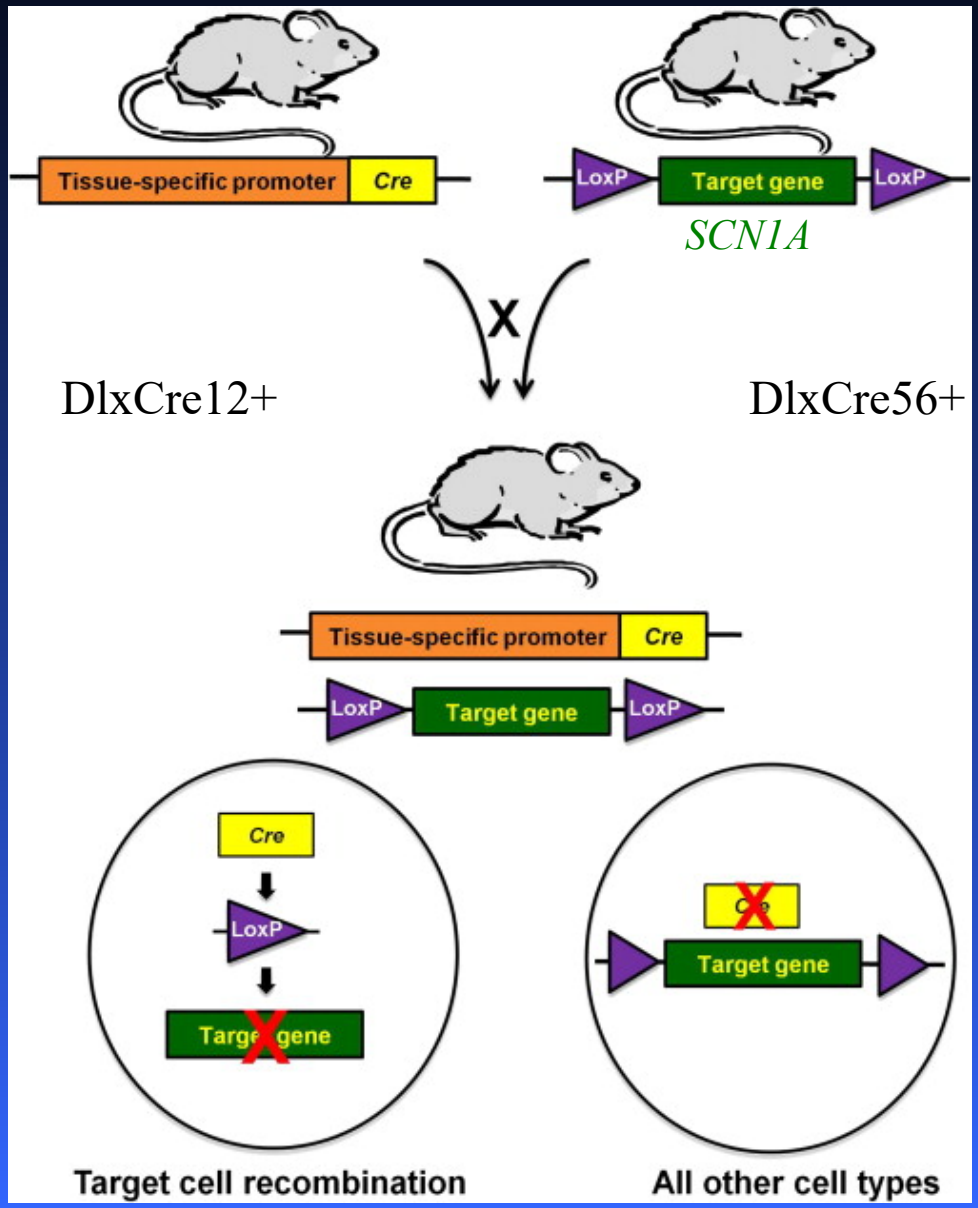
Circadian Abnormalities in the Mouse Model of Dravet Syndrome

Seizure disorder
due to mutation in *SCN1A*/$Na_V1.1$

Our specific aim:

Whether deletion of *Scn1a* specifically in interneurons alone is sufficient to cause Circadian dysfunction

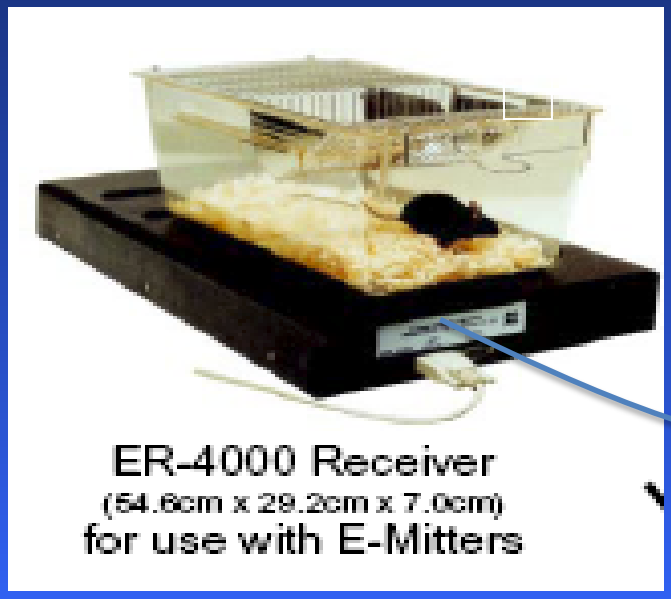
CreLoxP System for Interneuron specific deletion of *SCN1A*



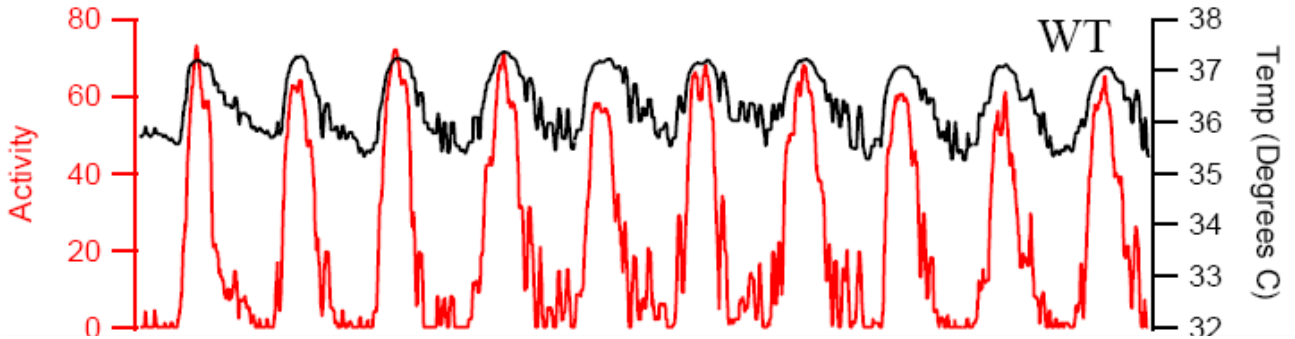
Methods


EMitter

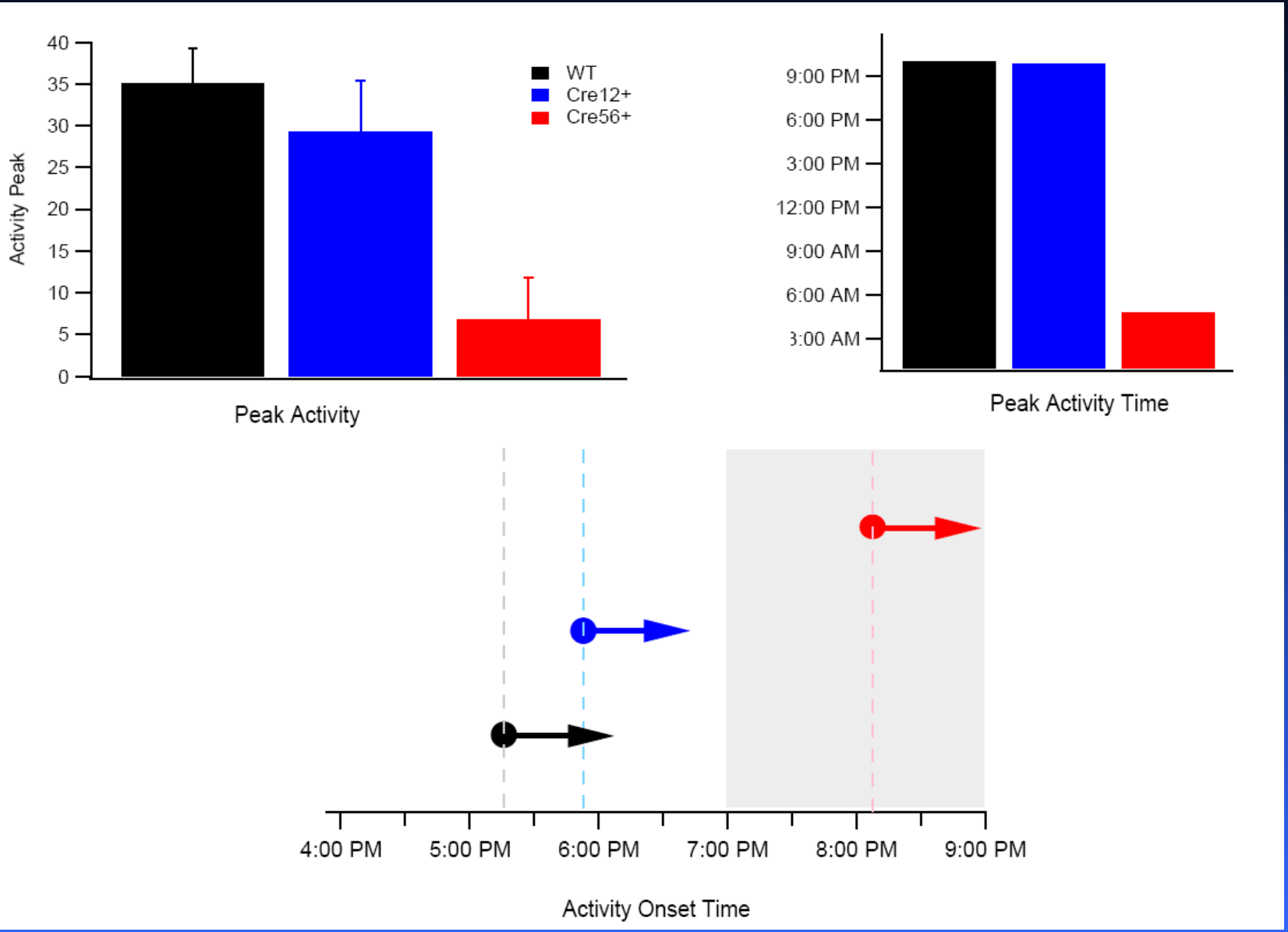

K1251
K1262
K1292
K1294


ER-4000 Receiver
(54.6cm x 28.2cm x 7.0cm)
for use with E-Mitters

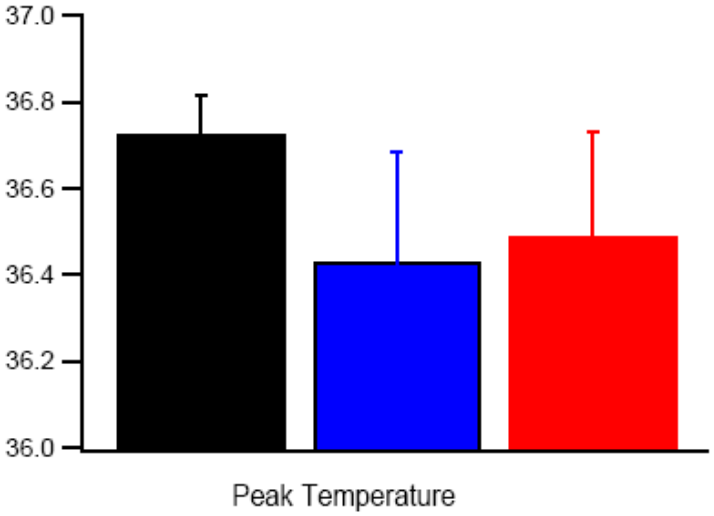

DELL


WT
Activity
80
60
40
20
0
38
37
36
35
34
33
32
Temp (Degrees C)

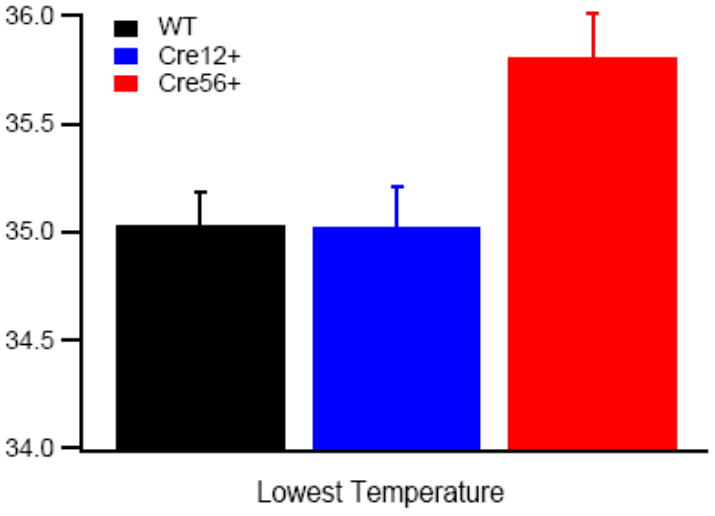
Activity Modulation over Two Days



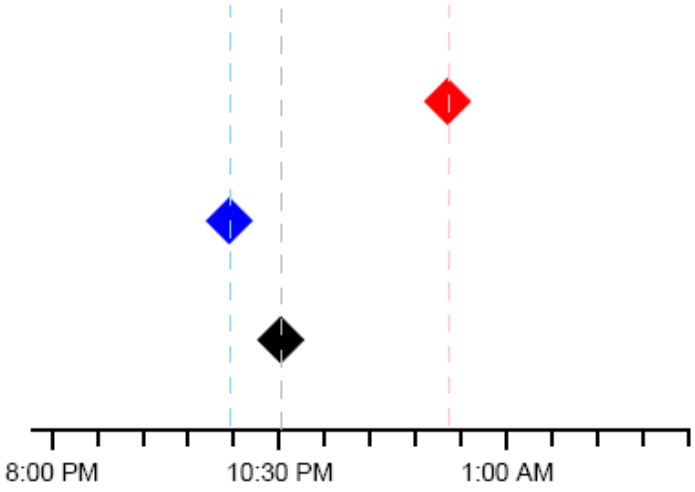
Temperature Modulation over two Days



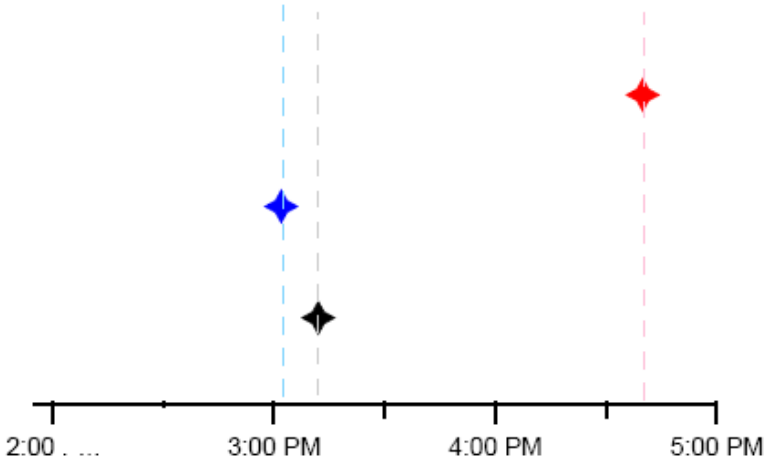
Peak Temperature



Lowest Temperature



Time of Peak Temperature



Time of Lowest Temp

Conclusion

- Deletion of *SCN1A* in interneurons with DlxCre 56 impairs Circadian Rhythm
  - Irregularity of activity oscillations, decrease in activity, delayed activity onset time.
  - Slight decrease in peak temperature (not statistically significant), increase in lowest temperature, delayed peak and lowest temperature time.
- Deletion of *SCN1A* in interneurons with DlxCre12 did not significantly affect circadian rhythm.

Hypothesis and Future Direction

- Hypothesis: DlxCre56 is expressed in interneurons of the Suprachiasmatic Nucleus, the main regulator of circadian rhythm whereas DlxCre12 is not significantly expressed.
- Future Studies:
  - Comparative expression of DlxCre56 and DlxCre12 in the mutant mouse brain (In the SCN)

Thank You!

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  - Jim Pridgeon
  - Christina Buckman
- Lab partners:
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- Seattle Children's Research Institute
  - CIBR
  - UW/Harborview Medical Center

References

- *Kalume et al., JNS 2010*
- *Catterall et al., Jphys 2010*
- *Kalume et al., JCI 2013*