Drug Repurposing

Strategies and Approaches for Discovering New Uses of Existing Drugs

Indication expansion

New therapeutic uses

Signature matching

Disease signature comparison

Network propagation

Disease module identification

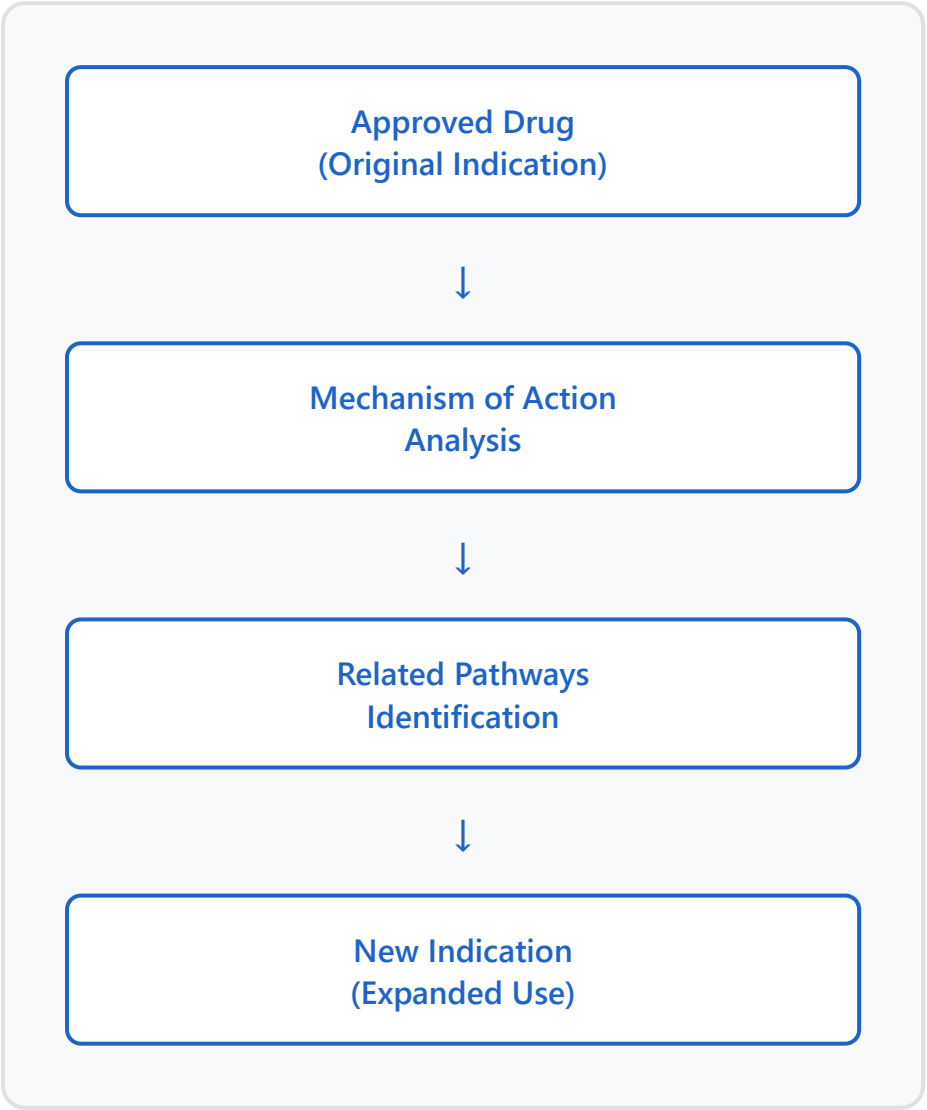
Clinical evidence

Real-world validation

IP considerations

Patent and exclusivity

1. Indication Expansion



Overview

Indication expansion involves identifying new therapeutic applications for drugs already approved for other conditions. This approach leverages existing safety and pharmacokinetic data, significantly reducing development time and costs.

The strategy relies on understanding the drug's mechanism of action and identifying other diseases that share similar molecular pathways or biological targets. This can reduce development time by 3-12 years compared to traditional drug development.

Example: Sildenafil (Viagra)

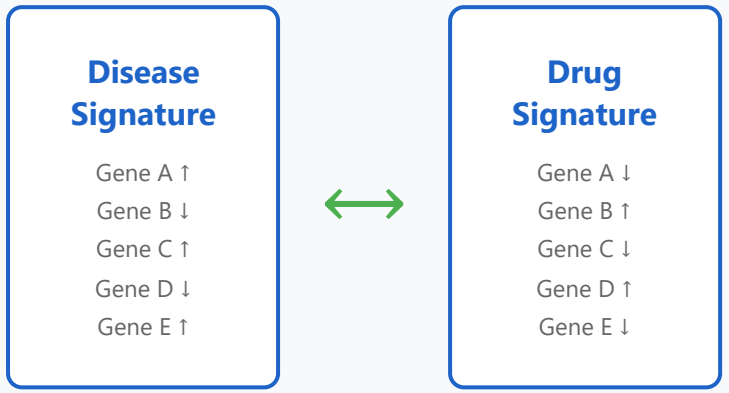
Originally developed for hypertension and angina, sildenafil was later repurposed for erectile dysfunction and subsequently for pulmonary arterial hypertension, demonstrating successful indication expansion.

Key Advantages:

- Known safety profile reduces risk
- Shorter regulatory pathway

- Lower development costs (50-60% reduction)
- Faster time to market

2. Signature Matching



Overview

Signature matching uses computational approaches to compare gene expression patterns between diseases and drug effects. The goal is to find drugs whose expression signatures are inversely correlated with disease signatures.

This method utilizes large-scale gene expression databases like the Connectivity Map (CMap) and LINCS L1000, which contain expression profiles of thousands of drugs across multiple cell lines.

Example: Topiramate for Inflammatory Bowel Disease

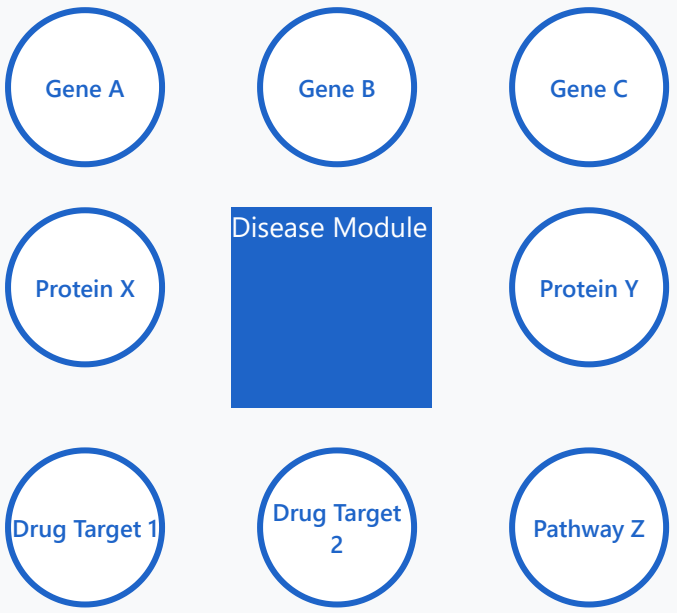
Computational signature matching identified topiramate, an antiepileptic drug, as a potential treatment for IBD based on inverse gene expression patterns, later validated in preclinical studies.

Key Components:

- Disease gene expression profiling
- Drug-induced expression changes
- Correlation analysis algorithms

- Statistical validation methods
- Experimental verification requirements

3. Network Propagation



Network-based approach identifies drug targets connected to disease modules

Overview

Network propagation leverages biological network data (protein-protein interactions, metabolic pathways, signaling cascades) to identify disease modules and potential drug targets within these interconnected systems.

This approach uses algorithms to propagate information through molecular networks, starting from known disease genes to identify proximal drug targets that may not be immediately obvious from traditional analyses.

Example: Metformin for Cancer

Network analysis revealed that metformin, a diabetes drug, affects multiple pathways connected to cancer metabolism and proliferation, leading to clinical trials for cancer prevention and treatment.

Key Methodologies:

- Protein-protein interaction networks
- Random walk algorithms
- Module identification techniques
- Network proximity measures

- Multi-omics data integration

4. Clinical Evidence

Accelerated pathway for repurposed drugs

Overview

Clinical evidence for drug repurposing can come from multiple sources including real-world evidence, electronic health records, observational studies, and serendipitous clinical observations.

The validation process for repurposed drugs is often faster because safety has already been established. However, efficacy must still be demonstrated through appropriate clinical trials, though these can sometimes skip early safety phases.

Example: Thalidomide for Multiple Myeloma

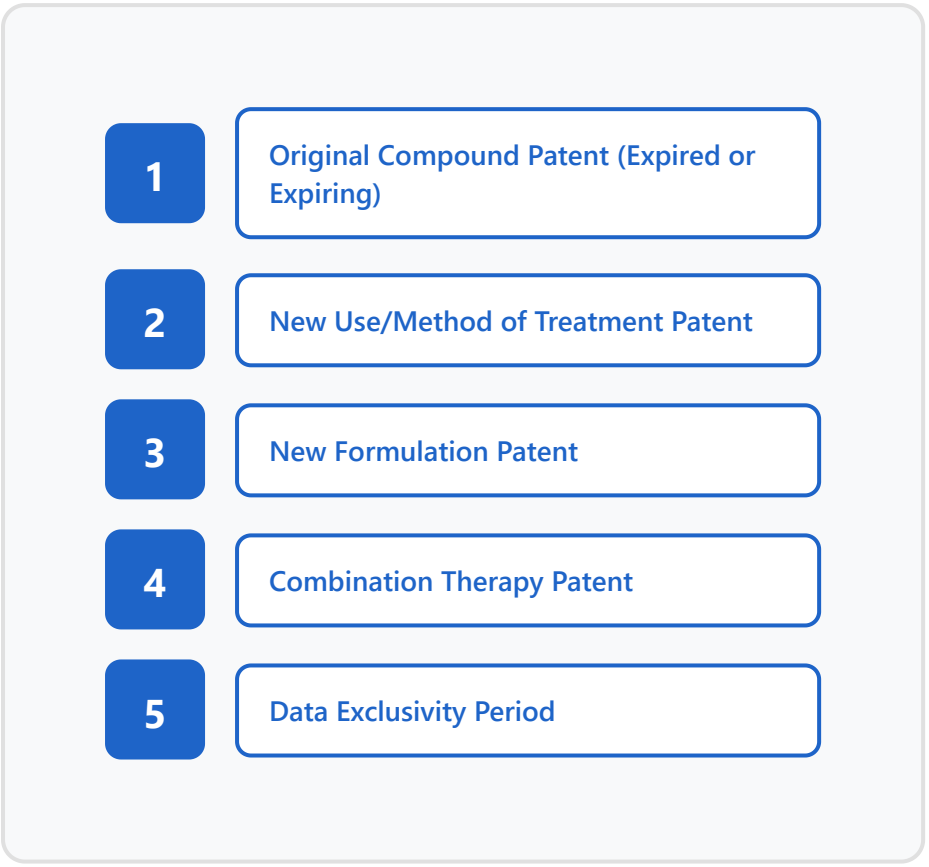
Despite its tragic history, thalidomide was successfully repurposed for multiple myeloma after clinical observations and trials demonstrated significant efficacy, receiving FDA approval in 2006.

Evidence Sources:

- Electronic health records (EHR) mining
- Real-world data analysis
- Case reports and observational studies

- Phase II/III clinical trials
- Post-marketing surveillance data

5. IP Considerations



Overview

Intellectual property strategy is crucial for drug repurposing success. While the original compound patent may have expired, new patents can be obtained for novel uses, formulations, or combination therapies.

Companies must carefully navigate the patent landscape to ensure sufficient protection for their investment while adhering to regulatory requirements. Market exclusivity can also be obtained through orphan drug designation or pediatric exclusivity.

Example: Aspirin

Though aspirin's compound patent expired long ago, new method-of-use patents have been granted for cardiovascular disease prevention, demonstrating ongoing innovation opportunities in repurposed drugs.

IP Strategies:

- Method-of-use patents for new indications
- New formulation development (extended-release, etc.)

- Combination therapy patents
- Orphan drug exclusivity (7 years in US)
- Pediatric exclusivity extensions (6 months)
- Data exclusivity periods (varies by region)

Summary

Drug repurposing represents a powerful strategy to accelerate therapeutic development by leveraging existing drugs for new indications. By combining computational approaches (signature matching, network propagation) with clinical evidence and strategic IP planning, researchers can identify promising candidates more efficiently than traditional drug development. Success requires integration of multiple data types, rigorous validation, and careful consideration of regulatory and commercial factors.