Assessing the Hypoxic Response in Intestinal Organoids

Romina Falahaty¹, Dr. Neeraj Kumari ¹ and Dr. Cullen M. Taniguchi MD, PhD.²

¹²Department of Radiation Oncology, UT MD Anderson Cancer Center, Houston, TX, USA.

**Background**

- The close proximity of small intestine to the pancreas subjects the sensitive tissue to radiotoxicity from exposure to high-dose radiation,
- There are no approved therapies to prevent, mitigate, or treat GI-ARS (Gastrointestinal-Acute-Radiation Syndrome).
- Stabilization of Hypoxia Inducible Factor 2 (HIF2) mitigates and protects against radiation induced GI toxicity.
- Here performed a preliminary study to elucidate the effect of hypoxia or FG4592 treatment on HIF2 expression.

**Significance**

- A selective GI radioprotector may allow cancer patients to receive a higher, and potentially curative, dose of radiation for tumors located near the intestines (e.g. pancreatic cancer).

**Methods & Results**

Patient-derived enteroids (PDEs) were obtained with from the Baylor Digestive Disease Core Lab of culture of enteroids, 3D structure, and treatment experimentation. Diagram B demonstrates the procedure of a western blot.

**Maximal HIF-2 Expression Under Normoxia at Protein Level**

We observed no morphological changes in enteroids grown in either normal (20%) or low oxygen (5%) levels, however there was greater HIF2 stabilization at baseline at 5% compared to normoxia. The addition of FG-4592 led to enhanced HIF2 expression detectable starting at 48 hours of incubation, with maximal expression at 72 hours. The protein expression of HIF2 was normalized by the protein expression of Actin (loading control).

**Key Takeaways**

- Our results demonstrate that the radioprotective drug FG-4592 is raising HIF2 in human enteroids.
- Further testing will need to be done to verify the radioprotective effects of FG-4592 in these PDEs.
- This will potentially open avenues for ablative radiation in unresectable pancreatic cancer.

---

@TaniguchiMD

Romina.falahaty@gmail.com