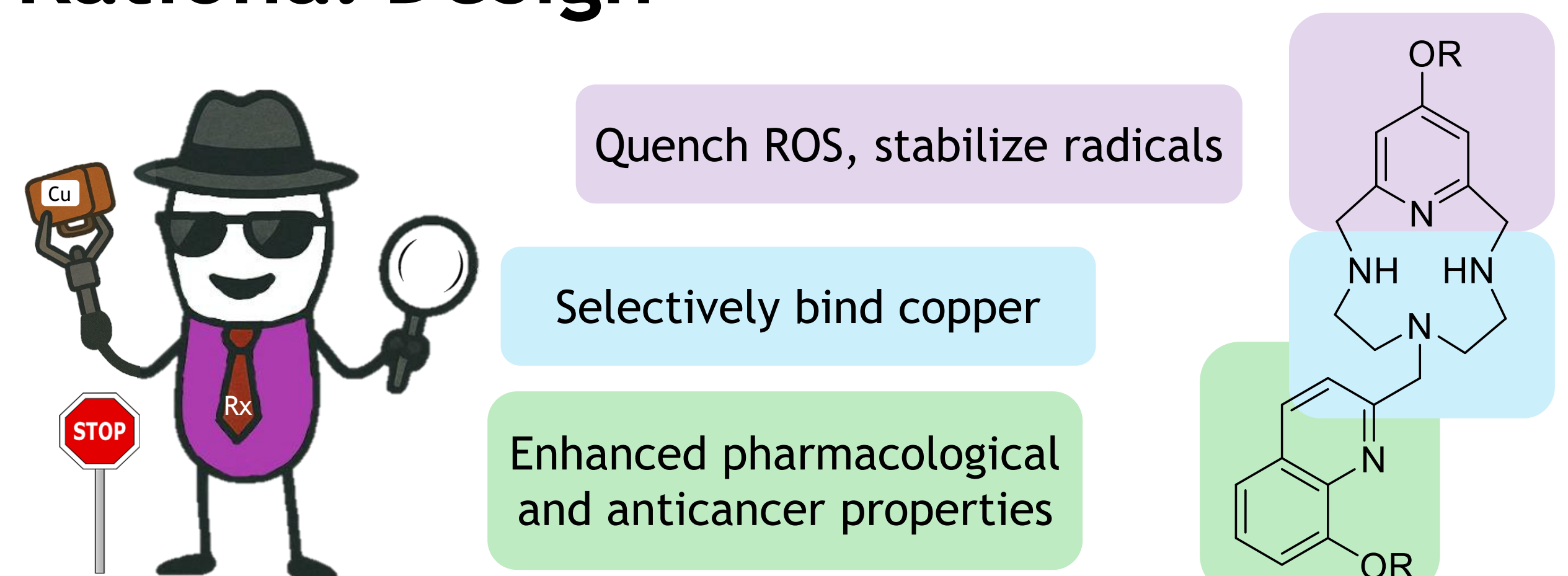
Ligand	P_e Value (10^{-6} cm/s)	$-\log P_e$ Value	% Acc	% Don	% Mem
CN-PyN ₃	0.00	10.00	0	96.7	3.2
COOH-PyN ₃	0.00	10.00	0	98.4	1.7
NMe ₂ -PyN ₃	0.22±0.11	6.69±0.21	0.36	95.79	3.80
CF ₃ -PyN ₃	0.66±0.38	6.87±1.75	0.94	89.46	9.40
Cl-PyN ₃	6.07±2.10	5.24±0.17	9.1	88.7	2.3
I-PyN ₃	7.04±0.66	5.15±0.04	10.9	89.1	0.00
OMe-PyN ₃	31.58±11.48	4.52±0.15	37.0	59.7	3.3
L6	TBD	TBD	TBD	TBD	TBD
L7	TBD	TBD	TBD	TBD	TBD
L8	TBD	TBD	TBD	TBD	TBD
L9	TBD	TBD	TBD	TBD	TBD
L10	TBD	TBD	TBD	TBD	TBD

Future Directions

- Optimization of current synthesis and development of new ligands.
- Continued characterization of novel ^RPyN₃-Q ligands.
- Continued *in vitro* biological assays.



Rational Design



References

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