Intellectual Property (IP) considerations are critical in drug repurposing efforts. It can be wrong to assume that the entity owning the molecule being assessed for repurposing will be supportive of drug repurposing efforts. The owner may have ultimate control of the process. It is therefore important to understand the issues related to IP at the outset of the program and to engage with the owner of the drug at the earliest opportunity.

The requirement for sufficient evidence to attract the necessary funds for completion of clinical programs to achieve the ultimate goal. This typically involves the generation of new Intellectual Property (IP). However, while the generation of new IP is certainly attractive and important to potential investors, often what might superficially appear to be new IP has often already been captured by the innovator company that first developed the drug? The lack of sufficient funds to complete a clinical program often results in the publication of preliminary clinical reports that are underpowered and insufficient to alter clinical behaviour. As such, these reports only serve to expand the CV of the researchers.

A consideration of the clinical and regulatory development path to generate clinical data supporting the drug in the repurposed indication. This might involve large phase 3 clinical studies that directly compare the repurposed drug with the existing standard of care, with a requirement to show equivalence or superiority over the existing agents.

For deadly diseases, drug repositioning is a "universal strategy" because: 1) a reduced number of required clinical trial steps could reduce the time and costs for the medicine to reach market; 2) existing pharmaceutical supply chains could facilitate "formulation and distribution" of the drug; 3) the known possibility of combining with other drugs could allow for more effective treatment; and 4) The repositioning may make it easier to find "novel mechanisms of action" for ancient people.".

Breakthroughs in human genomes, network biology, and chemoproteomics have all aided drug repurposing. It's sometimes referred to as a serendipitous process, in which repurposable drugs are discovered by chance. It's now possible to find promising repurposing candidates by looking for genes implicated in a certain disease and determining if they interact with other genes in the cell that are known drug targets. According to studies, medications that target human genetic targets are twice as likely to succeed as all other drugs in development. Because it can be a time and cost effective strategy for treating dreadful diseases like cancer, drug repurposing is being employed as a solution-finding technique to combat the COVID-19 pandemic.

There have been a number of successes, the most notable of which being sildenafil (Viagra) for erectile dysfunction and pulmonary hypertension, as well as thalidomide for leprosy and multiple myelomas. Posaconazole and ravuconazole have been tested in clinical studies for Chagas disease. Clotrimazole and ketoconazole, two more antifungal drugs, have been studied for anti-trypanosome therapy. Antimicrobial repositioning has resulted in the development of broad-spectrum medicines that are effective against a variety of infections. Repurposed medications are emerging as viable choices for treating severe mental illnesses in psychiatry.

As a result of these under-appreciated challenges, drug-repurposing typically fails to fulfil its promise. There are multiple examples of drugs proposed for repurposing that have failed to demonstrate any success and prominent among them is the diabetes therapy, metformin. Metformin has >25,000 publications suggesting therapeutic potential in cancer, >240 clinical trials but with little evidence of any benefit to cancer patients [5]. Another prominent example is the anti-parasitic drug, ivermectin, that was initially proposed for repurposing as a potential treatment for COVID-19 but that was ultimately demonstrated in randomised clinical trials not to have sufficient activity to provide patient benefit [8,9].

There are however, rare examples of successful drug repurposing. The most deserving examples include thalidomide, moxidectin, dimethylfumurate and most recently fluvoxamine as a treatment for COVID-19 [10-12].

There are also common misconceptions, so some often cited examples of drug repurposing are actually more appropriately considered examples of industry's data-driven approach to drug development (e.g. sildenafil and minoxidil) or "label expansion" or "line extensions" that were conceived from the outset of the program.

There are, however, genuine examples of industry's success at drug repurposing. Selected examples include bevacizumab (from cancer indications to age-related macular degeneration), rituximab (from non-Hodgkin's lymphoma to rheumatoid arthritis, immune thrombocytopenia), adalimumab (from rheumatoid arthritis to autoimmune diseases more broadly) [5].

DISCUSSION AND CONCLUSION

In conclusion, while there are genuine opportunities for drug repurposing, and important examples of success. Although intuitively this might appear to be a simple and straight forward process, that is seldom the case. It is critical therefore to understand and address the challenges that could derail well-intentioned drug repurposing efforts.

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