Therapeutic discovery for pain

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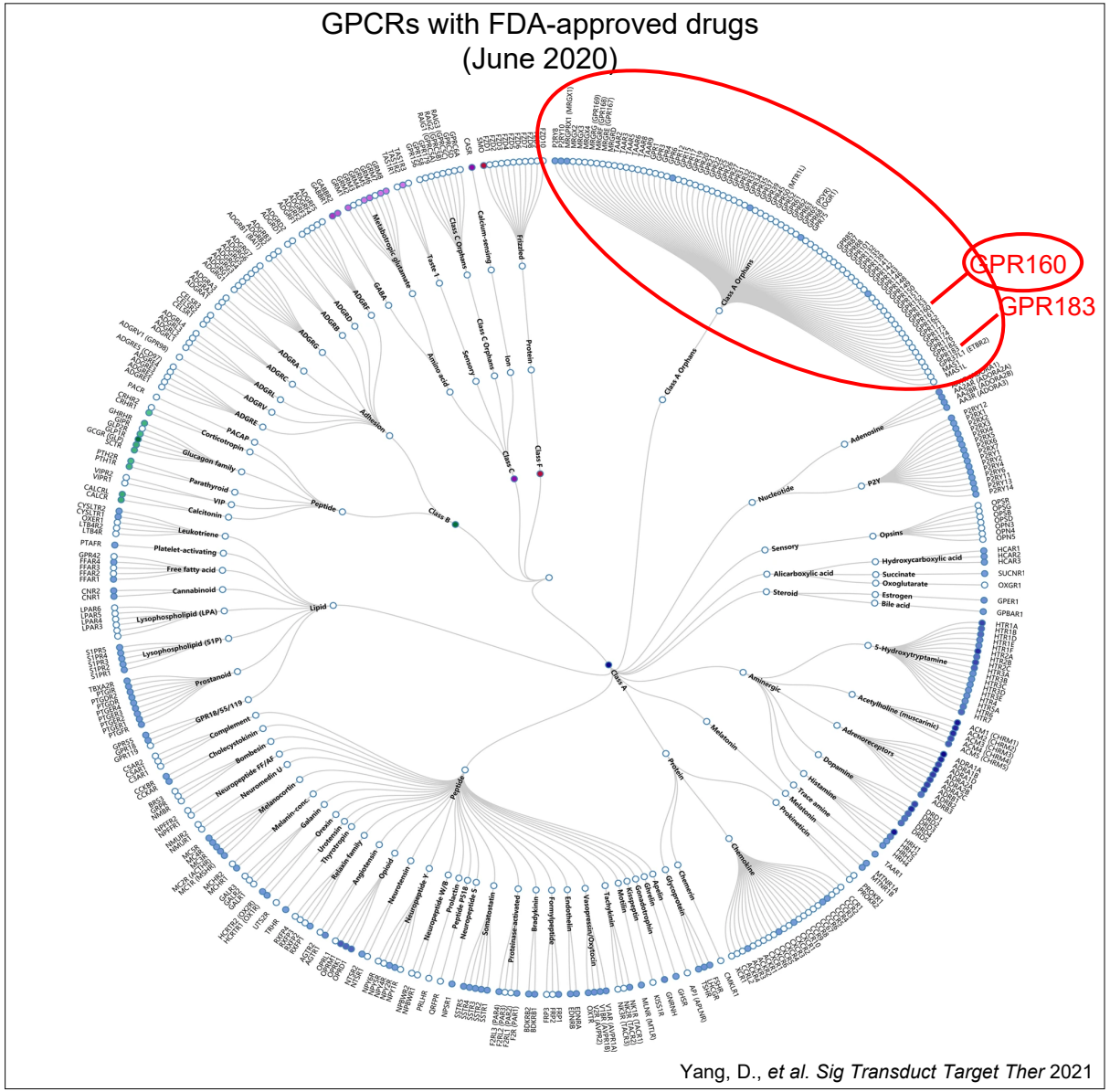
G protein-coupled receptors (GPCRs), the largest class of membrane proteins, represent the most druggable targets to make it to market

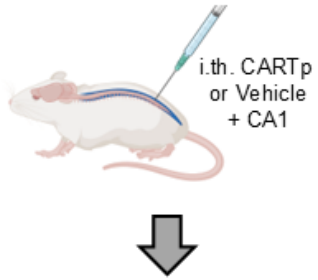
- There are 826 human GPCRs.
- ~350 non-olfactory GPCRs are considered druggable
- ~175 GPCRs are validated drug targets (Yang et al., 2020)
- The rapid increase in structural studies have yielded
  - 1,296 GPCR structures
  - 842 GPCR structure models
  - 743 refined models
- ~35% of all FDA-approved drugs target GPCRs (527 drugs) (Yang et al., 2020).
- Yet, there are ~120 orphan GPCRs whose endogenous ligands are still not known.
- Only a few FDA-approved drugs target orphan GPCRs.



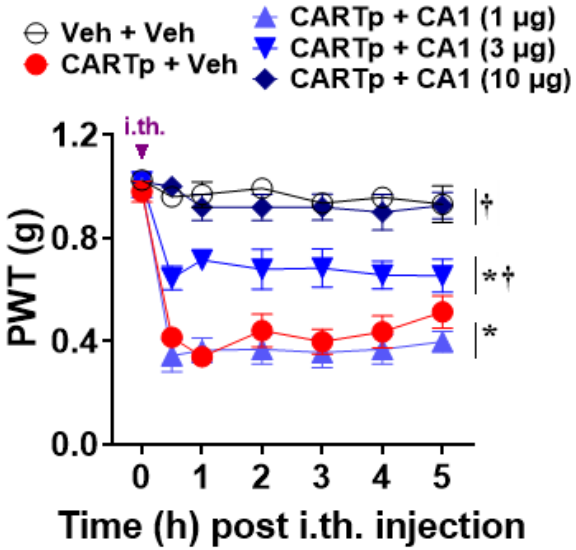
Yang, D., et al. *Sig Transduct Target Ther* 2021
Pándy-Szekeres G., et al. *Nucleic Acids Res. 2023*
Hauser, A. et al., *Nat Rev Drug Discov 2017*
Sriram K, et al., *Mol Pharmacol*. 2018

Targeting orphan GPCRs: breaking barriers to novel analgesic drug

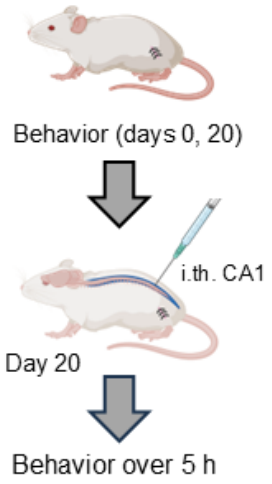
CA1 blocks CARTp-induced mechano-allodynia and reverses CCI-induced mechano-allodynia in mice

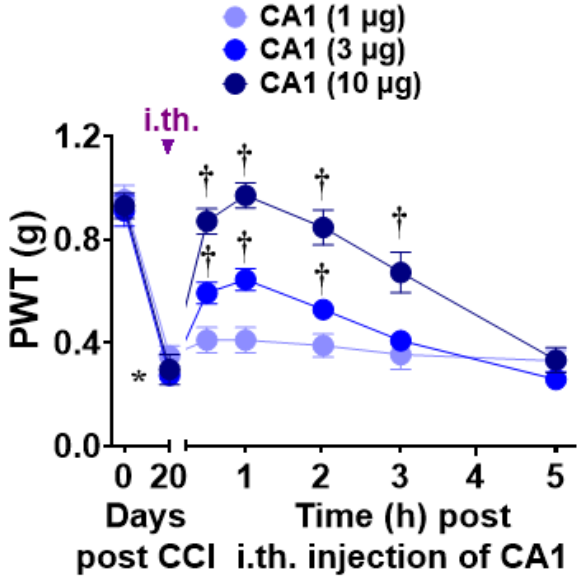


Behavior over 5 h



EC_{50}: 2.8 µg (95%CI:1.7-4.4)
6.1 nmol (95%CI:3.8-9.7)





EC_{50}: 2.4 µg (95%CI:1.5-4.0)
5.3 nmol (95%CI:3.2-8.7)

N=4-5 (M)

- Disco tates in roden
- Using
- We i ation of GPR1
- Decip *ini PAIN* ***2024a***
- Virtua GPR160 antag
- GPR1 gress.
- Lead of start-up and commercialization).