

Repurposing drugs in the genomics era: bioinformatics approaches

Abbreviations: DNI, drugs of new indications; FDA, federal drug administration; GWAS, genome-wide association studies; PheGenI, phenome-genome integrator

Editorial

Conventional drug discovery approaches is time consuming with a high failure rate.¹ In recent years discovering new uses for already approved drugs is becoming increasingly attractive.²⁻⁵ This approach, termed as “drug repurposing” offers several advantages. For an approved drug, considerable information such as molecular targets, pathways, dosage, formulation, side effects, pharmacology and toxicology is available. This can considerably shorten the clinical trials and the approval process for a new indication. For diseases with limited options such as pancreatic cancer or for the neglected diseases involving various infectious diseases, such an approach would provide a rationale for therapy in the short run.^{6,7}

The era of repurposed medicine started with the success of Pfizer in 1998 when Sildenafil (Viagra) was repurposed from angina to erectile dysfunction.⁸ The anti nausea drug, Thalidomide (Thalomid) was repurposed for the treatment of leprosy in 1998⁹ and multiple myeloma in 2006 by Celgene.¹⁰ The list of repurposed drugs for the treatment of diverse diseases continues to evolve.¹¹ A drug target is often implicated in multiple pathways. These pathways are frequently shared across diverse cell types and consequently in multiple disease phenotypes. Thus, it is reasonable to expect an approved drug for one disease indication may offer therapeutic advantage in other diseases. Often a hint of repurposing use for a drug stems from epidemiological studies and clinical practice. Bioinformatics approaches can be used effectively to develop a database of repurposed drugs.^{12,13}

Mining of the genome- and -knowledge oriented databases is an attractive starting point for drug targets discovery. The availability of genome databases such as the NCBI Phenome-Genome Integrator, PheGenI,¹⁴ the Genome-wide Association Studies Catalogue, GWAS,¹⁵ human protein atlas,¹⁶ human protein map,¹⁷ proteomics dB¹⁸ the Uniprot knowledgebase¹⁹ and canSar protein annotation tool²⁰ can facilitate a systematic characterization of drug targets. The implication of a drug target in multiple diseases can be inferred from disease-oriented databases such as the GeneCards,²¹ the MalaCards,²² and the DisGeNet.²³ Molecular targets for approved drugs can be inferred from the drug bank,²⁴ US Federal Drug Administration database (FDA) and Drugs of New Indications (DNI) database.¹³

Using such an approach, recently series of FDA approved drugs were predicted for possible repurposing in the treatment of Vitiligo, an autoimmune disease,²⁵ Ebola Virus disease^{26,27} and the Zika virus infection.²⁸ The drug classes included antidiabetics, anti estrogens, antineoplastics, antithrombotics, antivirals, antihypertensives, statins as well as nutraceuticals. These results provide a strong rationale for therapeutic validation for repurposing efforts for these infectious diseases. For diseases such as the Ebola virus disease and the Zika virus disease with global implications, such a repurposing of existing drugs could help meet the urgent needs.

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Commercialization challenges including patent protection, competition from the generics and pricing of an existing drug for new indication exist to the concept of repurposing medicine.²⁹ Nevertheless, for diseases with limited treatment options, neglected diseases and global healthcare emergencies, repurposing existing drugs is a necessary approach for urgently needed therapeutics. Systematic bioinformatics mining of the genome can help improve the odds of finding the right drug with the molecular target implicated in specific diseases. Repurposing medicine together with conventional drug discovery approaches can help move the discoveries closer to bedside at a faster rate and meet unmet demands. One can anticipate that repurposing becomes a standard drug discovery approach in the future.

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Conflict of interest

The author declares no conflict of interest.

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