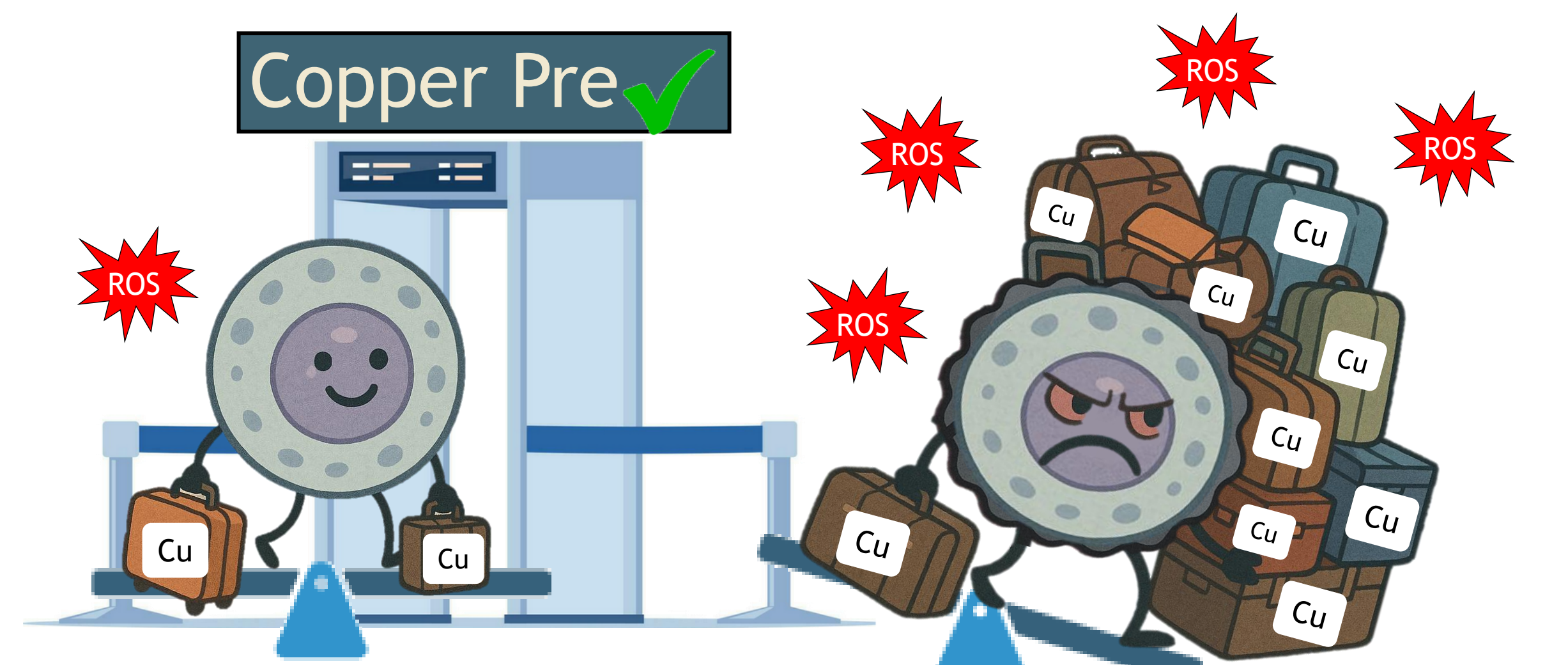


Influence of Quinoline Moieties on the Pharmacological Properties and Anticancer Activity of Tetra-aza Pyridinophanes

Sarah Dunn, Nora Del Bosque, Christina Mantsorov, Giridhar Akkaraju, Ph.D., Kayla N. Green, Ph.D., Department of Chemistry and Biochemistry

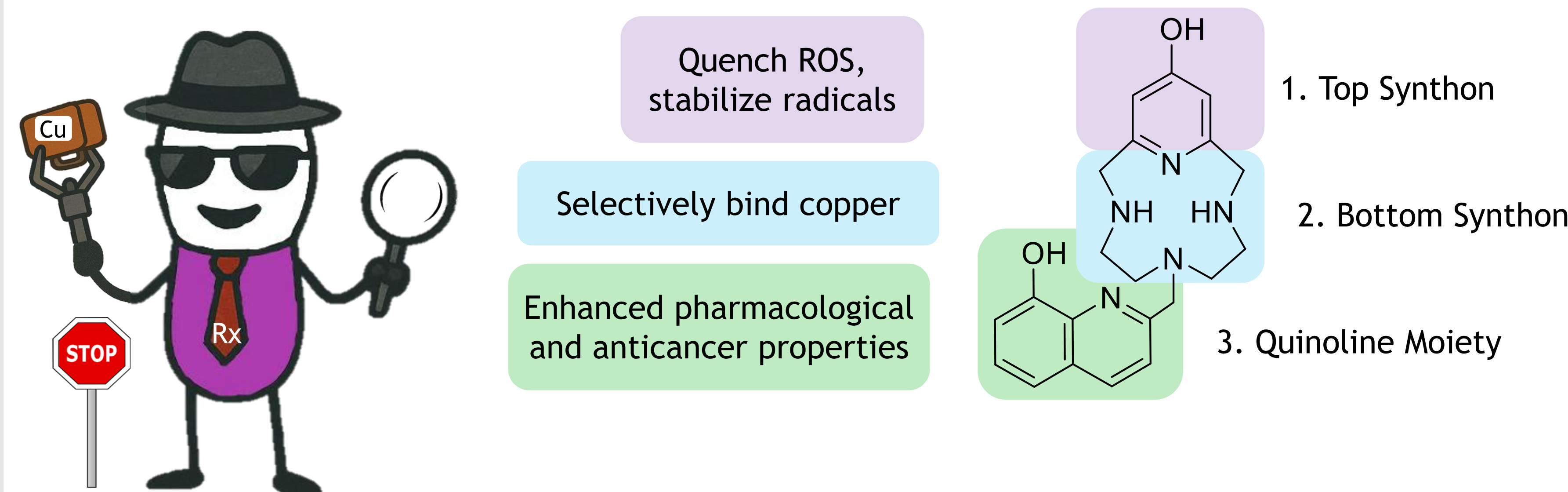
Abstract



- | Healthy Cell | Cancerous Cell |
|-------------------------------|---|
| • Grows and divides normally | • Grows and divides rapidly |
| • Undergoes apoptosis | • Resists apoptosis |
| • Follows immune system rules | • Doesn't follow immune system rules |
| • No DNA mutations | • DNA mutations |
| • Controlled amount of copper | • Unregulated, high amount of copper |
| • Low ROS levels | • High ROS levels |

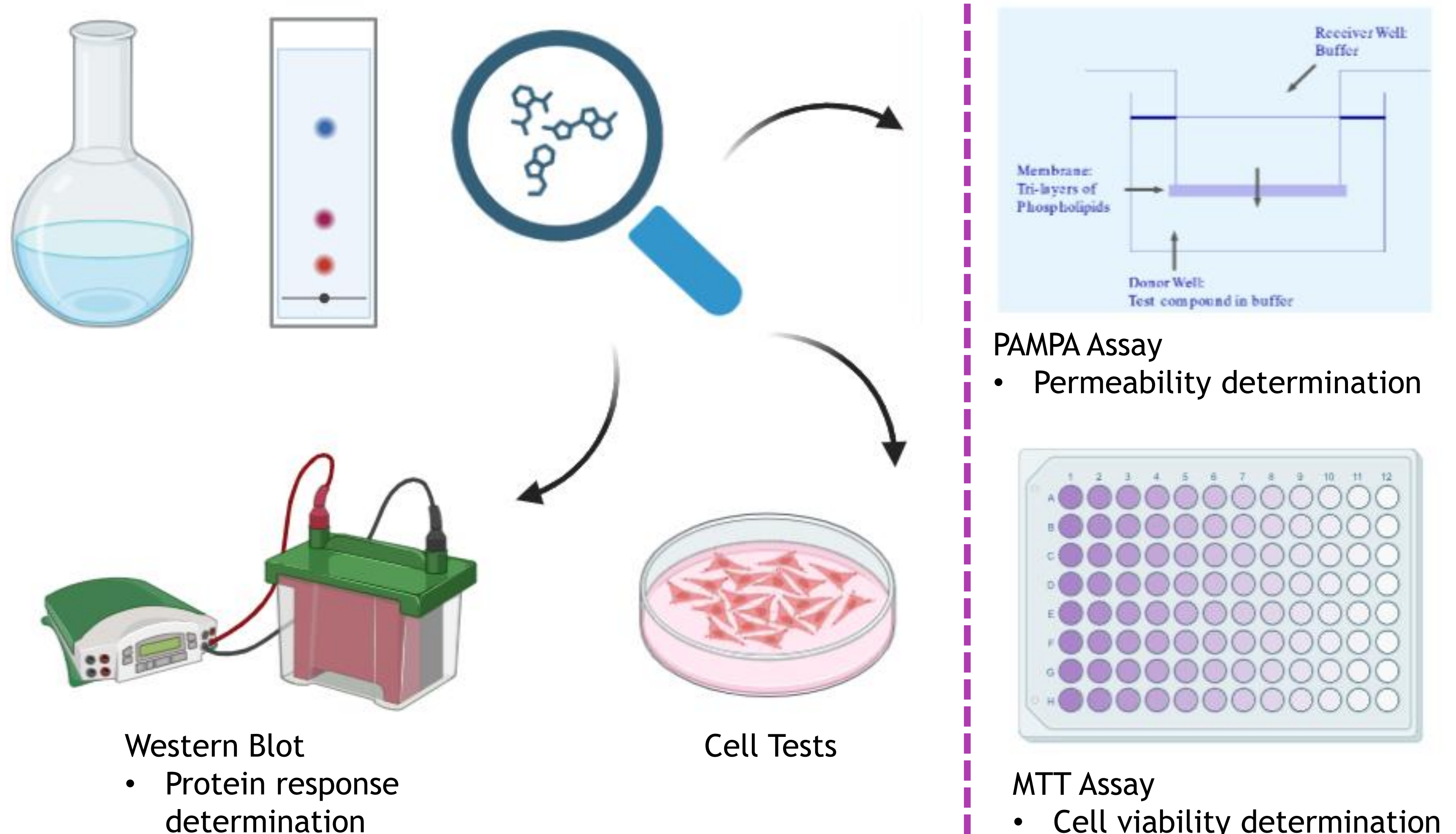
Objective: Synthesizing Multi-Function Ligands for Addressing Elevated Copper and ROS Levels in Diseased Cells

Rational Design

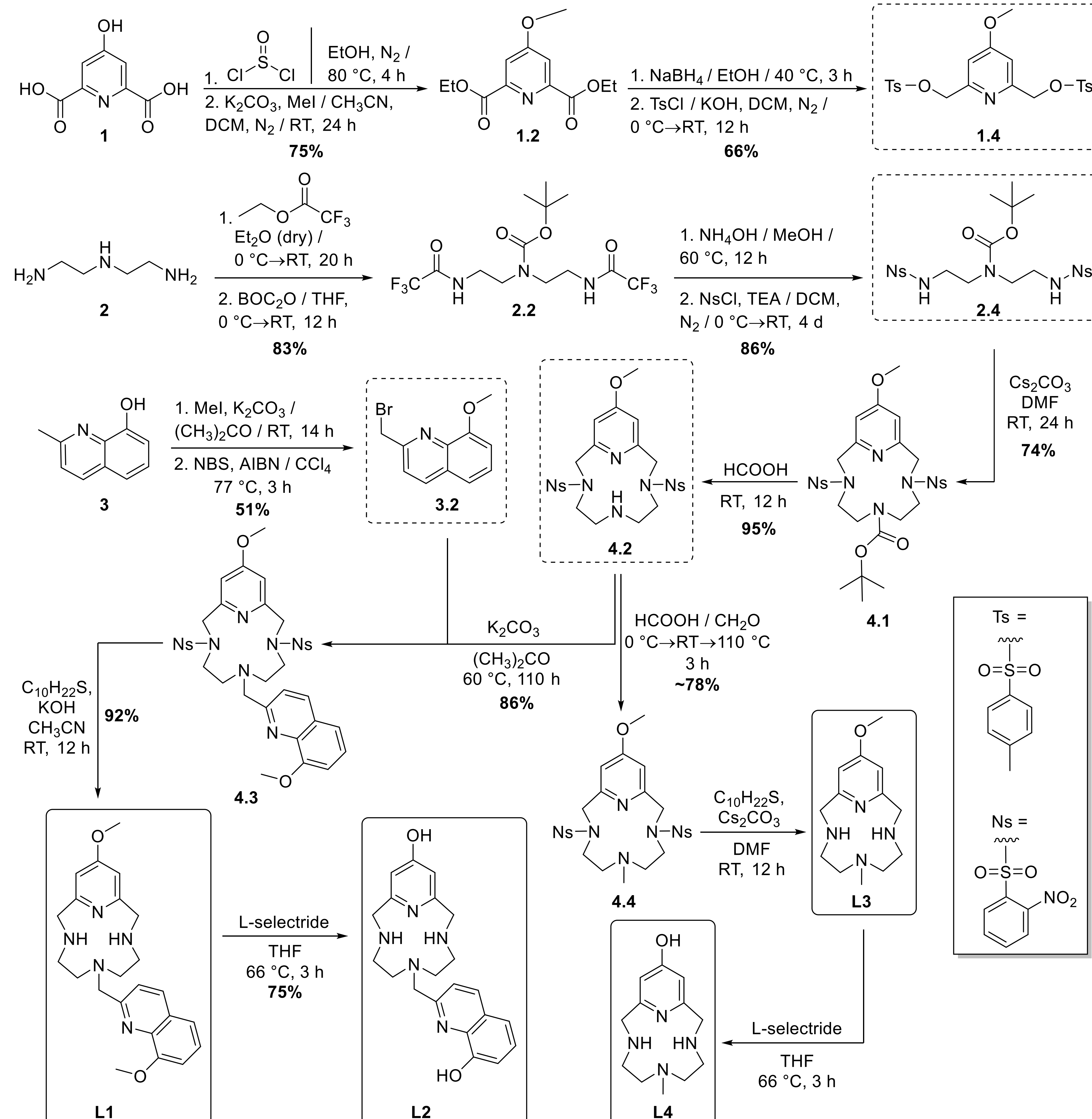


Workflow

Synthesis, Purification, and Characterization of Ligands



Synthetic Scheme for New ^RPyN₃-R' Ligands



ROS, Copper, and Cancer

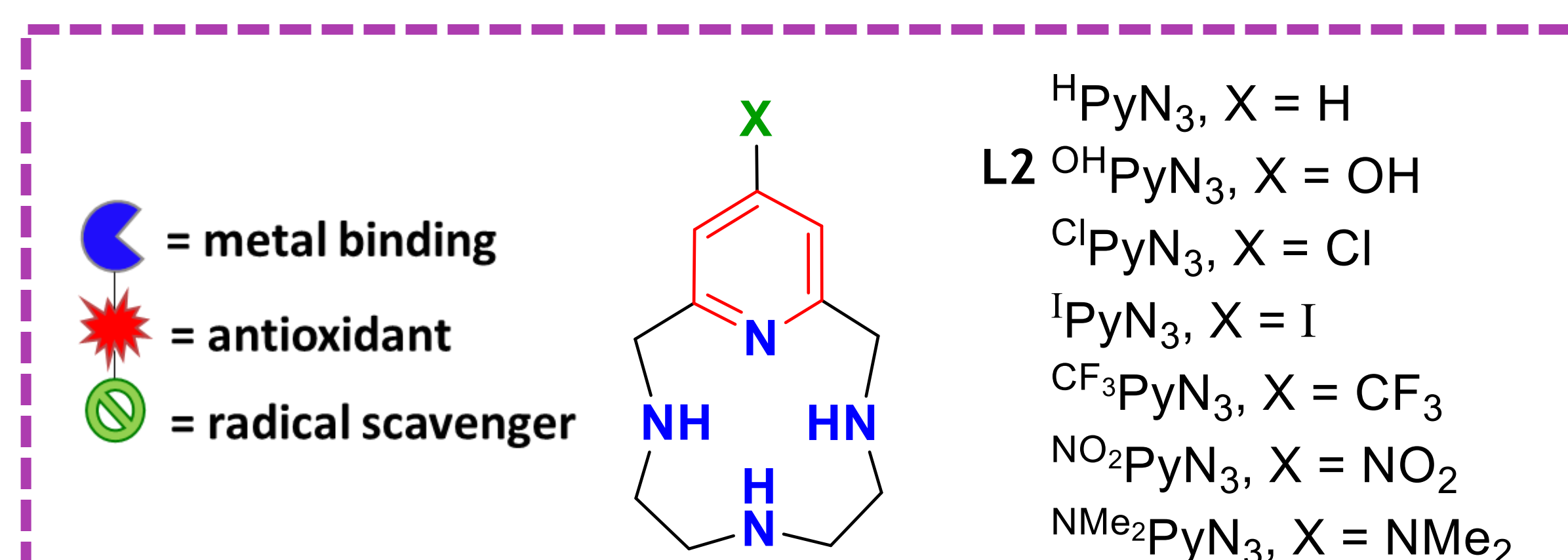
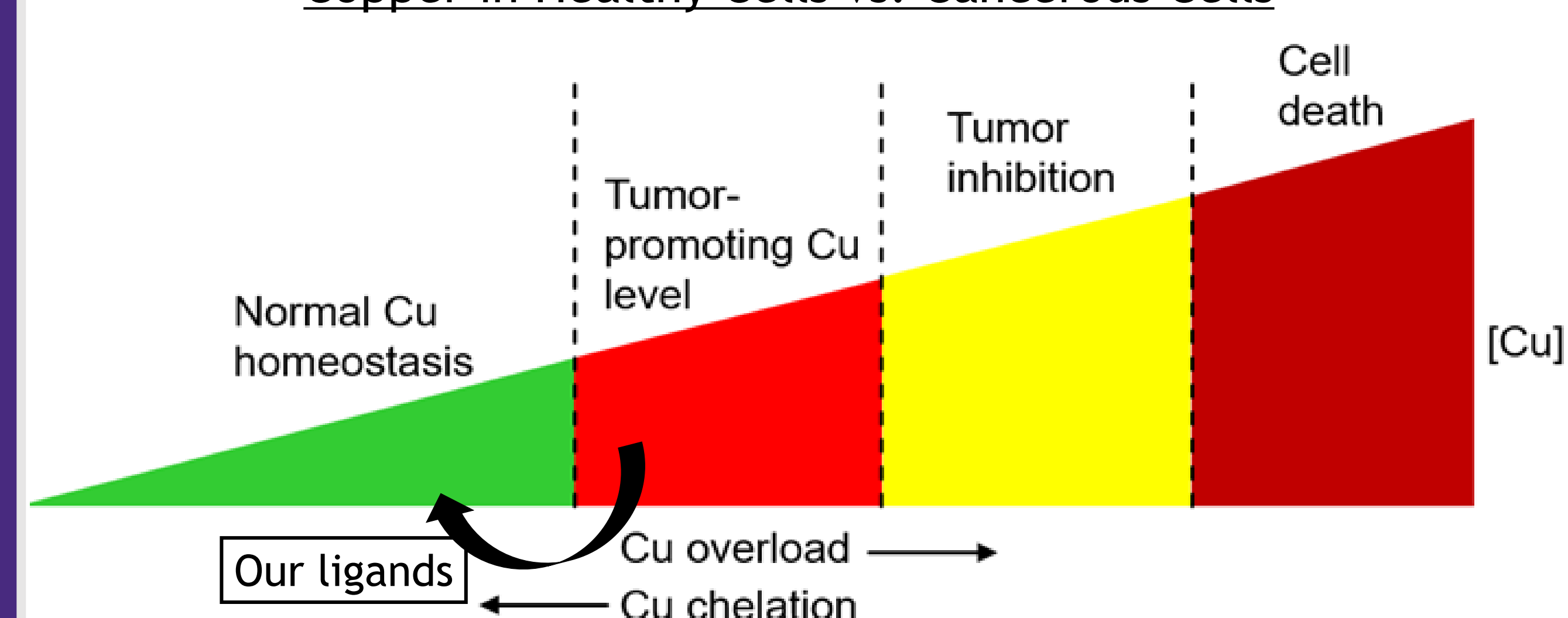
Current Therapeutics:

- Quench ROS
- Stabilize radicals
- Bind copper

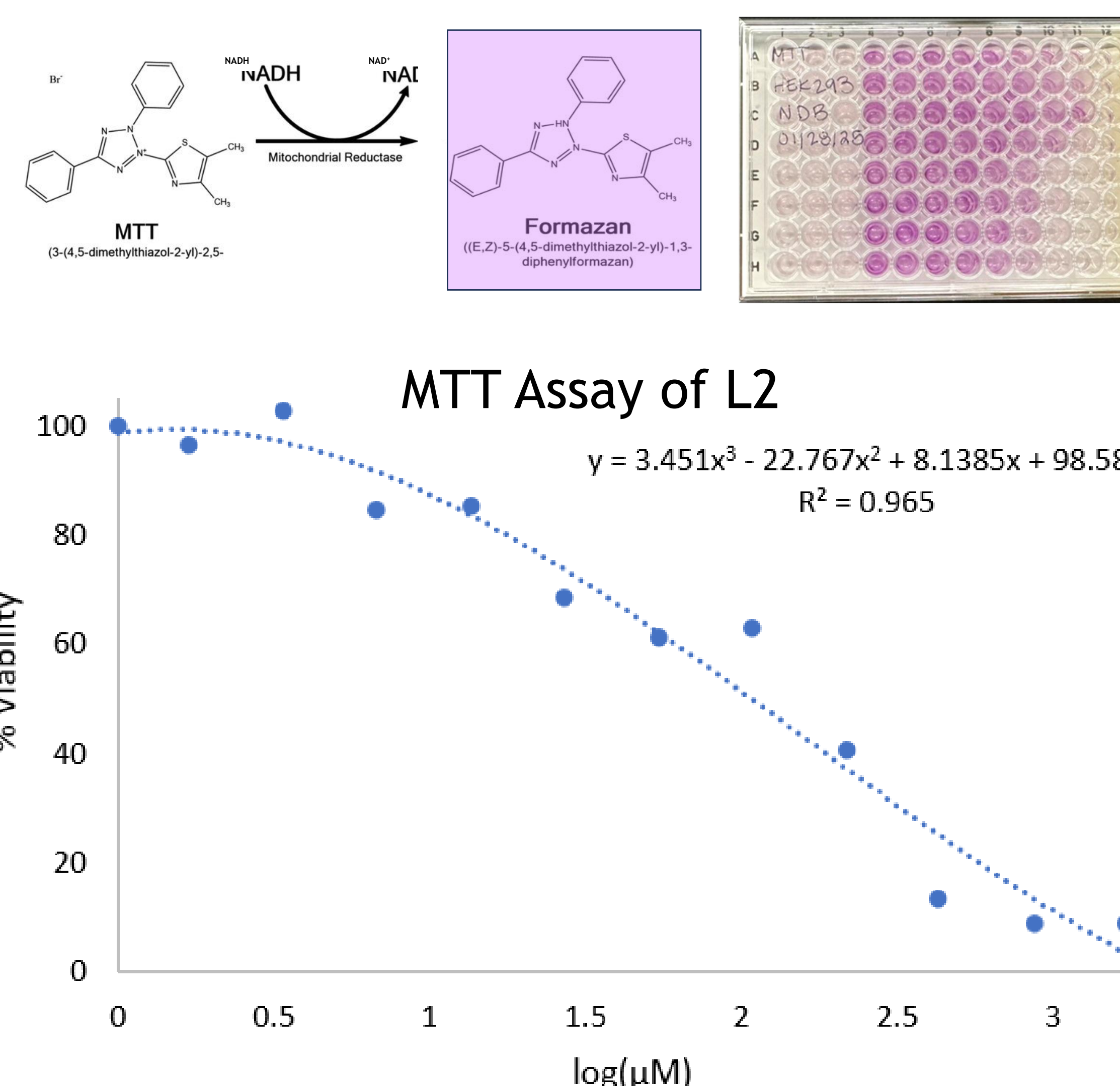
Proposed Therapeutics:

- Combined effects

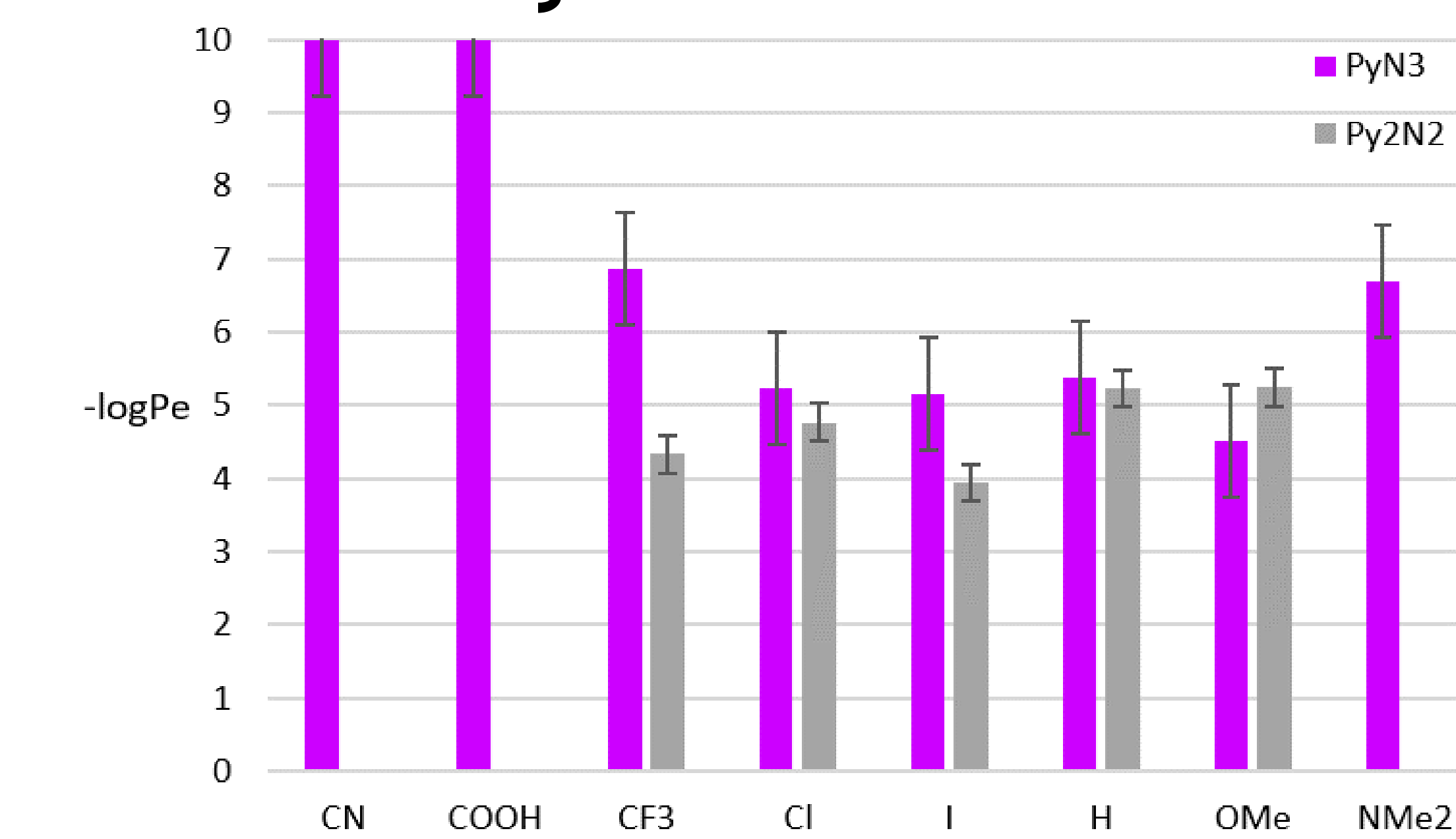
Copper in Healthy Cells vs. Cancerous Cells



MTT Assay



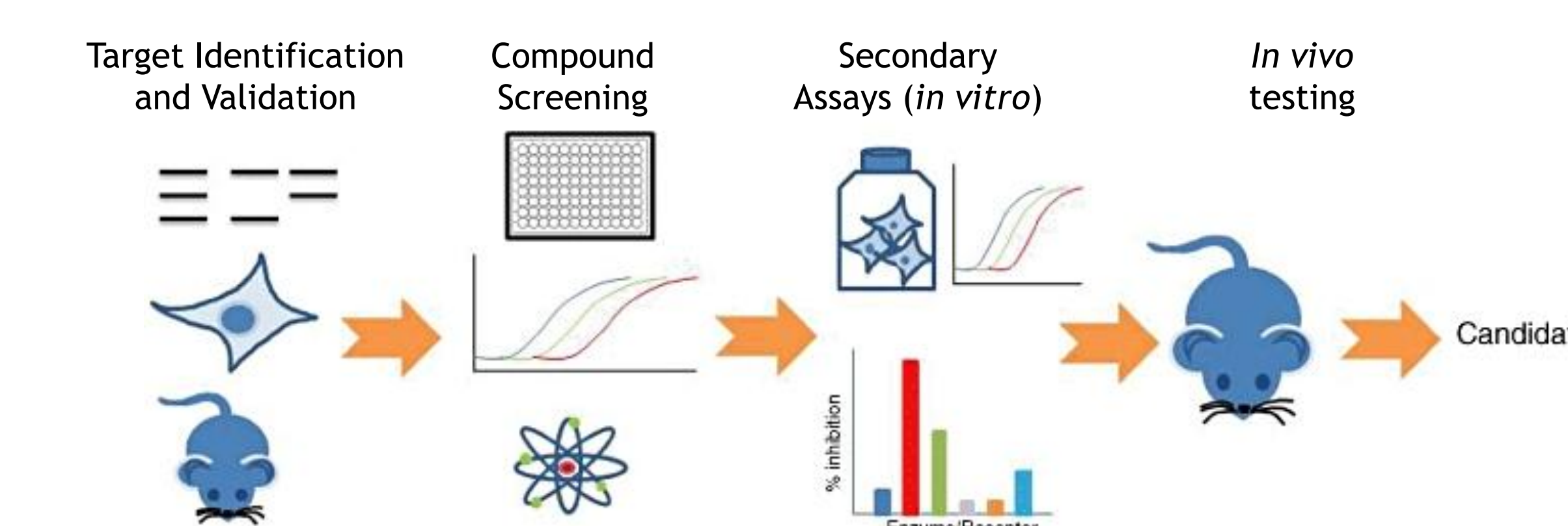
PAMPA Assay



Ligand	P _e Value (10 ⁻⁶ cm/s)	-logP _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
OMe-PyN ₃ -Q	TBD	TBD	TBD	TBD	TBD

Future Directions

- Optimization of current synthesis and development of new ligands.
- Continued characterization of novel PyN₃-Q ligands.
- Continued *in vitro* biological assays on cancer cell lines



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