

Sustained anti-pruritic effect in mice with TP-2021, a kappa opioid agonist peptide, delivered by subdermal ProNeura[®] Implants

B. B. Land¹, S. Sreedharan², R. Patel², T. Beck³, K. DeVarney², M. Rubin²,
*C. Chavkin¹;

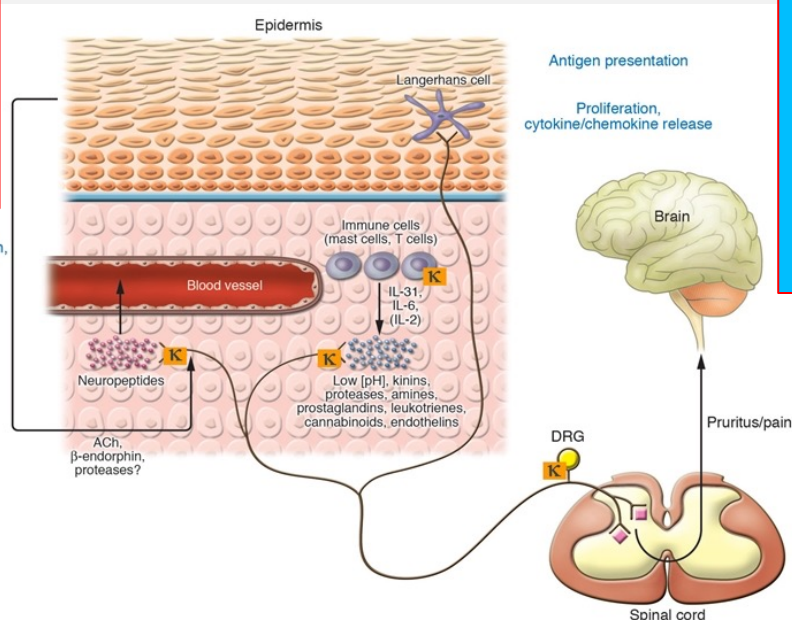
¹Pharmacol., Univ. of Washington, Seattle, WA; ²Titan Pharmaceuticals, South San Francisco, CA; ³Med. Univ. of South Carolina, Charleston, SC



KAPPA OPIOID RECEPTOR AGONISTS IN CHRONIC PRURITUS



Proliferation,
plasma extravasation,
edema



Nalfurafine



Difelikefalin

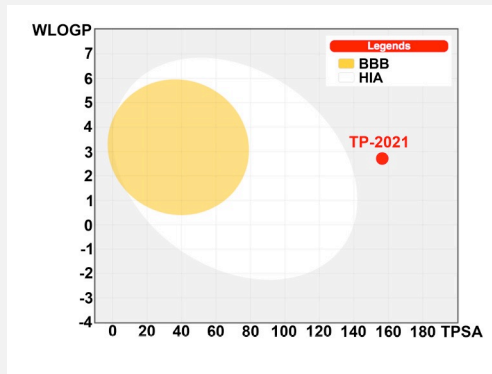
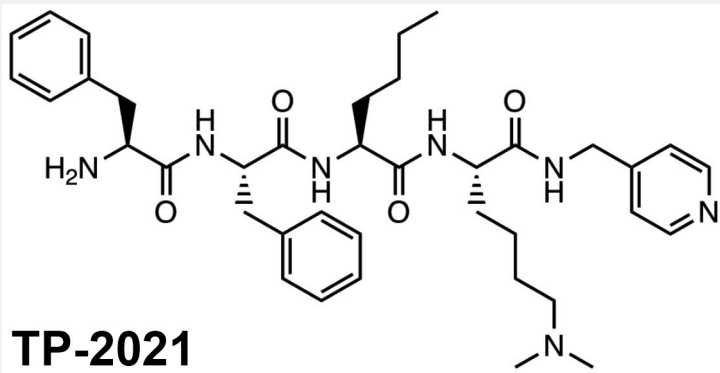


5

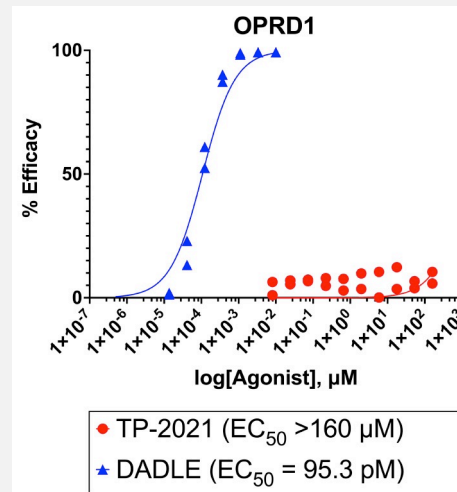
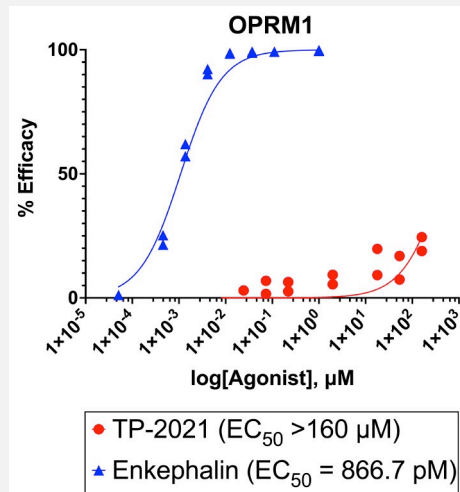
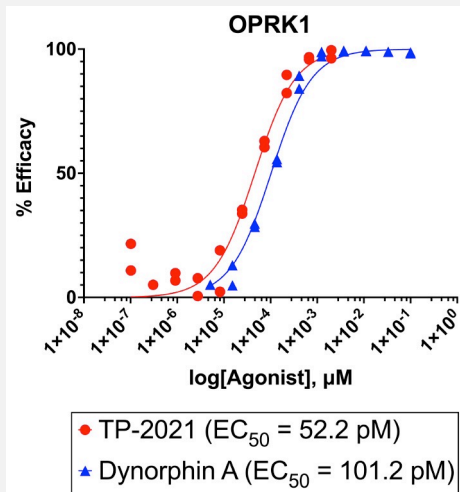
Source: Paus et al., J Clin Inv, 2006

CARA
THERAPEUTICS

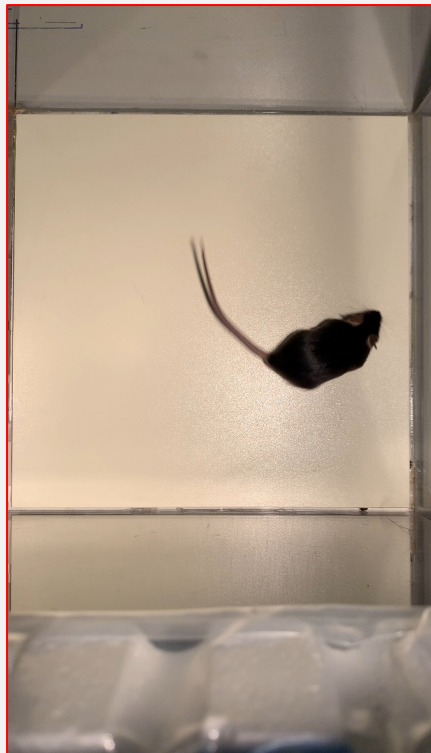
TP-2021 - A PERIPHERAL KAPPA OPIOID RECEPTOR AGONIST



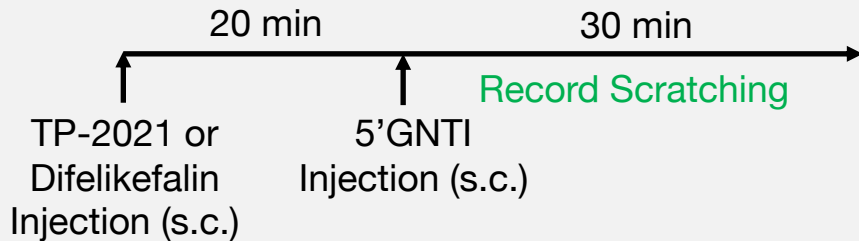
TP-2021 BINDS SELECTIVELY TO KAPPA OPIOID RECEPTORS



MOUSE PRURITUS MODEL



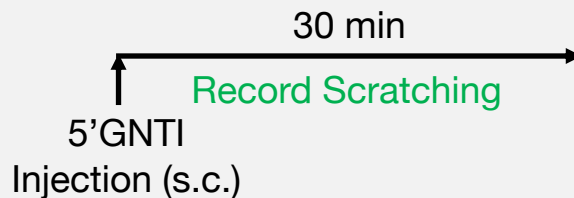
Acute Bolus Injection



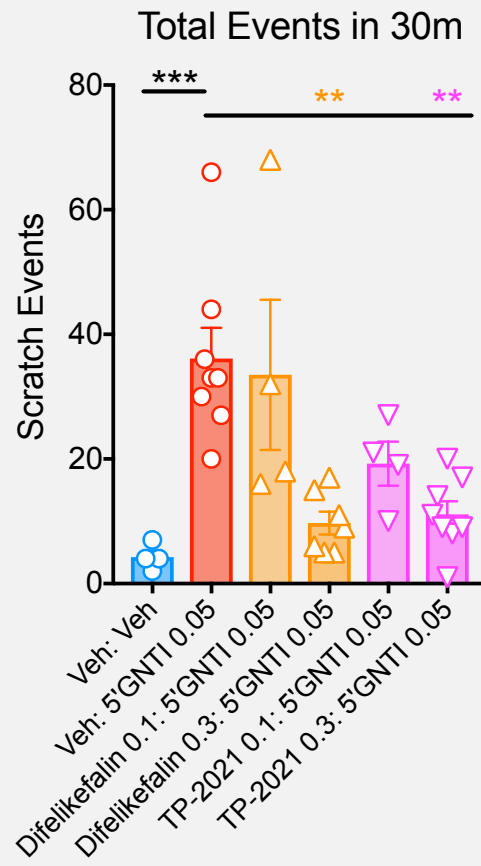
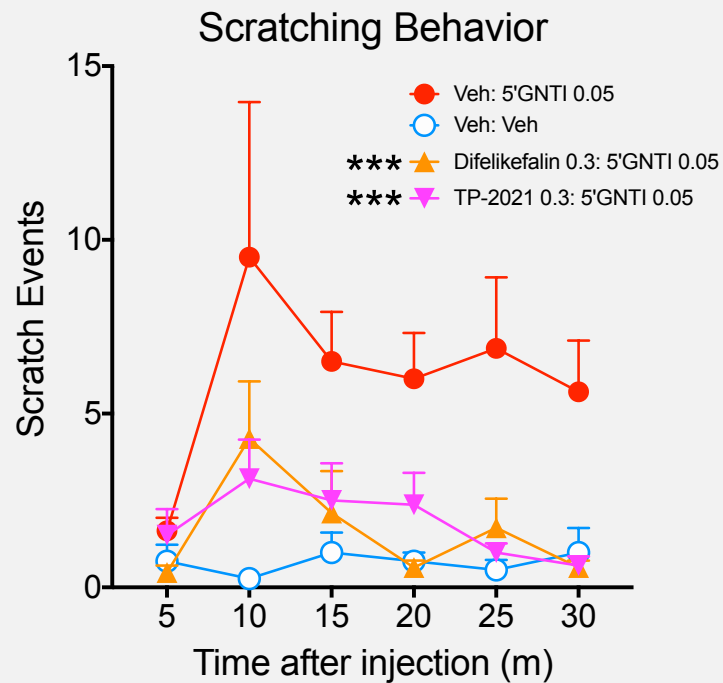
Chronic Subdermal Implantation

Day 0: Implant or control

Days 1, 14, 28, 56: 5'GNTI Challenge



EVALUATION OF TP-2021 SC BOLUS IN MOUSE PRURITUS MODEL



PRONEURA - A LONG-TERM DRUG DELIVERY PLATFORM



EVA POLYMER

+



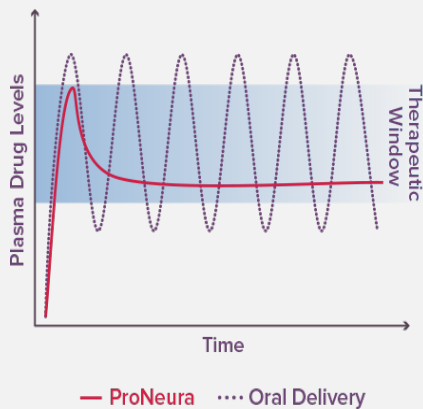
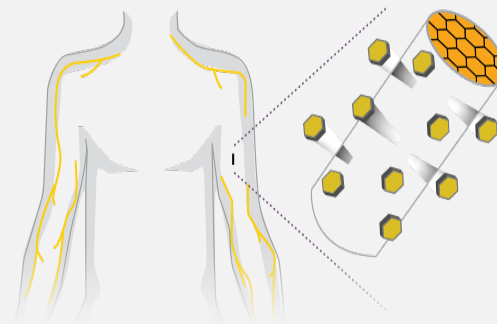
API

>

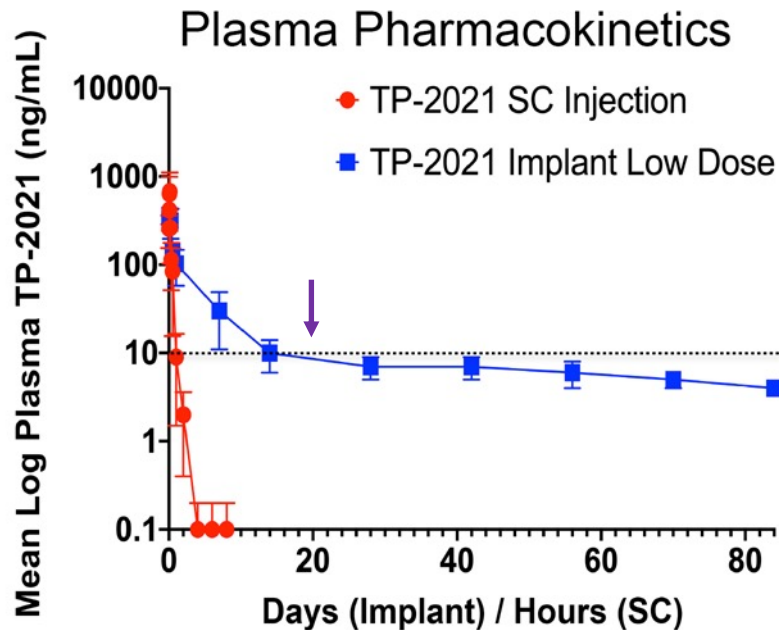
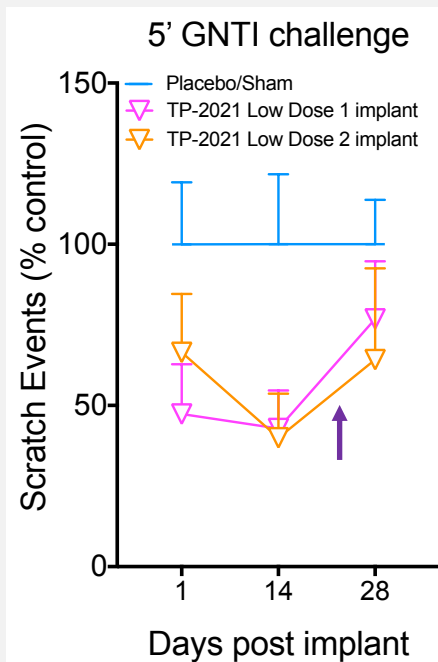
BLENDED &
EXTRUDED



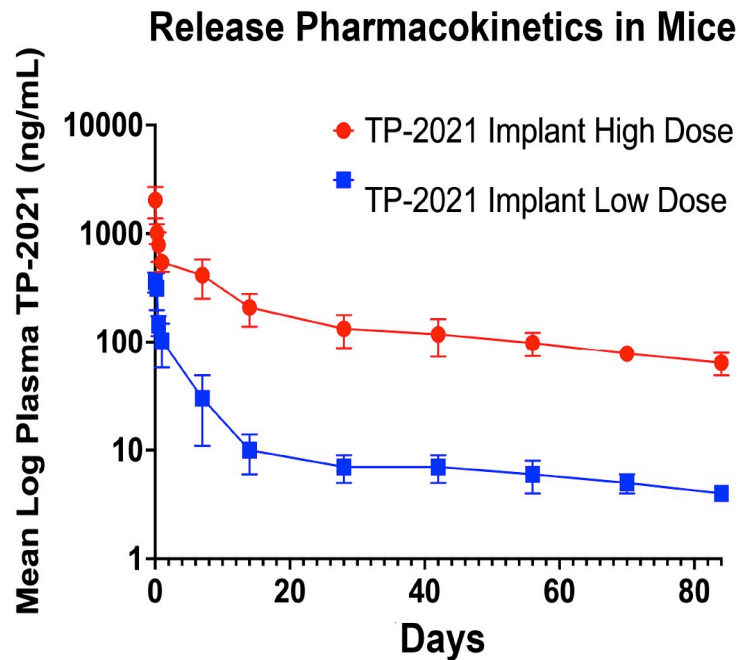
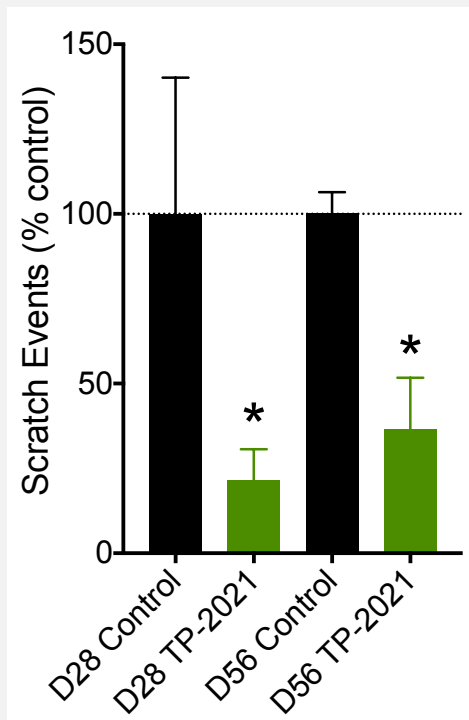
IMPLANT



LOW-DOSE TP-2021 IMPLANTS IN MOUSE PRURITUS MODEL



HIGH-DOSE TP-2021 IMPLANTS IN MOUSE PRURITUS MODEL



SUMMARY

- TP-2021 is a highly selective and potent kappa opioid receptor agonist
- TP-2021 shows similar anti-pruritic efficacy and potency to Difelikefalin when delivered by subcutaneous injection
- Low dose subdermal TP-2021-ProNeura implants show anti-pruritic efficacy, which diminishes after 2 weeks
- A single high-dose TP-2021-ProNeura implant shows sustained anti-pruritic efficacy, thus far through Day 56, with further efficacy assessments continuing

CONCLUSION

- TP-2021-ProNeura implants present a viable solution for treatment of chronic pruritus and related conditions for potentially 6 months or longer
- A single administration of TP-2021-ProNeura implant could potentially abrogate the need for daily administration, even if a peptide with oral bioavailability is therapeutically achievable

CONTRIBUTORS

University of Washington

Benjamin Land, Ph.D.
Charles Chavkin, Ph.D.
Sophia Mar

Funding

University of Washington

Reagents

Titan Pharmaceuticals

Titan Pharmaceuticals

Sunil Sreedharan, Ph.D.
Raj Patel, Ph.D.
Tyler Beck
Kate DeVarney, Ph.D.
Marc Rubin, M.D.