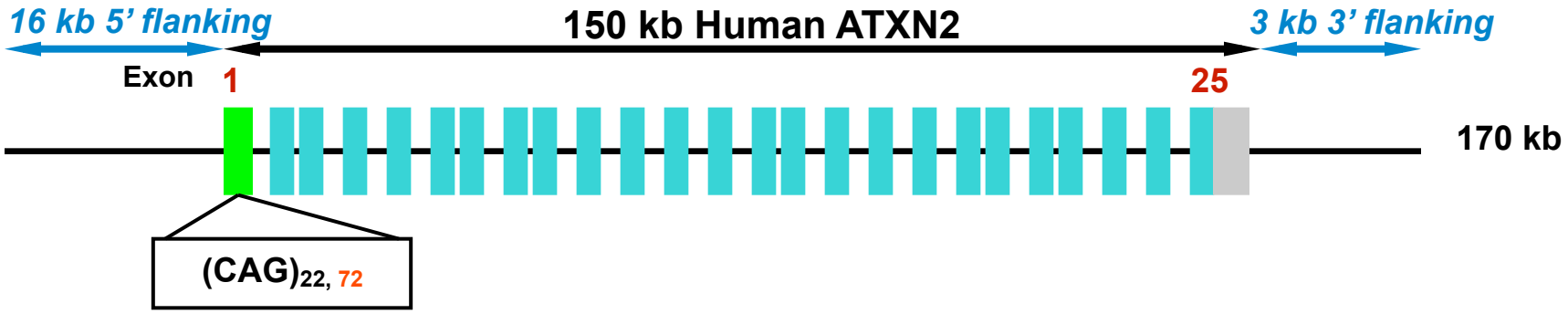
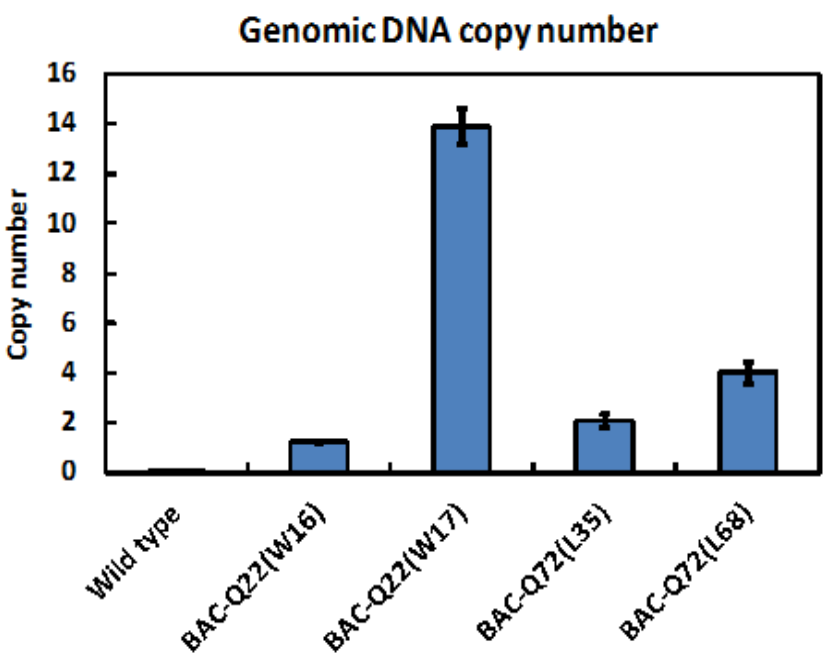
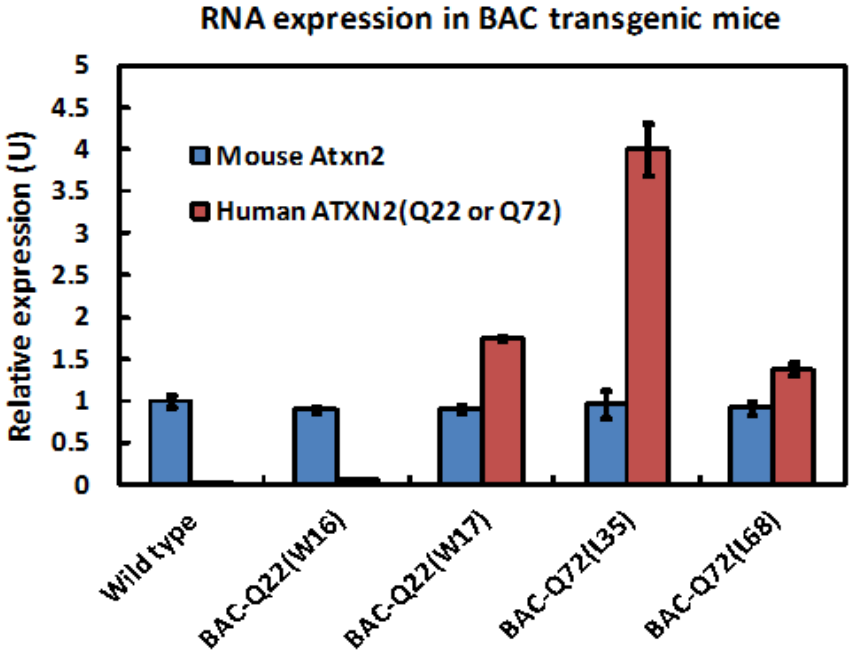
# BAC SCA2 transgenic mice

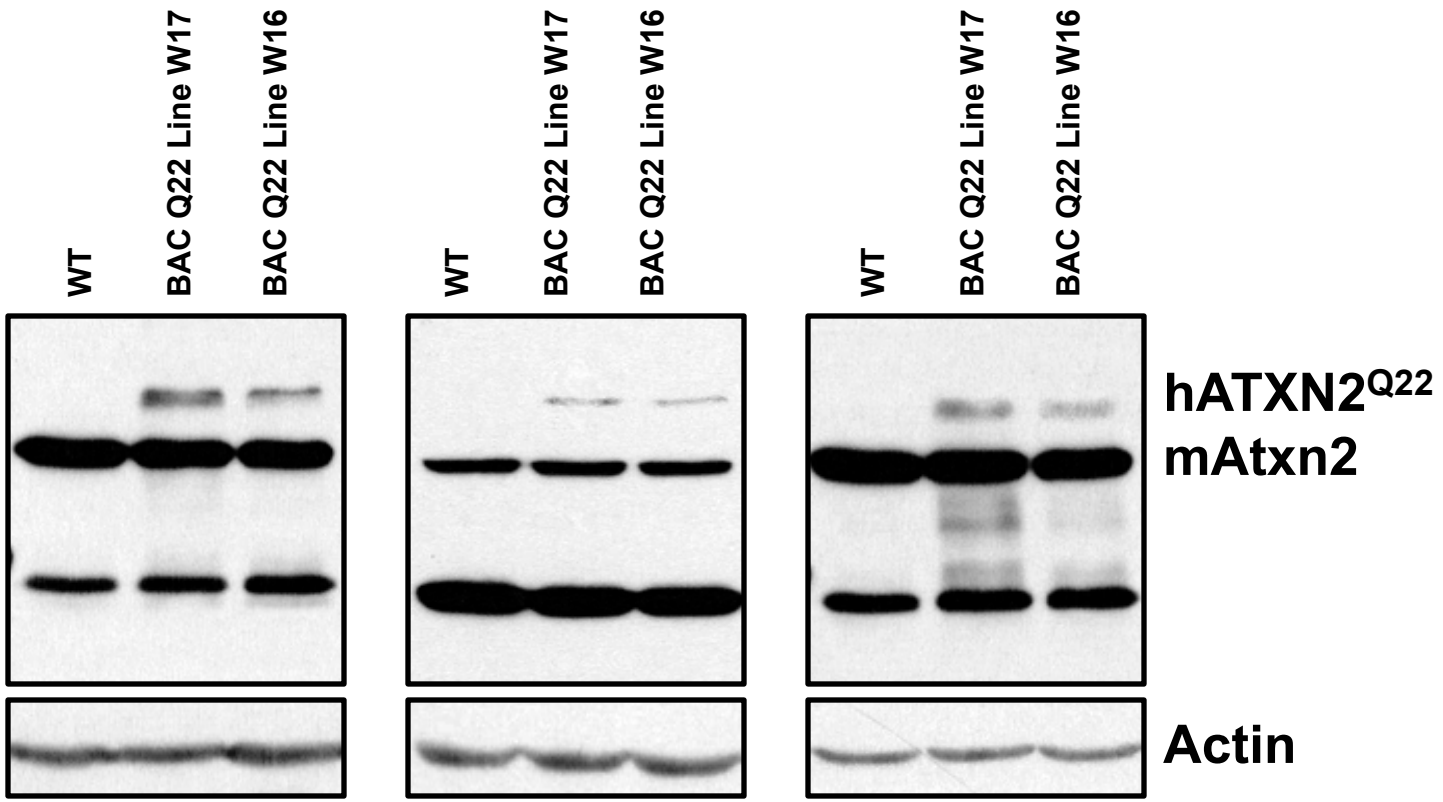
Lab Meeting 8-31-12


16 kb 5' flanking
150 kb Human ATXN2
3 kb 3' flanking
Exon
1
25
170 kb
(CAG)22, 72

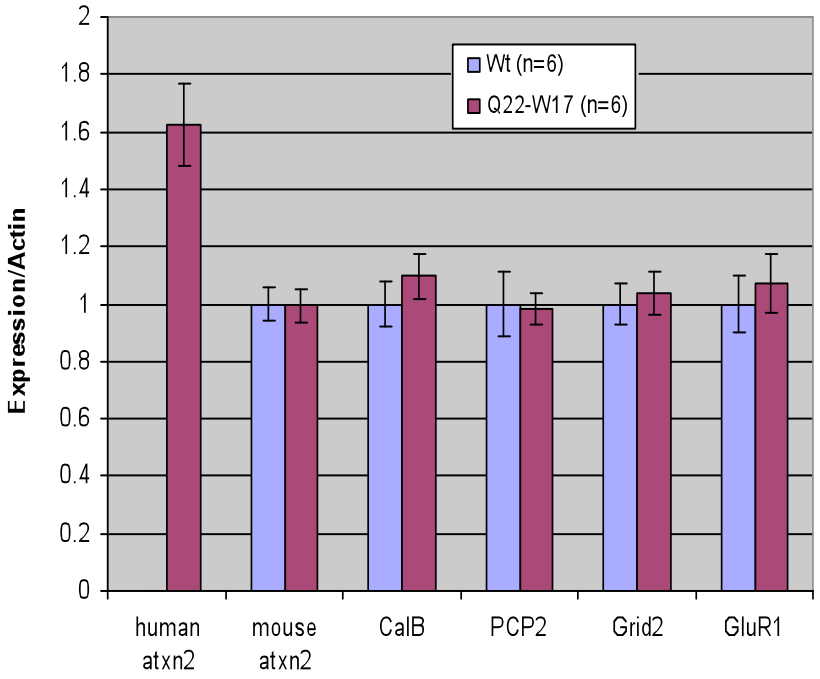

Genomic DNA copy number
Copy number
16
14
12
10
8
6
4
2
0
Wild type
BAC-Q22(W16)
BAC-Q22(W17)
BAC-Q72(L35)
BAC-Q72(L68)

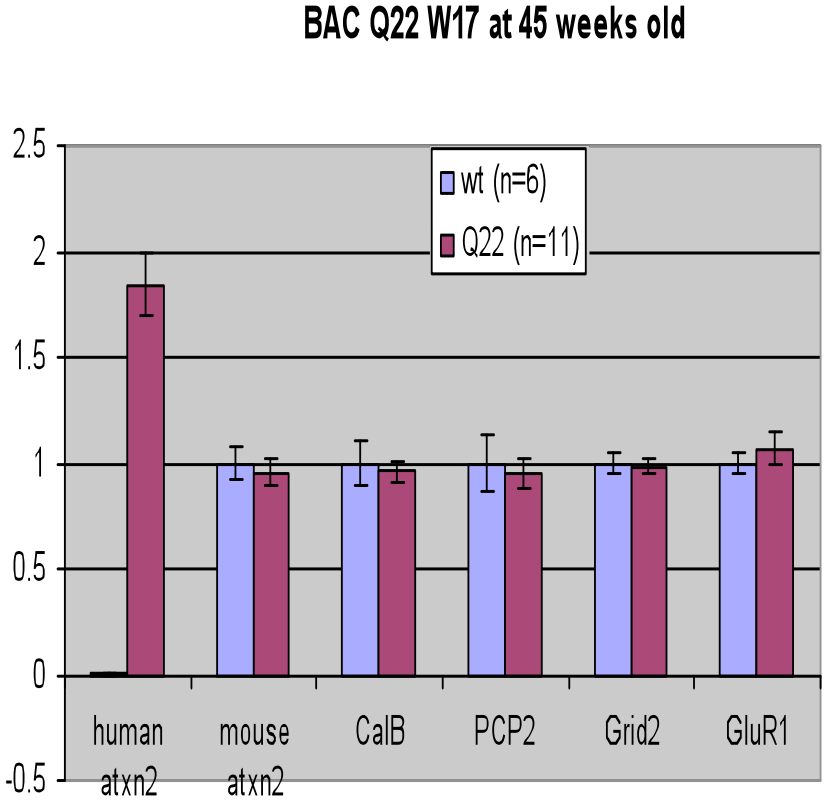

RNA expression in BAC transgenic mice
Relative expression (U)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
Mouse Atxn2
Human ATXN2(Q22 or Q72)
Wild type
BAC-Q22(W16)
BAC-Q22(W17)
BAC-Q72(L35)
BAC-Q72(L68)

## *Human Ataxin 2 expression in BAC Q22 Transgenic mice*



# *Gene expression profile in BAC Q22 mice*

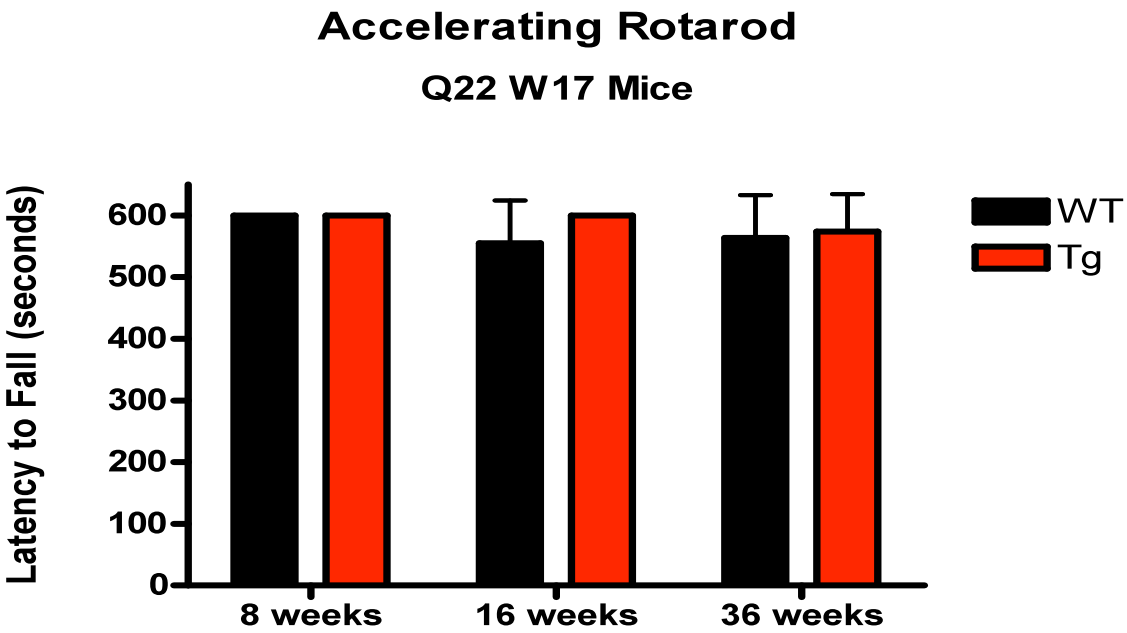


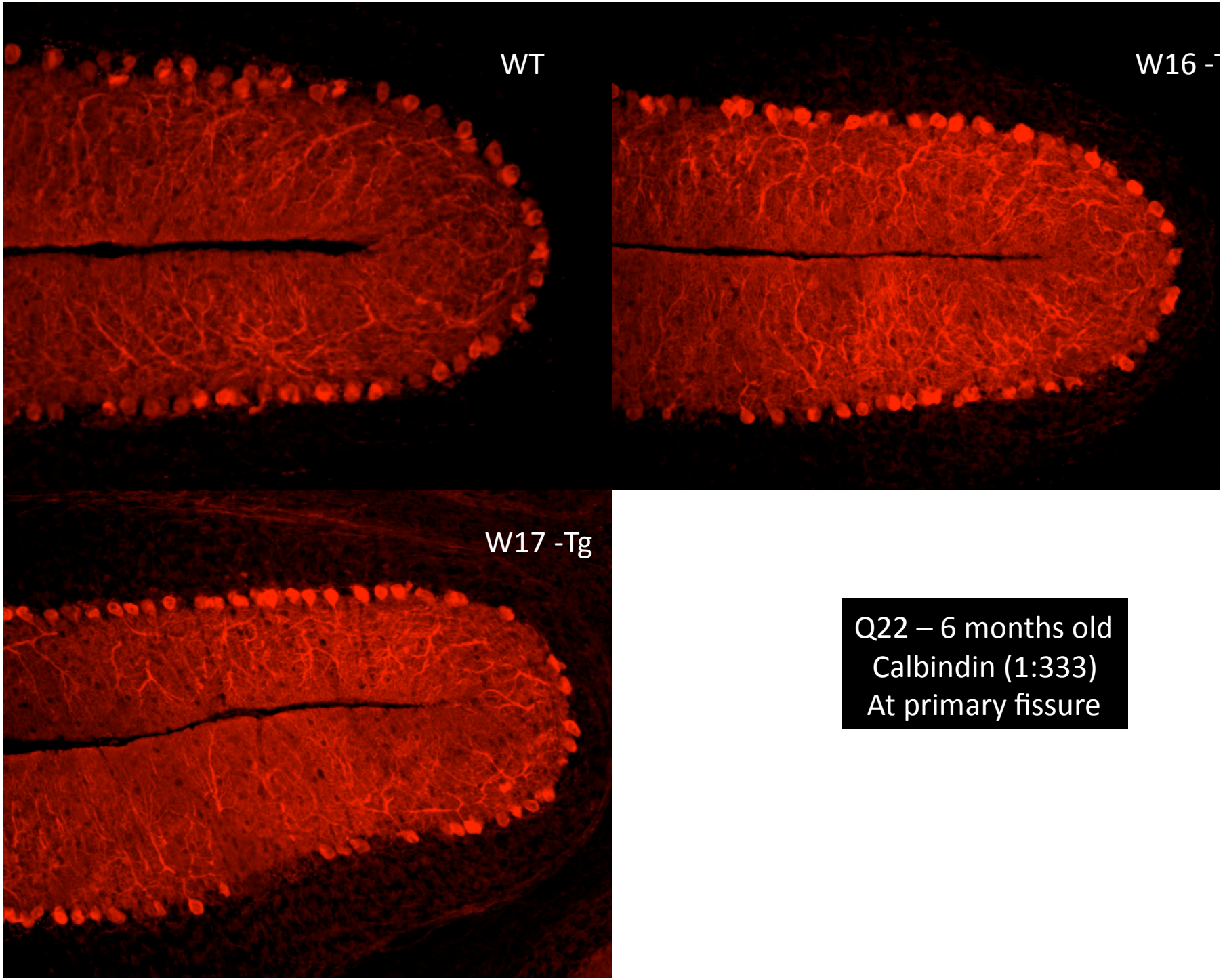
# Accelerating Rotarod

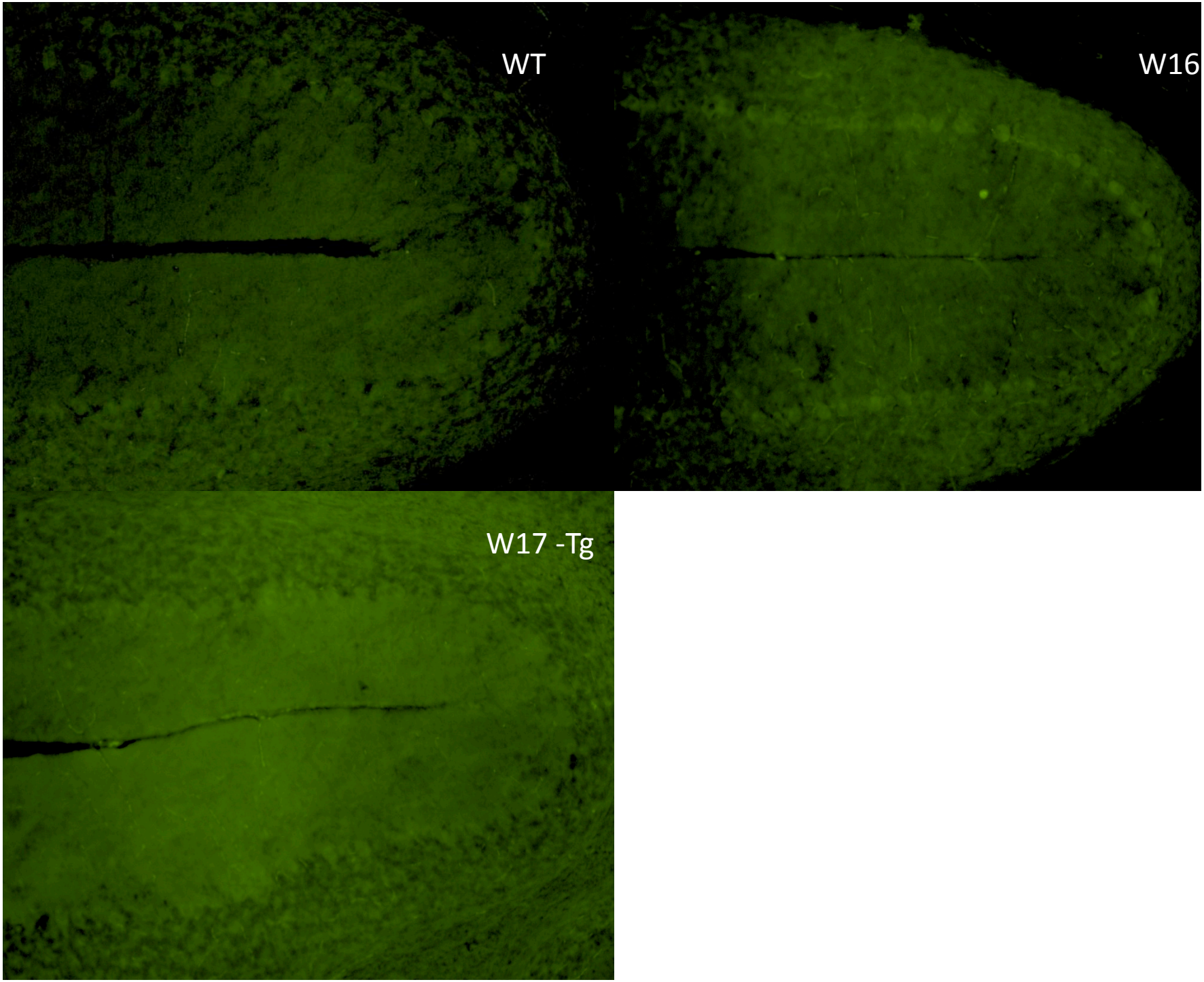
## BAC Q22$^{+/-}$ vs Wildtype

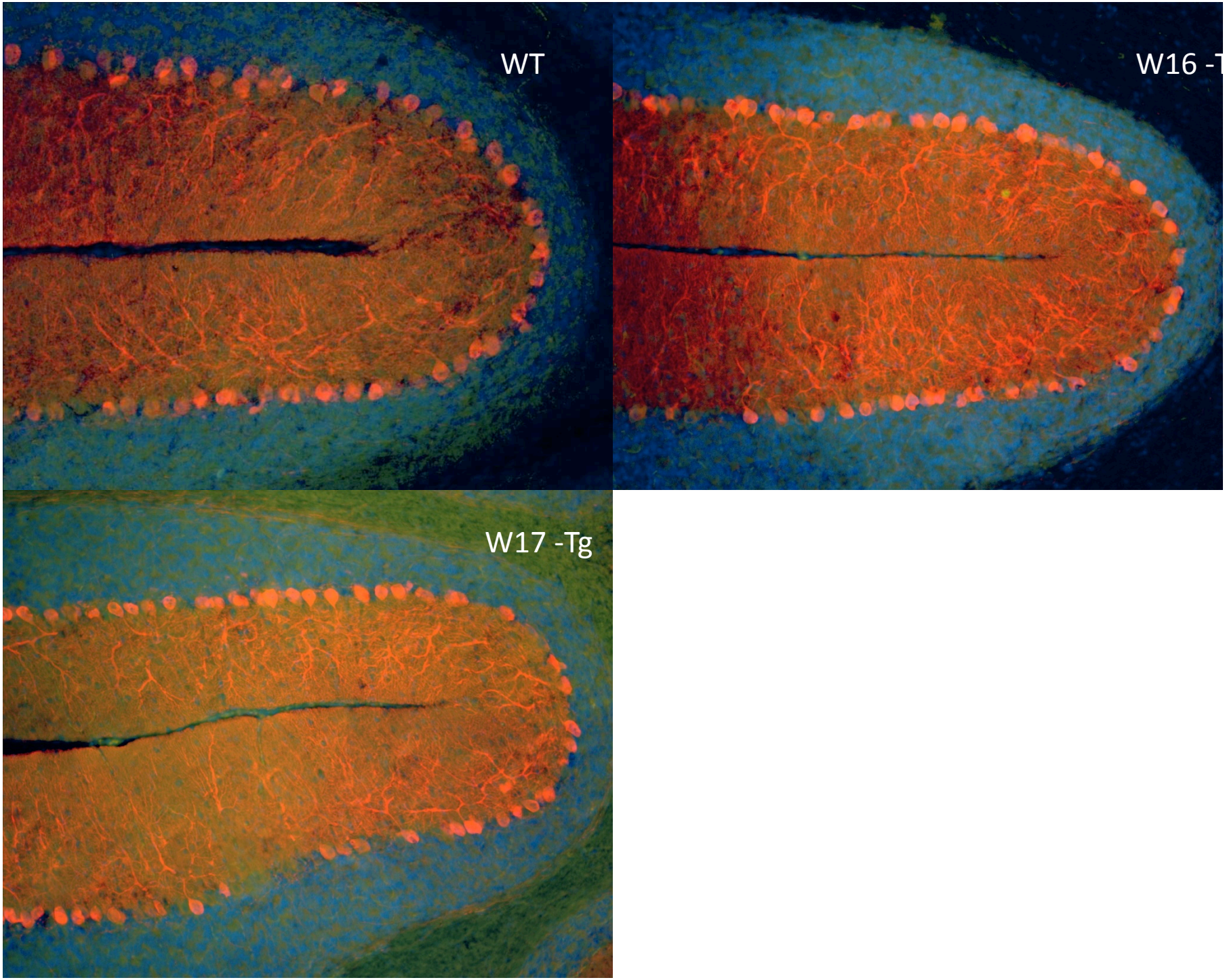
### Comparison of Day 3 means



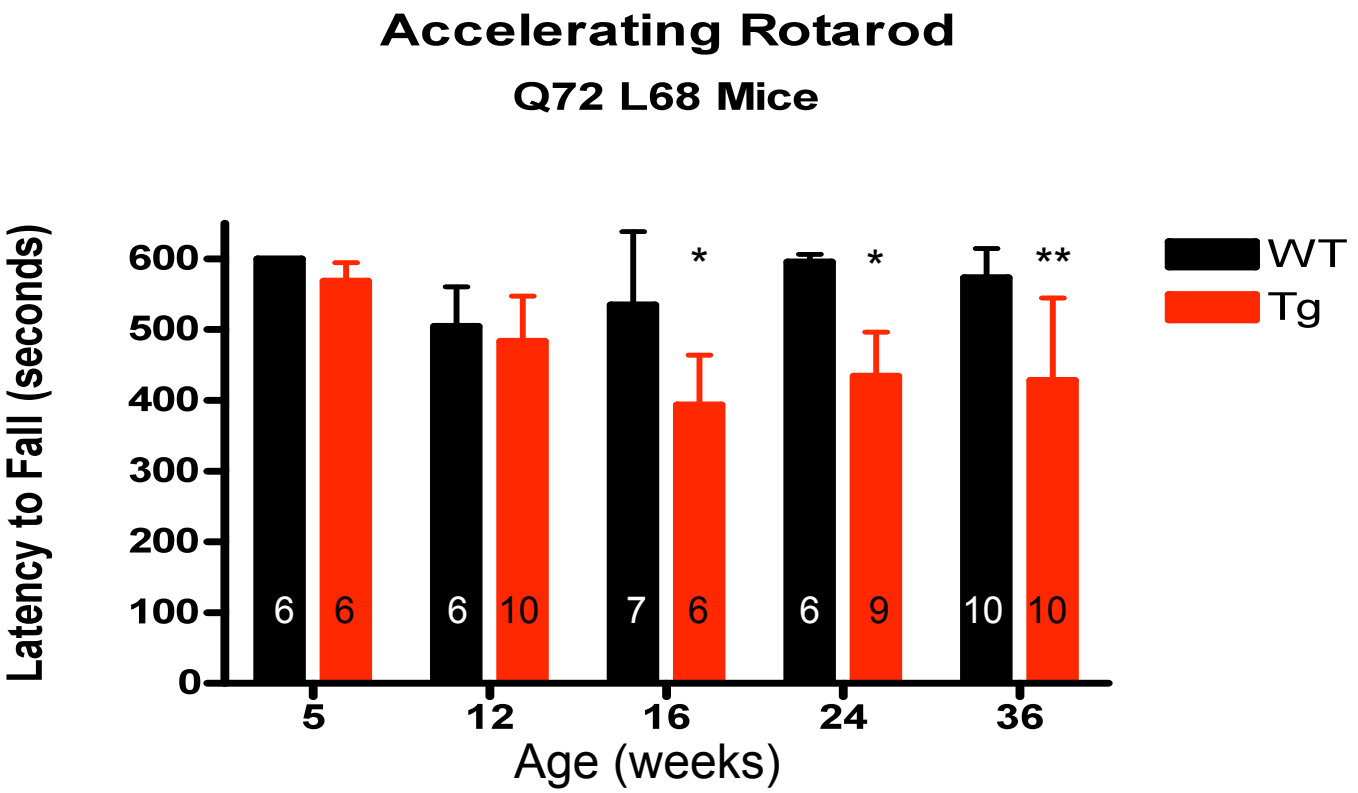

-Comparison between BAC Q22 (W17) mice and wild-type litter mates (8, 16, and 36 weeks of age) of performance on the accelerating rotarod. Mice completed three trials per day for three days. The figure shows the average of all trials per day. Rotarod settings: 4-40 rpm from 0-600 seconds. Two-way ANOVAs followed by Bonferroni post-hoc tests were used to test for statistical significance (*, $p < 0.05$). Error bars represent standard deviation of the mean.


WT
W16 -
W17 -Tg
Q22 – 6 months old
Calbindin (1:333)
At primary fissure


WT
W16
W17 -Tg


WT
W16 -T
W17 -Tg

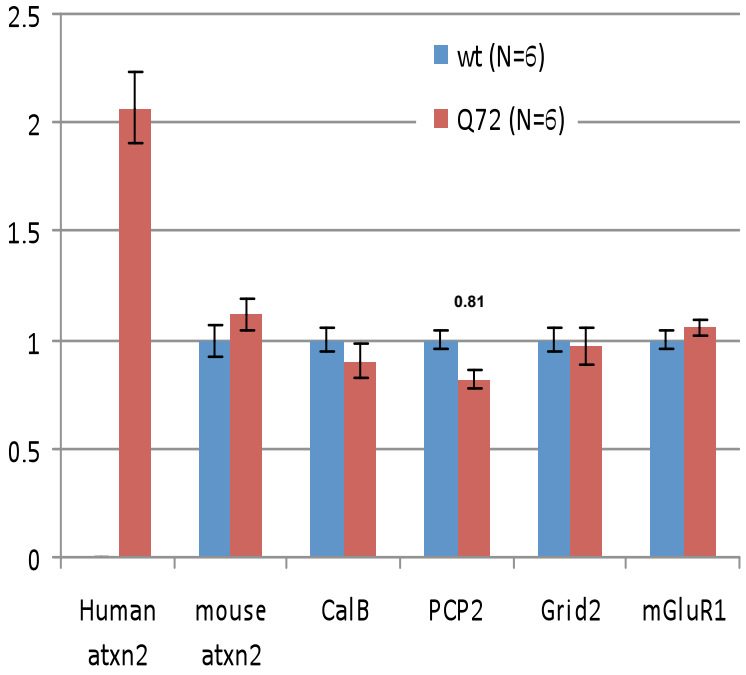
# BAC Q72 Line 68 mice



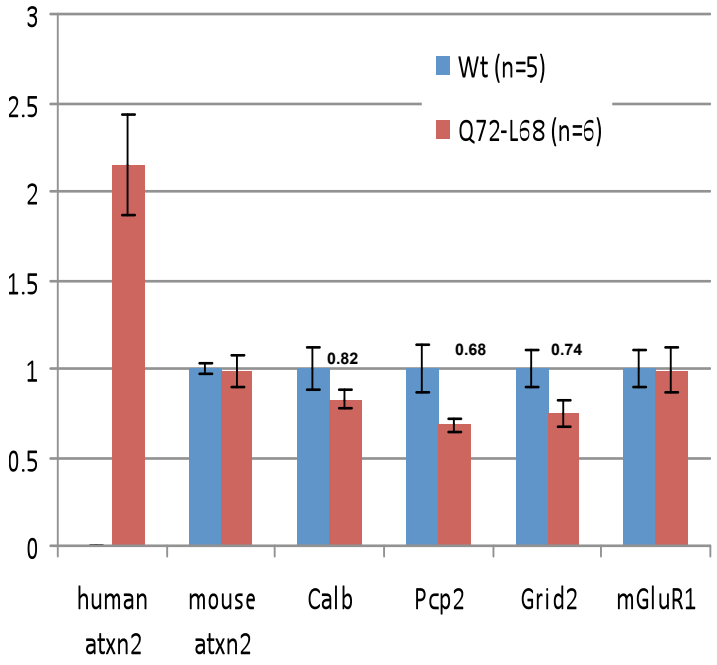

Two-way ANOVA shows a difference between wild-type and transgenic Q72 mice (L68) at 16, 24, and 36 weeks. There are no differences within wild-type or transgenic groups across different ages. Bonferroni post-hoc tests. * $p<0.01$; ** $p<0.0001$

# *Gene expression profile in BAC Q72 Line 68 by qPCR*

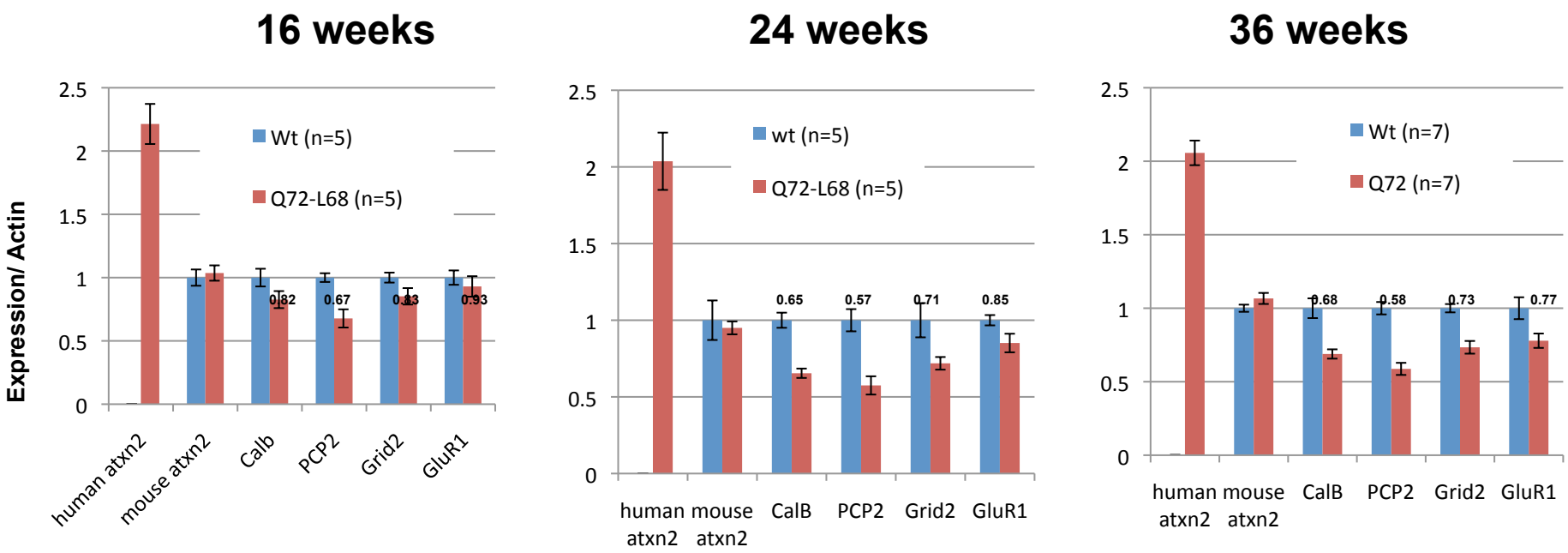
## 5 weeks



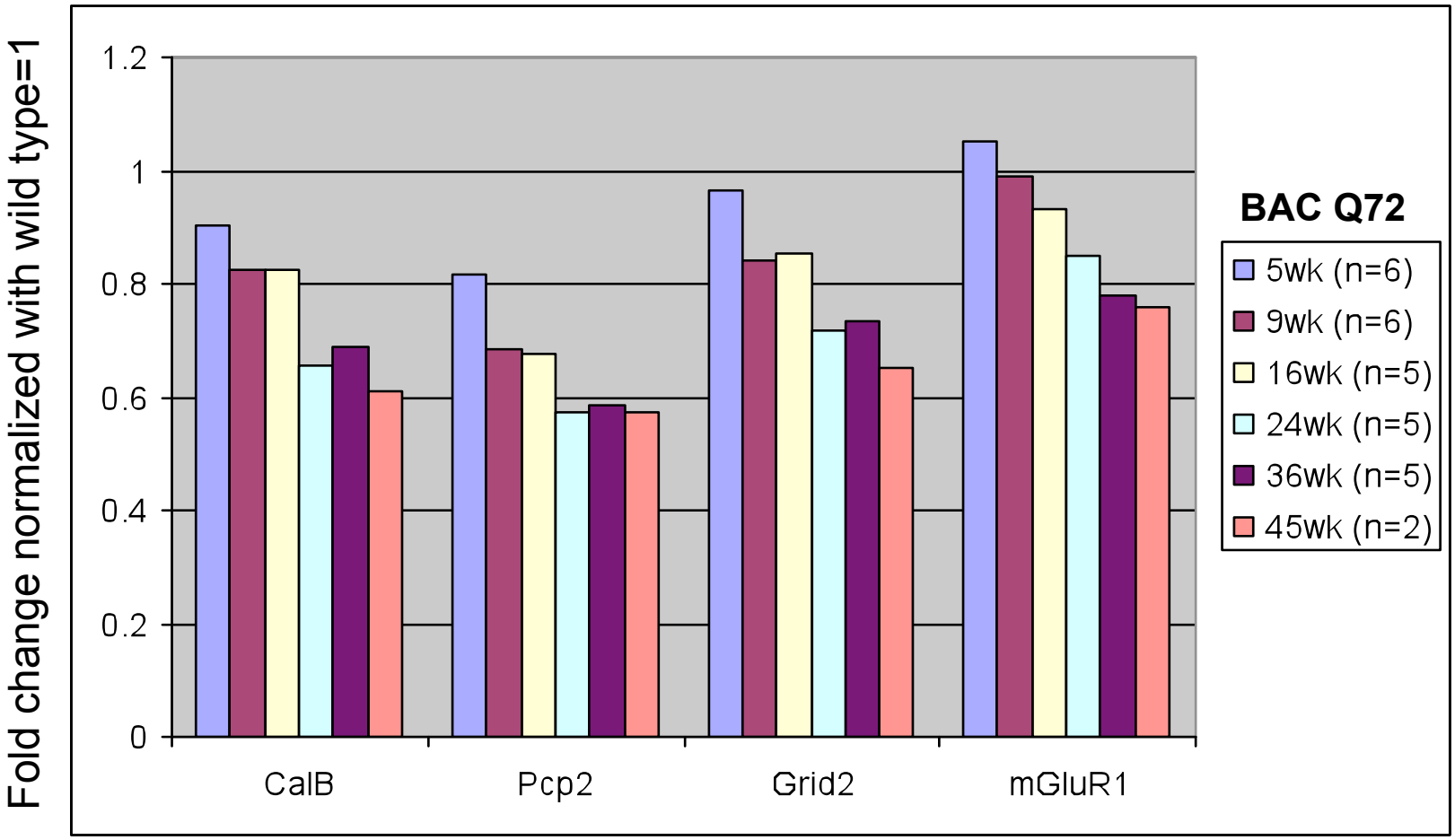

## 9 weeks



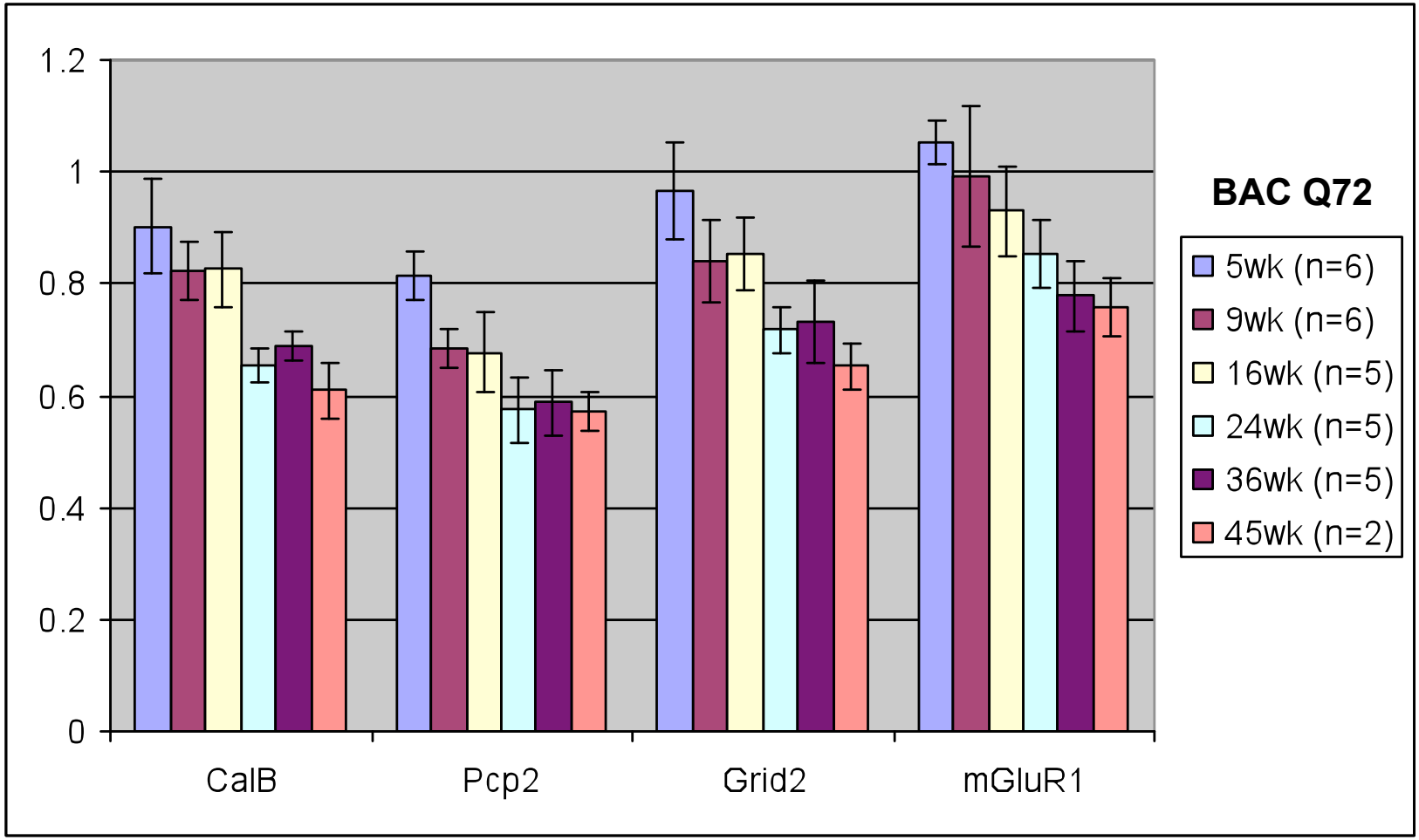
# *Gene expression profile in BAC Q72 Line 68 mice by qPCR*



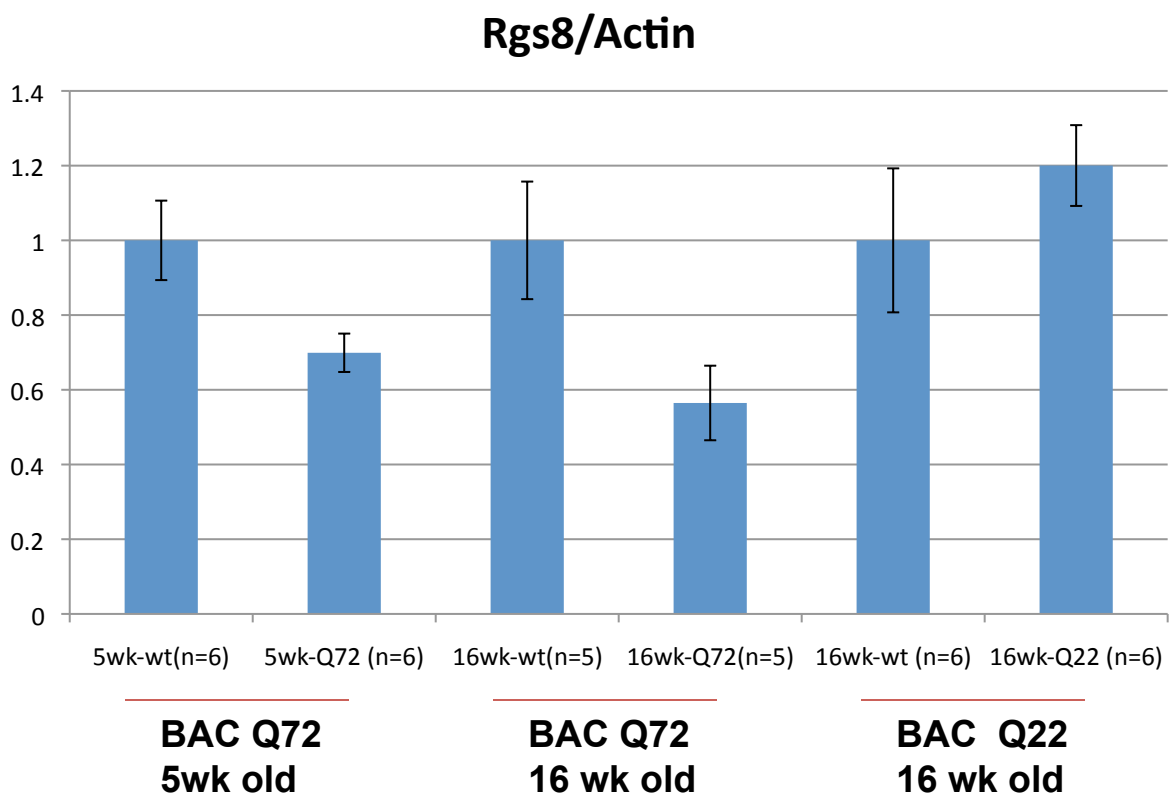
## *Expression of Purkinje cell markers in 6 time points of BAC Q72 L68*



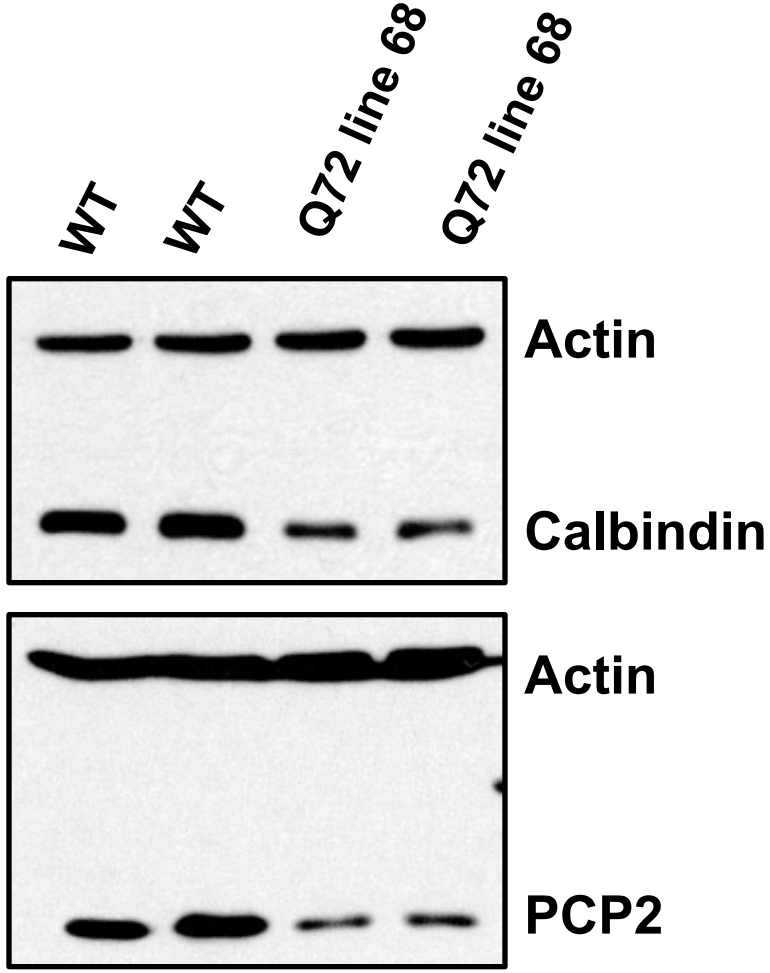
***Expression of Purkinje cell markers in 6 time points of BAC Q72 L68***

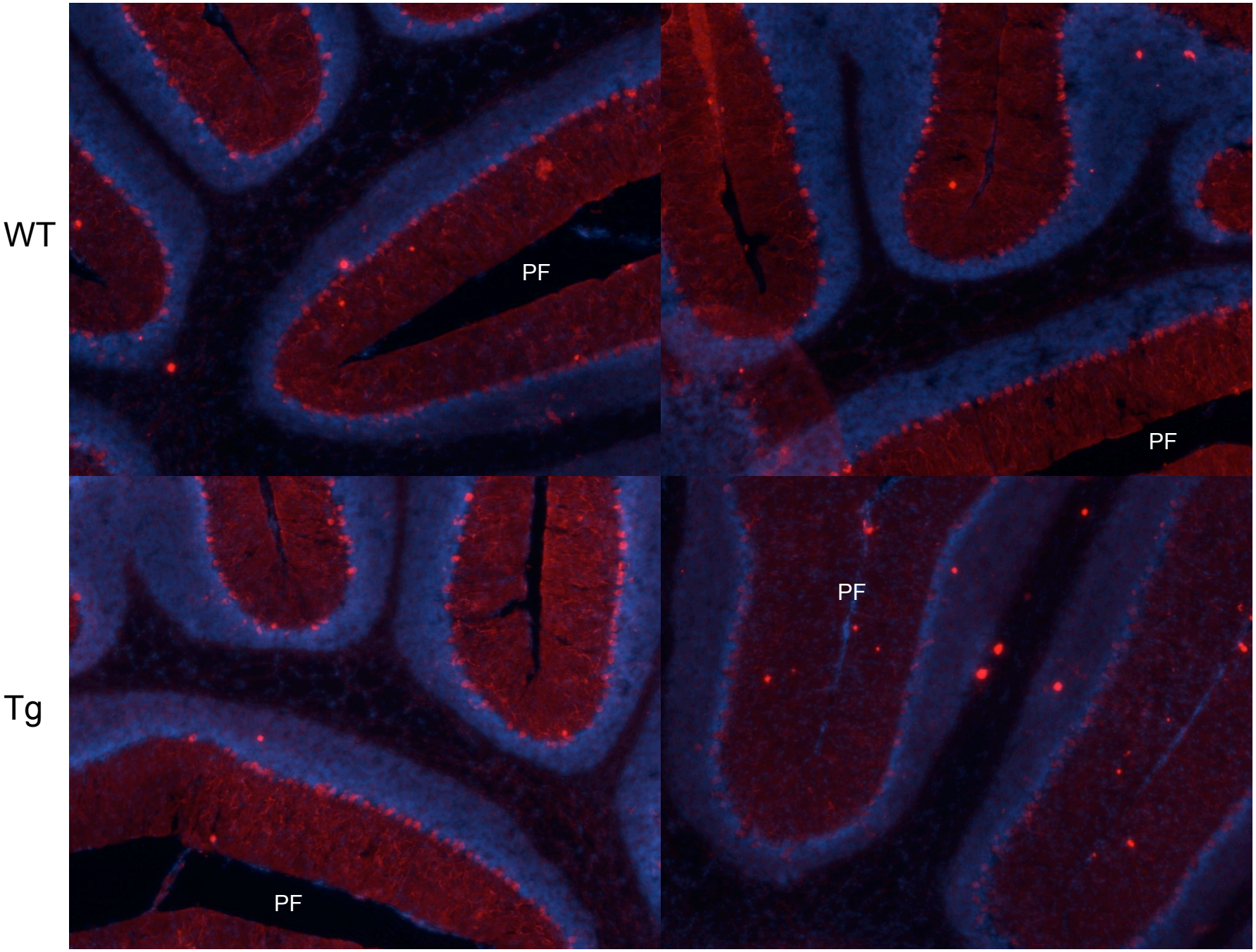


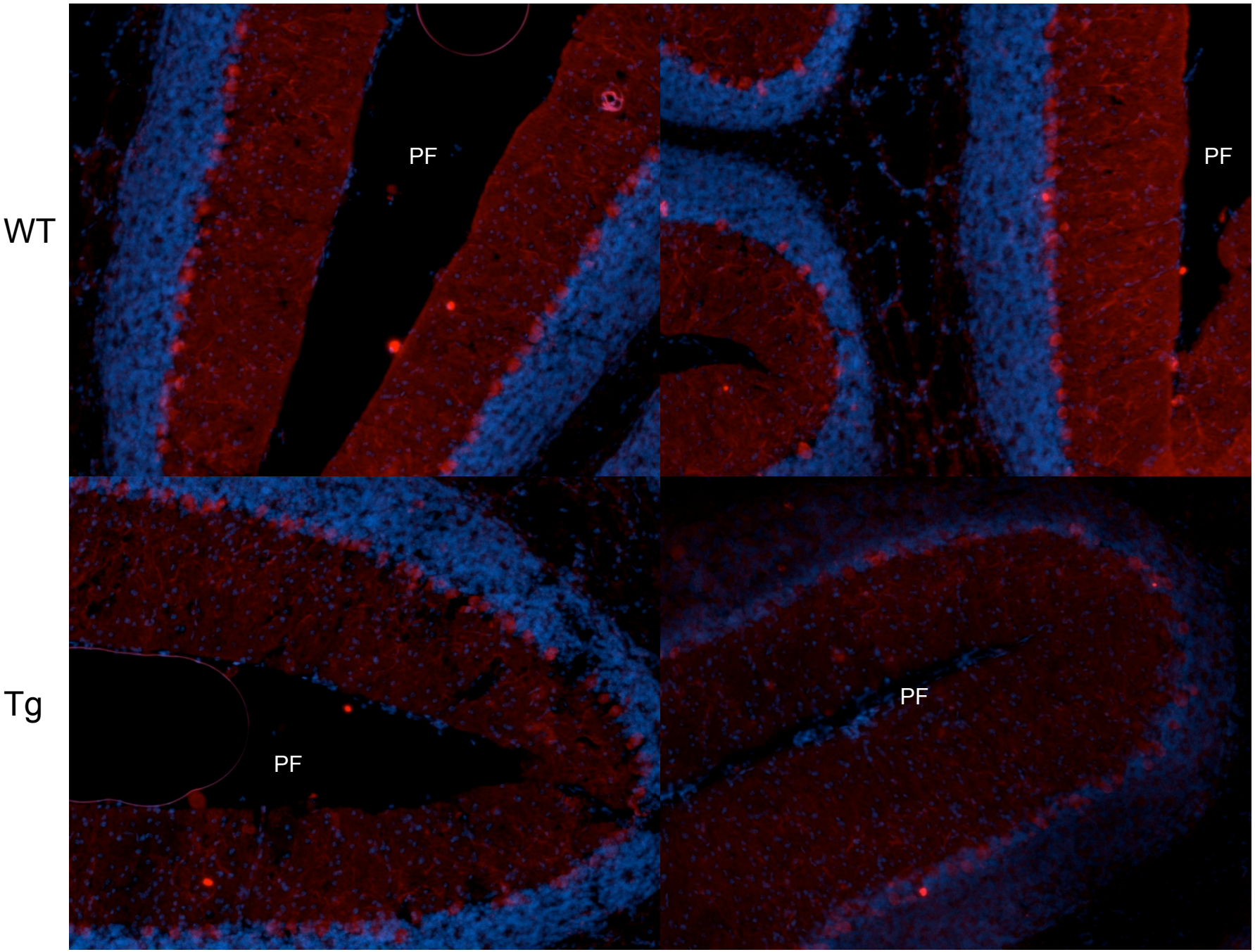
# *Down regulation of Rgs8 in BAC Q72*



***BAC Q72 Line 68 at 24 weeks old***



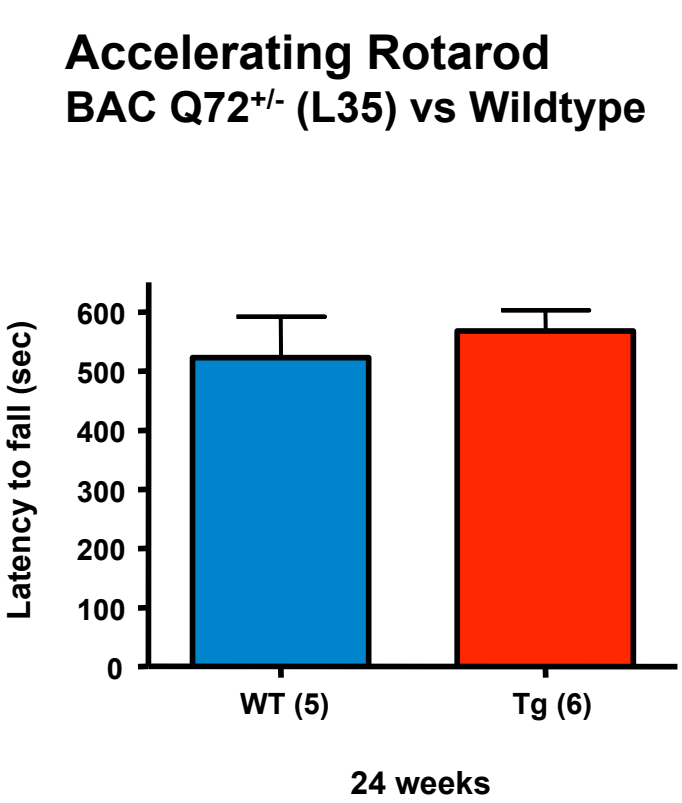

WT
Tg
PF
PF
PF
PF

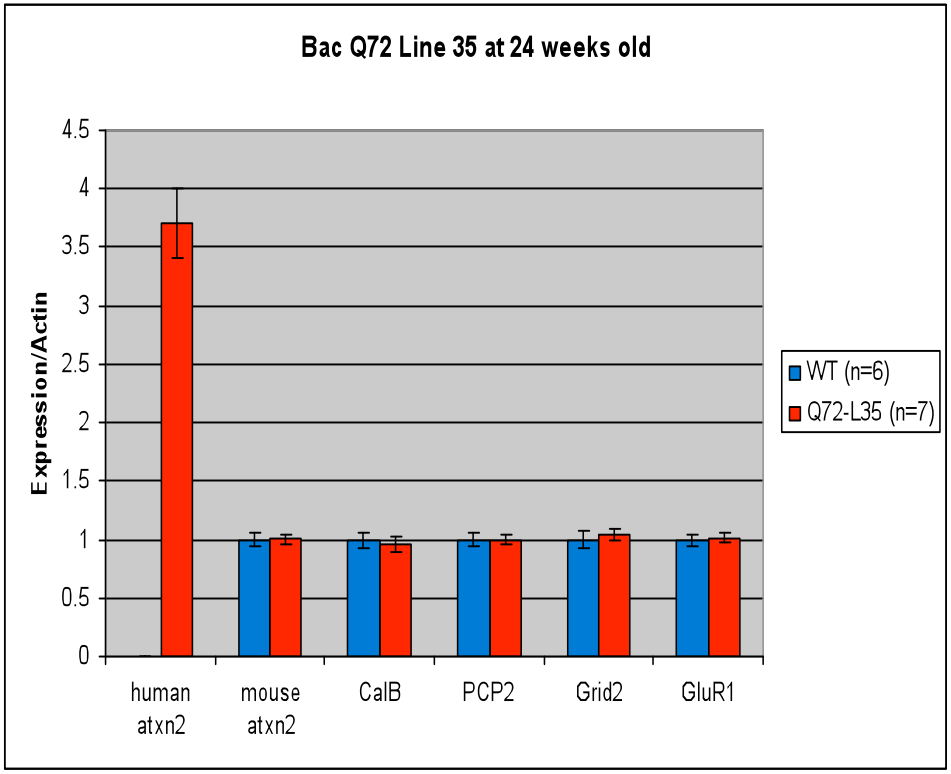

WT
Tg
PF
PF
PF
PF

# Q72 – L68 phenotype

- Tg mice are displaying an open-cage behavioral phenotype (see video).
- Significant difference in weight starting around 12 weeks (same age and same sex).
- Female Tg mice appear to be less fertile.
  - 1 in 8 gave birth. That litter lived only a few days. Female never became pregnant again (two more prolonged attempts).

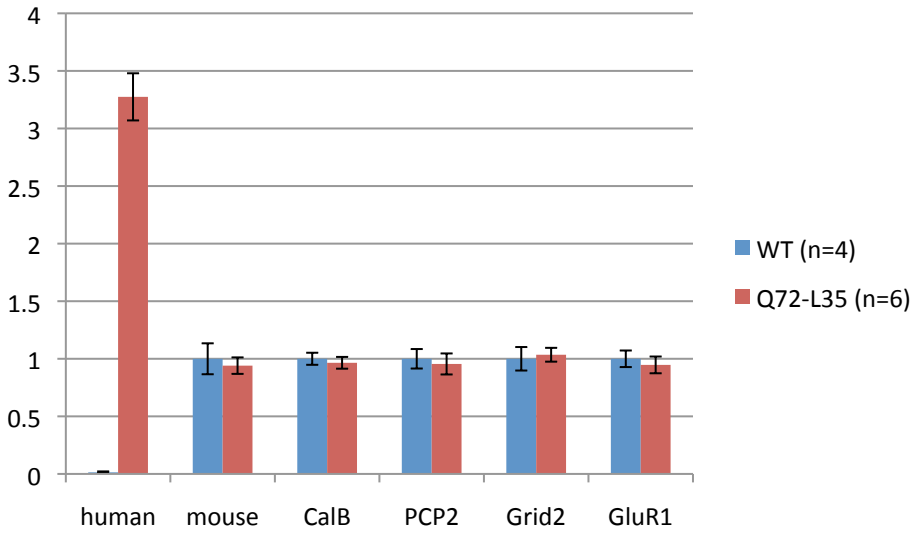
# *BAC Q72 Line 35 at 24 weeks old*




-Comparison between BAC Q72 (L35 line) mice and wild-type litter mates (24 weeks of age) of performance on the accelerating rotarod. Mice completed three trials per day for three days. The figure shows the average of all trials on day 3. Rotarod settings: 4-40 rpm from 0-600 seconds. Two-way ANOVAs followed by Bonferroni post-hoc tests show no difference in rotarod performance.

# BAC *Q72* Line 35 at 36 weeks old

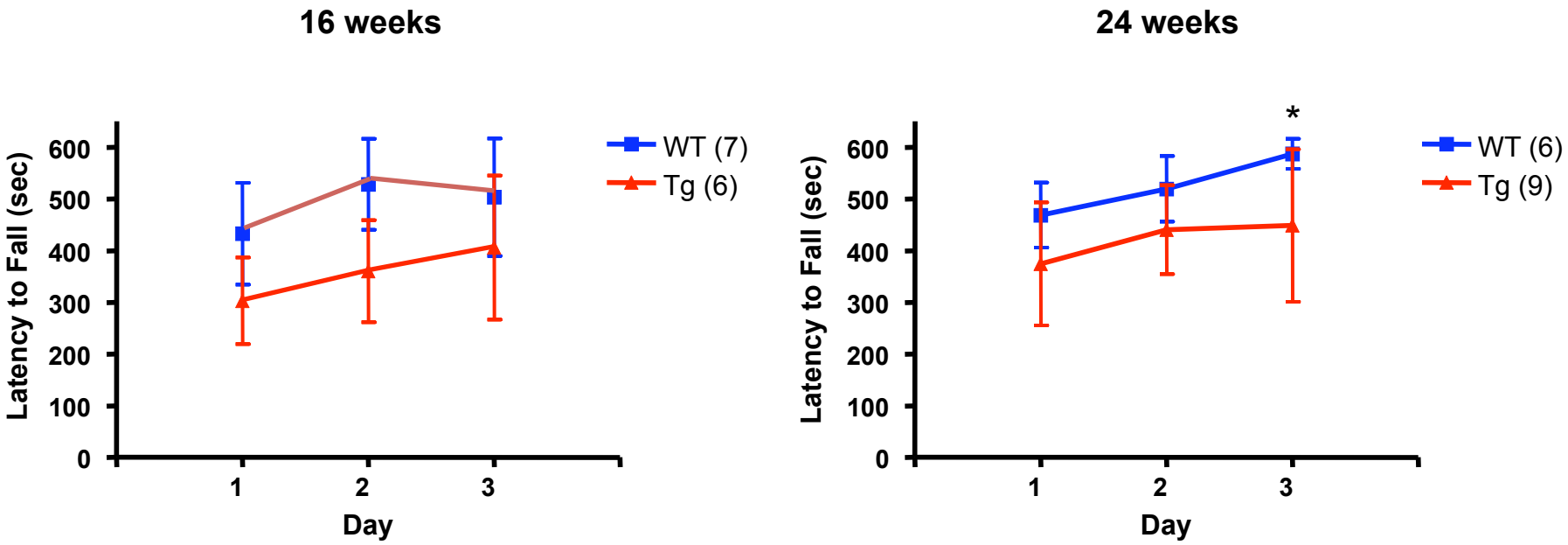


# Q72 – L35 phenotype

- Mice appear healthy
- No difference in weight
- Prolific breeders

# Accelerating Rotarod

## BAC Q72$^{+/-}$ (L68) vs Wildtype

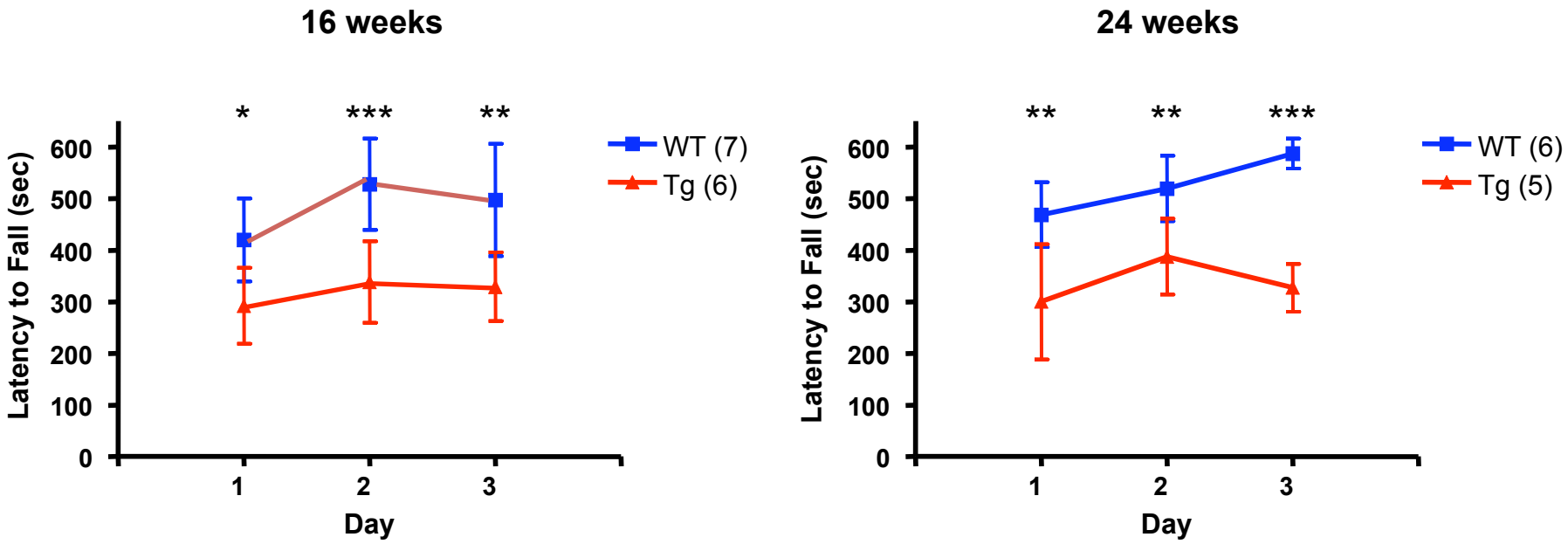



-Comparison between BAC Q72 mice and wild-type litter mates (16 and 24 weeks of age) of performance on the accelerating rotarod. Mice completed three trials per day for three days. The figure shows the average of all trials per day. Rotarod settings: 4-40 rpm from 0-600 seconds. Two-way ANOVAs followed by Bonferroni post-hoc tests were used to test for statistical significance (*, $p < 0.05$).

# Accelerating Rotarod

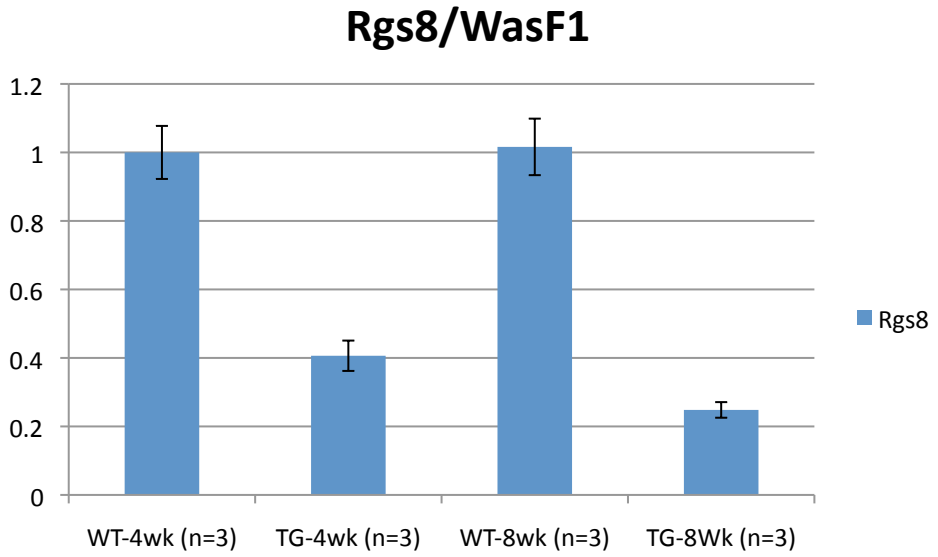
## BAC Q72$^{+/-}$ (L68) vs Wildtype

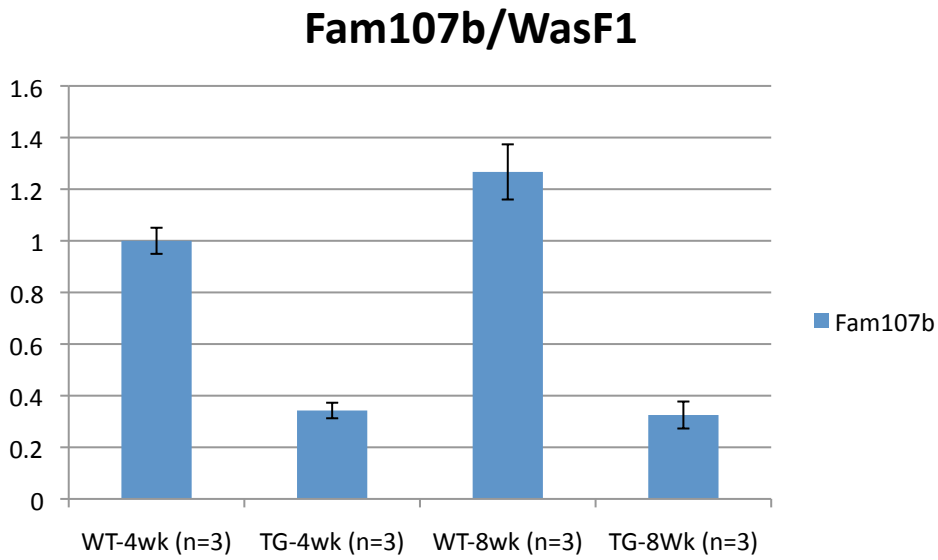
**-corrected for spins and holding**



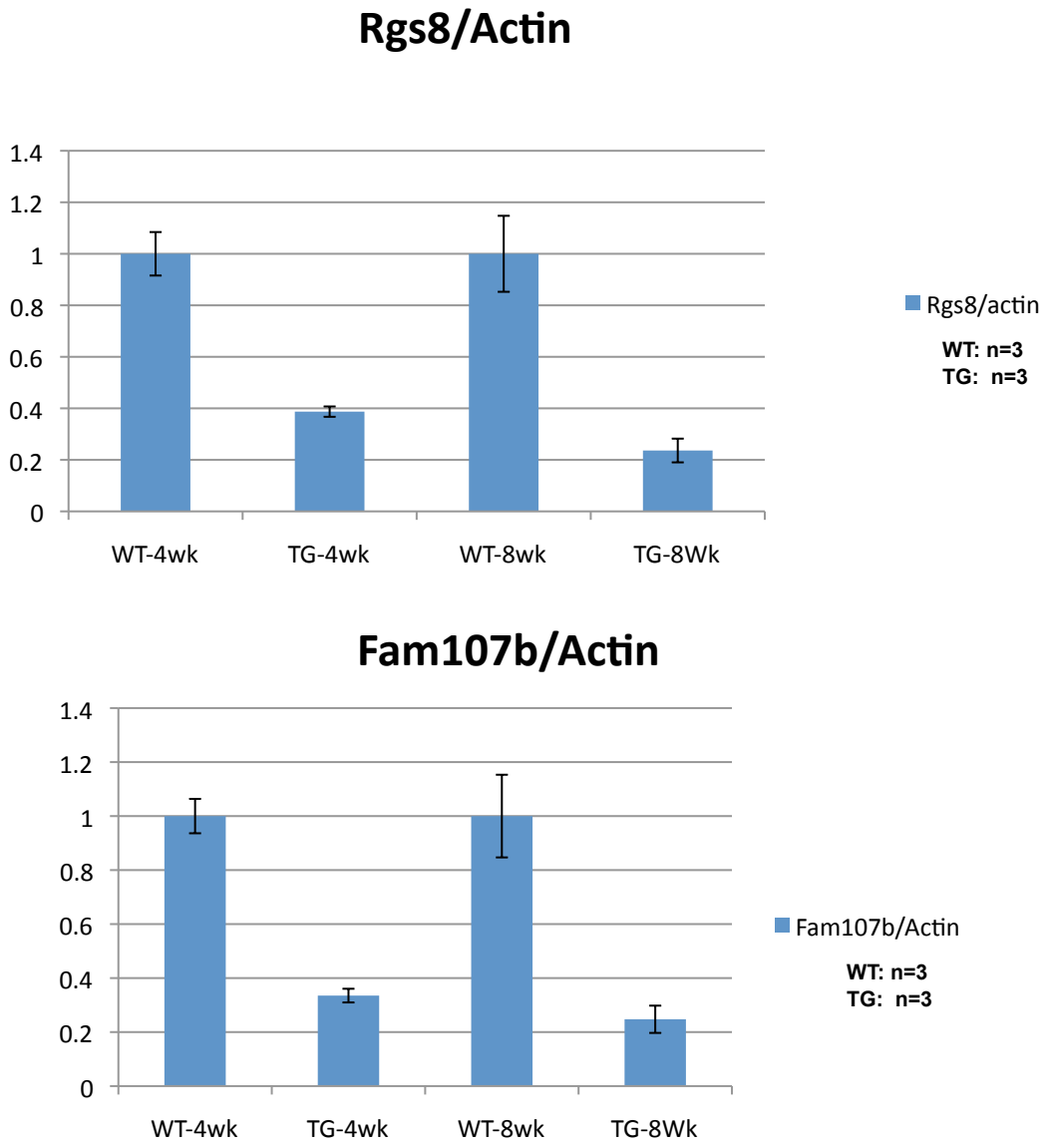

-Comparison between BAC Q72 mice and wild-type litter mates (16 and 24 weeks of age) of performance on the accelerating rotarod similar to previous slide. However, data was corrected for mice that held onto the rod and spun for 5 or more consecutive revolutions. Mice completed three trials per day for three days. The figure shows the average of all trials per day. Rotarod settings: 4-40 rpm from 0-600 seconds. Two-way ANOVAs followed by Bonferroni post-hoc tests were used to test for statistical significance (*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$).

# SCA2-Q127

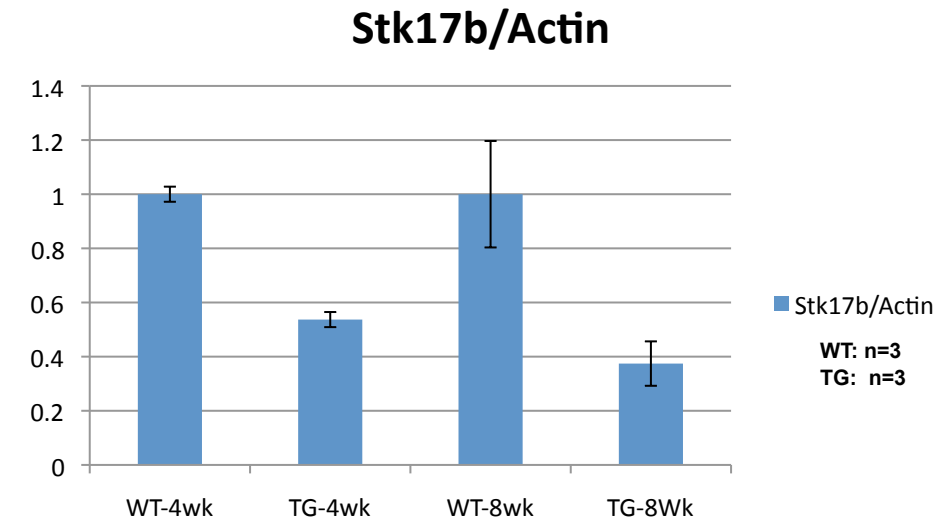

Rgs8/WasF1
1.2
1
0.8
0.6
0.4
0.2
0
WT-4wk (n=3)
TG-4wk (n=3)
WT-8wk (n=3)
TG-8Wk (n=3)
Rgs8

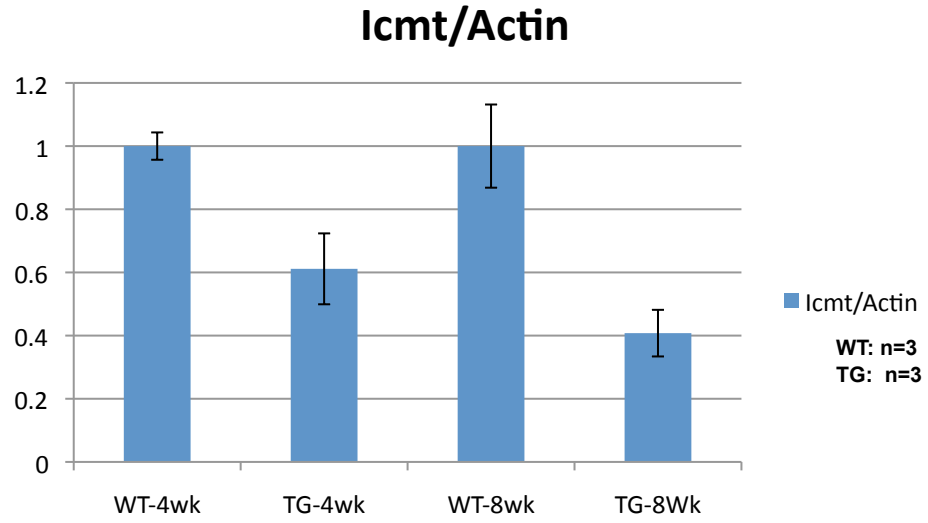

Fam107b/WasF1
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
WT-4wk (n=3)
TG-4wk (n=3)
WT-8wk (n=3)
TG-8Wk (n=3)
Fam107b

# SCA2-Q127


Rgs8/Actin
1.4
1.2
1
0.8
0.6
0.4
0.2
0
WT-4wk
TG-4wk
WT-8wk
TG-8Wk
Rgs8/actin
WT: n=3
TG: n=3
Fam107b/Actin
1.4
1.2
1
0.8
0.6
0.4
0.2
0
WT-4wk
TG-4wk
WT-8wk
TG-8Wk
Fam107b/Actin
WT: n=3
TG: n=3

# SCA2-Q127


Stk17b/Actin
1.4
1.2
1
0.8
0.6
0.4
0.2
0
WT-4wk
TG-4wk
WT-8wk
TG-8Wk
Stk17b/Actin
WT: n=3
TG: n=3


Icmt/Actin
1.2
1
0.8
0.6
0.4
0.2
0
WT-4wk
TG-4wk
WT-8wk
TG-8Wk
Icmt/Actin
WT: n=3
TG: n=3