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SJSU Undergraduate Research Grants

Effects of increased intracellular pH on autophagy in mammalian cells

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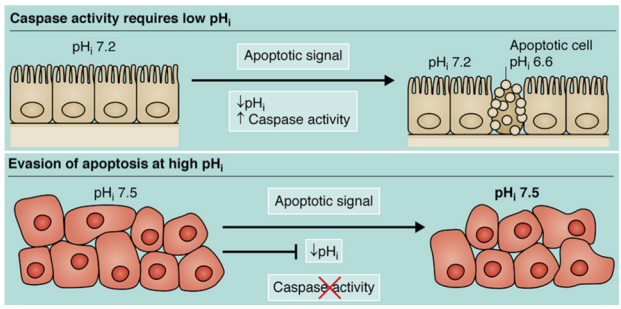
Abstract

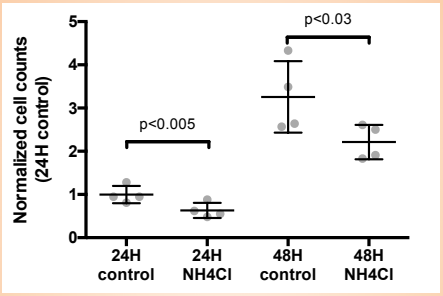
Increased intracellular pH (pHi) has been linked to driving several hallmarks of cancer in Dr. Grillo-Hill's previous research (White et al. 2017). Proliferation, tumorigenesis and metastasis are seen to increase at raised pHi. However, less intuitively, so does cell death. In the form of autophagy, perishing cells feed the tumor from within by recycling cell parts. Unpublished data in the Grillo-Hill lab show an increase in autophagy at raised pHi in the Drosophila eye imaginal disc. To test the conservation of this mechanism from Drosophila to mammals, this project replicates the test conditions in cultured canine epithelial cells. The research aims to broaden available understanding of how cancerous cells avoid death in human patients.

Research Questions



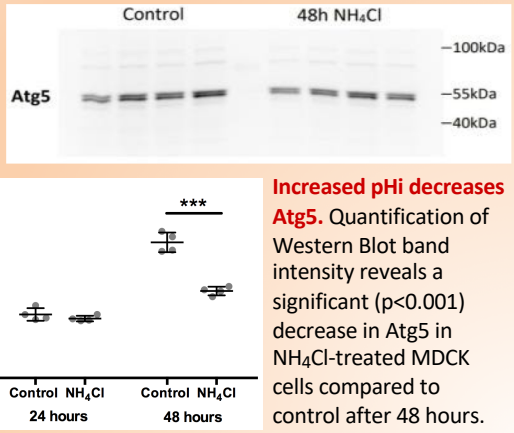
Does increased pHi allow cells to avoid apoptosis?
If so, is autophagy the primary mode of cell death?

Figure 1.



Increased pHi decreases cell number. MDCK cells treated with NH_4Cl for 24 or 48 hours showed significantly decreased cell numbers when compared to untreated controls.

Figure 2.



Increased pHi decreases Atg5. Quantification of Western Blot band intensity reveals a significant ($p<0.001$) decrease in Atg5 in NH_4Cl-treated MDCK cells compared to control after 48 hours.

Procedures and Findings

Procedure 1:

- **Chemically increase intracellular pH with NH_4Cl.**
- **Count cells after 24 and 48 hours of treatment.**

Finding 1:

- **Confirmed that cell numbers significantly decrease in response to raised pHi (Figure 1).**

Procedure 2:

- **Perform Western Blot analysis of the known autophagy marker Atg5.**

***Finding 2*:**

- **Observed a significant decrease in Atg5 as a result of raised pHi (Figure 2).**

Citations

1. **Ulmschneider, B, Grillo-Hill, BK, Benitez, M, Azimova, D, Barber, DL, and Nystul, NG. 2016. *J. Cell Biol.* 215:345-355.**
2. **White KA, Grillo-Hill BK, and Barber DL. 2017. *J. Cell Sci.* 130:663-669.**

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