Metalloenzymes as therapeutic targets

Aims & Scope:

In the last decade, the growing interest on Metalloenzymes is mainly related to the increasing amount of insights about their key roles in the pathophysiology and pathogenesis of a variety of human disorders. The dysregulation of metalloenzymes activity is a widespread and pivotal event associated with the onset of the most common diseases of our age, including tumours growth and spread, CNS and neurodegenerative diseases like Epilepsy, Alzheimer and Parkinson, some bacterial and viral infections, hypertension and obesity.

In the last twenty years, the fine-tuning of new technologies has allowed the scientific community to better define the structure of the catalytic sites of some metalloenzymes and the role played by the metal. Relying on this information, high affinity inhibitors/ligands, able to modulate the activity of these enzymes, have been successfully identified.

The goal of this special issue is to provide an overview about the most relevant and recent advancements in this field. This special issue will be focused on metalloenzymes wherein the metal center plays catalytic role and which are involved in pathophysiology and pathogenesis of human disorders. Thus, it will include, but will not be limited to:

- Zn(II)-containing metalloenzymes: matrix metalloproteinases (MMPs), histone deacetylases (HDACs), E3 Ubiquitin Ligases, histidinol dehydrogenase (HDH), carbonic anhydrases (CAs), Angiotensin Converting Enzyme (ACE), botulinum neurotoxins (BoNTs);
- Fe(III)-containing metalloenzymes: cytochrome P450 superfamily (Cyt p450), 5-lypoxigenase (5-LOX);
- Cu(II)-containing metalloenzymes: mushroom tyrosinase (TY);
- Mg(II)-containing metalloenzymes: Human immunodeficiency virus integrase (HIV-1 IN).
In particular, it is planned to present and discuss the state of the art about the key data on the most drugable metalloenzymes, and the breakthrough in the new emerging structural and mechanistic insights that would be useful to design new inhibitors or to investigate new implications of metalloenzymes in diseases. We also exhort to submit high quality, original articles on the synthesis and binding studies of new inhibitors/ligands of this peculiar class of enzymes. Thus, potential topics include, but are not limited to:

- Emerging structural and mechanistic studies on metalloenzymes;
- Relevant insights concerning the impact of the metal related to the catalytic activity of specific metalloenzymes;
- Screening, identification and synthesis of new inhibitors/ligands;
- New integrated approach to gain atomic-level information for the structure or the dynamics of the metalloenzymes or their complexes;
- Development of new functional assays to define the protein-inhibitors binding;
- Identification of new biochemical pathways, where metalloenzymes might be implicated and play key roles in disease processes.

**Keywords:**
Metalloenzymes, pathophysiology, matrix metalloproteinases, bacterial metalloenzymes inhibitors, C-cinnamoyl glycosides, ER aminopeptidase inhibitors, carbonic anhydrases, HIV-IN mutation, guanylate cyclase.

**Subtopics:**
- Mechanism of substrate recognition and processing by Matrix Metalloproteinases
- Inhibitors of ER aminopeptidase 1 and 2: from design to clinical application
- Epigenetic metalloenzymes
- C-cinnamoyl glycosides: an emerging “tail” for the development of selective carbonic anhydrase inhibitors
- State of the Art on Carbonic Anhydrases Modulators for Biomedical Purposes
• The design of new HIV-IN mutation resistant inhibitors using multiple microdomain targeting strategies
• Adynamins as potential drug targets.
• Inhibitors of serine/threonine protein phosphatases
• Bacterial Metalloenzymes Inhibitors
• Therapeutic targeting of the soluble guanylate cyclase

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