1-Slide U54 summary received from the NCI

Acquired Resistance to Therapy and Iron (ARTI) Center

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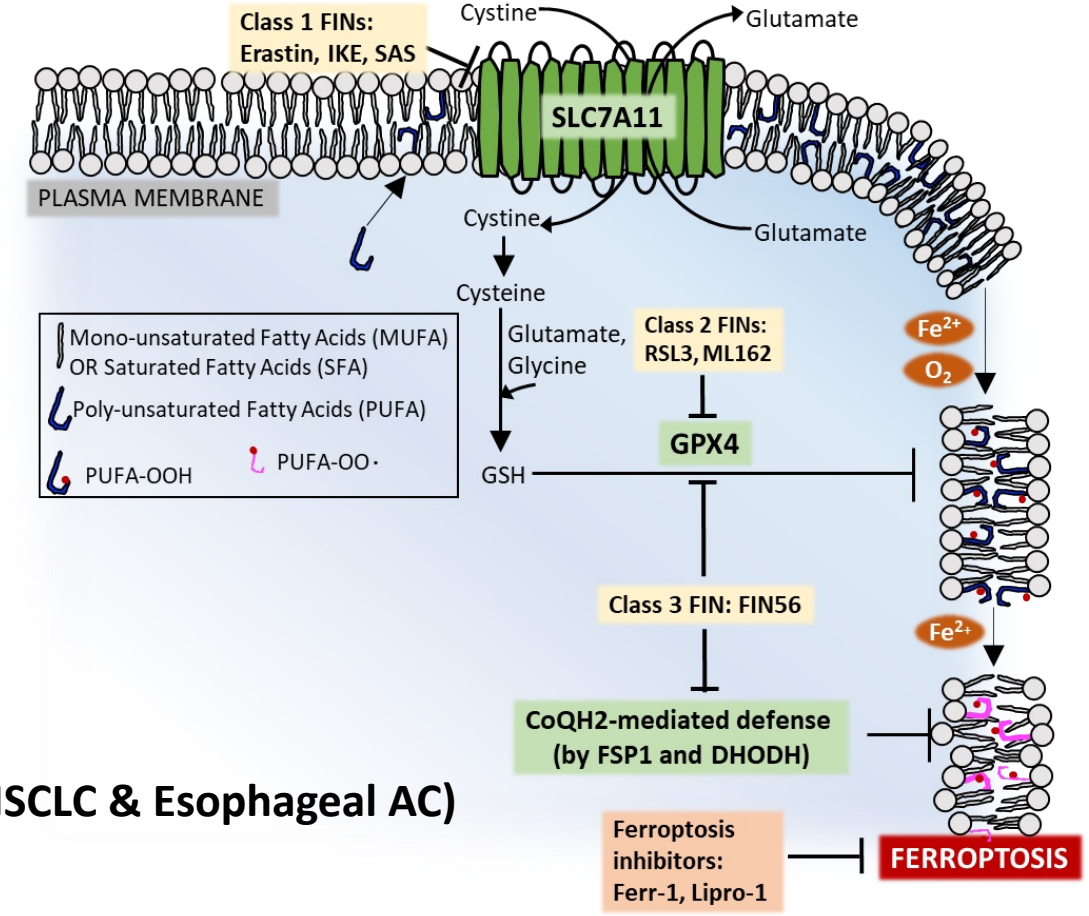
- Acquired RT resistance *via* cell death/iron-ferroptosis
- Immune & TME profiles
- Physical drivers - hypoxia



(NSCLC & Esophageal AC)

- *How do cancer cells adapt to radiation & avoid cell death?*
- *Molecular controls for iron-oxygen-redox in suppression of ferroptosis*
- *Tests ways to reverse-prevent acquired radioresistance with FIN drugs*

- **P1 Mechanisms of Ferroptosis in Acquired Radioresistance**
  - ✓ *NSCLC - intrinsic p53-Nrf2-KEAP mutations pathways*
  - ✓ *Paired models of acquired resistance (pre-post radiation)*
  - ✓ *PDX, organoids, comparative CRISPR screens/KOs*

- **P2 Hypoxia & Ferroptosis in Acquired Radioresistance**
  - ✓ *NSCLC - functional PET tracers (hypoxia, redox, and metabolism)*
  - ✓ *Testing of hyperbaric oxygen, HIF-ATF4 small molecular inhibitors*

- **P3 Genomic & TME in Ferroptosis Acquired Radioresistance**
  - ✓ *Esophageal AC - CyTOF heterogeneity, CNV single cell analysis*
  - ✓ *Longitudinal patient biopsies - evolution of acquired res. with RT*
  - ✓ *Examine role of neutrophil-myeloid infiltrates*

- **Molecular Imaging Core**
  - ✓ *Leverages MDACC P30 to integrate imaging with –omics across projects*