

Preface

The idea to write this book arose from the interest and discussion around our recent review covering the structural and functional aspects on gamma-glutamyl transpeptidases [1]. In the summer of 2012, Dr. Beatrice Menz, Life Sciences Editor of Springer, generously invited us to consider expanding this interesting subject and to publish it within Springer Briefs Series. We kindly accepted this invitation as we consider the topic to be of great interest for the scientific community and for a large part of readers and researchers who approach the extended literature on these enzymes.

The interest in gamma-glutamyl transpeptidases has been increased in the years due to their functional versatility and their potential applications in biotechnology and clinics. The enzymes play a key role in crucial cellular events such as aging, senescence and cancer, thanks to its involvement in glutathione metabolism, the most abundant antioxidant molecule in the cells which regulates redox homeostasis. A fascinating aspect emerging from our studies is that gamma-glutamyl transpeptidases can be considered from different point of views, a moonlighting protein, that is a protein, usually an enzyme, which can perform more than one function in different contexts, cell types, tissues, or during evolution. A number of the currently known moonlighting proteins are evolutionarily derived from highly conserved enzymes, also called ancient enzymes. Indeed, gamma-glutamyl transpeptidase is present in many different organisms and this increases the chance to develop secondary moonlighting functions. Our previous investigations on gamma-glutamyl transpeptidases isolated from extremophilic microorganisms, considered the first bacteria to colonize the earth, thanks to their ability to adapt to the extreme conditions of temperature and pressure, strongly suggest that these enzymes first evolved the ability to hydrolyze glutathione and only later with eubacteria and eukarya evolved a second function, to transfer the gamma-glutamyl group to amino acids and short peptides [2, 3]. A real gain of function that provided the cell for the uptake and recycle of amino acids for protein synthesis. An interesting prospective for this function is that the bacterial enzymes, which can accept a large spectrum of substrates (most of them still unknown), can be exploited to produce gamma-glutamyl compounds extremely useful for drug delivery. In addition, moonlighting provides a possible mechanism by which bacteria may become resistant to antibiotics. Interestingly, some mutations in

bacterial gamma-glutamyl transpeptidase confer the protein cephalosporin acylase activity, a sort of antibiotic resistance, which can be exploited for an eco-sustainable synthesis of antibiotics. As regards eukaryal enzymes, gamma-glutamyl transpeptidase is also involved in leukotrienes metabolism and in drugs detoxification. All these features together make the enzyme the center of an interesting debate about its known and unknown functions.

The present volume especially focuses on the structure and function relationship of gamma-glutamyl transpeptidases and on fallout on cell life, with a particular emphasis on biotechnological and biomedical applications. In the final part, we summarize some interesting findings about the involvement of the enzyme in cancer and other diseases. For this topic, we take a lot of advantage from the more recent reviews of Pompella et al., which have given a strong contribution in understanding the role of gamma-glutamyl transpeptidase in cell proliferation. For these reasons, we thank all the researchers who have contributed with their work to our knowledge in the field.

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References

1. Castellano I, Merlino A (2012) Gamma-glutamyl transpeptidases: sequence, structure, biochemical properties, and biotechnological applications. *Cell Mol Life Sci* 69 (20):3381–3394
2. Castellano I, Merlino A, Rossi M, La Cara F (2010) Biochemical and structural properties of gamma-glutamyl transpeptidase from *Geobacillus thermodenitrificans*: an enzyme specialized in hydrolase activity. *Biochimie* 92 (5):464–474
3. Castellano I, Di Salle A, Merlino A, Rossi M, La Cara F (2011) Gene cloning and protein expression of gamma-glutamyl transpeptidases from *Thermus thermophilus* and *Deinococcus radiodurans*: comparison of molecular and structural properties with mesophilic counterparts. *Extremophiles* 15 (2):259–270

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