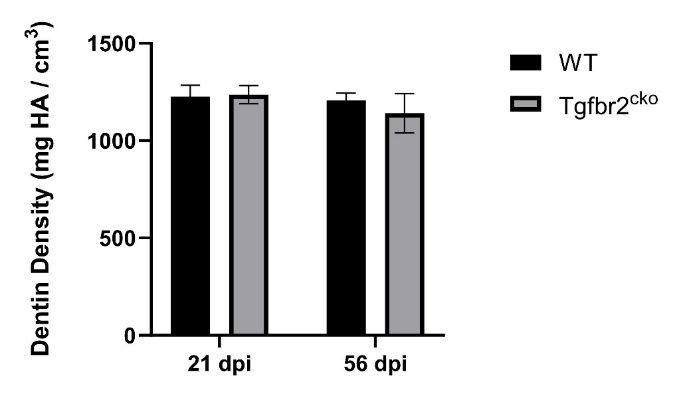
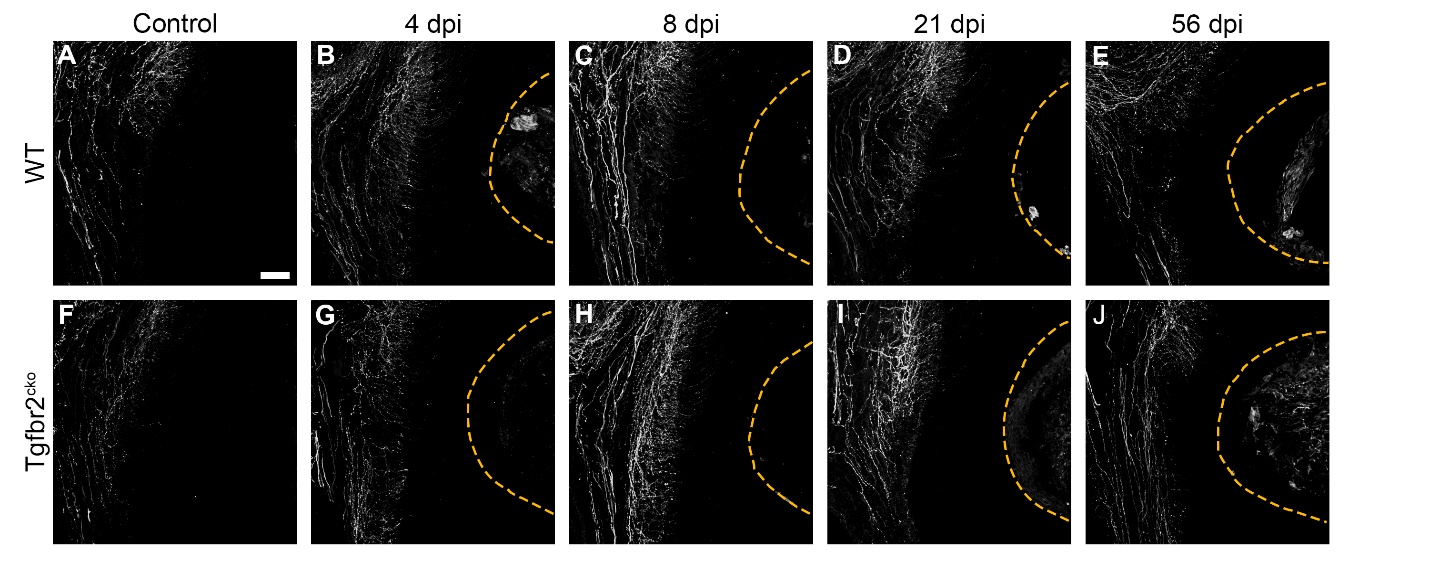
**Appendix A**



**Figure A1. Micro-CT analysis of dentin density.** No differences in dentin density were found at 21 or 56 dpi between WT and Tgfbr2cko M1s.



**Figure A2. Isolated CGRP+ axon sprouting in response to injury.** Timeline of isolated CGRP+ axon outgrowth (white) in uninjured, and 4, 8, 21, and 56 dpi WT (A-E) and Tgfbr2cko (F-J) M1s, demonstrating divergent outgrowth patterns from 4-21 dpi between genotypes. Dotted yellow lines indicate areas of dentin injury. Scale bar in (A) = 50 μm.

**Table A1. Results from the fitted GEE, accounting for repeated measures from evaluating two sections from each sample.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **term** | **estimate** | **std.error** | **statistic** | **p.value** |
| Intercept | 1875690 | 199702 | 88.218 | <0.0001 |
| WT | 355742 | 272975 | 1.698 | 0.1925 |
| Ctl | -301958 | 302287 | 0.998 | 0.3178 |
| 8dpi | 92072 | 308701 | 0.089 | 0.7655 |
| 21dpi | 355390 | 335635 | 1.121 | 0.2897 |
| 56dpi | -548734 | 463553 | 1.401 | 0.2365 |
| WT:Ctl | -719330 | 412341 | 3.043 | 0.0811 |
| WT:8dpi | -560670 | 413896 | 1.835 | 0.1755 |
| WT:21dpi | -1161959 | 407350 | 8.137 | 0.0043 |
| Ctl:8dpi | -93531 | 414278 | 0.051 | 0.8214 |
| Ctl:21dpi | -18368 | 448516 | 0.002 | 0.9673 |
| WT:56dpi | -824827 | 521689 | 2.5 | 0.1139 |
| WT:Ctl:8dpi | 1354414 | 581367 | 5.428 | 0.0198 |
| WT:Ctl:21dpi | 921794 | 576407 | 2.557 | 0.1098 |
| Reference group: Tgfbr2cko, Day 4, injured | | | | |

Generalized Estimating Equations (GEE) is a method for fitting (generalized) linear regression models to clustered data, which yields from having more than one measurement per mouse. By using the Huber-White method to estimate standard errors, valid inferential results are expected even when the working correlation is misspecified. In particular, we considered an identity link, normal variance, and working independence. The injured group was used as reference (as opposed to the control) since data from 56 dpi was only available for injured mice. However, results are equivalent since only two groups (injured and control) were considered. Overall, A:B denotes the interaction term between factor A and factor B, and A:B:C denotes the 3-way interaction between factors A, B, and C. The statistically significant findings are described below:

* WT:21dpi: The change from 4 dpi CGRP to 21 dpi CGRP in Wild Type mice is significantly different than the change from 4 dpi CGRP to 21 dpi CGRP in Tgfbr2cko mice. In other words, the effect of changing dpi from 4 to 21 is significantly different between genotypes, with a p-value of 0.00434.
* The difference in the change from Day 4 dpi CGRP to Day 8 dpi CGRP between Wild Type mice and Tgfbr2cko mice in control teeth is significantly different than the difference in the change from Day 4 dpi CGRP to Day 8 dpi CGRP between Wild Type mice and Tgfbr2cko mice in injured teeth, with a p-value of 0.0198.

Taken together, this indicates that due to the long time period in which the axon sprouting is equivalent at the beginning and at the end, we found many similarities between the CGRP levels. However, we found that the timeline from 4 dpi to 21 dpi was different between the genotypes, indicating a differential healing response via CGRP.