

Systematic Drug Repositioning: Data and Informatics Showcase?

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Computational Biology, Quantitative Sciences
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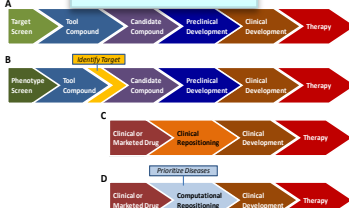
"The most fruitful basis for the discovery of a new drug is to start with an old drug" ... Sir James Black

Repurposing

Drug repositioning or repurposing is the application of known drugs and compounds to new disease indications.

Drug	Original indication	New indication
Viagra	Hypertension	Erectile dysfunction
Wellbutrin	Depression	Smoking cessation
Minoxidil	Hypertension	Hair loss
Thalidomide	Antiemetic	Leprosy
AZT	Cancer?	AIDS

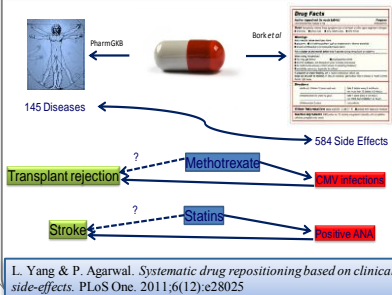
Shorter timelines



Patient Benefit: Better Safety

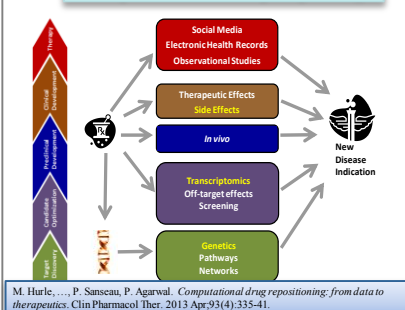
Corporate Benefit: Less Risk

Systematic Use of Clinical Side Effects



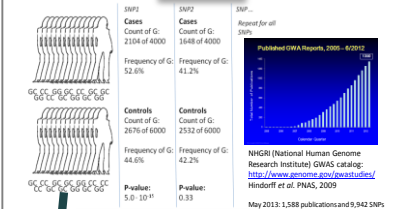
L. Yang & P. Agarwal. Systematic drug repositioning based on clinical side-effects. PLoS One. 2011;6(12):e28025

Computational Repurposing

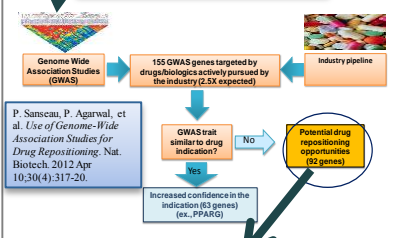


M. Hurl, ..., P. Sanseau, P. Agarwal. Computational drug repositioning: from data to therapeutics. Clin Pharmacol Ther. 2013 Apr;93(4):335-41.

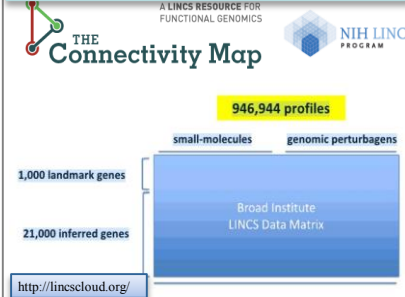
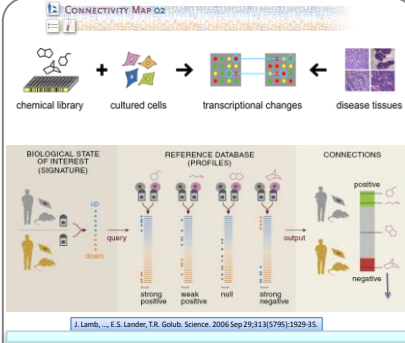
GWAS



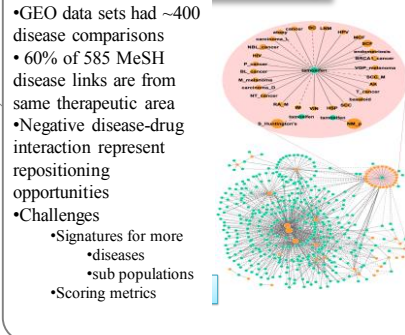
Repurposing with GWAS



Drug name	First substance developed	Gene	Current drug indication	GWAS trait (new potential drug indication)	GWAS reference
Dorsiphenolol	Launched/reagent	TM6SF1	Osteoporosis/cancer	Colic's disease	2
EPN-790	Phase 1	IL27	Adrenoleukodystrophy	Colic's disease/teratogenic bowel disease	2,16
Reparatol	Phase 2	3BP1	Cocaine withdrawal/insulin drop diabetes	Smoking cessation	7
Bio-053	Phase 1	LINC01	Multiple sclerosis	Essential tremor	4,5
ANG-557	Phase 1	CSG5L5	Systemic lupus erythematosus	Colic's disease/colic's disease/teratogenic bowel disease	13-19
Deo-021	Preclinical	TC4	Cancer	Factor's cancer therapy	20



Large-scale mining



Key Evidence

- External PubMed
 - F. Agarwal and D Scalls. Can literature analysis identify innovation drivers in drug discovery? Nat Rev Drug Discov. 2009 Nov;8(11):865-78.
- Internal Knowledge Management: Socrates Search
 - is a Google-like application that has been enhanced for chemistry, biology and disease search. The system has indexed more than 20 terabytes of electronic lab notebooks (ELNs), Documentum archives, SharePoint sites, emails and databases. The system uses sophisticated text indexing and analytics to identify chemical structure, gene, species and disease entities. Bio-IT World 2013 Best Practices Award.

Take Home: Systematic Repurposing



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Electronic Health Records (EHRs)

