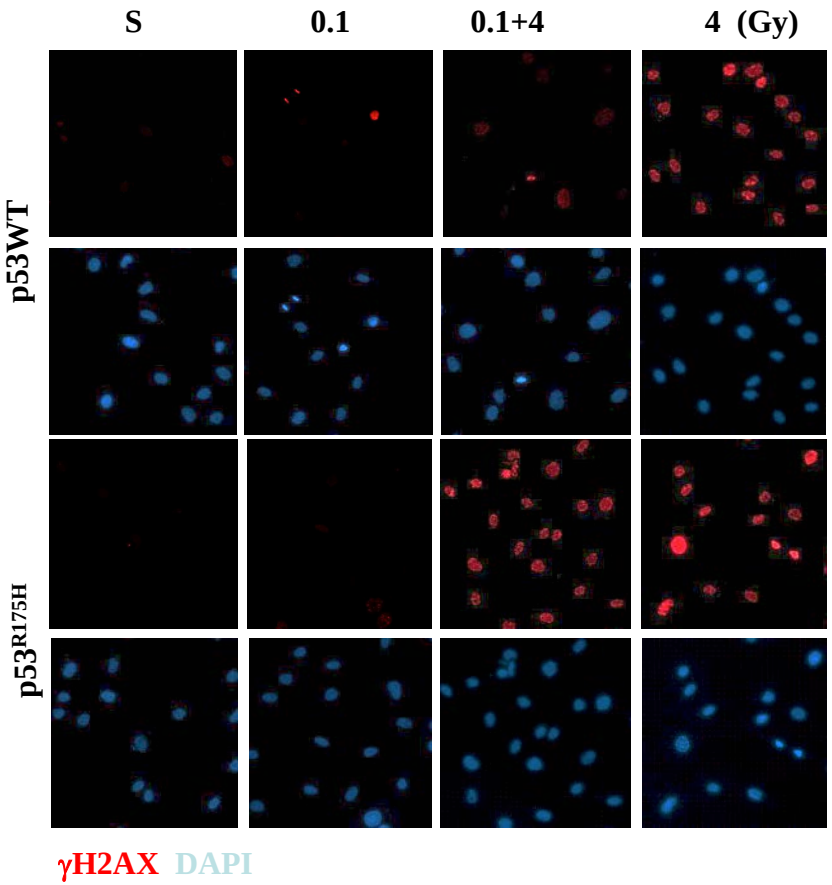
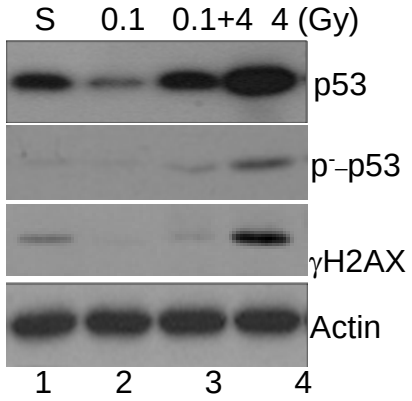
A p53-mediated metabolic response to low doses of radiation

Zhi-Min Yuan

JOHN B. LITTLE
CENTER FOR RADIATION SCIENCES
HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

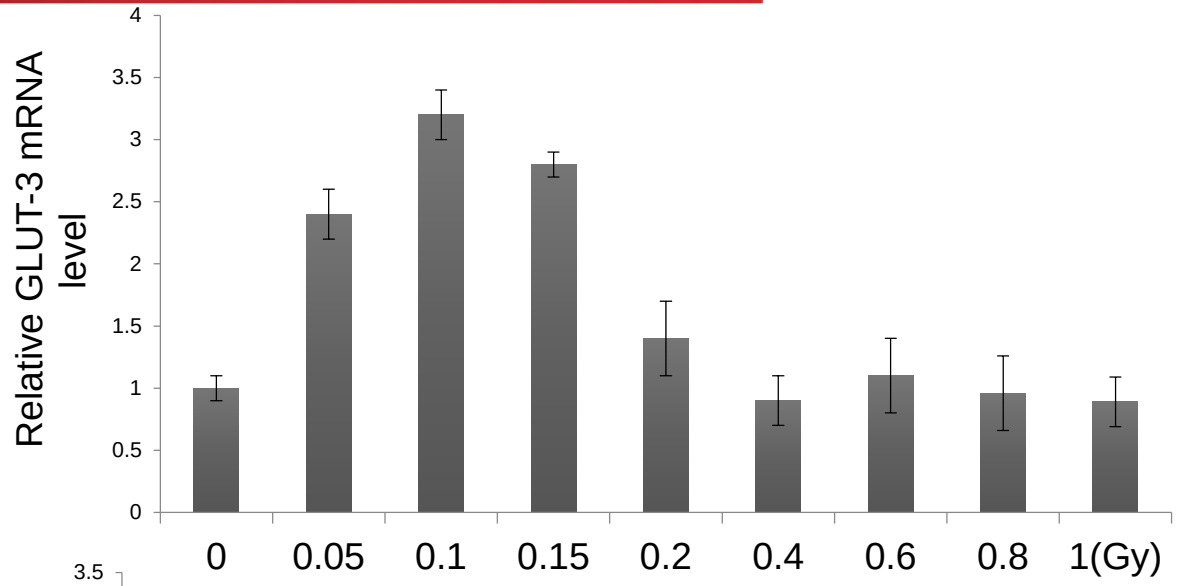
Radioadaptive response is p53-dependent

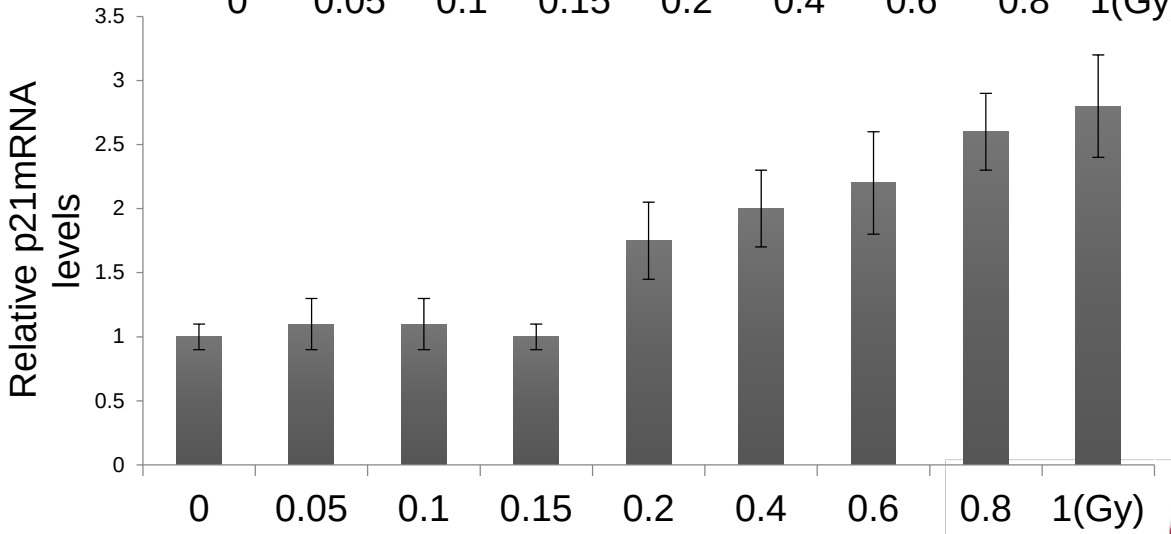




JOHN B. LITTLE
CENTER FOR RADIATION SCIENCES
HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

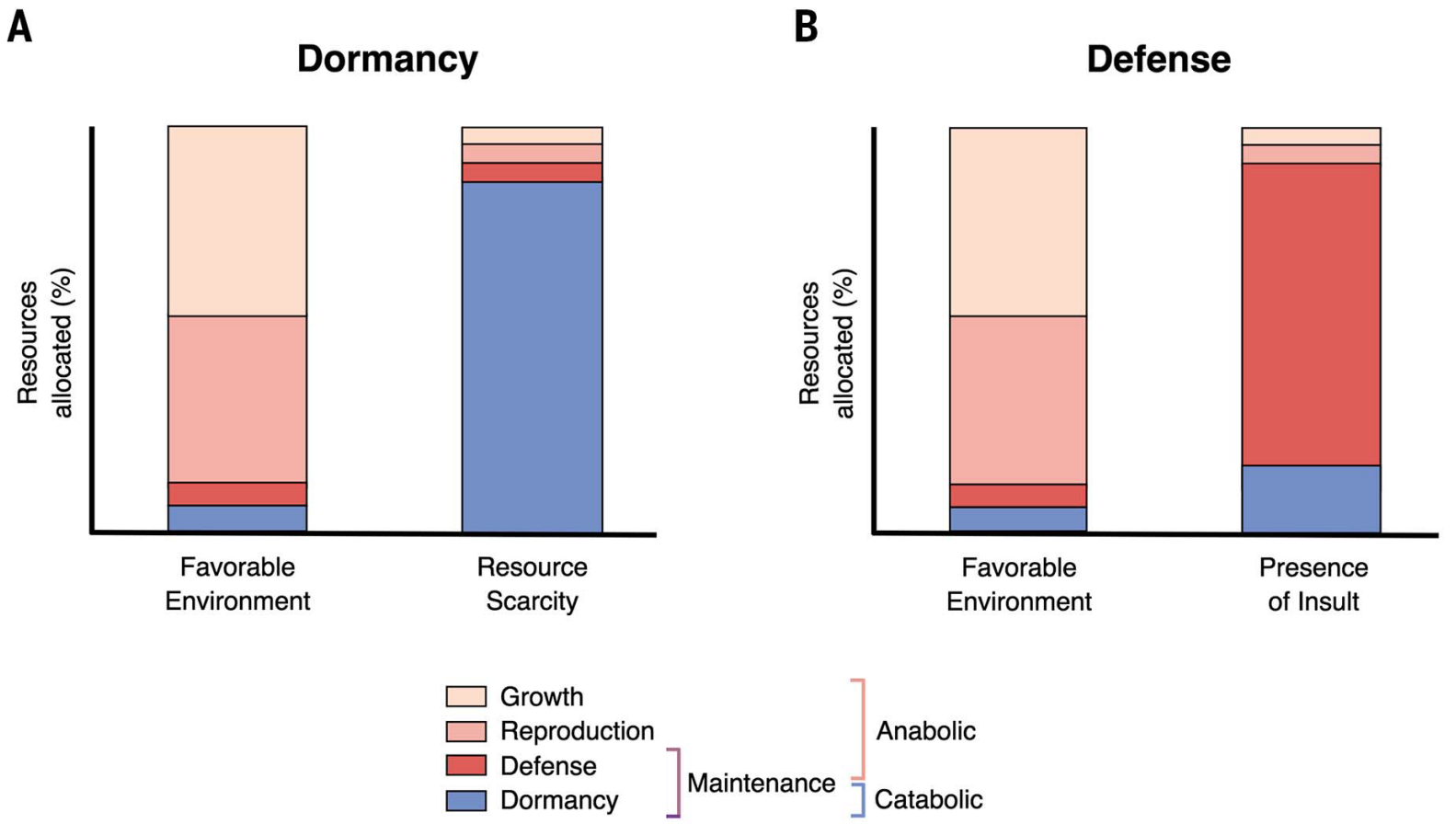
Distinct dose response of HIF-1α and p53





JOHN B. LITTLE
CENTER FOR RADIATION SCIENCES
HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

Cellular defense is supported by anabolic metabolism



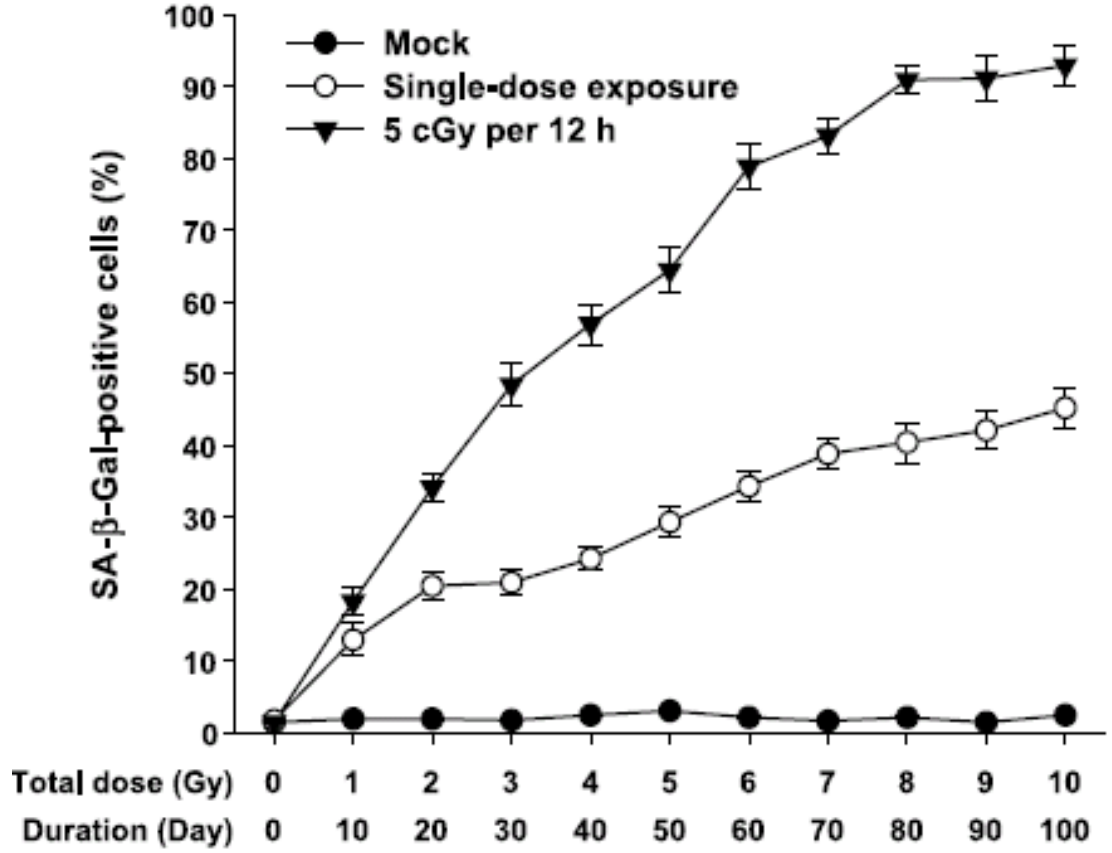
Wang et al., Science 363, 140 (2019) 11 January 2019

JOHN B. LITTLE CENTER FOR RADIATION SCIENCES
HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

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-1a induction
4. A threshold IR dose ~0.2Gy, 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

Take home message

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

JOHN B. LITTLE
CENTER FOR RADIATION SCIENCES
HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH