# Network pharmacology: drug re-purposing and discovery of multi-drug therapies by analytical approaches

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**Executive Summary**

The intrinsic robustness of living systems against perturbations is a key factor that explains why many single-target drugs have been found to provide poor efficacy or lead to significant side effects.

**THE PROBLEM:**
Rather than trying to design selective ligands that target individual receptors only, network polypharmacology aims to modify multiple cellular targets to tackle the compensatory mechanisms and robustness of disease-associated cellular systems, as well as to control unwanted side effects that limit the clinical utility of many conventional drug treatments. However, the exponentially increasing number of potential drug target combinations makes the pure experimental approach quickly unfeasible, and translates into a need for design principles to determine the most promising target combinations to effectively control complex disease systems.

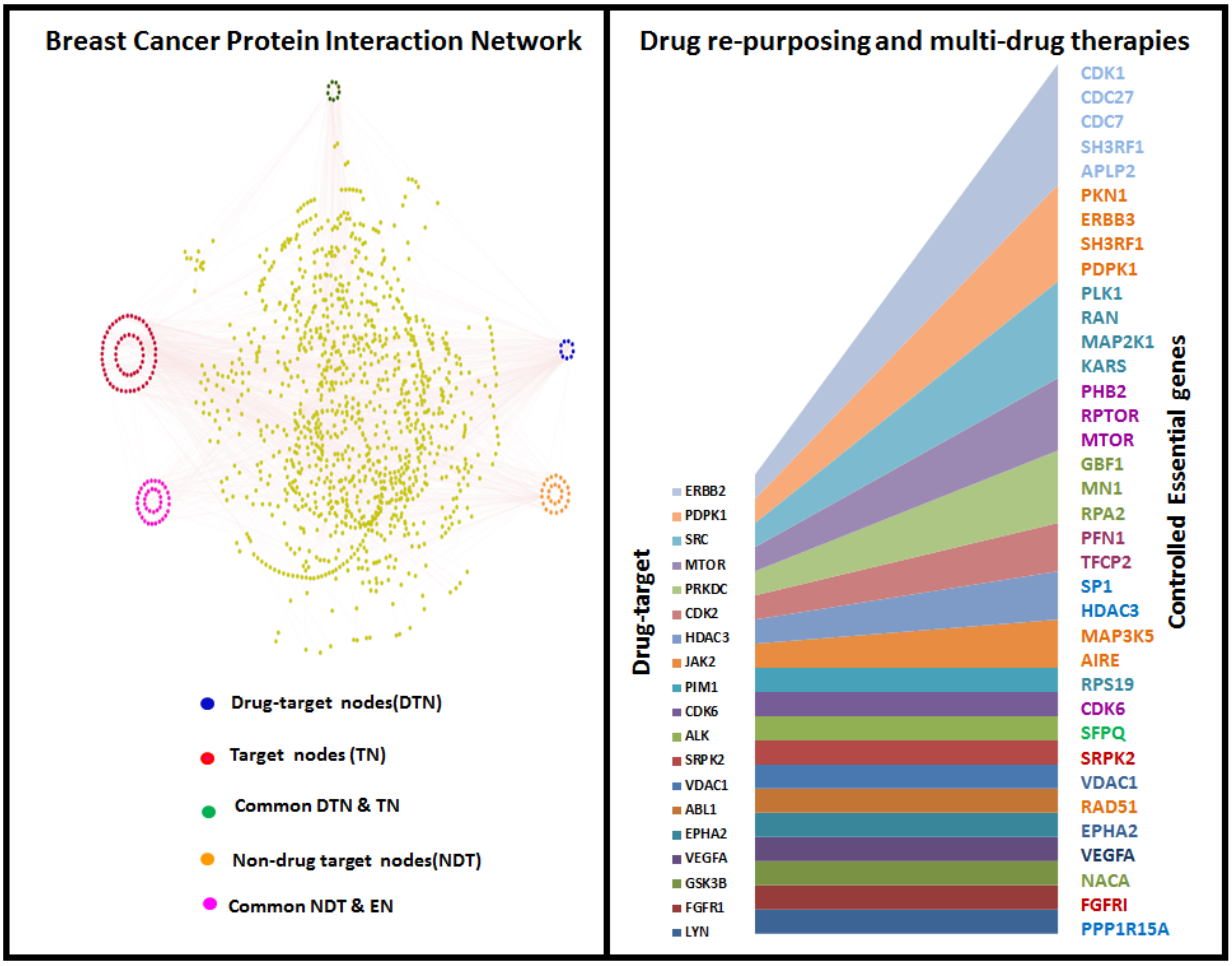
**OUR SOLUTION:**
Although diseased cells may harbor hundreds of genomic alterations, only a subset of these alterations is driving the disease initiation and progression; these are known as (disease specific) essential genes.

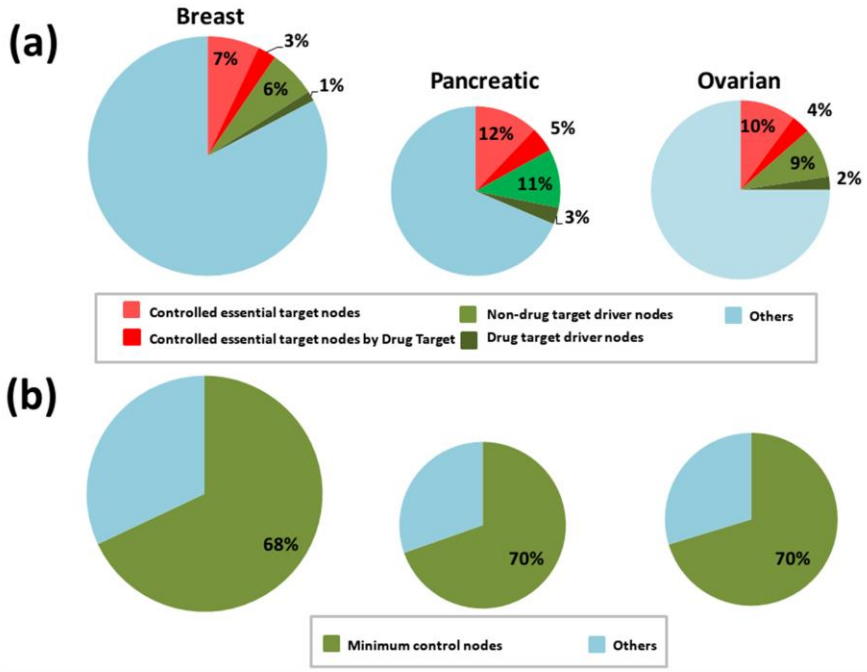
Our approach focuses on controlling disease-specific essential genes, as acting upon them is guaranteed to kill the diseased (and only the diseased!) cells. Our new machine learning algorithms identify nodes targetable by FDA-approved drugs, which lead to controlling essential genes, through (sometimes many) cascading effects in the network. Additionally, since essential genes are crucial for disease proliferation, targeting even a subset of them induces significant gains.

In a recent study we considered the disease networks of breast, pancreatic, and ovarian cancer. In case of breast cancer for example, we found out that a combination of 5 already available FDA-approved drugs has the potential of controlling over 19 breast-cancer essential genes.

**THE BUSINESS:**
Our approach can pinpoint not only pairs or triples of available drugs for cumulative therapy testing, but can analytically predict combinations of 6-10 drugs which are mathematically proved to have an influence over disease specific essential genes. The use of already existing, and approved, drugs in our predicted cumulative therapy is a significant advantage for a pharmaceutical company, as in the case of successful experimental testing it does not need to go through the extremely lengthy and costly process of approving a new drug. Also, our personalized disease network control analysis can be added to the list of services offered by specialized bio-medical data analysis companies offering personalized medical data analysis services. This will ultimately allow the health providers to offer personalized therapies based on our high-end analysis.

**THE PRODUCT**
The target outcome of this project is to develop a customizable bioinformatics platform allowing for data integration and analysis with the purpose of providing analytical suggestions of new multi-drug therapies (of specific diseases) by drug re-purposing. The platform will also be the subject of several custom modifications, as particularly fitted for our commercial partners.




**Controlling of cancer networks.**

The radius of the circles is proportional with the number of nodes in the networks. (a) The percentage of controlled target nodes by drug-target nodes and non drug-target nodes, w.r.t. the total number of nodes. (b) Required minimum control nodes for the control of the whole cancer networks.