Technology Transfer Brief

KOREA UNIVERSITY SEJONG CAMPUS

A Urea/Carbamate-Based Allosteric Antagonist Platform for Functional Modulation of P2X7 Signaling in CNS Neuroinflammation

Medicinal Chemistry Laboratory

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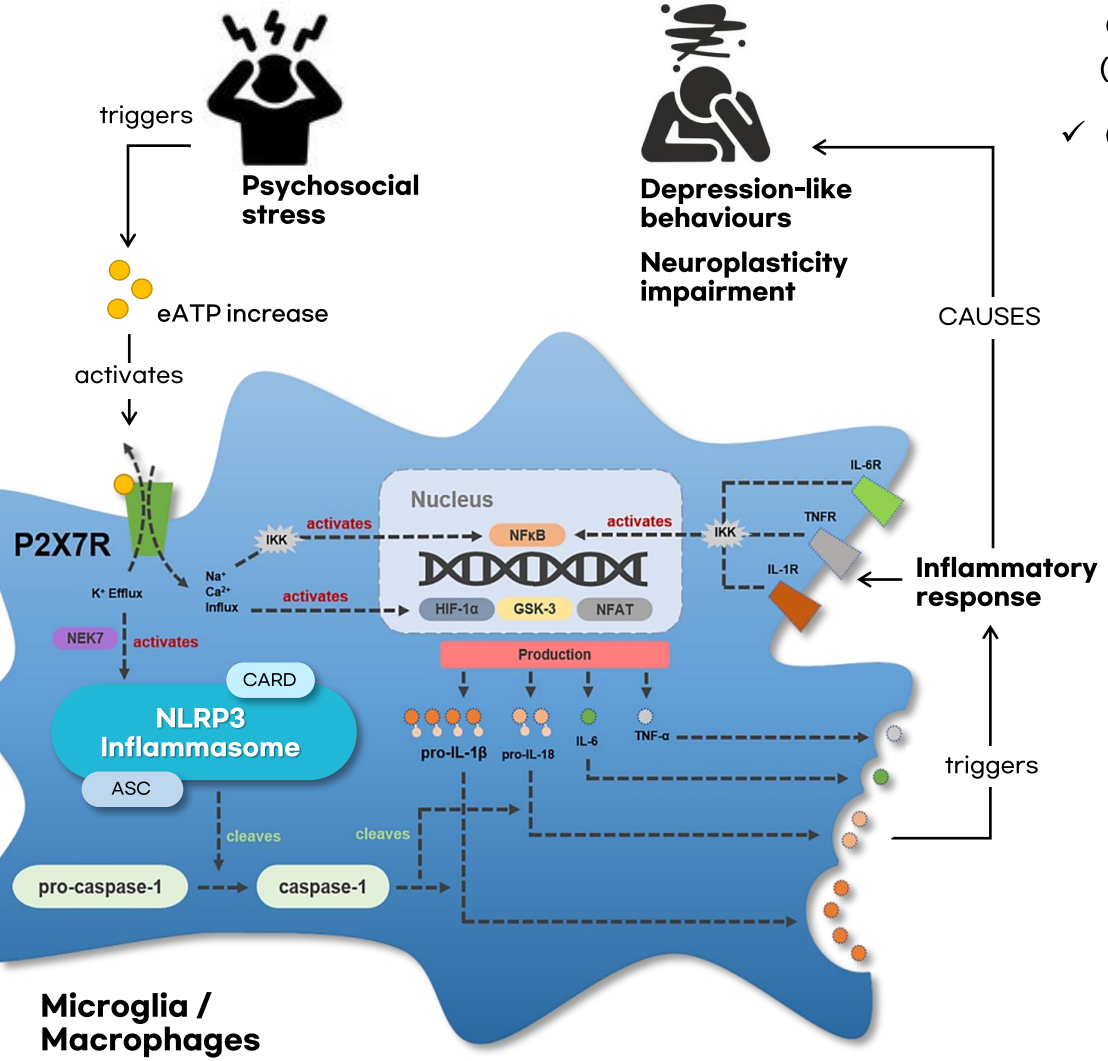
Technology Transfer Brief

A Urea/Carbamate-Based Allosteric Antagonist Platform for Functional Modulation of P2X7 Signaling in CNS Neuroinflammation

Content

01 CNS Neuroinflammation Is an Upstream Signaling Problem



(*Source: von Muecke-Heim *et al.*, European Archives of Psychiatry and Clinical Neuroscience, 2021)

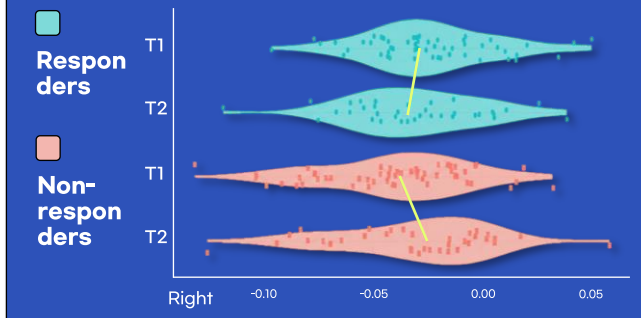
✓ **P2X7 receptor-mediated activation of NLRP3 inflammasome : key upstream driver of neuroinflammation in CNS disorders.**

(*Inflammation-associated depression, Parkinson's disease, Alzheimer's disease)

✓ **Conventional therapeutic limitations :** (in inflammation-associated depression)

1. **Antidepressants** : Target monoaminergic neurotransmission, with limited efficacy in inflammation-associated depressive subtypes.
2. **P2X7 receptor antagonists** : Developed for peripheral inflammatory diseases, with limited efficacy against CNS pathological processes.

Structural Brain Recovery Fails in SSRI Non-Responders



Total Hippocampus Laterality Index

- Structural recovery after SSRI treatment is limited to responders, with persistent structural pathology in non-responders.
- Limitations of symptom-focused antidepressant therapy.

Inflammatory Burden in Moderate to Severe Depression

- High inflammatory burden in patients with severe depression.
- Need for combination therapeutic strategies in severe cases.

02 Technology Overview

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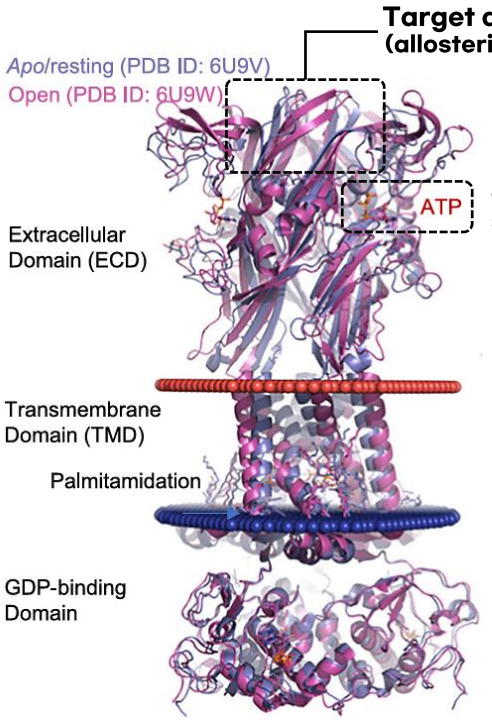
- ✓ **Existing P2X7 antagonists establish the PCP as a functional allosteric target.**
- ✓ **The remaining challenge is how to accommodate structural diversity across PCP sub-pockets at the chemical design level.**



P2X7 is an ATP-gated trimeric ion channel whose extracellular conformational changes drive channel opening and downstream neuroinflammatory signaling.

- CNS-focused P2X7 antagonists target the allosteric site at the portal of the central pocket (PCP), distinct from the ATP-binding site.
- **Allosteric sites** : **regulates channel gating** by controlling key structural elements such as the flipper, lower body, and central pocket.

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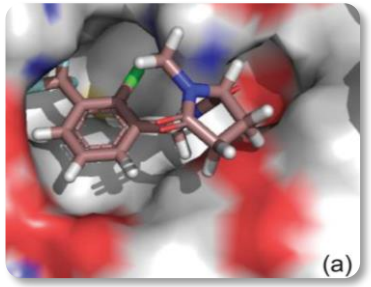

- Chemotype : Diaryl/heteroaromatic small-molecule scaffold.
- An early reference P2X7 antagonist used to establish allosteric binding at the PCP region.
- **Rigid binding mode.**

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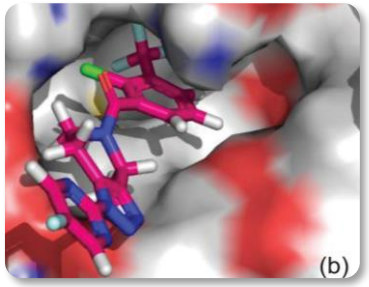

- Chemotype : Polycyclic aromatic scaffold.
- A clinically advanced P2X7 antagonist demonstrating PCP engagement in CNS-targeted development.
- **Limited sub-pocket adaptability.**

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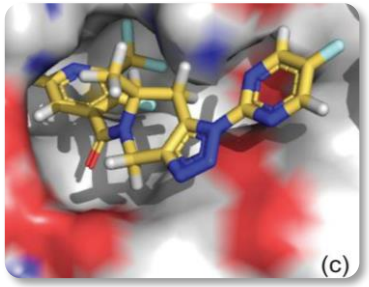
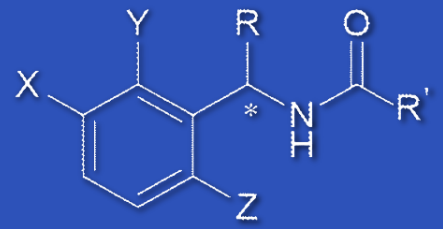


- Chemotype : Bulky heteroaromatic scaffold.
- A later-generation antagonist illustrating distinct binding modes within the PCP allosteric site.
- **Bulky scaffold constraints.**

A Flexible Allosteric Antagonist Platform for P2X7R



- **Urea/carbamate** chemotypes : Enable flexible binding across heterogeneous PCP sub-pockets.
- **Chemically tunable scaffold** : Adapts to allosteric gating conformations, stabilizing non-conductive P2X7 states.

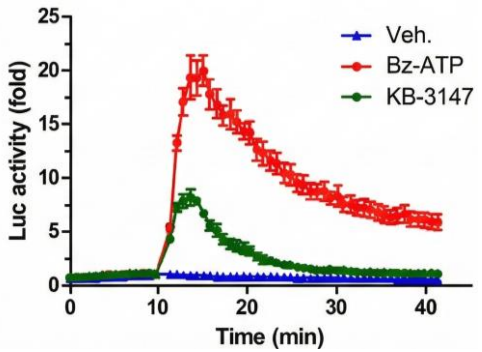
(*Source: Guo *et al.*, Nature Communications, 2025)

03 Key Features & Advantages

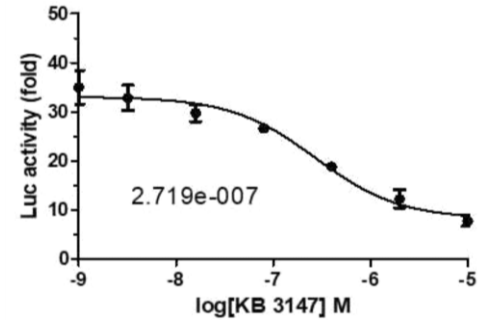
❶ Inhibition of Functional Activation

- **Luciferase signal** : Suppressed both the peak response and sustained activity over time, consistent with reduced Ca^{2+}-dependent signaling.
- **Dose response** : Inhibited in a dose-dependent manner, demonstrating high functional potency in the sub-micromolar range.

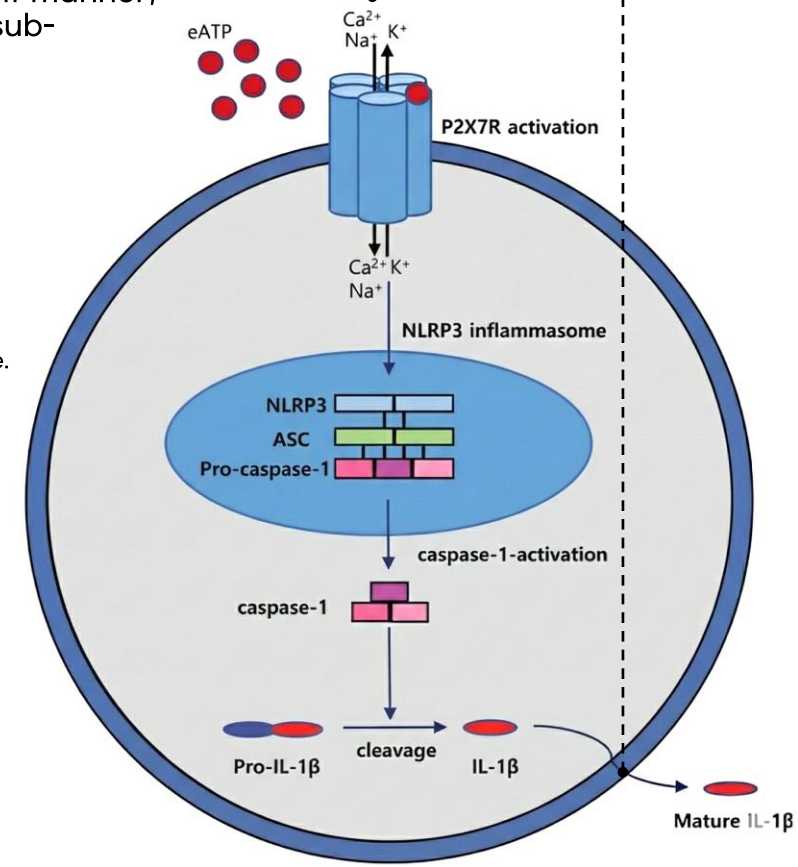
P2X7 : BZ-ATP/KB 3147



- Reduced peak luciferase response.
- Reduced sustained luciferase activity over time.

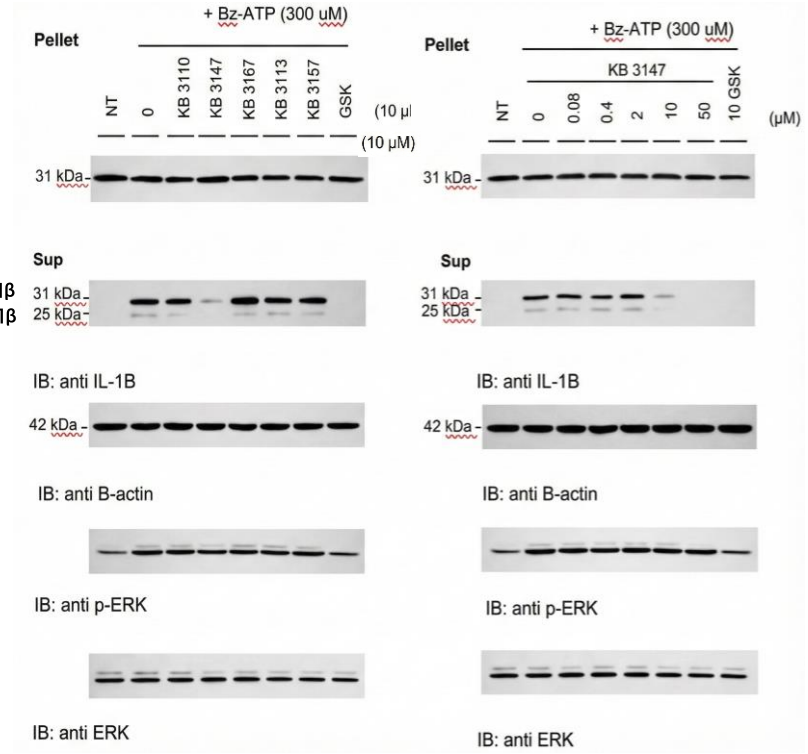


- Dose-dependent reduction of luciferase activity.
- Sub-micromolar functional potency.



❷ IL-1β Secretion Suppression

- **P2X7R antagonist (KB3147)** : Dose-dependently inhibits Bz-ATP-induced IL-1β secretion in the culture supernatant.
- **Preserved Intracellular IL-1β and ERK Signaling** : Excludes inhibition of cytokine production and nonspecific cytotoxic effects.



04 Strategic Business Opportunities

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- ✓ **Business Vision :** A urea/carbamate-based allosteric approach to functionally modulate P2X7 receptor signaling in CNS neuroinflammation.
- ✓ **Engagement Model :** Staged licensing and preclinical co-development partnerships.

Collaborative development opportunities

❶ Allosteric chemotype expansion

- Structure-guided design and synthesis based on urea/carbamate scaffolds.
- Chemotype strategies addressing structural heterogeneity of PCP sub-pockets.

❷ Functional efficacy validation (P2X7R-specific)

- P2X7R-specific functional assays including Ca^{2+} signaling, luciferase, and IL-1β secretion.
- Functional inhibition-based efficacy evaluation.

❸ CNS-relevant translational framework

- Neuroinflammatory subtype and biomarker-linked translational readouts.
- Mechanism-to-phenotype validation toward CNS indications.

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Medicinal Chemistry Lab
(College of Pharmacy)

Collaborative R&D

Mechanism- and subtype-driven preclinical co-development

IP license (Option/Exclusive)

P2X7 Allosteric Antagonist Platform

- Pharma (CNS & Neuroinflammation)
- Biotech (P2X7 / Immuno-neuro)
- Discovery CRO / Translational Research Platforms

Commercial License

Pharmaceutical Development Partners

- Pharma (CNS & Neuroinflammation Programs)
- Biopharma with IND-enabling capabilities
- Strategic licensing or co-development partners

Intellectual Property

- Title : NOVEL UREA-BASED OR CARBAMATE-BASED P2X7 RECEPTOR ANTAGOIST, AND PHARMACEUTICAL COMPOSITION FOR PREVENTING OR TREATING MAJOR DEPRESSIVE DISORDER, COMPRISING SAME AS ACTIVE INGREDIENT.
- Patent : PCT/KR2022/018104, KR 10-2022-0152551 (Date : Nov. 16, 2022)

CONTACT US

For inquiries regarding technology licensing, collaborative R&D, or partnership opportunities, please contact :

- Technology Transfer Agency : **IBU Inc.**
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Partnering to unlock new business opportunities through innovation.

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