EDITORIAL

Drug Repurposing in Cancer: Now and Beyond

Drug repurposing, also called drug repositioning, is an attractive approach that seeks to identify new targets or treatments for existing drugs. This approach saves not only significant amounts of money, but also time invested in drug design and development. This is especially so since pharmaceutical industry suffers from high attrition rates, delay in the approval of new drugs as well as other regulatory requirements, all of which result in higher drug costs. While serendipity played an initial role in sparking interest in drug repurposing, observational studies lend great support for the garnered success of repositioning several drugs, such as sildenafil, metformin, or edaravone to name a few. This repositioning offers new and big hopes for integrating already approved drugs, especially off-patent ones, in the management/treatment of off-target diseases. This is the first of a two parts thematic issue dealing with drug repurposing. Here, deep learning-based drug-target interactions (DTIs) prediction approaches are discussed, along with drugs repurposed for cancer.

Schcolnik-Cabrera *et al.* discuss how drug repurposing helps patients meet their needs to access new treatments [1]. In their paper, the authors highlight the notion that drug repurposing approaches allow for faster preclinical evaluation and clinical trials of the compound of interest, reduction in budgeting research and development costs, as well as improvement of biosafety risks. The authors call upon increased advertising of repurposing in the health community in order to reduce prescribing bias where appropriate.

Abbasi *et al.* write an elegant piece where they investigate the existing deep learning-based drug-target interactions (DTIs) prediction approaches from multiple perspectives [2]. They then explore these approaches in an attempt to identify the deep network architectures that can be employed to extract valuable and relevant information from drug compound and protein sequences. This paper also explores the process of how to combine descriptors for drug and protein features, elements that may prove helpful in the race for drug discovery, especially when repurposing is desired. Similarly, Falvo *et al*. discuss computational approaches, preclinical models and clinical trials that are employed for repurposing drugs to treat different types of cancer, especially ones resistant to commonly used anticancer drugs [3].

A central feature of this thematic issue revolves around combatting cancer with repurposed drugs that are currently used for diseases other than cancer. Antoszczak *et al.* discuss how some antidepressants (citalopram, fluoxetine, paroxetine, sertraline) and antipsychotics (chlorpromazine, pimozide, thioridazine, trifluoperazine) could be repositioned for cancer treatment [4]. Likewise, Zhang *et al.* discuss how pioglitazone, metformin, losartan, syrosingopine, prazosin aspirin, celecoxib chloroquine, artemisinin, pyrimethamin, flubendazole, mebendazole, itraconazole, rapamycin, sertraline, fluoxetine, paroxetine, as well as antibacterial drugs such as sulfisoxazole and azithromycin can be intelligently employed for cancer therapy [5]. Allegra *et al.* discuss how bromocriptine, chlorprothixene, mebendazole, flubendazole, quinacrine, furazolidone, verteporfin, telmisartan, clarithromycin, or nelfinavir among others can be repositioned for acute lymphoblastic leukemia, chronic myeloid leukemia (CML), and lymphomas [6]. Similarly, for CML, Nehme *et al.* elaborate the use of acriflavine (ACF) in blocking growth of solid and and hematopoietic tumor cells [7]. In this paper, the authors discuss how tyrosine kinase inhibitors (TKIs) such as imatinib (IM) are effective in CML therapy; yet 15% of patients are refractory to IM. The authors then move to suggest the repurposing of ACF in CML after IM failure or in combination with IM to improve the anti-tumor effects of IM especially in resistant cancer populations. Paliogiannis *et al.* present a state of the art review on repurposing anticancer drugs for use in idiopathic lung disease, and anti-fibrotic drugs for use in cancer therapy [8].

Iratni *et al.* discuss how sildenafil, commonly used for erectile dysfunction, can be reprofiled as a potential anticancer drug [9]. The authors discuss how the pro-apoptotic effect of Sildenafil lies in its ability to potentiate nitric oxide (NO)/ phosphodiesterase type 5 (PDE5)-dependent mechanisms. In addition, the authors discuss sildenafil's ability to induce autophagy and potentiate anti-tumor immune responses. Alaaeddine *et al.* discuss in a rather elegant way the value of designing multi-target directed ligands (MTDLs) modifying the activity of COX-2, 15-LOX, and PPARγ in cancer and metabolic disorders [10]. The authors then propose that concerted future effort to translate these early results facilitating the adoption of these, and similar, molecules in clinical research.

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We hope readers enjoy this part of the thematic issue. We invite them to read the second part which is primarily dedicated to repositioning drugs for neurodegenerative and cardiovascular diseases.

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