

A CAF-targeting TME normalizer, Penetrium, overcomes stromal resistance in NSCLC

Sandip Patel¹, Jin-Ho Choy², Sue Jang³, Eunice Choi⁴, Geun-woo Jin^{3,4}

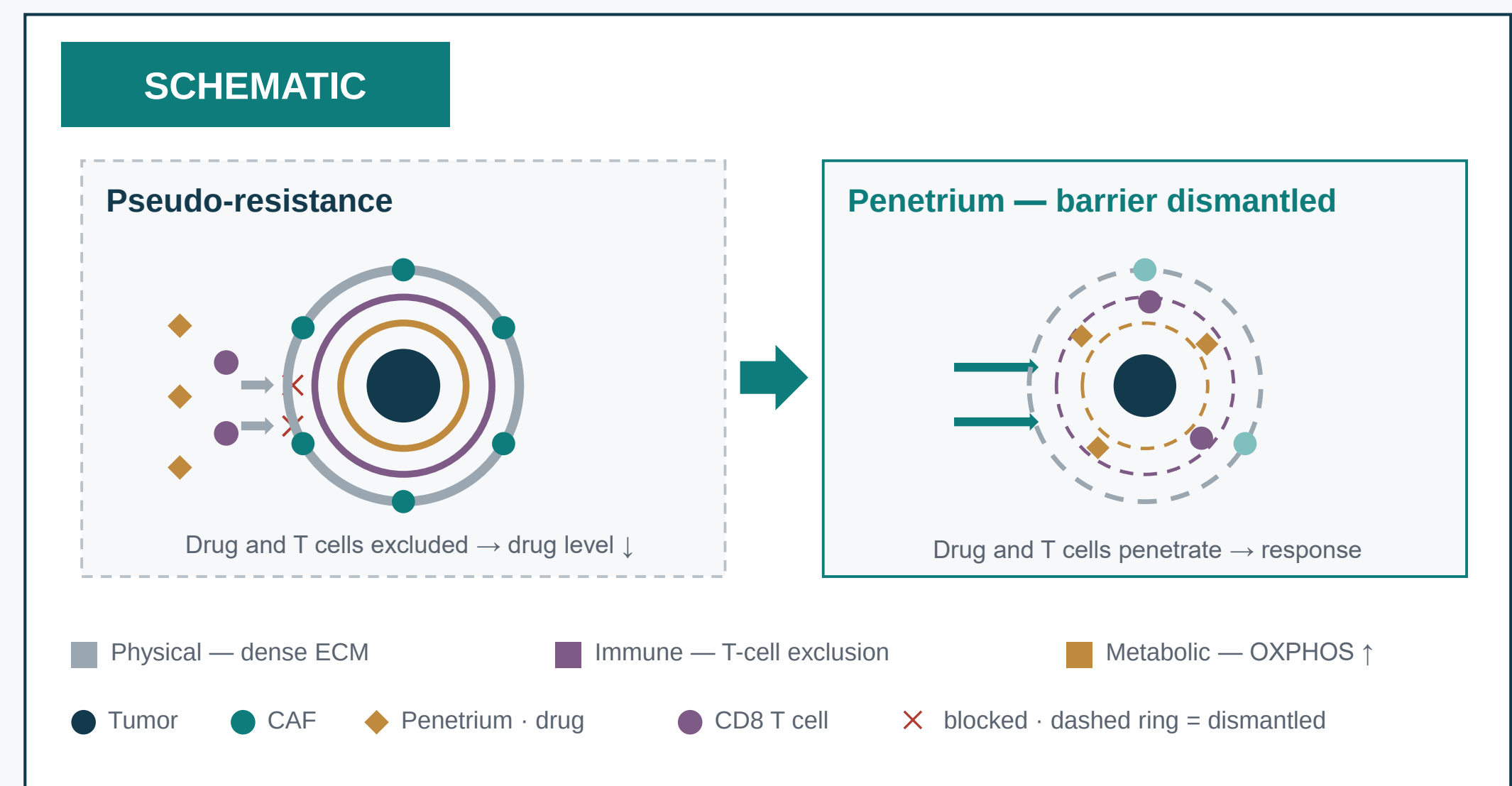
¹UC San Diego Moores Cancer Center, La Jolla, CA, USA · ²Dankook University, Seoul, Republic of Korea · ³Penetrium Bioscience, Inc., Seoul, Republic of Korea · ⁴Hyundaibioscience, Co. Ltd., Seoul, Republic of Korea

Background

Modern anticancer therapy has largely focused on vulnerabilities intrinsic to tumor cells. However, tumor-directed therapy alone may therefore face an inherent therapeutic ceiling. Effective cancer treatment may require targeting not only the heterogeneous tumor cells themselves, but also the stromal microenvironmental barriers that protect them.

Cancer-associated fibroblasts (CAFs) are central organizers of this resistant tumor microenvironment (TME), creating physical, immune, and metabolic barriers through ECM overproduction, immune-evasion signaling, and mitochondrial OXPHOS hyperactivation. These barriers can restrict effective drug access and suppress antitumor immunity across mechanistically distinct therapies.

Penitrem, a novel oral formulation of niclosamide, was developed as a first-in-class TME normalizer designed to selectively target pathologically hyperactivated stromal cells, dismantle CAF-mediated barriers, and restore the efficacy of tumor-directed therapies.



Methods

Patient-derived organoid-CAF co-culture system

- Lung cancer
- Pancreatic cancer
- Ovarian cancer

LL/2 syngeneic mouse model

Conclusion

Across chemotherapy, targeted therapy, and immunotherapy, Penetrium restores the activity of mechanistically distinct agents through a compartment-selective, complementary mechanism — the partner drug targets the heterogeneous tumor cell while Penetrium normalizes the protective stroma. By targeting a shared stromal barrier rather than specific tumor-specific alteration, Penetrium offers a pan-tumor strategy to address stromal resistance, including in NSCLC.

