

The effects of PAK1 deletion on cardiomyocyte contraction and Ca^{2+} release in neonatal mouse ventricular myocytes

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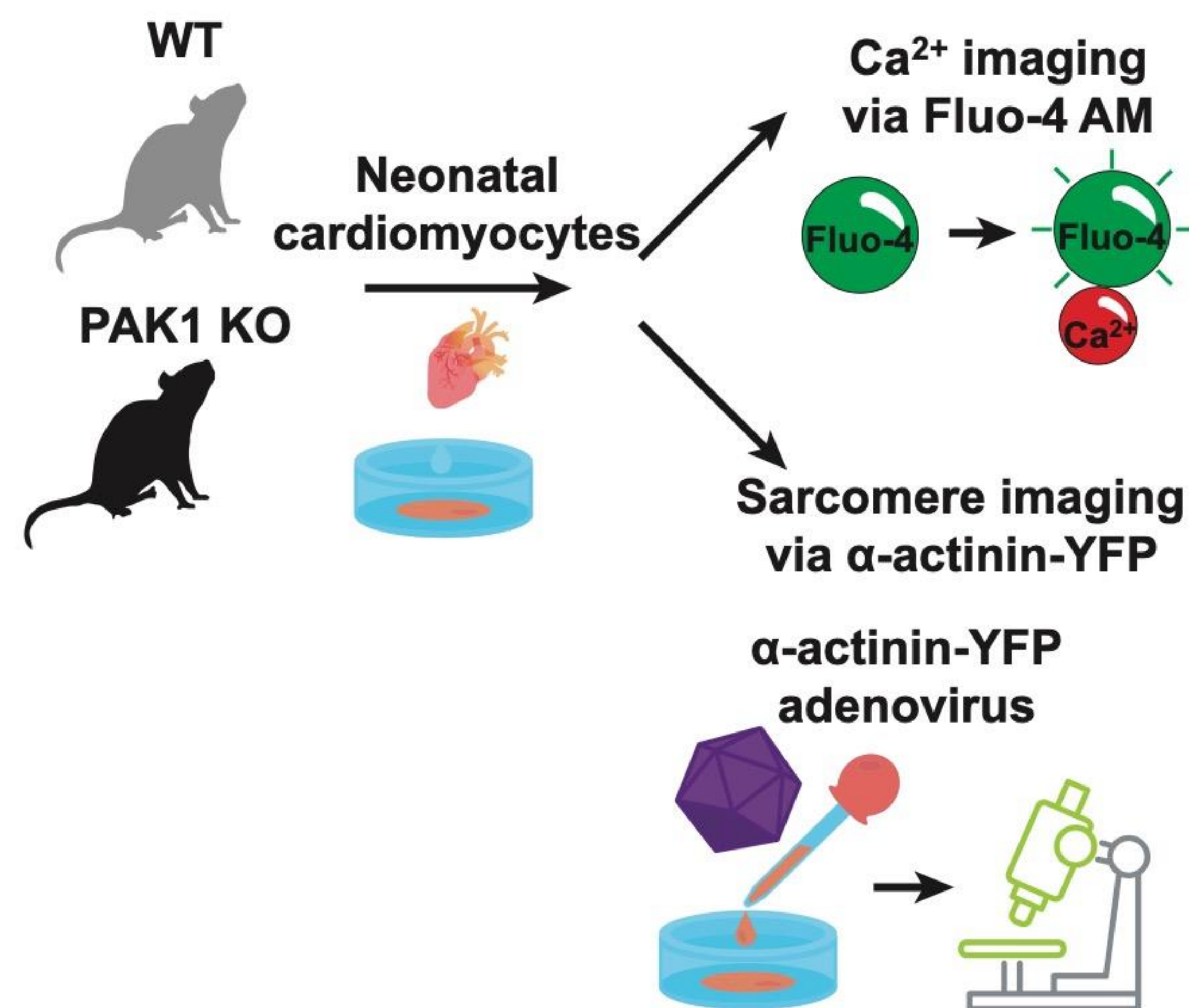
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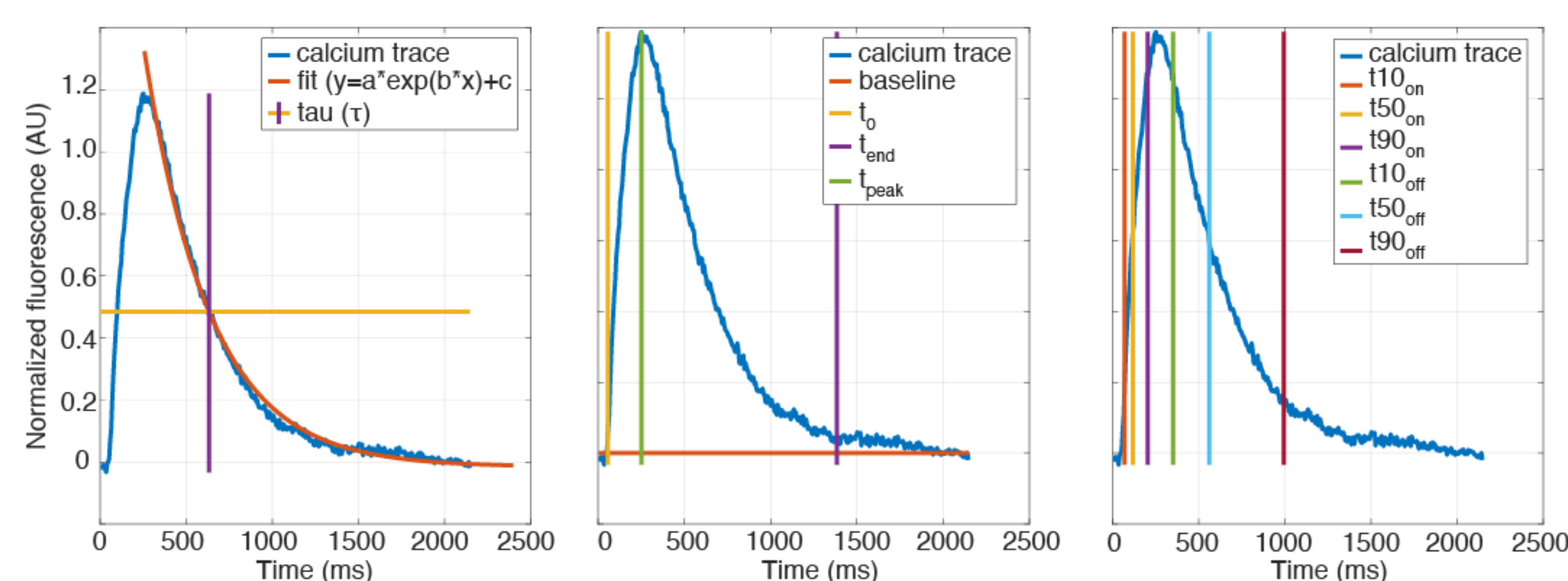
Introduction

- PAK1 is a protein kinase known for influencing the structure and motility of cells.
- In adult mouse cardiomyocytes, the removal of PAK1 results in decreased calcium ion (Ca^{2+}) release and contraction rates.
- This research focuses on determining whether PAK1 deletion in neonatal cardiomyocytes influences Ca^{2+} release and sarcomere contraction rates.
- Analyzed Wild-Type (WT) and Knockout (KO) sarcomere microscopy videos via video analysis softwares SarcTrack and CalTrack.
- Significant findings could support a novel therapeutic for heart disease patients.

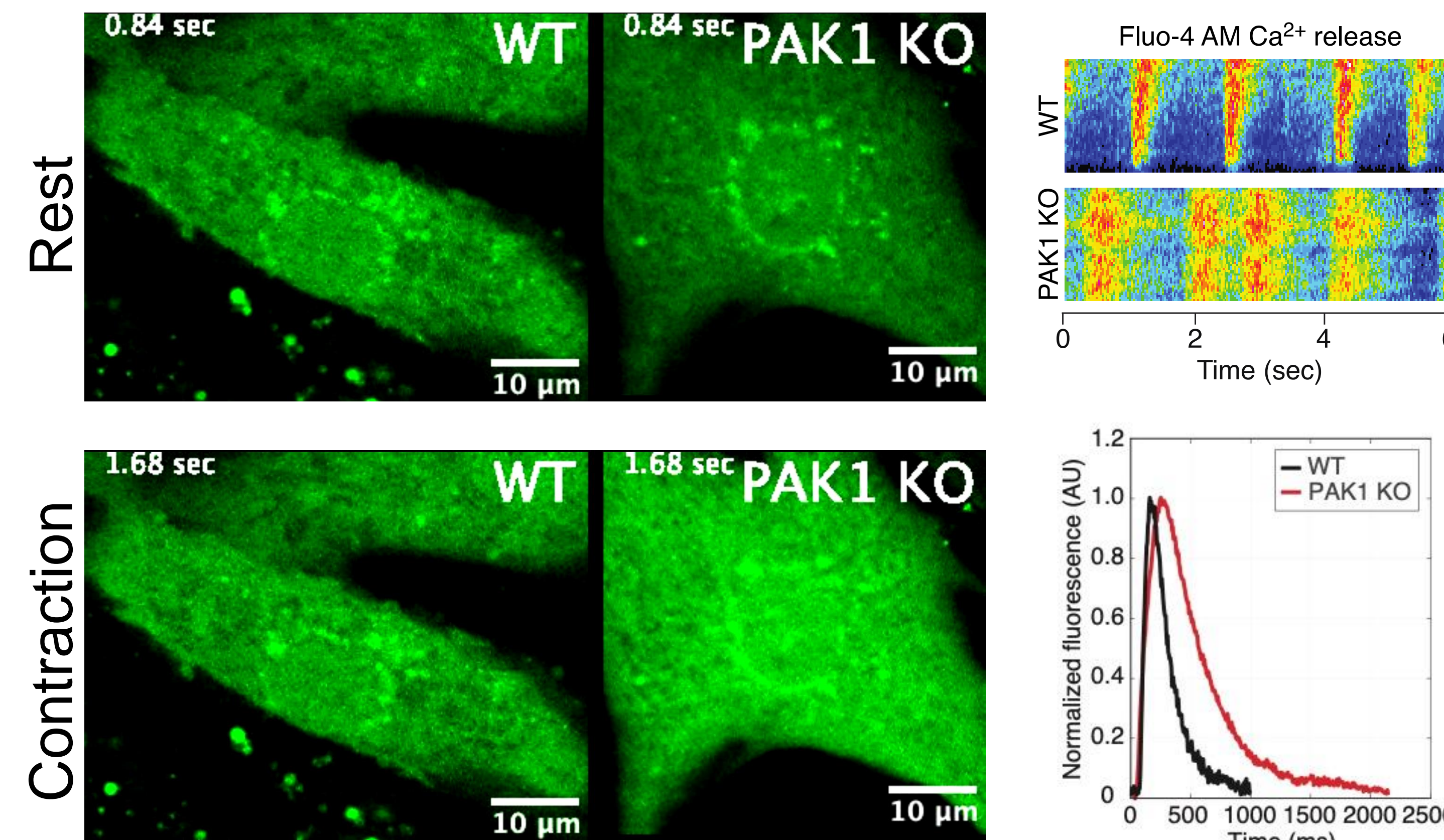
Materials and Methods



Ca²⁺ kinetics curve fitting parameters

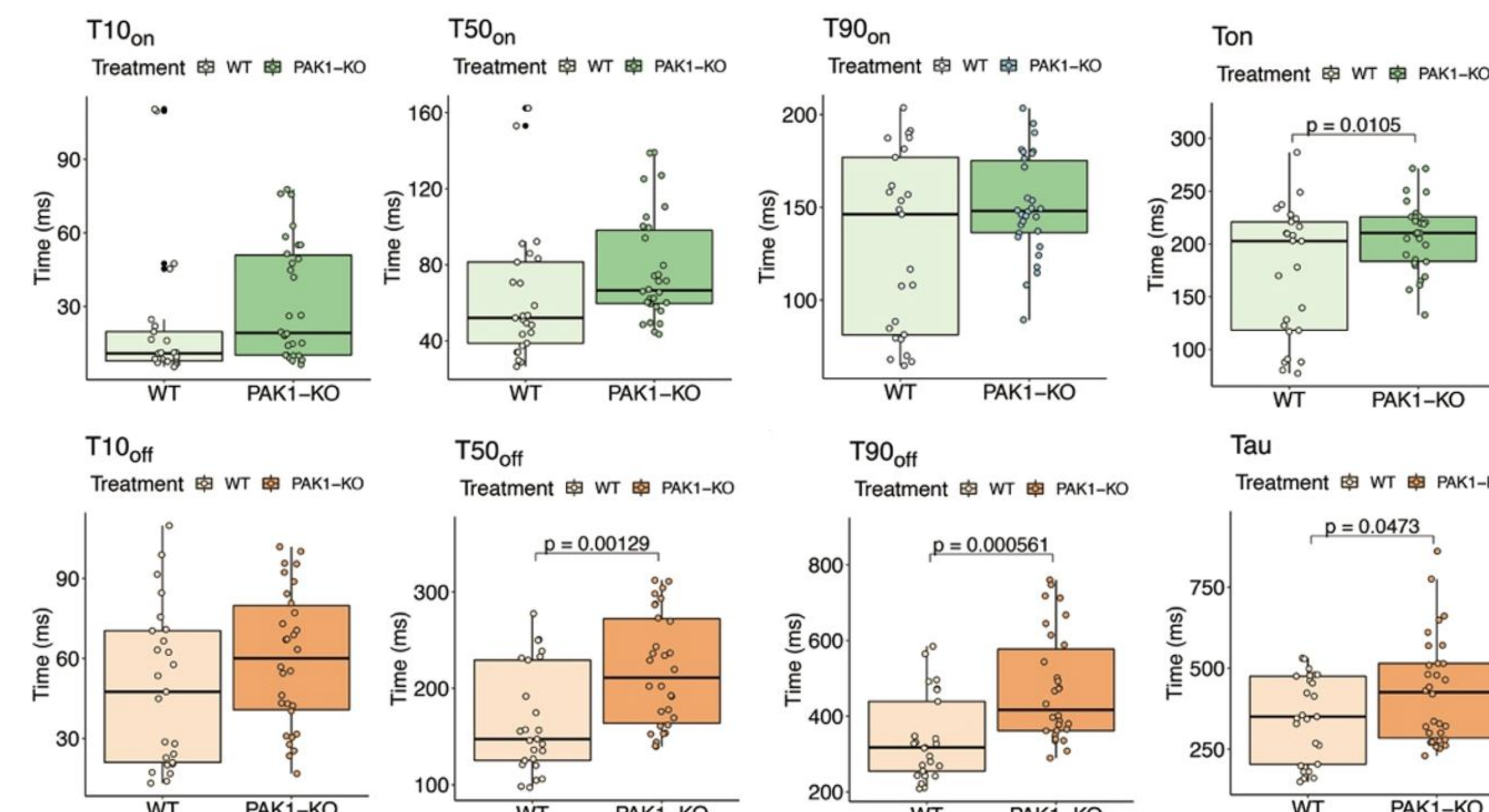


Ca²⁺ kinetics are slowed in PAK1 KOs



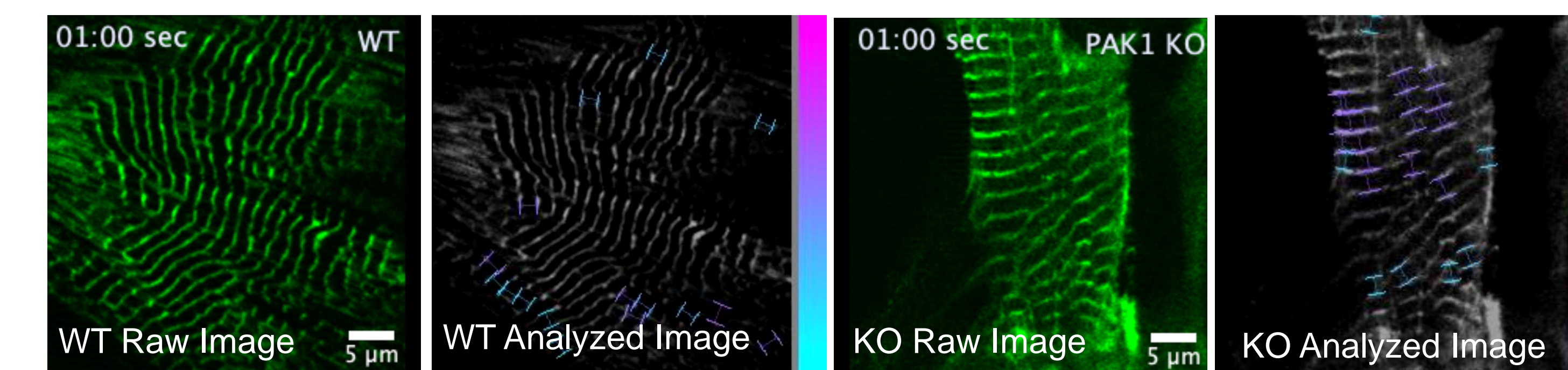
- Ca^{2+} ions tagged with Fluo-4 AM fluorescent indicator.
- Ca^{2+} released during contraction, absorbed during relaxation.
- Ca^{2+} release takes longer in PAK1 KO than WT.

PAK1 KOs exhibit delayed Ca²⁺ release and reuptake kinetics

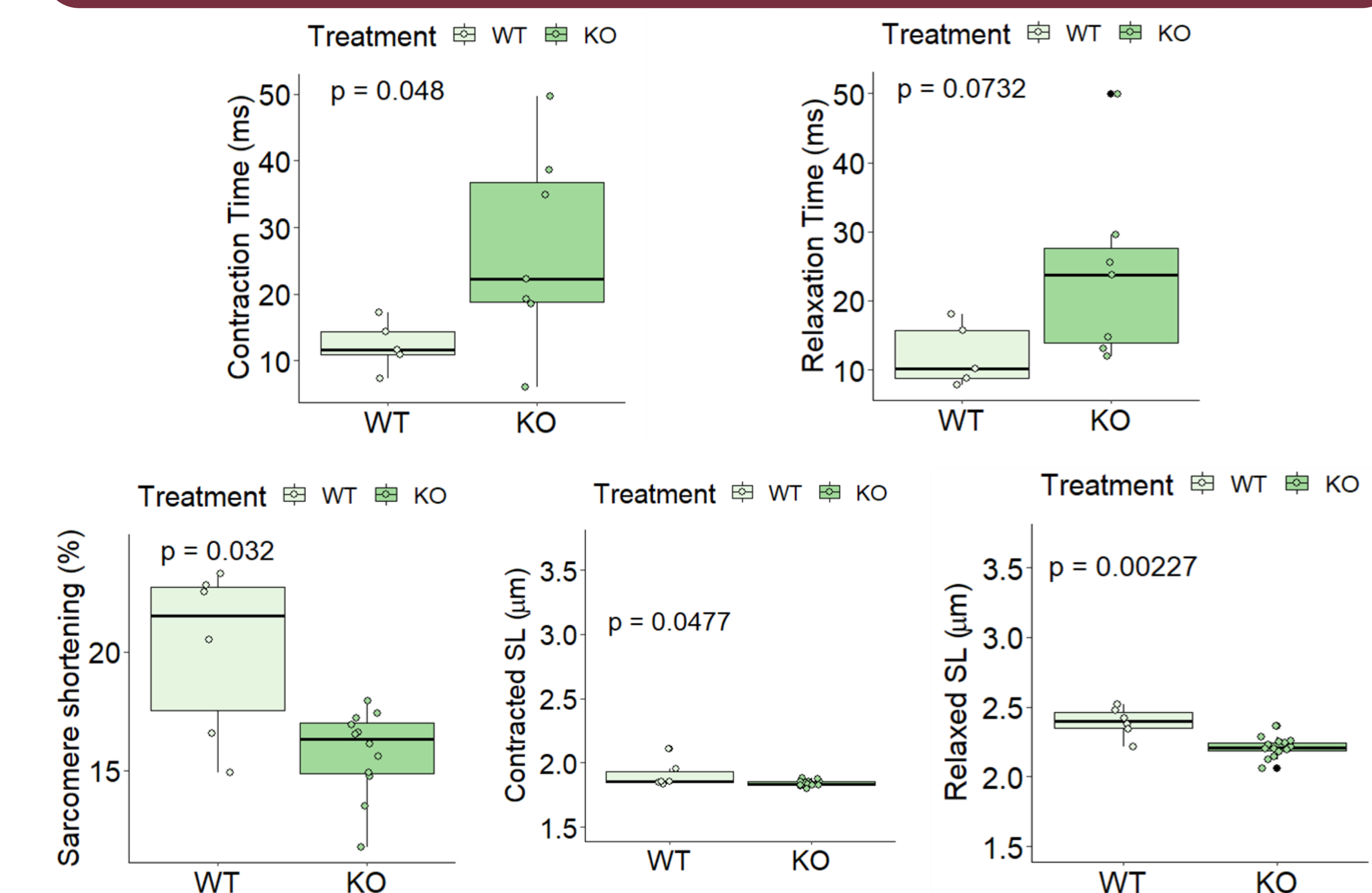


- Contraction time is significantly longer in PAK1 KO than WT.
- Sarcomere shortening percent, contracted length, and relaxed length were all significantly longer in PAK1 WT than KO.

Shortening dynamics tracked by α -actinin-YFP



PAK1 KO delays contractile kinetics as well as percent shortening



Conclusions

- PAK1 KO reduces Ca^{2+} release and reuptake kinetics
- PAK1 KO delays contractile kinetics as well as percent shortening and sarcomere lengths
- Overall, PAK1 KO reduces the kinetics of contraction and relaxation in neonatal cardiomyocytes

References

1. Batra, A., et. al. (2021). Molecular and cellular biochemistry, 476, 1337-1349.
2. Toepfer, C. N., et. al. (2019). Circulation research, 124(8), 1172-1183.
3. Psaras, Y., et. al. (2021). Circulation research, 129(2), 326-341.