How Does AI Enable Combination Therapy Optimization?

Rasit Dinc

Rasit Dinc Digital Health & AI Research

Abstract

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Introduction

Combination therapy, the use of two or more therapeutic agents, has become a cornerstone of treatment for complex diseases like cancer. The rationale is to attack the disease from multiple angles, potentially leading to increased efficacy, reduced toxicity, and a lower likelihood of developing drug resistance [1]. However, the sheer number of possible drug combinations makes it practically impossible to test them all experimentally. This is where Artificial Intelligence (AI) is making a transformative impact. By leveraging sophisticated algorithms and vast datasets, AI is revolutionizing how we identify and optimize combination therapies, paving the way for more personalized and effective treatments.

The Data Challenge and AI's Role

The complexity of human biology and disease presents a significant data challenge. Every individual has a unique genetic makeup, and diseases like cancer are characterized by a multitude of genetic and molecular abnormalities. Effective combination therapy requires an understanding of how different drugs interact with each other and with the patient's specific biological landscape. This involves analyzing massive datasets, including genomic data, proteomic data, drug-target information, and clinical data. AI, particularly machine learning, is exceptionally well-suited for this task. Machine learning algorithms can sift through these vast and complex datasets to identify patterns and relationships that would be impossible for humans to discern. By learning from existing data, these models can predict which drug

combinations are most likely to be effective for a particular patient or disease subtype.

Predictive Modeling for Synergy

One of the most exciting applications of AI in this field is the development of predictive models for drug synergy. A synergistic interaction occurs when the combined effect of two or more drugs is greater than the sum of their individual effects. Identifying these synergistic combinations is a key goal of combination therapy. Recent studies have demonstrated the remarkable ability of AI to predict drug synergy with a high degree of accuracy. For instance, a 2025 study published in *Nature Communications* detailed how machine learning models were used to predict synergistic drug combinations for pancreatic cancer [2]. Researchers trained their models on a dataset of 496 drug combinations and then used them to predict the efficacy of 1.6 million possible combinations. Subsequent experimental validation showed a hit rate of up to 60%, a testament to the predictive power of AI. These models often employ advanced techniques like Graph Convolutional Networks (GCNs) and Deep Neural Networks (DNNs) to learn from the chemical structures of drugs and the genetic features of cancer cells.

Personalization and Optimization

Beyond predicting synergy, AI is also enabling the personalization of combination therapies. The concept of "one-size-fits-all" medicine is becoming increasingly obsolete. AI algorithms can analyze a patient's unique genomic and molecular profile to recommend a combination therapy tailored to their specific needs. This approach, often referred to as precision medicine, holds the promise of delivering the right treatment to the right patient at the right time. Furthermore, AI can be used to optimize the dosage and scheduling of combination therapies in real-time. Models like CURATE.AI, for example, can dynamically adjust drug doses based on a patient's response to treatment, maximizing therapeutic benefit while minimizing side effects [1]. This dynamic optimization is a significant step towards truly personalized and adaptive cancer care.

Conclusion

The integration of AI into the field of combination therapy is not just an incremental improvement; it is a paradigm shift. By harnessing the power of machine learning and big data, we can move beyond the trial-and-error approach of the past and towards a future of rationally designed, personalized, and optimized combination therapies. While challenges related to data quality, model interpretability, and clinical validation remain, the potential of AI to revolutionize cancer treatment and improve patient outcomes is undeniable. As AI technologies continue to mature, we can expect to see even more sophisticated and powerful tools for designing the next generation of cancer therapies.

References

[1] Ambreen, S., Umar, M., Noor, A., Jain, H., & Ali, R. (2025). Advanced AI

and ML frameworks for transforming drug discovery and optimization: With innovative insights in polypharmacology, drug repurposing, combination therapy and nanomedicine. *European Journal of Medicinal Chemistry*, *284*, 117164. https://doi.org/10.1016/j.ejmech.2024.117164

[2] Pourmousa, M., Jain, S., Barnaeva, E., Jin, W., Hochuli, J., Itkin, Z., ... & Zakharov, A. V. (2025). AI-driven discovery of synergistic drug combinations against pancreatic cancer. *Nature Communications*, *16*(1), 4020. https://doi.org/10.1038/s41467-025-56818-6

[3] Abd El-Hafeez, T., El-Hoseny, H., & El-Shemeisy, A. (2024). Harnessing machine learning to find synergistic combinations for FDA-approved cancer drugs. *Scientific Reports*, *14*(1), 2449. https://doi.org/10.1038/s41598-024-52950-z