Quantitative Analysis of the Efficacy of 5-Iodo-2’-Deoxyuridine as a Radiosensitizer When Incorporated into Human Dermal Fibroblasts

Olivia Suggs1; Endre Takacs, Ph.D2; Delphine Dean, Ph.D.3
1Department of Chemistry and Biochemistry, Spelman College
2Department of Physics and Astronomy, Clemson University
3Department of Bioengineering, Clemson University

Background
- The microenvironment of a solid tumor (TME) contains a complex extracellular matrix and various stromal cells, including fibroblasts.
- The vasculature of tumors is often leaky and accumulates molecules in the blood stream to a greater extent than in normal tissue.
- Preliminary data suggests that this imbalance can hinder the effective administration of drug therapeutics to the tumor.
- Ionizing radiation (IR)—located in the upper region of the electromagnetic spectrum—carries enough energy to remove electrons from atoms and molecules, with the potential to penetrate cells in the human body.
- One of the most widely recognized forms of IR exposure is radiation therapy—considered to be one of the cornerstones of cancer therapy—which can influence the process of vasculature remodeling.
- To achieve selectivity at the tumor, therapeutic molecules must be able to navigate the biological barriers found in the TME.
- Radiation sensitization with IR treatment, we expect to see a cytotoxic effect.
- Double-stranded DNA breaks are considered to be one of the trademarks of IR-mediated radiosensitization.

Preparation of samples
50,000 cells seeded into each polyethylene cup
4 conditions (3 cups/treatment):
- Control/Control
- Control/Radiation
- IUdR/Radiation
- IUdR/Control

Irradiation Procedure
Constant Conditions:
- Energy: 5.35E-10 J
- Dose Rate: 0.174 mGy/min
- Voltage: 50 keV

Treated samples received 1 mGy of radiation over 5 m46s

Results

<table>
<thead>
<tr>
<th></th>
<th>Hour 0</th>
<th>Hour 72</th>
</tr>
</thead>
<tbody>
<tr>
<td>+/-</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
<tr>
<td>-/+</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td>+/+</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Discussion
The results of this experiment demonstrate that IUdR does function as an effective radiosensitizer when coupled with low-energy, low-dose x-ray radiation. The result of the MTS assay show similar trends in metabolic activity between the Control/Control and IUdR/Radiation samples, both decreasing overtime. However, cell staining images suggest a cytotoxic effect in the samples treated with IUdR/Radiation. This evidence indicates sensitization did take place in cooperation with low-dose radiation. Future studies should consider immunofluorescent staining using γ-H2AX and vimentin to confirm the presence of double-strand DNA breaks.

This research suggests that cells treated with IUdR in conjunction with low-dose radiation will experience decreased cell survival.

References

Acknowledgements
This work was supported by the National Science Foundation Grant no. 1757658 with funding from DBI and the EBSCoR Program. I gratefully acknowledge the guidance of Dr. Takacs and Dr. Dean.