Utilization of 5-ALA in Functional Pituitary Tumors: Pre-Clinical Work in Pituitary Cell Lines

Keiko Kang, BS\textsuperscript{1,2}, Anudeep Yekula, MBBS\textsuperscript{1}, Leonora Balaj, PhD\textsuperscript{1}, Bob Carter, MD, PhD\textsuperscript{1}, Pamela Jones, MD, MS, MPH\textsuperscript{1}

\textsuperscript{1}Department of Neurosurgery, Massachusetts General Hospital and Harvard Medical School and Harvard Medical School, Boston, MA.

\textsuperscript{2}School of Medicine, University of California, San Diego, La Jolla, CA.
Disclosures

• The authors have no other financial or organizational relationships with commercial interests or other entities
Introduction

• 5-aminolevulinic acid (5-ALA) is used for fluorescent guided surgery (FGS) in glioblastoma; however, its role in the resection of other cranial tumors is unclear

• Pituitary adenomas (PA) can be difficult to differentiate from normal gland, leading to suboptimal surgical and neuroendocrine outcomes

• Here, we investigate uptake of 5-ALA in functional pituitary cell lines
Methods

- **Cell Lines:**
  - PDFS (non-functional, negative control)
  - Gli36 (glioma, positive control)
  - GH3 (growth hormone/prolactin)
  - AtT20 (ACTH)

- **5-ALA Dosing:** Cells were incubated in the following conditions:
  - 0 mM (mock), 0.2 mM, 0.4 mM, 0.8 mM, 8.0 mM, 16.0 mM for 24 hours

- **Image Flow Cytometry:** Excitation at 405nm, collection at 660-670nm; gated to isolate single cell, fluorescent events
Results

- The graph depicts fluorescence in positive (Gli36) and negative (PDFS) control cell lines dosed with 5-ALA relative to mock.
- Non-functional pituitary cell lines (PDFS) did not fluoresce after 5-ALA administration.
- We re-demonstrate fluorescence of glioma cells after administration of 5-ALA.

![Graph showing fold change of fluorescent intensity against 5-ALA dose](image)
Results

- Functional pituitary cell lines demonstrate fluorescence after 5-ALA administration.
Results

- The functional pituitary cell lines demonstrated greatest fluorescent intensity after dosing with 0.4mM 5-ALA
- GH3 (p = 0.008) and AtT20 (p = 0.031) cells had significantly higher fluorescent intensity than the PDFS cells
Discussion

• We demonstrate uptake of 5-ALA in functional pituitary adenoma cell lines, which was significantly higher as compared to non-functional pituitary adenoma cell lines

• Our data demonstrates the potential of 5-ALA for FGS of functional PAs

• This work may pave the way for use of 5ALA in patients with MRI-negative, functional PAs
Summary

1. We demonstrate uptake of 5-ALA and fluorescence in the functional GH3 and AtT20 pituitary cell lines

2. Maximal fluorescent intensity in the GH3 and AtT20 cell lines was observed with a 5-ALA dose of 0.4mM

3. A significantly higher fluorescent intensity was observed in GH3 and AtT20 cells compared to PDFS cells at the optimal 5-ALA dose