Editorial

Recent Advances in the Development of New Therapeutic Tools Against Major Parasitic Diseases

Parasitic infections represent a major challenge for global health and economy. Despite their high prevalence and clinical impact, treatment options are still incomplete. There are a limited number of effective medicines, many have serious side effects, and increasing drug resistance is also a real threat. Even if these diseases have been largely neglected for drug development because they affect poor people in poor regions of the world, in recent years, the search for antiparasitic drugs received a new impulse. Thus, this issue will focus on recent efforts to reinvigorate the drug development targeting major parasitic diseases.

One interesting strategy recently used to fight these diseases is based on the inhibition of enzymes involved in metabolic pathways essential for parasite survival and/or infectivity and absent or sufficiently different at a structural level from those present in the host. In this context, the first paper of the issue [1] explores the possibility to target in trypanosomal diseases, the enzymes of the **pentose phosphate pathway**, which includes an oxidative branch, important in the maintenance of cell redox homeostasis, and a non-oxidative branch in which ribose 5-phosphate and erythrose 4-phosphate, precursors of nucleic acids and aromatic amino acids, are produced. In particular, the authors provide a comprehensive overview of the available chemotherapeutic options against trypanosomal diseases and discuss the potential of genetically validated enzymes from the pentose phosphate pathway of trypanosomatids to be explored as potential drug targets.

The second paper [2] analyzes **Carbonic Anhydrase** (CA) metallo-enzymes as a new possible drug targets for parasitic diseases. CAs catalyze the reversible hydration of carbon dioxide to bicarbonate and protons. Compelling data in the literature strongly indicate that interference with CA activity in various parasites leads to an impairment of parasite growth and virulence, which in turn leads to a significant anti-infective effect. All the existing studies on CAs from protozoa responsible for the major human parasitic diseases, namely Malaria, Leishmaniasis and Chagas disease, are analyzed, and the emerging role of these enzymes as targets for the development of new anti-parasitic drugs is critically discussed.

In the past, the lack of high-resolution structural information on parasitic proteins has been a big obstacle in structure based drug discovery programmes. However, the recent renaissance of **electron microscopy** (EM), which has seen a remarkable rise in the number of available structures, represents an important impulse in drug discovery for parasitic diseases. Thus, the third paper of the issue [3] addresses the challenges associated with the structural determination of parasitic proteins by EM and provides some examples of parasitic protein structures determined with this technique. Finally, limitations which need to be overcome before using EM as a mainstream technique in parasitic drug development are also discussed.

REFERENCES

[1] Loureiro, I; Faria, J.; Santarem, N.; Smith, T.K.; Tavares, J.; Cordeiro-da-Silva, A. Potential drug targets in the pentose phosphate pathway of trypanosomatids. *Curr. Med. Chem.,* **2018**, *25*(39), 5239-5265.

[2] D'Ambrosio, K.; Supuran, C.T.; De Simone, G. Are carbonic anhydrases suitable targets to fight protozoan parasitic diseases? *Curr. Med. Chem.,* **2018**, *25*(39), 5266-5278.

[3] Johnson, R.M.; Rawson, S.; McPhillie, M.J.; Fishwick, C.W.G.; Muench, S.P. The growing role of electron microscopy in anti-parasitic drug discovery. *Curr. Med. Chem.,* **2018**, *25*(39), 5279-5290.

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