

Systems Medicine

A Network-Based Approach to Understanding and Treating Disease

Network Medicine

Disease as network perturbations

Disease Modules

Interconnected disease components

Comorbidities

Shared molecular mechanisms

Drug Repurposing

Network-based drug discovery

Personalized Networks

Patient-specific network models

Detailed Explanations

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Network Medicine

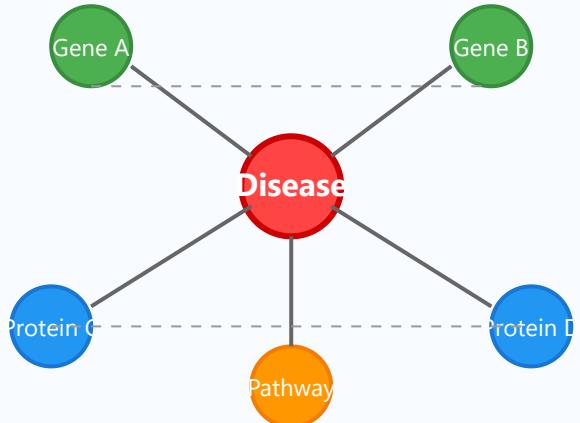
Network Medicine is a paradigm that views diseases not as isolated events, but as perturbations in complex biological networks. This approach integrates genomics, proteomics, and metabolomics data to understand disease mechanisms.

Key Concepts:

- **Interactome:** The complete set of molecular interactions in cells, including protein-protein, protein-DNA, and metabolic interactions
- **Network Perturbation:** Disease occurs when normal network structure or function is disrupted
- **Systems-level Analysis:** Understanding how multiple components interact simultaneously

Applications:

- Identifying disease-associated genes and pathways
- Predicting disease progression
- Understanding complex disease etiology



Key Insight:

Diseases rarely result from abnormalities in a single gene or protein, but from complex interactions within cellular networks.

Disease Modules

Disease modules are interconnected groups of genes, proteins, or other molecular components that collectively contribute to a disease phenotype. These modules represent functional units within the larger biological network.

Characteristics:

- **Modularity:** Disease components cluster together in the network
- **Functional Coherence:** Module members share biological functions
- **Topological Proximity:** Disease genes tend to interact directly or through few intermediates

Significance:

- Reveals disease mechanisms at the systems level
- Identifies potential therapeutic targets
- Explains genetic heterogeneity in diseases
- Enables disease classification based on molecular profiles



Key Insight:

Disease modules help explain why different genetic mutations can lead to similar disease phenotypes and why diseases share common molecular mechanisms.

3 Comorbidities

Comorbidities refer to the co-occurrence of two or more diseases in the same individual more frequently than expected by chance. Network medicine reveals that comorbidities often result from shared molecular mechanisms and overlapping disease modules.

Network-Based Explanations:

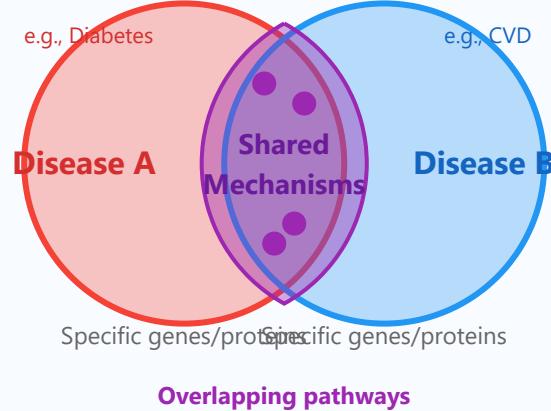
- **Overlapping Disease Modules:** Two diseases share common genes or proteins
- **Pathway Convergence:** Different diseases affect the same biological pathways
- **Shared Risk Factors:** Common genetic or environmental factors

Clinical Examples:

- Diabetes and cardiovascular disease
- Depression and chronic pain
- Obesity and metabolic syndrome
- Autoimmune diseases (e.g., rheumatoid arthritis and psoriasis)

Implications:

- Improved disease prediction and prevention



- Comprehensive treatment strategies
- Understanding disease progression patterns

Key Insight:

Network analysis reveals that comorbidities are not random but follow predictable patterns based on shared molecular mechanisms, enabling better patient stratification and treatment planning.

4 Drug Repurposing

Network-based drug repurposing identifies new therapeutic uses for existing drugs by analyzing their effects on biological networks. This approach can significantly reduce the time and cost of drug development.

Network-Based Strategies:

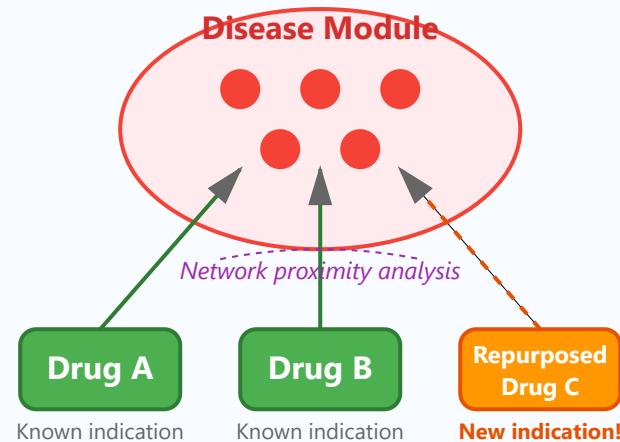
- **Target-Based:** Identifying drugs that target proteins in disease modules
- **Pathway-Based:** Finding drugs that modulate disease-relevant pathways
- **Network Proximity:** Measuring closeness between drug targets and disease genes
- **Module-Based:** Drugs affecting the same network modules as diseases

Success Stories:

- Aspirin: Originally for pain → cardiovascular protection
- Metformin: Diabetes → cancer prevention, aging
- Thalidomide: Sedative → multiple myeloma treatment
- Sildenafil (Viagra): Hypertension → erectile dysfunction

Advantages:

- Reduced development time (3-12 years vs 10-17 years)
- Lower costs (\$300M vs \$2-3B)
- Known safety profiles
- Higher success rates



Key Insight:

By analyzing network proximity between drug targets and disease genes, we can systematically identify repurposing opportunities that would be missed by traditional approaches.

5 Personalized Networks

Personalized networks integrate individual patient data (genomics, transcriptomics, proteomics, clinical data) to create patient-specific network models. This enables precision

medicine approaches tailored to each patient's unique molecular profile.

Data Integration:

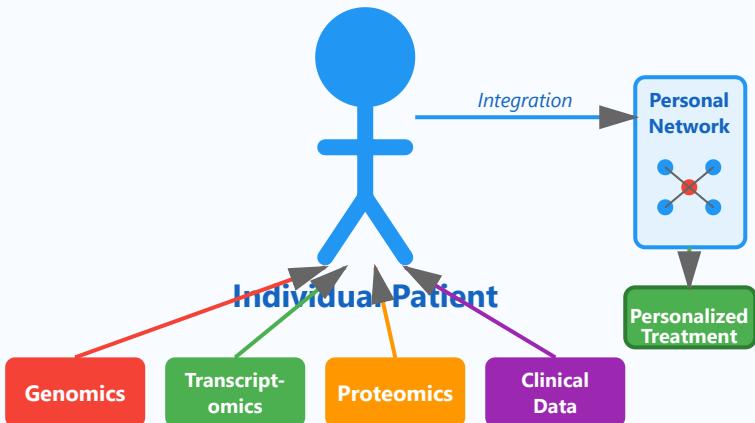
- **Genomic Data:** Mutations, SNPs, structural variants
- **Transcriptomic Data:** Gene expression patterns
- **Proteomic Data:** Protein abundance and modifications
- **Metabolomic Data:** Metabolite profiles
- **Clinical Data:** Symptoms, disease history, treatment response

Applications:

- Predicting individual disease risk
- Selecting optimal treatments
- Identifying personalized drug targets
- Predicting treatment response and adverse effects
- Monitoring disease progression

Challenges:

- Data integration complexity
- Computational requirements
- Clinical validation
- Cost and accessibility



Key Insight:

Personalized networks enable true precision medicine by capturing each patient's unique molecular landscape and identifying optimal therapeutic strategies based on individual network perturbations.