WELCOME LETTER

Dear Colleagues and Friends,

We are thrilled to welcome you to the 54rd Annual Meeting of the Brazilian Society of Biochemistry and Molecular Biology (SBBq), at the Majestic Hotel Convention Center in Águas de Lindóia, SP, May 17 to 20, 2025.

SBBq´s annual meeting is one of Brazil's most esteemed scientific events, having been held continuously for over four decades. It is a vital forum for scientific exchange, promoting the advancement of knowledge in Biochemistry, Molecular Biology, and related fields. It also fosters discussions on scientific education and training, as well as consensus positions in the field, contributing towards public policies.

This year, the organizing committee has created an engaging interdisciplinary program that features 8 plenary lectures and 18 symposia led by world-class scientists. These sessions will highlight the latest advancements and current challenges across various research topics in Biochemistry and Molecular Biology. We are also pleased to include policy thinkers who will assess the landscape of science and technology in our country.

We eagerly anticipate your presence in Águas de Lindóia!

Alicia J. Kowaltowski

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08361 - Sessão de Cartazes I

D.35 - Impacto de Mutações R81A, H107A e D111A no Domínio Zinc-finger da hHep1 na Estrutura e Interação com Hsp70: Abordagens Computacionais e Biofísicas

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INTRODUCTION: Molecular chaperones, also known as Heat-Shock Proteins (HSPs), are essential proteins for maintaining cellular proteostasis. They play several critical roles in ensuring the proper folding and functionality of cellular proteins, from assisting newly translated polypeptides to directing misfolded proteins for degradation. The human Hsp70-escort protein 1 (hHep1) is a small mitochondrial protein that regulates the solubility and stimulates the activity of Hsp70 family. Dysfunction of hHep1 leads to the aggregation of Hsp70, causing cellular damage and contributing to the development of neurodegenerative diseases. Biochemical studies have demonstrated that point mutations at three charged residues within the Zinc-finger domain of hHep1 (R81A, H107A, and D111A) result in the aggregation of hHep1 and, consequently, Hsp70, raising questions about the molecular mechanisms underlying this process. OBJECTIVES: The objective of this study is to investigate the impact of single, double, and triple mutations at conserved residues (R81A, H107A and D111A) on the structural integrity of hHep1 and its interaction with Hsp70. MATERIALS AND METHODS: The structural models of hHep1 and its point mutants were generated using AlphaFold3 and validated using tools based on conformational similarity, stereochemical geometry and machine learning. Recombinant plasmids of single, double, and triple mutations were constructed in pET28A using the Q5 Site-Directed Mutagenesis Kit (New England Biolabs) and transformed into Escherichia coli DH5α strain. The mutations were confirmed by plasmid sequencing. Recombinant protein production was carried out in E. coli BL21(DE3) cells. DISCUSSION AND RESULTS: In silico analyses of the mutants indicate that R81A and H107A mutants preserved the threedimensional structure of hHep1. However, all three mutations, including D111A, which causes global destabilization, reduce the free energy of unfolding, consistent with a loss of functionality. CONCLUSION: Comparative biophysical characterization assays are currently in progress to quantify the impact of the mutations on the hHep1 structure. Further analyses, including circular dichroism, fluorescence spectroscopy, and size-exclusion chromatography, will be performed.

Keywords: Hsp70, hHep1, Chaperonas moleculares
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08460 - Sessão de Cartazes II

D.36 - Study of the modulation of the catalytic activity of cysteine proteases (cruzain, cathepsin L, and B) by 3,5-diaryl-1,2,4-oxadiazole analogs.

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INTRODUCTION: Cysteine proteases are proteolytic enzymes involved in essential physiological and pathological processes, including immune response regulation, cancer progression, protein degradation, and extracellular matrix remodeling. These enzymes are also promising targets for therapeutic strategies against parasitic diseases and cancer. OBJECTIVES: This study aimed to evaluate the inhibitory potential of 3,5-diaryl-1,2,4-oxadiazole analogs on the cysteine proteases cathepsin B, cathepsin L, and cruzain. MATERIALS AND METHODS: IC_{50} values were determined by incubating cathepsin B and cruzain in sodium acetate buffer (100 mM), EDTA (5 mM), NaCl (100 mM), Triton X-100 (0.01%), 20% glycerol, and DTT (3 mM). Cathepsin L was incubated in a similar buffer (without Triton X-100) at pH 5.5. Enzymatic activity was measured by spectrofluorimetry using Z-FR-MCA as a substrate (λ_{ex} = 360 nm; λ_{em} = 480 nm) at 37°C. DISCUSSION AND RESULTS: The analogs displayed selective inhibitory activity. For cruzain, D09 and D14 were most effective, with D14 showing an IC_{50} of 21.86 µM. For cathepsin L, D13 was the most potent inhibitor (IC_{50} = 4.84 µM), followed by D07 and D06. Regarding cathepsin B, D08, D16, and D17 were prominent, with D17 exhibiting the lowest IC_{50} (3.76 µM). Bulky substituents, such as multiple methoxyphenyl groups, negatively impacted efficacy due to steric hindrance. D03 and D14 inhibited cruzain via simple non-competitive inhibition (INCLS). The same mechanism was observed for D06 and D13 with cathepsin L, and D17, D18, and D19 with cathepsin B. D08 showed non-competitive inhibition with positive cooperativity, indicating allosteric modulation and enhanced interaction with the enzyme–substrate–inhibitor complex. CONCLUSION: Structural variations in 3,5-diaryl-1,2,4-oxadiazole analogs influence cysteine protease inhibition. Ligand size plays a crucial role in modulating enzyme interaction and inhibitory efficacy.

Keywords: Cathepsins, 3,5-diaryl-1,2,4-oxadiazole analogues co, Inhibitory Potential
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