EDITORIAL

Drug Repurposing in Neurodegenerative and Cardiovascular Diseases

This is the second part of our thematic issue about drug repurposing. Here, the topics focus on neurodegenerative and cardiovascular diseases. Drugs discussed in this issue include antibiotics, anti-mycobacterials, antivirals, anti-fungals, chelating agents, PPAR modulators, metformin, modulators of the renin-angiotensin system, including angiotensin receptor blockers, and anticancer drugs. In addition, repurposing of andrographolide, edaravone, cilostazol, sildenafil and sialidase inhibitors is also presented.

Repurposing drugs for neurodegenerative diseases is a major part of this issue. In their review, Rampa *et al.* discuss the treatment of Alzheimer's disease by recently repositioned drugs in various classes such antibiotics, anti-mycobacterials, antivirals, antifungals, chelating agents, PPAR modulators, metformin, modulators of the renin-angiotensin system including angiotensin receptor blockers, and anticancer drugs [1]. The authors then dissect new hypotheses proposed regarding the pathogenesis of this disease. Such hypotheses, the authors argue, could unhide previously overlooked therapeutic regimens. El Massry *et al.* reassess the mechanisms through which metformin exerts its effects. and elegantly discuss how metabolic stress could be a powerful instigator of neural insults [2]. In particular, the authors discuss how metabolic stress contributes to the pathobiology of Alzheimer's disease and depression. The authors conclude with the therapeutic benefits of repurposing metformin for the reversal of brain injury though they caution that further studies are warranted. Ren *et al.* discuss the potential repurposing of andrographolide for use in the management of Alzheimer's disease, Parkinson's disease, as well as cancer, inflammation, and cardiovascular disease [3]. The authors then provide a perspective on pharmacological enhancement of andrographolide such as derivatives, chemical modifications with potent biological activity and drug delivery. Traumatic brain injury (TBI) is a debilitating disease that is putting a lot of financial and other burdens on different countries. Shakkour *et al.* discuss how edaravone, is a potent free-radical scavenger that has been in the market for more than 30 years can be repositioned for TBI [4]. In their review, the authors discuss the biochemical properties of edaravone along with its effects on several neurological disorders in the hope that it can be adopted for treating TBI patients. Anwar *et al.* present an interesting paper about targeting COVID-19 in Parkinson's patients, and how drug repurposing can help patients with COVID-19 who are already suffering from Parkinson disease [5]. The authors discuss how amantadine, a common drug possessing both antiviral and anti-Parkinson properties can be utilized.

Another section of this issue deals with drugs repurposed for cardiovascular disease. El-Hachem *et al.* discuss how cilostazol, a selective inhibitor of phosphodiesterase-III, originally prescribed to treat intermittent claudication, can be repurposed for the management of Raynaud's phenomenon [6]. This is largely due to this drug's antiplatelet and vasodilating properties. Poitras *et al.* present a very interesting paper about the chemistry and pharmacology of PDE5 inhibitors [7]. They also revisit sildenafil's use for erectile dysfunction and pulmonary arterial hypertension. The authors then end with a critical review of emerging evidence suggesting that sildenafil can be repurposed for the treatment for persistent pulmonary hypertension of the newborn. Sobenin *et al.* present an exciting hypothesis that decreasing LDL enzymatic desialylation reduces lipid accumulation in arterial wall, thus suppressing atherogenesis [8]. The authors then discuss the potential of repurposing sialidase inhibitors for use in the treatment or management of atherosclerosis.

We hope readers enjoy both parts of the issue where we tried to cover leading causes of global death. We hope that by discussing drug repositioning in metabolic, neurodegenerative, and cardiovascular diseases, as well as in cancer, in addition to deep learning-based drug-target interactions (DTIs) prediction approaches and computational approaches, our readers would benefit from this diverse array of topics.

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