

Kinetic and pharmacological properties of P2X₃ and P2X_{2/3} receptors

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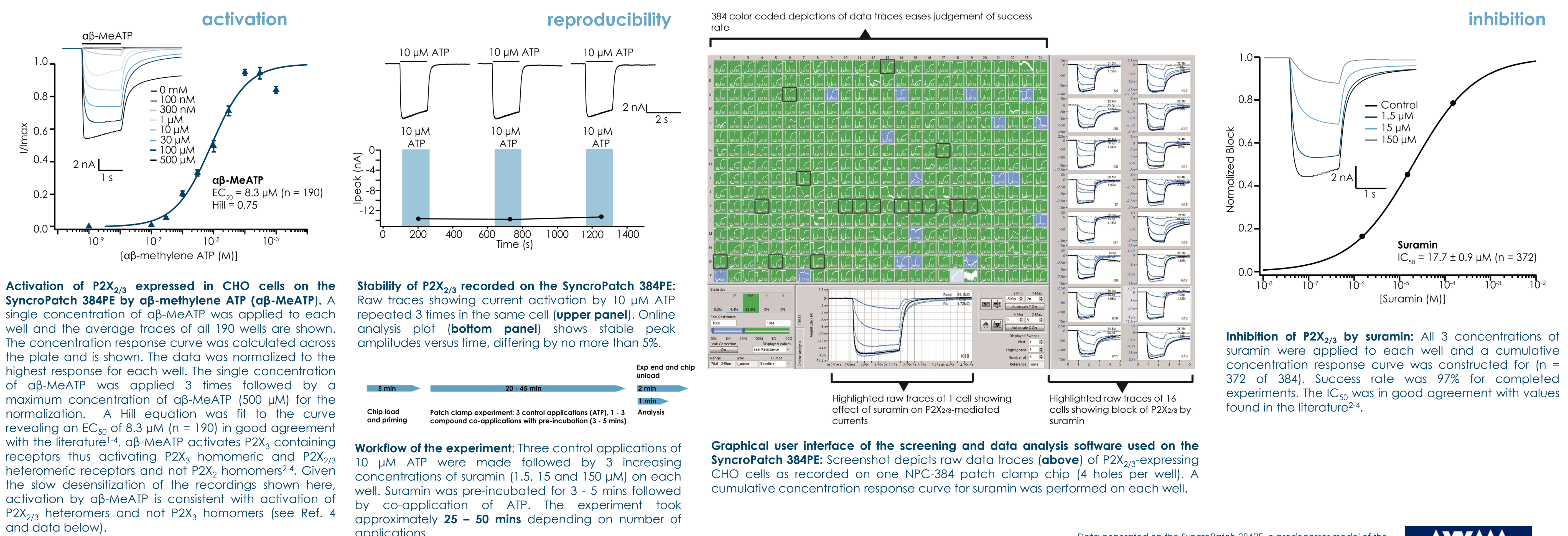
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Introduction

P2X receptors are ligand-gated ion channels activated by extracellular ATP. They are permeable to small monovalent cations, some having significant divalent or anion permeability. The P2X₂ and P2X₃ subunits are predominantly expressed in primary sensory neurons and have been proposed to play a role in thermal sensation, taste and pain. They form functional hetero- or homotrimers which are activated by ATP or αβ-methylene ATP (αβ-MeATP). The stoichiometry of P2X_{2/3} heteromers appears to be dependent on the relative abundance of the two subunits. A mixture of P2X₂ and P2X₃ homomers as well as P2X_{2/3} heteromers are likely to exist, which can be distinguished through their biophysical and pharmacological properties. The receptors open in response to an increase in extracellular ATP which occurs under pathological conditions such as tissue damage. The resulting depolarization leads to propagation of the pain signal. Due to its role in nociception and pain signaling, these receptors are considered to be important targets for pain management.

Here we present data collected on automated patch clamp (APC) systems showing activation and inhibition of P2X_{2/3} and P2X₃ receptors expressed in CHO cells with rapid and brief application of ligand and pre-incubation of inhibitors.

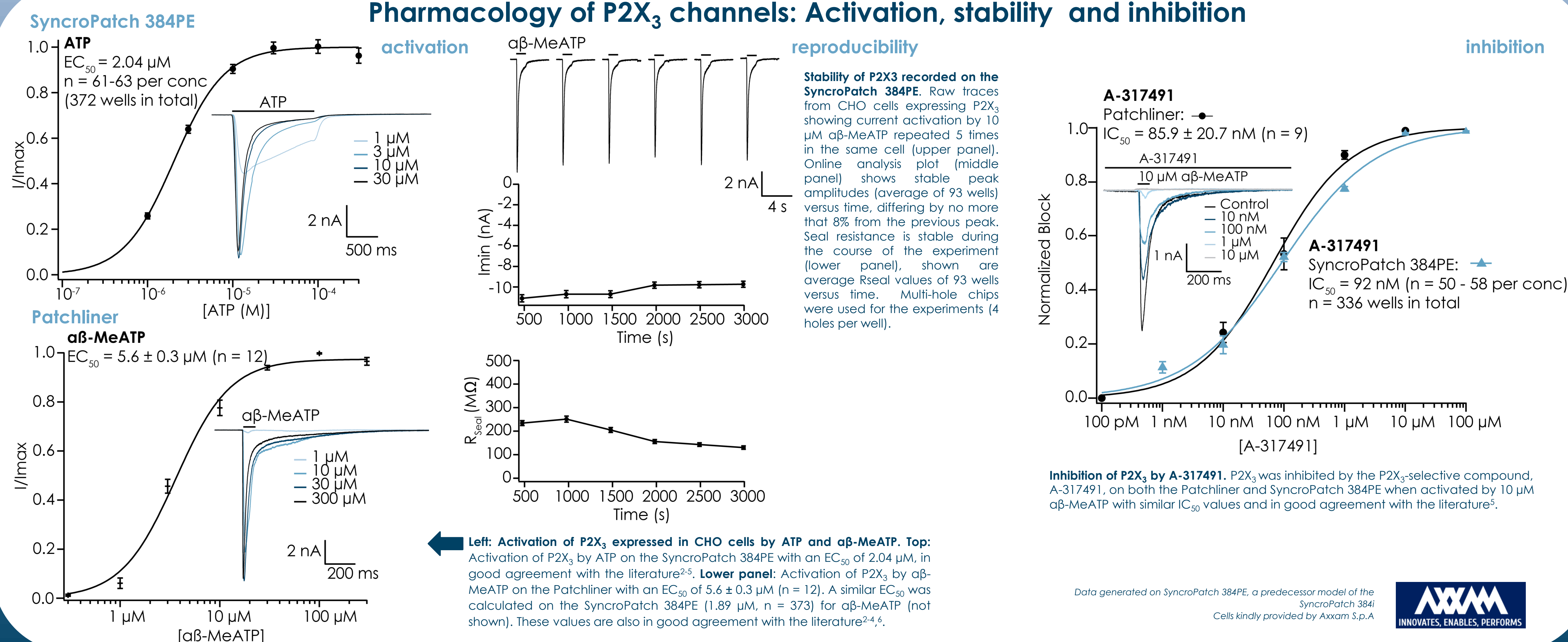
Pharmacology of P2X_{2/3} channels: High throughput activation, stability and inhibition



Data generated on the SyncroPatch 384PE, a predecessor model of the SyncroPatch 384i. Cells kindly provided by Axxam S.p.A.



Pharmacology of P2X₃ channels: Activation, stability and inhibition



Conclusions

- ✓ Ion channel currents mediated by P2X_{2/3} heteromers expressed in CHO cells were **activated by ATP and αβ-MeATP** on the SyncroPatch 384PE at high throughput.
- ✓ P2X_{2/3} heteromeric receptors were **inhibited by suramin** in a concentration-dependent manner with expected IC₅₀.
- ✓ P2X₃ homomers were successfully recorded on the **Patchliner** and **SyncroPatch 384PE**, displaying faster activation and inactivation kinetics compared to the P2X_{2/3} heteromers.
- ✓ Currents mediated by P2X₃ were highly **reproducible**, activated by ATP or αβ-MeATP.
- ✓ P2X₃-mediated currents were **blocked** by the specific inhibitor **A-317491**.
- ✓ **Patchliner** and **SyncroPatch 384i** can be used to measure different P2X-mediated currents and test compounds for specificity.

References

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