A p53-mediated metabolic response to low doses of radiation

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Radioadaptive response is p53-dependent

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<th>S</th>
<th>0.1</th>
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<tbody>
<tr>
<td>p53WT</td>
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<td>p53R175H</td>
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γH2AX  DAPI

radioadaptive response is p53-dependent
Distinct dose response of HIF-1α and p53
Cellular defense is supported by anabolic metabolism

Summary of radioadaptive response

1. Radioadaptive response is mediated by ROS, which is extremely sensitive to oxygen pressure
2. Low-dose irradiation induces a metabolic reprogramming from oxidative phosphorylation to glycolysis
3. The metabolic response to low-dose IR is mediated by p53 downregulation concurrent with HIF-1α induction
4. A threshold IR dose ~0.2 Gy, that determines whether a protective or damaging effect is induced.
Fractionated LDR exposure is more potent in induction of SIPS in HMFs.

LDR-induced p53 downregulation becomes sustained during chronic LDR exposure resulting in persistent upregulation of anabolic metabolism, which drives senescence.
1. When acute, LDR-induced adaptive response is protective

2. When chronic, LDR-induced adaptive response may become detrimental

3. Chronic LDR exposure induces prolonged p53 downregulation concomitant anabolic reprogramming resulting in disruption of homeostasis

4. Methods of averting mild stress-induced reduction in p53 may be attractive strategies for the maintenance of homeostasis and disease intervention