

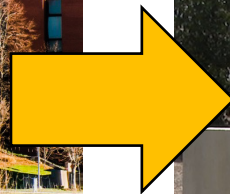
Studying the relationship between DNA damage in cancer cells and immune responses

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PAVES 2021

My Personal Journey



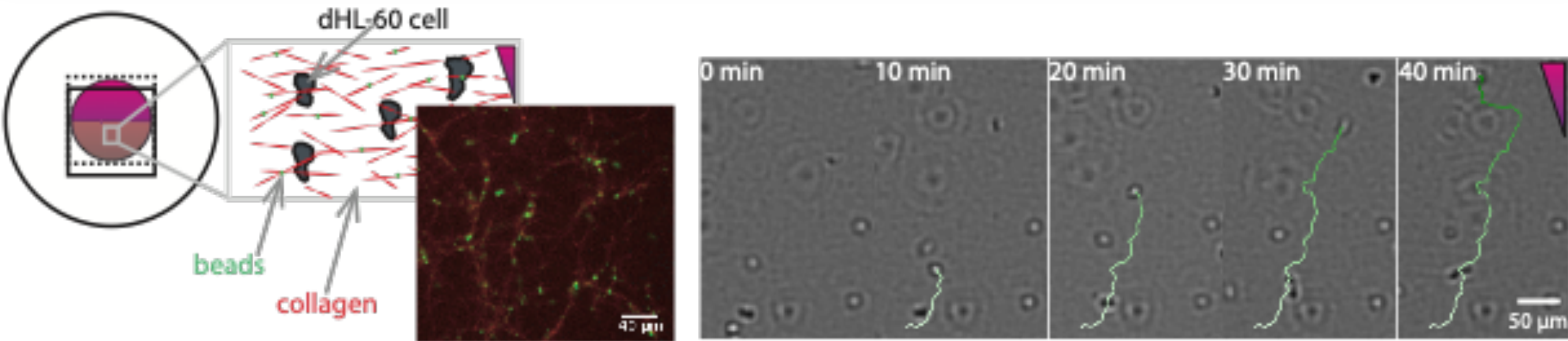
**University of Maryland,
Baltimore County**

B.S. Mechanical Engineering

**University of California,
San Diego**

Ph.D. Bioengineering

Mechanics of Neutrophil Migration in 3-D environments



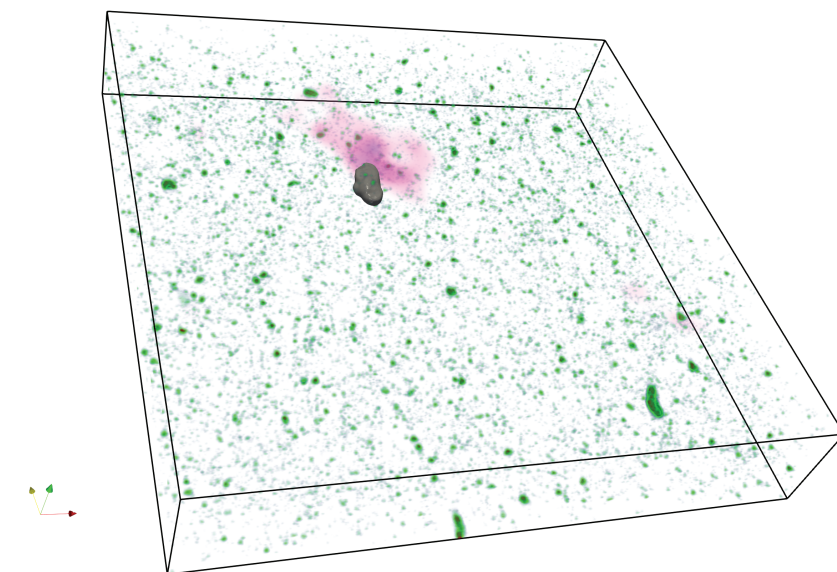
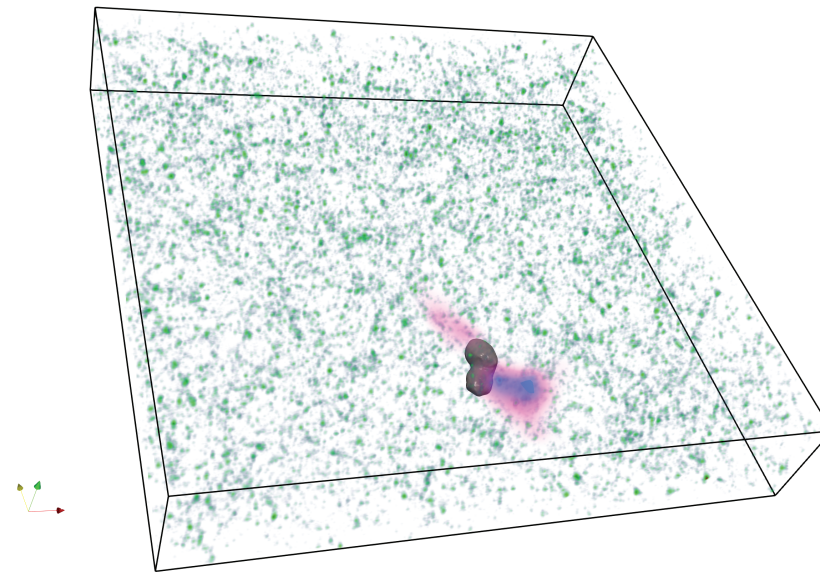
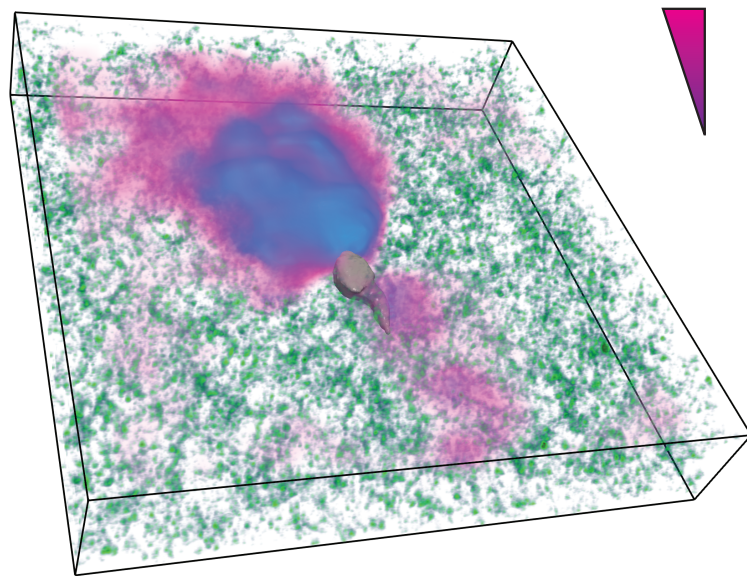
- *Built custom migration chamber for directed 3-D neutrophil migration in collagen gels*
- *Developed automated label and label-free cell tracking methods for tracking > 20,000 cells*

3-D neutrophil migration is dependent on ability to deform local environment and turn

0.25 mg/mL, untreated

0.25 mg/mL, blebbistatin

0.25 mg/mL, ck666



Mag. Incr.
Disp. (μm) 0 1.25 2.5

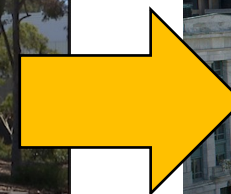
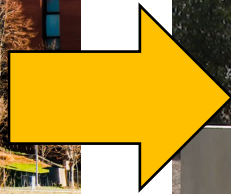
Findings

Low-Density 3-D Environments: Neutrophils rely on ability to deform surroundings

High-Density 3-D Environments: Neutrophils rely on ability to turn

Proteins involved in cell contractility, and turning crucial for neutrophil migration in 3-D environments

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Fellow,
Systems Biology

p53 dynamics can alter cell fates

p53 recognizes cellular stress

- DNA damage
- unusual growth signals
- oncogene activation
- hypoxia
- etc.

Different p53 dynamics linked to fate

- Pulsatile -> DNA damage repair
- Sustained -> Senescence

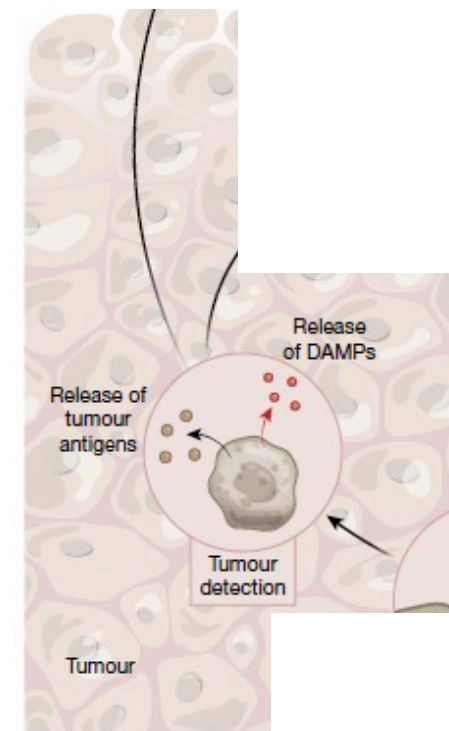
Cellular stress signals in tumors can illicit immune responses

Immune system can respond to tumor cells after cellular stress

Innate and adaptive responses

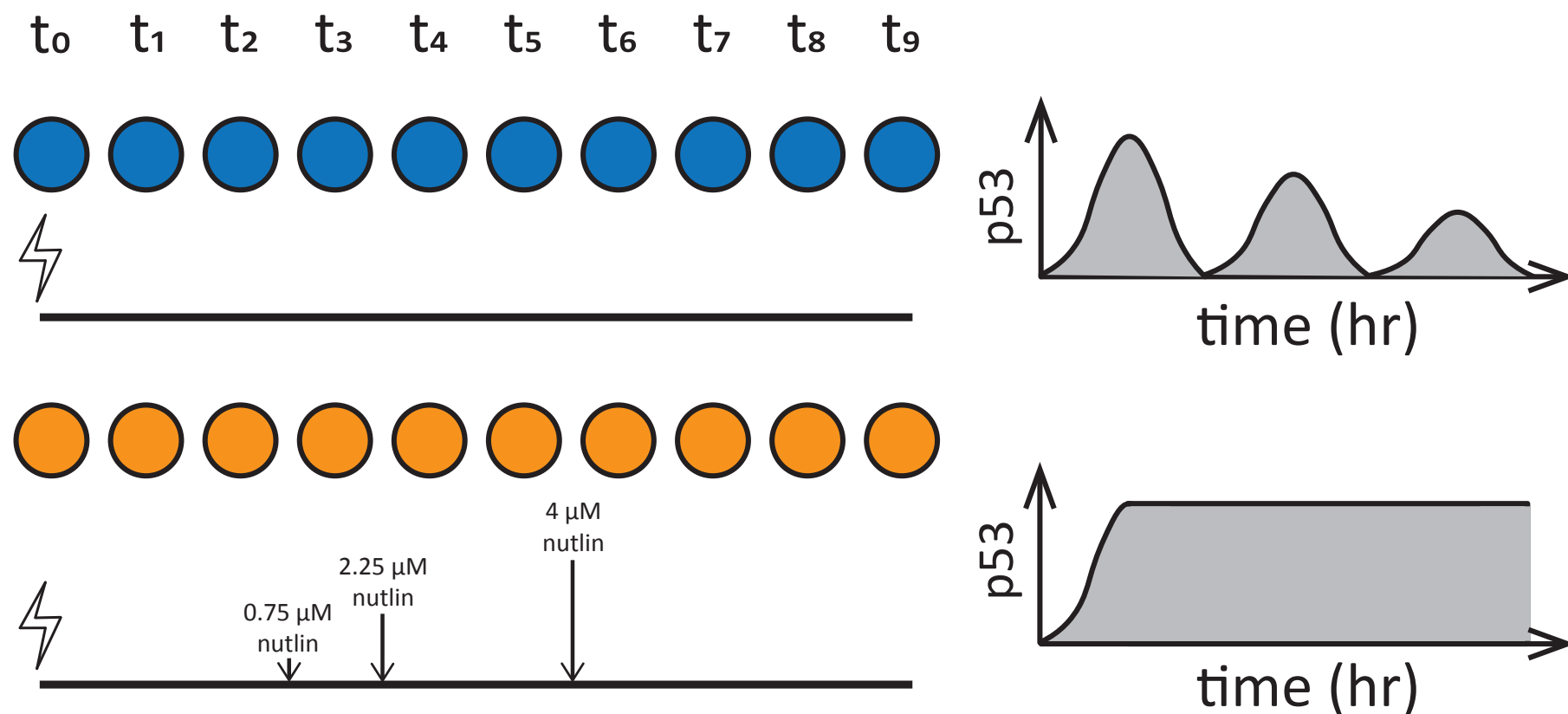
- Priming of adaptive immune cells
- Amplification of innate immune response
- Innate and adaptive immune cell mediated killing

Major cellular stress sensor is p53



Can p53 dynamics in cancer cells alter immune responses?

Time course analysis of gene expression in MCF-7 cells after DNA damage

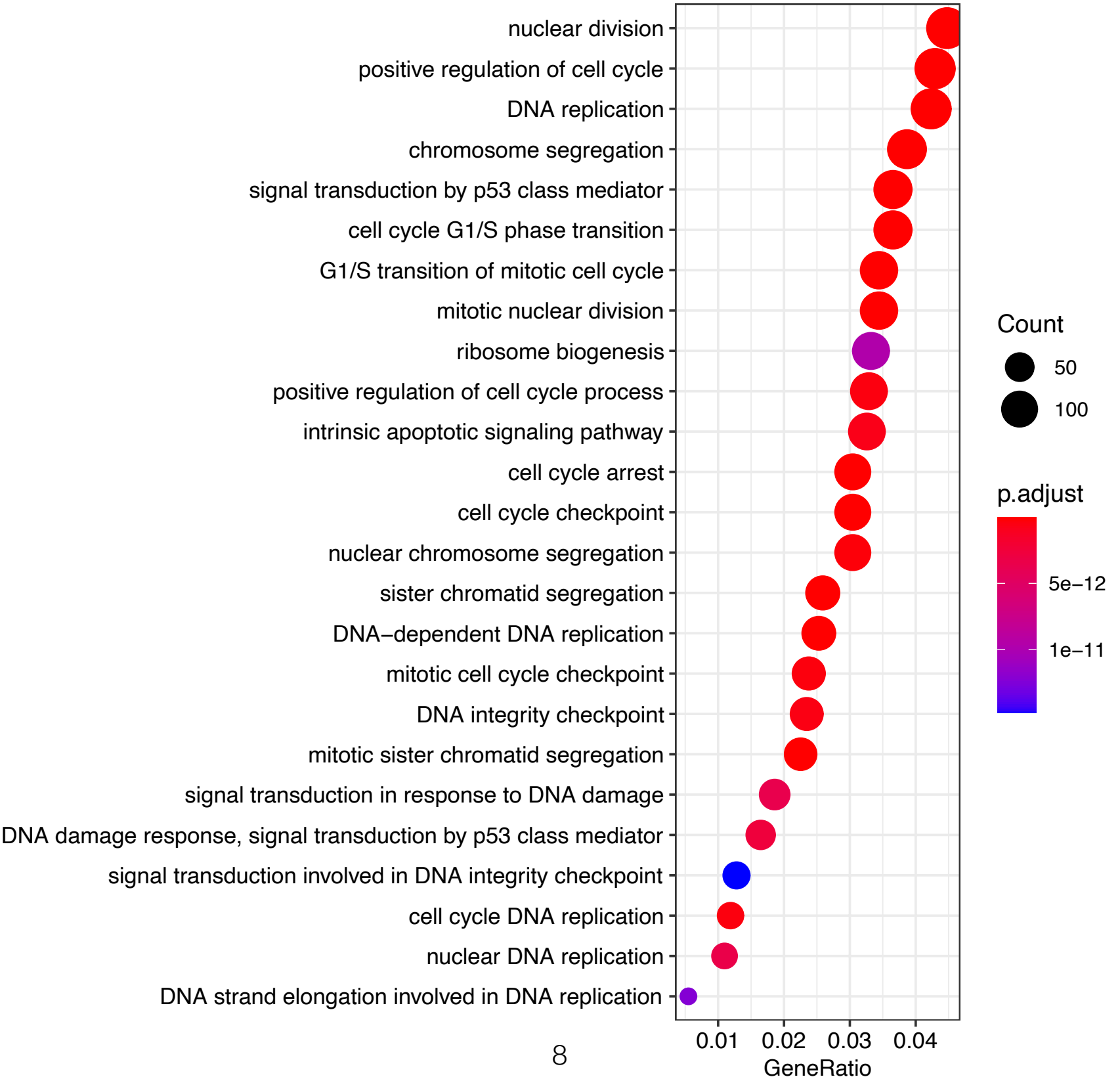


*Do p53 dynamics induce the expression of immune response related genes? **Yes!***

*Are some of these immune response genes p53-dependent? **Yes!***

*Do p53-dependent immune response gene expression dynamics differ with pulsatile or sustained p53 expression? **Yes!***

Over-representation of genes belonging to gene ontologies expected to be involved in DNA damage pathways



Results and Current/Future Work

Preliminary results

- Differential DNA damage responses in cancer cells result in expression of p53-dependent immune response genes

Current/Future work

- Experimentally validate gene expression dynamics of CSF-1, PAI-1, TNFRSF10B, and FAS
- Investigate functional consequences of differential expression dynamics for immune cells

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