Programma Nazionale di Ricerche in Antartide (PNRA)

Final project report

Project ID	2004/1.8
Title	Molecular basis of the structural adaptation of enzymes from antarctic organisms
Principal investigator	Stefano Pascarella
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Duration	2 years
Assigned funding	11000,00 Euro

Activities and results

A comparative analysis between enzymes from cold adapted organisms and their homologs from meso- and thermophilic species was carried out with the aim to identify the "static" and "dynamic" properties potentially related to the functional adaptation to low temperatures. Indeed, such enzymes show high catalytic efficiency in the 0-20 °C temperature range, temperatures at which counterparts from mesophilic or thermophilic organisms do not allow adequate metabolic rates to support life or cellular growth. The analysis took into account several "static" structural and chemical-physical characteristics of the enzymes such as number of inter-residue interactions, surface hydrophobicity, amino acid composition and the like. The comparisons of the dynamics properties of a few enzymes selected gave valuable indications on the role of the local and/or global flexibility of the polypeptide chain. Indeed, it is now accepted that flexibility is one of the major factors involved in cold adaptation.
The results obtained contributed to the understanding of the principles underlying catalysis in the cold temperatures and suggested possible strategies for the rational engineering of enzymes with biotechnological potential. In particular, part of the research focused on the structural adaptation occurred at the subunit interface of oligomeric cold adapted enzymes. The most significant chemical-physical variations found are: increase of the ionic interactions; decrease of the number of hydrogen bonds; decrease of the fraction of apolar surface; decrease of the hydrophobic contact surface. Several simulations of molecular dynamics have been carried out on psycrophilic and mesophilic elastases and trypsins with the aim to explore the variations within a specific enzymatic class. These enzymes possess fewer interdomain interactions compared to their mesophilic counterparts. Moreover, they display a higher flexibility in regions close to their functional sites. Apparently, both enzymes utilized the same evolutionary pathway to cold adaptation and therefore represent an interesting example of molecular evolutionary convergence.

Products

A – papers in scientific magazines

1. Papaleo E, Riccardi L, Villa C, Fantucci P, De Gioia L., Flexibility and enzymatic cold-adaptation: a comparative molecular dynamics investigation of the elastase family. Biochim Biophys Acta. 2006;1764:1397-1406. IF = 3,078
2. Papaleo E, Olufsen M, De Gioia L, Brandsdal BO., Optimization of electrostatics as a strategy for cold-adaptation: a case study of cold- and warm-active elastases. J Mol Graph Model. 2007;26:93-103. IF = 1,932
3. Tronelli D, Maugini E, Bossa F, Pascarella S., Structural adaptation to low temperatures--analysis of the subunit interface of oligomeric psychrophilic enzymes. FEBS J. 2007;274:4595-4608. IF = 3,396

B – book chapters

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C - proceedings of international conferences

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D – proceedings of national meetings and conferences

1. Tronelli D, Maugini E, Bossa F, Pascarella S, Structural adaptation to low temperatures--analysis of the subunit interface of oligomeric psychrophilic enzymes. 6th PNRA Meeting on antarctic biology: critical issues and research priorities for the ipy and 2007-2009, 7-9 June 2007, Follonica
2. Papaleo E, Pasi M, Riccardi L, Fantucci P, De Gioia L, Comparative molecular dynamics simulations to study enzymatic cold adaptation, 6th PNRA Meeting on antarctic biology: critical issues and research priorities for the ipy and 2007-2009, 7-9 June 2007, Follonica

E – thematic maps

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F – patents, prototypes and data bases

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G – exhibits, organization of conferences, editing and similar

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H - formation (PhD thesis, research fellowships, etc.)

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Research units

Research Unit Roma La Sapienza
Stefano Pascarella
Daniele Tronelli
Alessandro Paiardini

Research Unit Milano Bicocca
Luca De Gioia
Elena Papaleo

Date:

Notes

The following papers have been published outside the time frame of the project. However, they report part of the work initiated and elaborated within the project itself.

Maugini E, Tronelli D, Bossa F, Pascarella S., Structural adaptation of the subunit interface of oligomeric thermophilic and hyperthermophilic enzymes. Comput Biol Chem. 200933:137-148. IF = 1,653

Olufsen M, Papaleo E, Smalås AO, Brandsdal BO., Ion pairs and their role in modulating stability of cold- and warm-active uracil DNA glycosylase. Proteins. 2008;71:1219-1230. IF = 3,354

Papaleo E, Pasi M, Riccardi L, Sambi I, Fantucci P, De Gioia L., Protein flexibility in psychrophilic and mesophilic trypsins. Evidence of evolutionary conservation of protein dynamics in trypsin-like serine-proteases. FEBS Lett. 2008;582:1008-1018. IF = 3,263