Role of HIF2 signaling in small intestine regeneration after radiation injury

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### Gastrointestinal -ARS

Symptoms appear within few hours to days

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Time of Onset</th>
<th>Manifestation</th>
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<tbody>
<tr>
<td>5 - 12 Gy</td>
<td>9 - 10 days</td>
<td>Gastrointestinal (GI) syndrome</td>
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</tbody>
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*Chemobyl* (HBO, 2019)

**Radiation Exposure**

**The Intestinal Crypt**
There are no approved treatments for GI-ARS

**FG-4592** - an oral HIF activator

- FDA approved for Anemia treatment and could be rapidly repurposed

- Hypoxia Inducible Factors (HIFs)
  - tissue regeneration
  - stem cell growth
  - epithelial integrity
FG-4592 induces intestinal stem cells markers

Intestinal Organoid (Mini-Guts)

Enteroids grown in L-WRN conditioned media

5 Gy or 4592 treatment

RNA isolation & qPCR

BMI
HOPX
DCLK1
MEX3A
TERT

0
5
10
15
20
Relative Expression

+4 stem cell markers

Veh
FG-4592
Veh + 5 Gy
FG-4592 + 5 Gy

✱
✱✱
✱✱✱
✱✱✱✱

GI radioprotection

FG-4592

† intestinal stem cell/crypt survival
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Thank you for your attention…….