

# NK Cells in Circadian Regulation of Lung Injury

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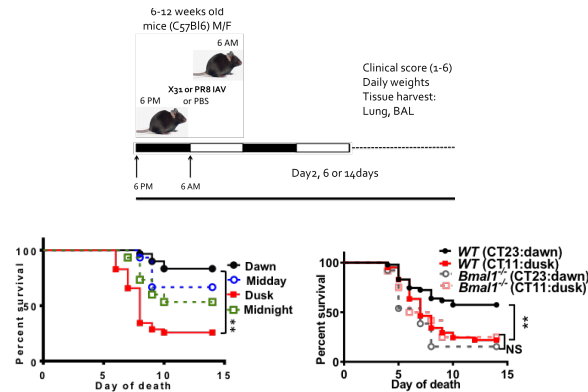


## Background

- influenza A virus (IAV) is an infection in the lungs that is the leading cause of mortality and morbidity
- circadian rhythm is the internal process that regulates the sleep/wake cycle
- circadian rhythm influences the innate immune response
- core clock "circadian" genes regulate expression of different proteins through a transcriptional translational feedback loop
- Natural Killer (NK) cells are crucial in innate immune response to infections
- NK cells aid in the process of protection against influenza infection

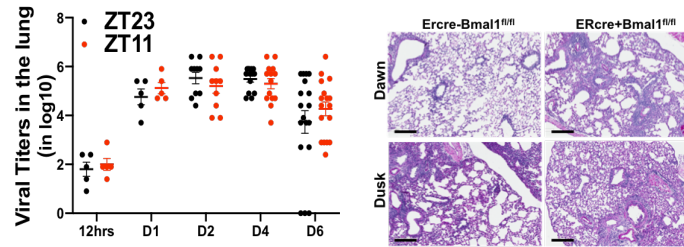
## Previous Work

- circadian rhythm controls the mortality and morbidity of mice infected with Influenza A

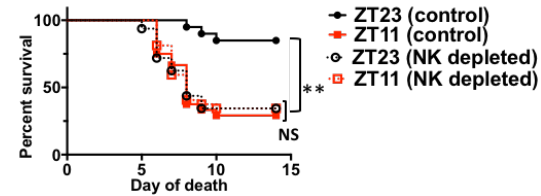


## Previous Work (cont'd)

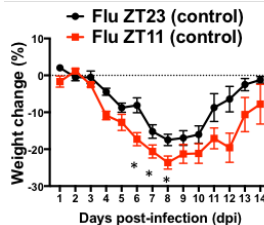
- circadian regulation effects mortality and morbidity by IAV through host tolerance not through antiviral response



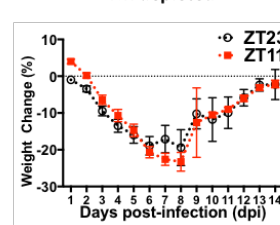
- depletion of NK Cells causes time of day difference in mortality and weight loss to be lost



### Controls (infected with IAV)



### NK depleted



## Specific Aims

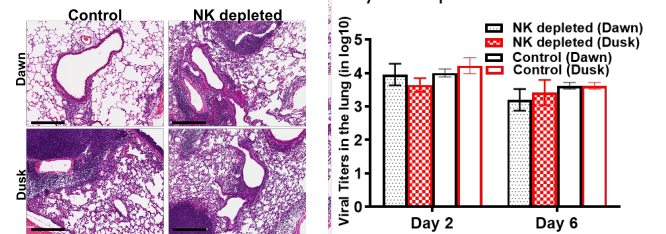
- determine the role of NK cells in lung inflammation during circadian regulation

## Methods

- mice aged 8-16 weeks housed 12 hr Light/Day cycles
- depletion of NK cells prior to infection with NK1.1 antibodies
- lungs were harvested at serial time points
- scoring of the damage in infected lungs was measured in four areas: peri-bronchial, peri-vascular, alveolar infiltrate and epithelial damage

## Results

- less severe lung injury among WT Dawn group but NK depletion eliminated any differences between dawn and dusk
- viral titers are not affected by NK depletion



## Conclusion

- temporal patterning of response to IAV is controlled by NK cells through worse lung histology as opposed to viral burden