The Ins2^{Akita} mouse as a model of vision loss and neurodegeneration in diabetes

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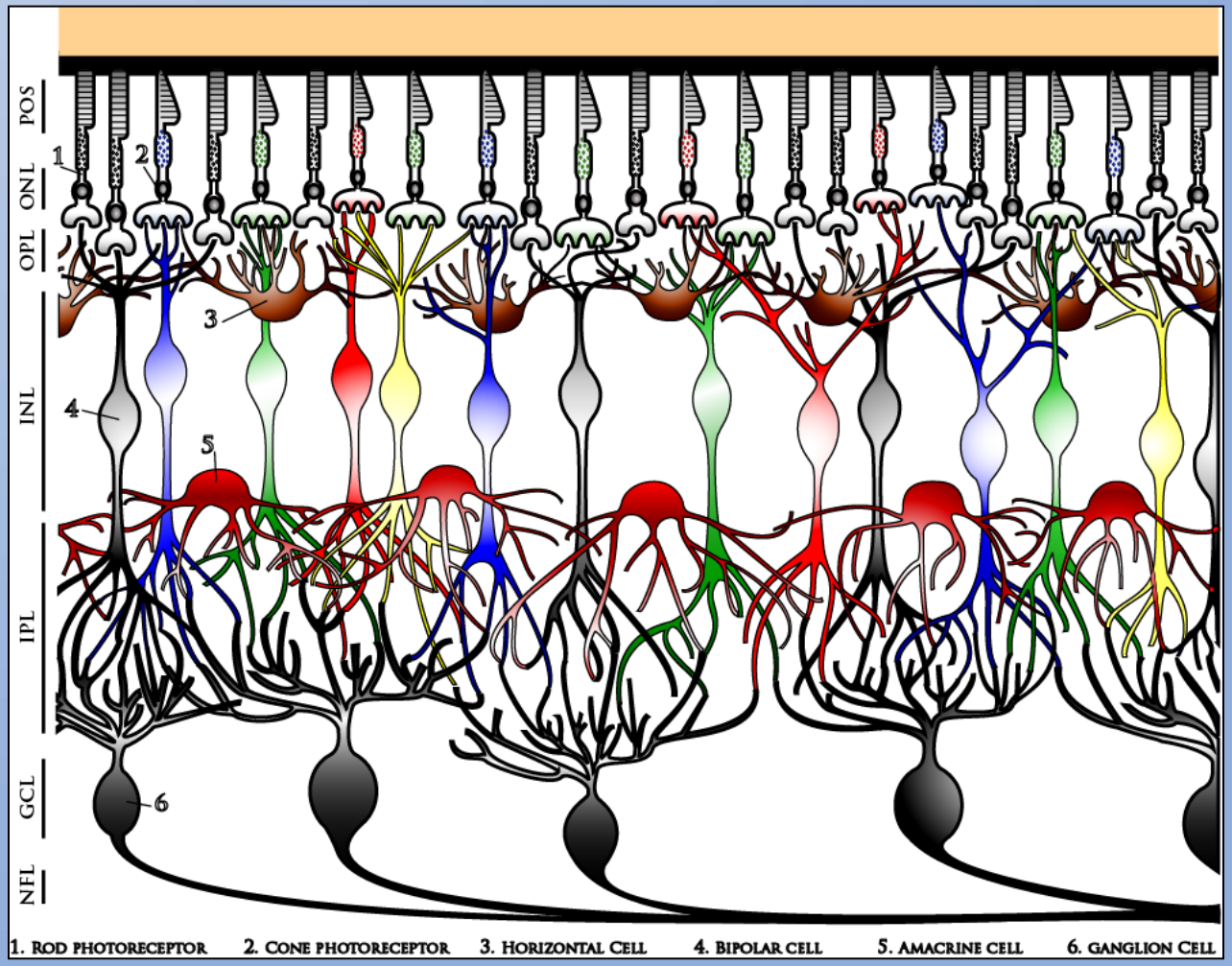
Diabetic retinopathy as a neurovascular disease

- Vascular pathology is very apparent by clinical exam
- Neuronal pathology less detectable due to transparency of tissue
- But loss of function is indicated by:
  - Electrophysiology
  - Poor night vision
  - Dark adaptation
  - Contrast sensitivity
  - Reduced acuity

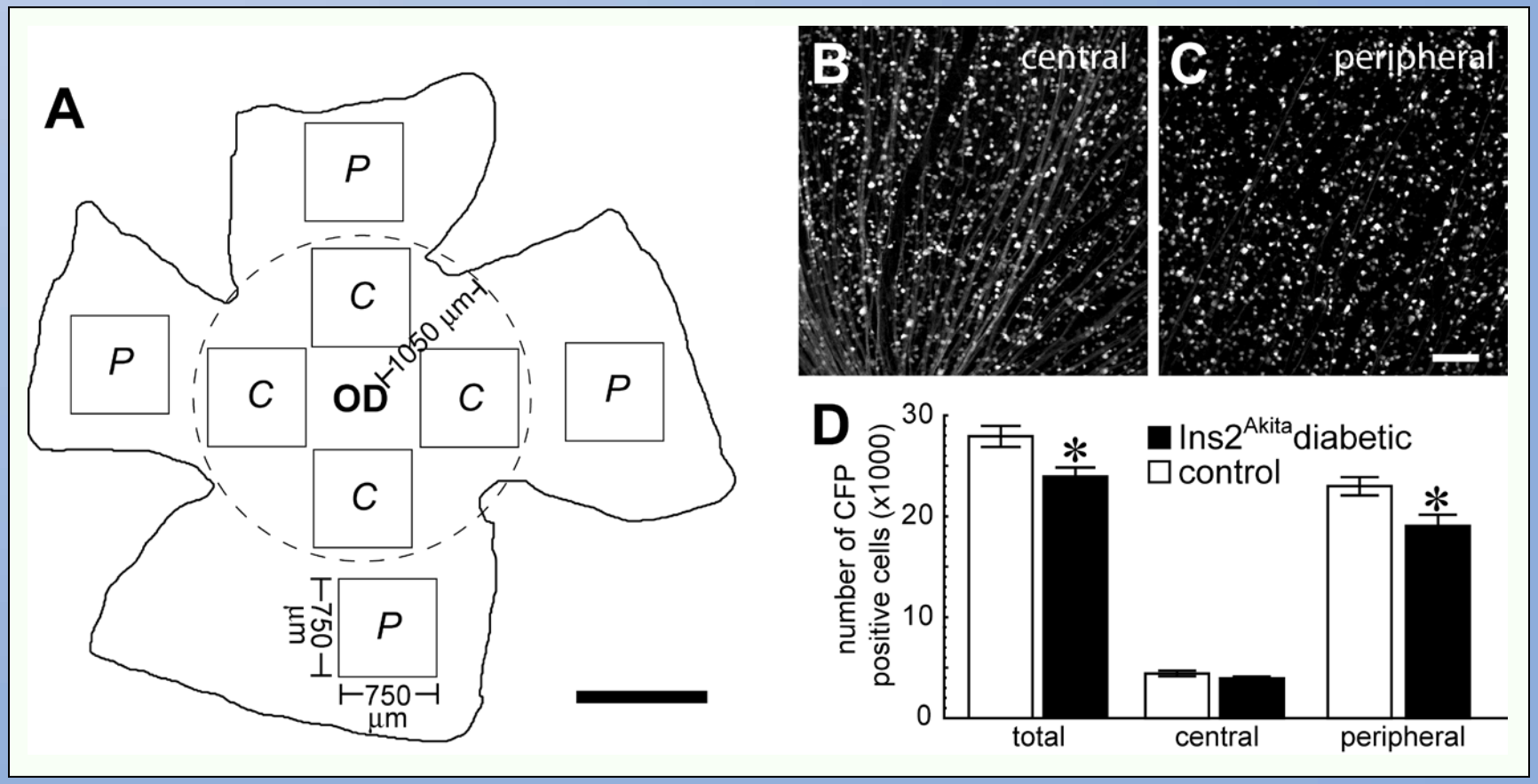
Neurons of the Retina



Transgenic mice to study retinal neurons and diabetes

- C57BL/6J $Ins2^{Akita}$
  - Spontaneous mutation of second insulin gene leading to ER stress in pancreatic beta cell
- Thy1-CFP: cyan fluorescent protein expressed under Thy1 promoter
- Thy1-YFP: Yellow fluorescent protein expressed under Thy1 promoter

CFP-Thy1 Retinal ganglion cells are depleted in Ins2^{Akita} diabetic mice



Gastinger et al, (2008) IOVS 49: 2635-2642

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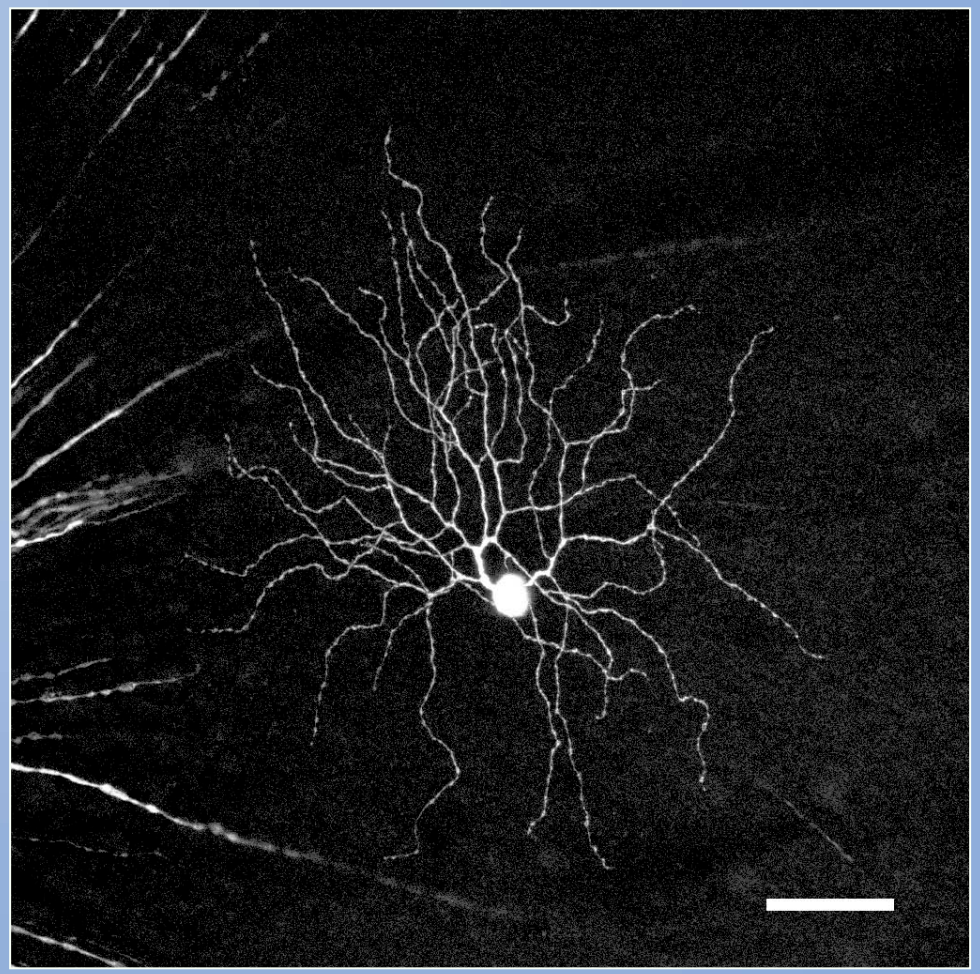
YFP-retinal ganglion cell morphology

- $INS2^{Akita}$ mice cross with Thy1-YFP to obtain diabetic mice with endogenously fluorescent retinal ganglion cells



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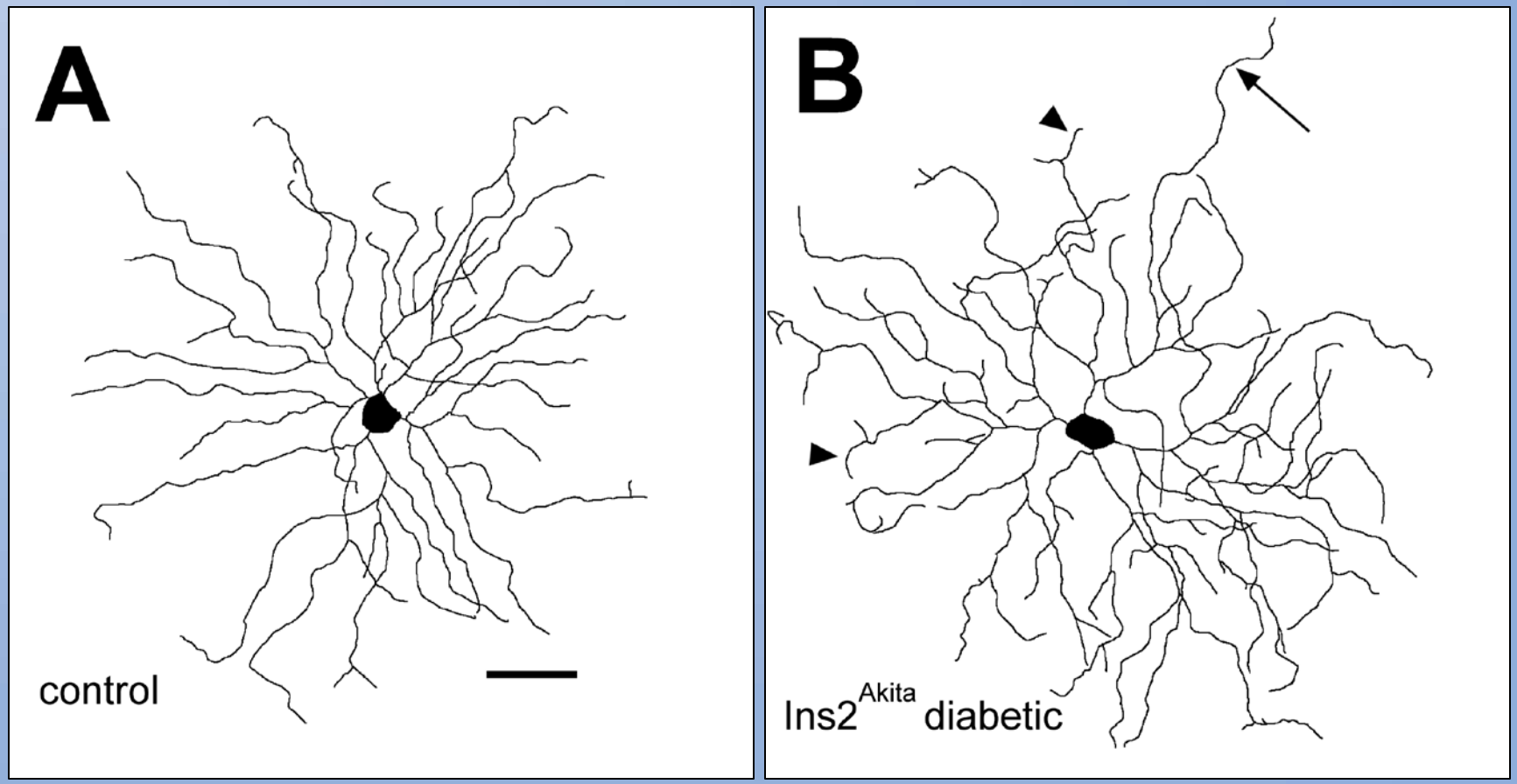
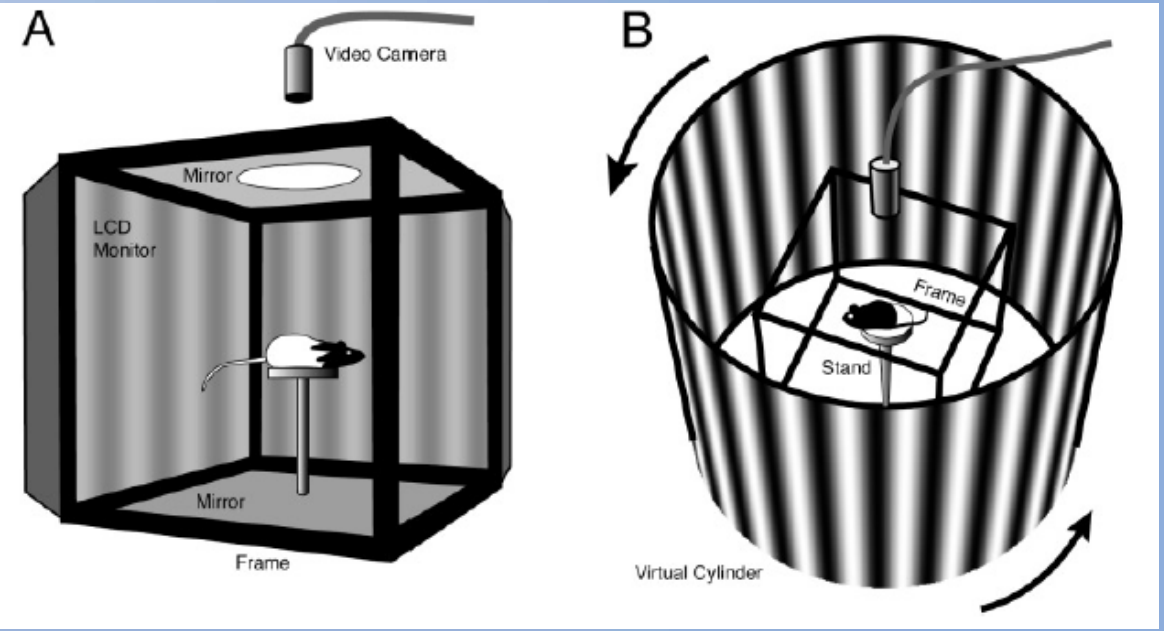
More complex dendritic branching patterns in diabetic Ins2^{Akita} mice



Gastinger et al, (2008) IOVS 49: 2635-2642

AMDCC grant: using the optokinetic reflex to measure vision in rodents

- 4 monitors form a box displaying moving grid
- Head movements track in direction of grid rotation
- Width of bars determines acuity
- Ratio of brightness of bars determines contrast sensitivity



Douglas et al, (2005) Visual Neuroscience, 22:677-684

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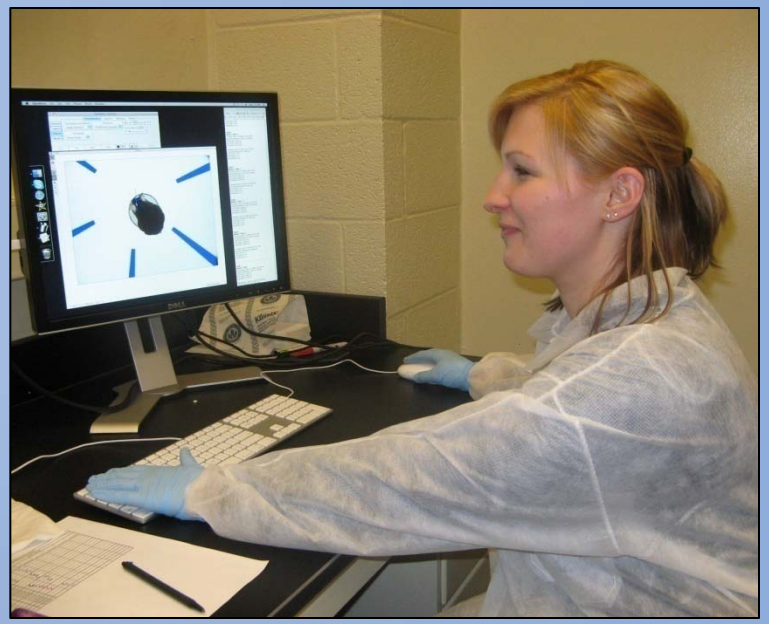
AMDCC grant: Using the optokinetic reflex to measure vision in rodents



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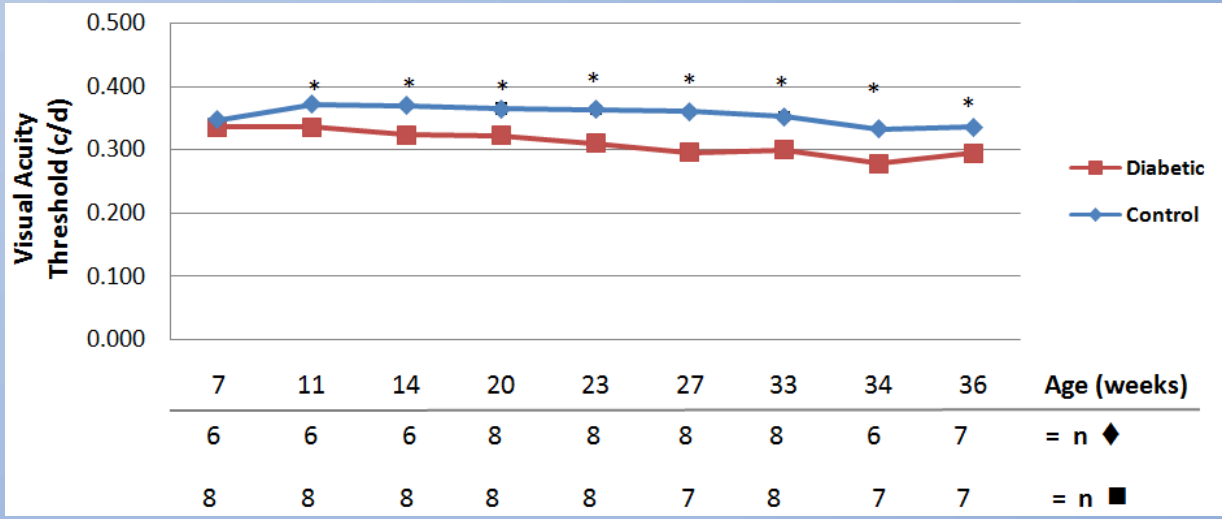
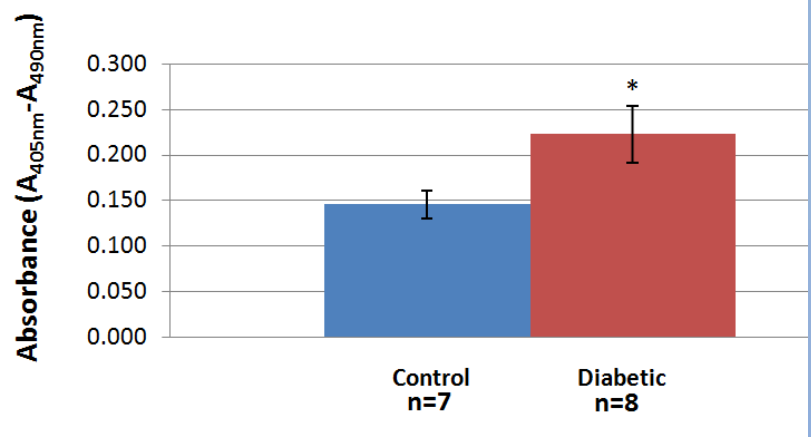
AMDCC progress





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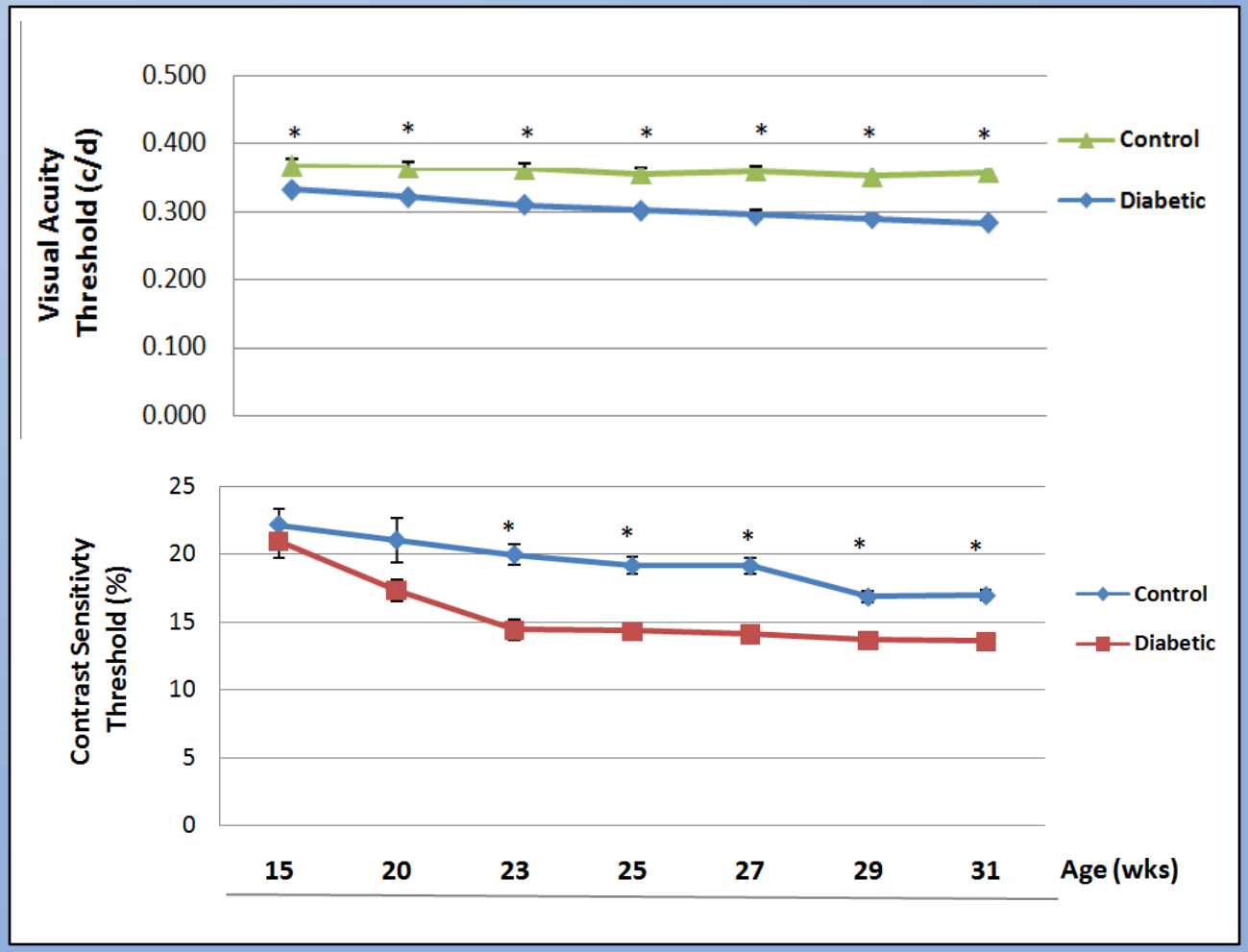
AMDCC progress



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Summary

- Ins2Akita model loss of visual acuity and contrast sensitivity
- Functional loss is accompanied by reductions and abnormalities in retinal ganglion cells

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