



# Effects of Atropine on Ventilation in Mouse Model of Dravet Syndrome

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Linda Lu and Nhu Y Thi Doan

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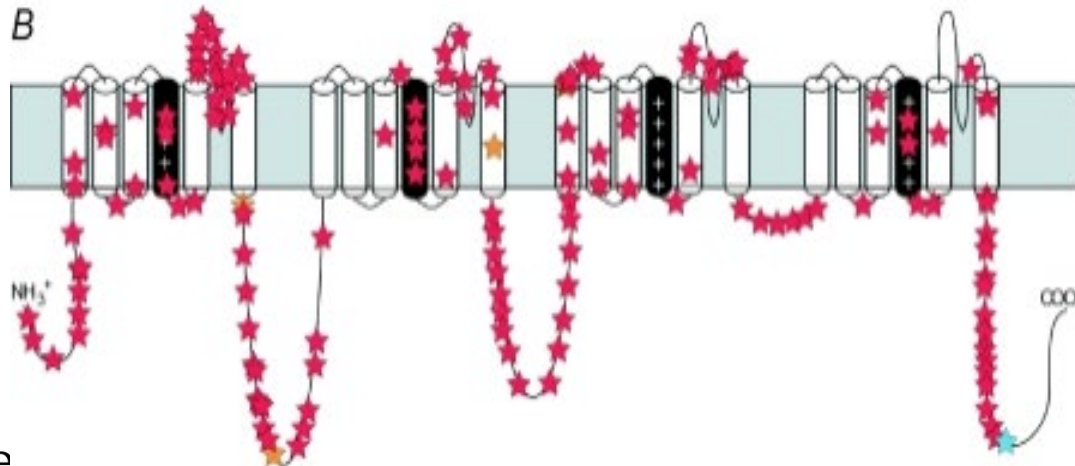
Dr. Franck Kalume

Seattle Children's Research Institute



# What is Dravet Syndrome?

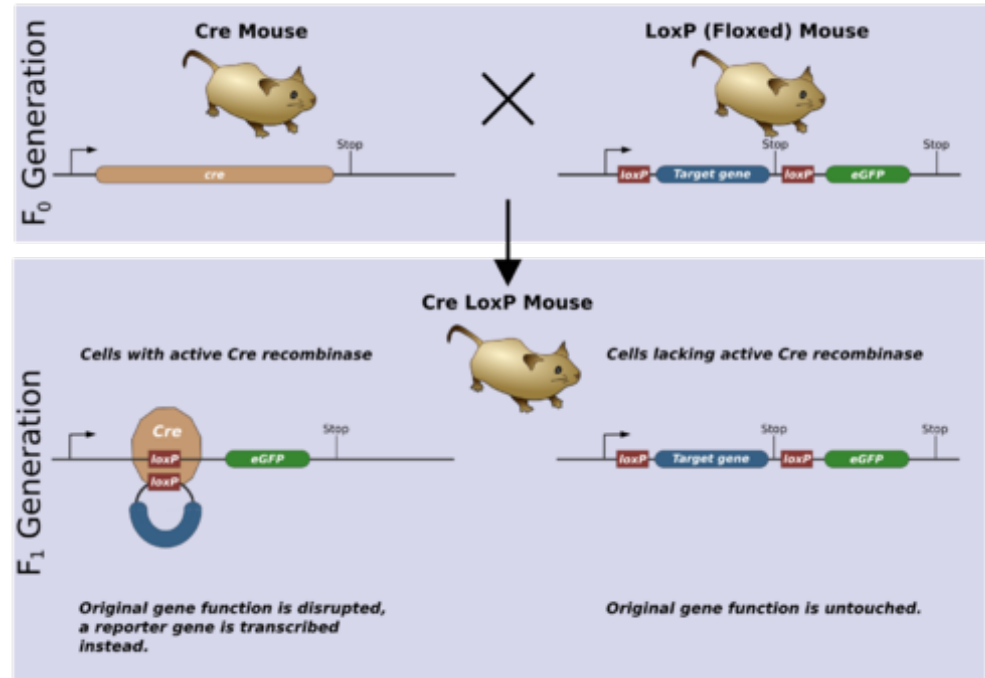
- Genetic epilepsy beginning in infancy that continues throughout adulthood
- Caused by mutation in Nav1.1 coded by SCN1A gene which results in a nonfunctional sodium channel that most affects inhibitory interneurons
- Patients can die of sudden unexpected death in epilepsy (SUDEP)



Catterall et al. *J. Physiology*, 2010

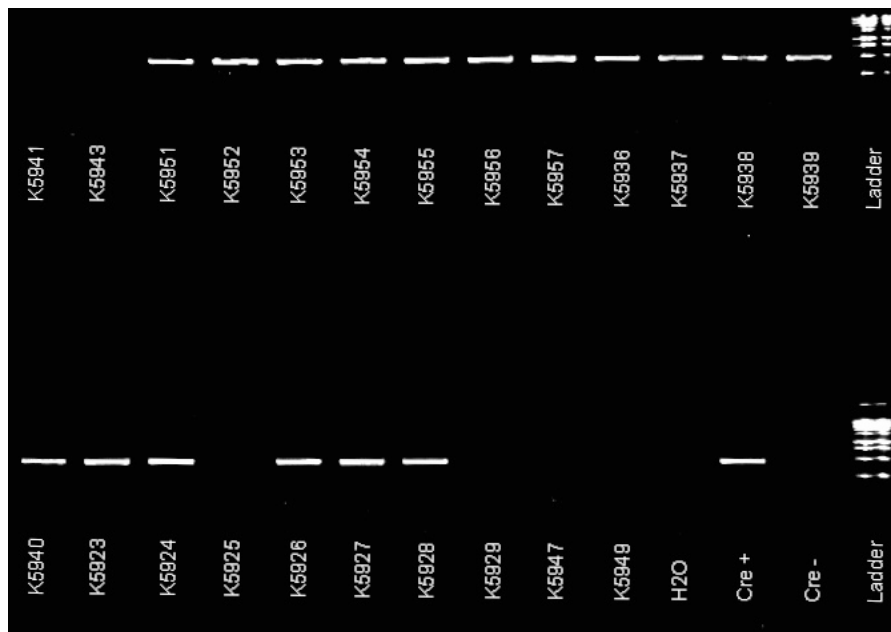
# Mouse Model of Dravet

- Engineered transgenic mice with global and conditional KO of SCN1A gene
- Cre-Lox recombinase system allows targeting of specific brain regions based on promoter activity
- Mice exhibit phenotypes similar to that observed in Dravet



# Genotyping

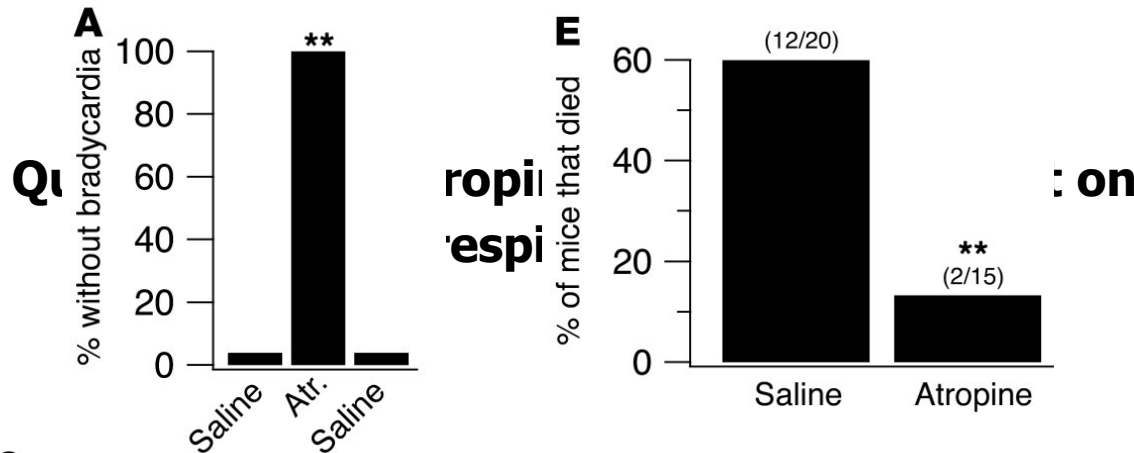
- Sample collection
- DNA extraction (Viagen method)
- PCR
- Gel electrophoresis and imaging
- Analysis of results





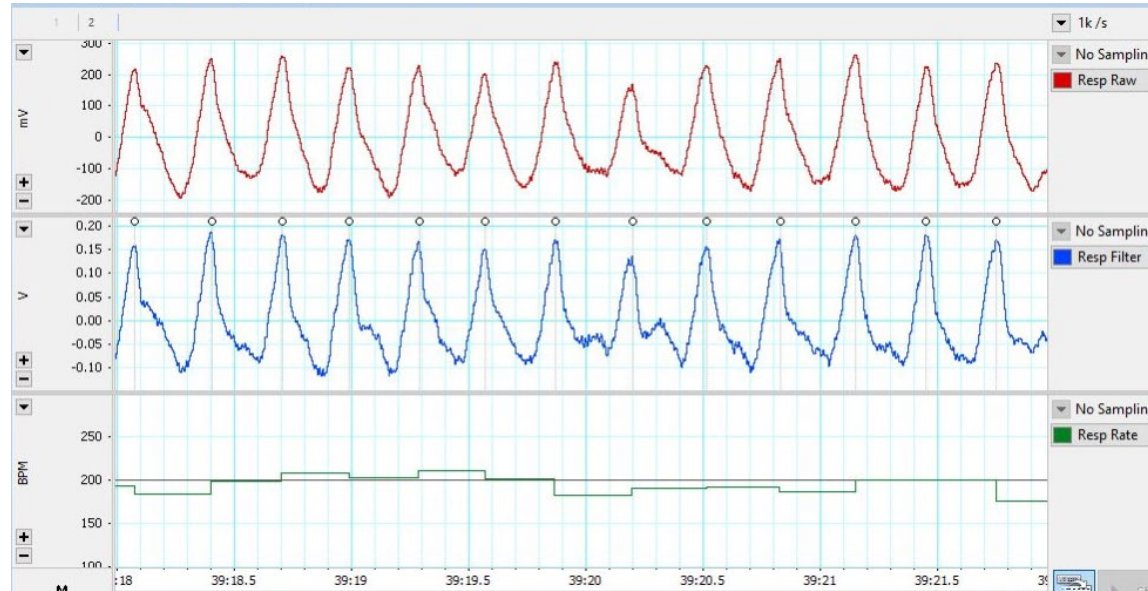
# Physiology of SUDEP

- SUDEP has previously been determined to be associated with abnormal cardiac activity and respiration
- Atropine blocks parasympathetic input to the heart and has been shown to prevent bradycardia and suppress death



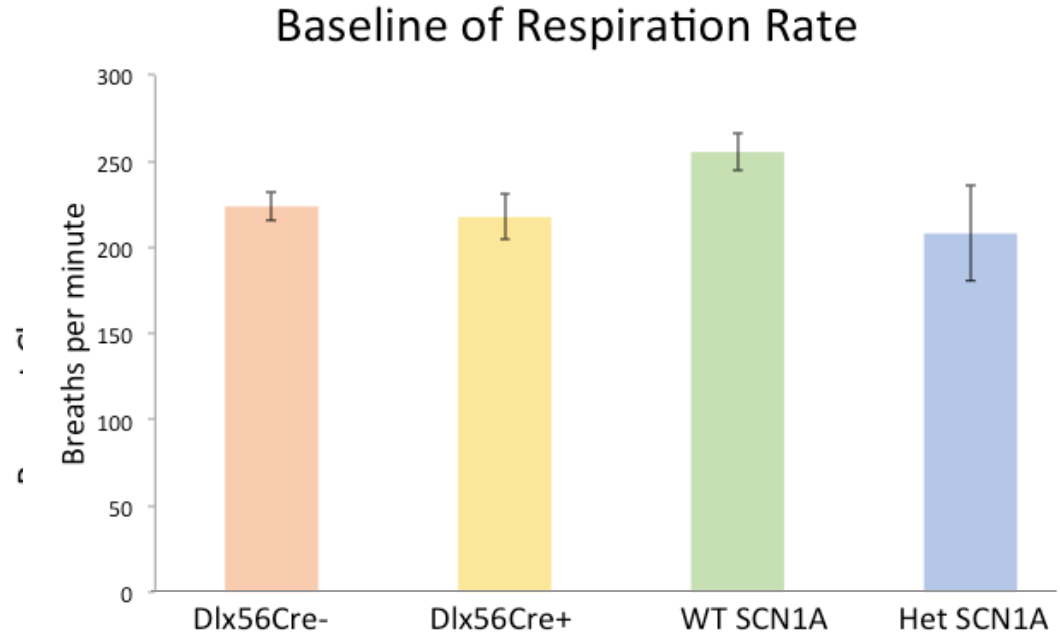
# Experimental Methods

- Conditional SCN1A WT (n=6) and KO mice (n=6)
- Global SCN1A WT (n=5) and KO mice (n=5)



# Respiration Rate

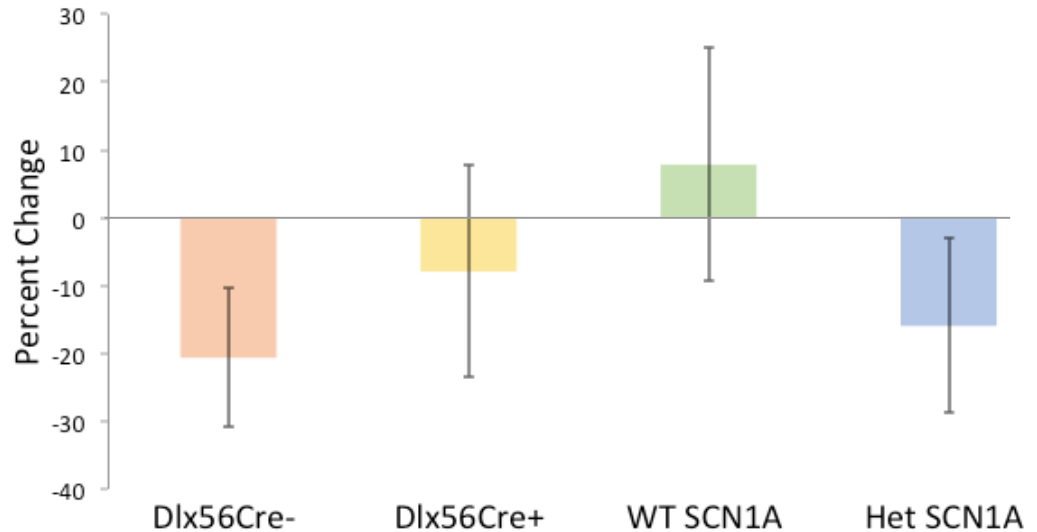
- Atropine decreased respiration rate in both WT and mutants
- No significant difference in change between WT and mutant



# Tidal Volume

- Tidal volume decreases except in WT SCN1A
- No significant difference in tidal volume between WT and mutant

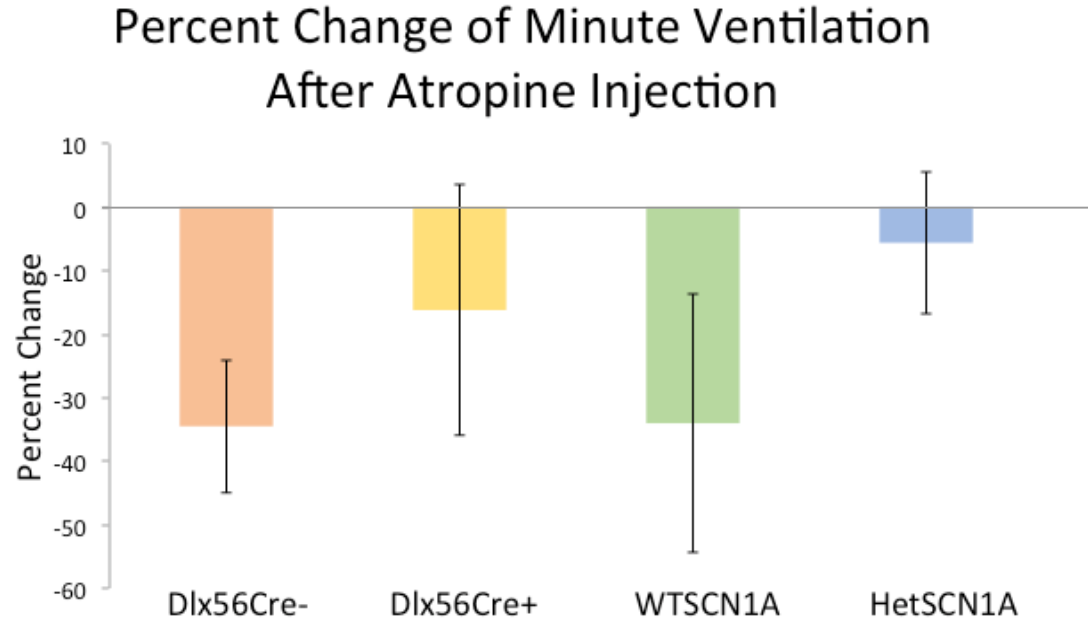
Percent Change of Tidal Volume After Atropine Injection





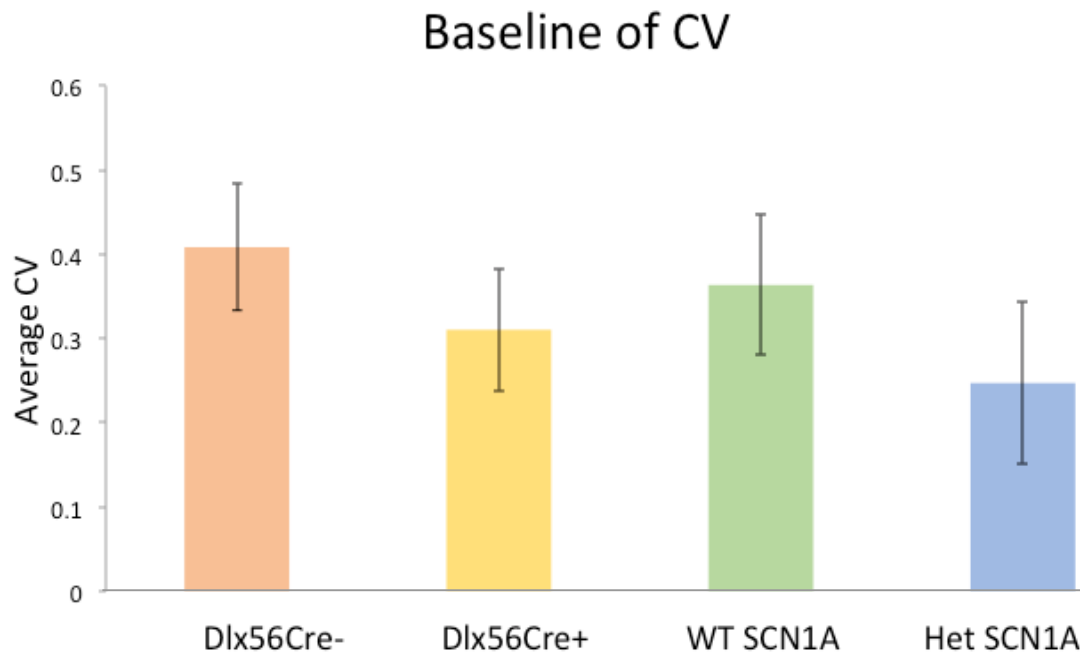
# Minute Ventilation

- Minute ventilation decreases after atropine injection
- Although it is not significant, atropine appears to have a smaller effect on the mutants



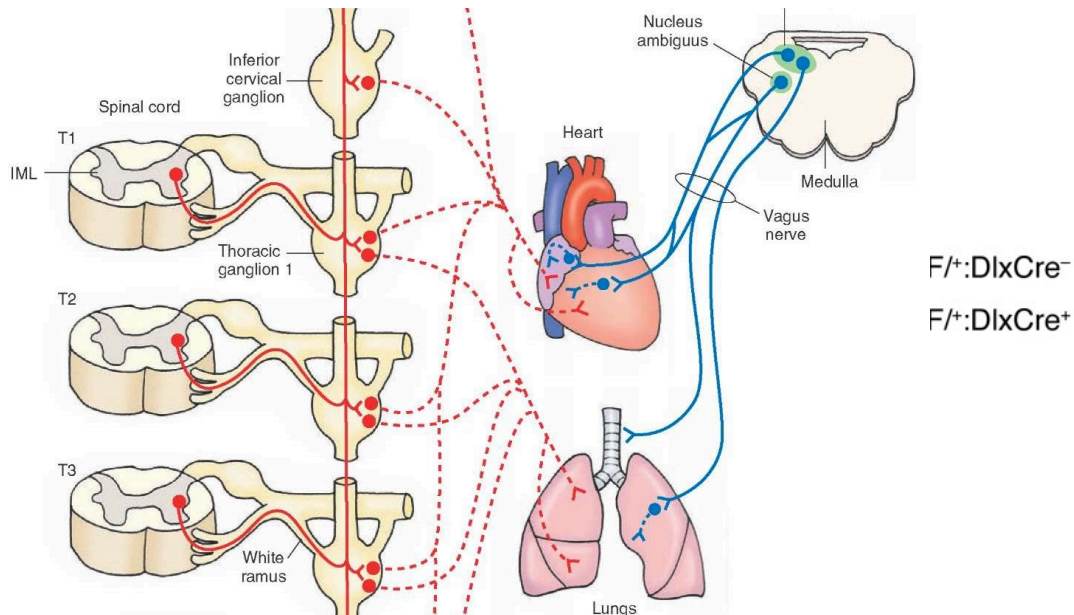
# Coefficient of Variation (CV)

- CV decreases in WT and increases in mutant
- No significant difference in CV between WT and mutant



# Conclusions

- Atropine decreased respiration rate and had no significant changes between WT and mutants in a mouse model of Dravet



Kalume et al *J. Clinical Investigation* 2013 Pt 3. What-when-how.



# Future Directions

- Longer baseline would allow more periods of stillness and better comparison between pre and post injection
- Analysis of respiration with other parameters simultaneously (e.g. EEG, EKG)
- Different dosages of atropine and comparison with other drugs (e.g. propranolol, N-methyl-scopolamine)



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