



UNIVERSITÀ DEGLI STUDI *MAGNA GRÆCIA* DI CATANZARO - DIPARTIMENTO DI SCIENZE DELLA SALUTE
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DOTTORATO DI RICERCA IN SCIENZE DELLA VITA - SCUOLA DI SPECIALIZZAZIONE IN FARMACIA OSPEDALIERA
PIANO PER L'ORIENTAMENTO E IL TUTORATO ORIENTARE ED ORIENTARSI TRA LE SCIENZE DEL FARMACO

SEMINARIO CORSO CV_S_155

HUMAN ASPARAGINE SYNTHETASE: STRUCTURAL INSIGHTS ABOUT AN EMERGENT ANTI-CANCER TARGET BY CRYO-EM AND MOLECULAR MODELLING TECHNIQUES



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Human Asparagine Synthetase (ASNS) is considered one emergent target in Medicinal Chemistry, due to its involvement in metastatic progression in breast cancer, sarcoma cell proliferation, and decreased effectiveness of clinical treatments for acute lymphoblastic leukemia¹. Recent advances in X-ray crystallography and cryogenic electron microscopy offer the opportunity of elucidating functionally relevant motions about this target. In this lecture those methods were used to investigate about the conformational changes of some key residues involved in the formation of a catalytically relevant intramolecular tunnel. The biophysical results are consistent with independent molecular dynamics (MD) simulations on a model generated from the X-ray structure of human ASNS, giving additional details about structural integrity of the tunnel in certain mutations².

Introduction

Prof. Vincenzo MOLLACE

Life Science Seminar Lecture

Prof. Nigel RICHARDS

Discussion and conclusions

Prof. Stefano ALCARO

References

- [1] Radadiya A, Zhu W, Coricello A, Alcaro S, Richards NGJ. *Improving the Treatment of Acute Lymphoblastic Leukemia*. *Biochemistry*. **2020**, 59, 3193-3200.
- [2] Coricello A, Nardone AJ, Lupia A, Gratteri C, Vos M, Chaptal V, Alcaro S, Zhu W, Takagi Y, Richards NGJ. *Cryo-EM and Molecular Dynamics Simulations Reveal Hidden Conformational Dynamics Controlling Ammonia Transport in Human Asparagine Synthetase*. *bioRxiv*, **2023**, 05.16.541009

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