

## Gamma-Glutamyl Transpeptidase and Glutathione Function

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$\gamma$ -Glutamyl transpeptidase (5-L-glutamyl-peptide: amino acid 5-glutamyl transferase; EC 2.3.2.2; abbreviated GGT), is a plasma membrane-associated enzyme that is located on the outer surface of the cells of secretory tissues [1]. It plays a central role in the metabolism of glutathione that is widely in various mammals [2]. The enzyme catalyzes the degradation of the extracellular glutathione in a well identified cycle known as the  $\gamma$ -glutamyl cycle. In addition, GGT plays a role in the formation of mercapturic acid and the slow reacting substance, leukotriene [3,4]. This enzyme in serum from normal subjects and liver disease patients was separated into multiple molecular forms, which differ in electric charge and relative molecular mass but have similar kinetic behavior [5]. GGT is usually assayed by using  $\gamma$ -glutamyl *p*-nitroanilide as a synthetic  $\gamma$ -glutamyl donor substrate. It is preferred more than the natural substrate glutathione due to the greater analytical convenience of the former compared to glutathione and the much greater solubility of the synthetic substrate [6].

It is generally agreed that clinically significant elevations of the catalytic activity of serum GGT associated almost exclusively with hepatobiliary disease [6], although the highest activity of GGT is found in the kidney [7]. Thus, measurements of total serum GGT activity and the multiple isoforms of serum GGT in normal and disease as well, were considered to be liver-specific [8,9]. It was found that serum GGT in advanced cases of *Schistosoma mansoni* infection was significantly increased [10] due to its effect on the liver. The alteration of GGT activity in schistosomiasis might be attributed to enzyme regulation and modifications [11]. The significant change of GGT in the liver may be an indication of altered degradation of glutathione and the formation of  $\gamma$ -glutamyl-amino acids [1]. It was reported that glutathionuria, growth failure and infertility are detected in genetic GGT deficient-mice [12]. Moreover, the genetic expression of GGT is increased during oxidative stress [1].

Glutathione, a ubiquitous tripeptide thiol found in virtually all cells, is considered as the main antioxidant [13]. It is important in the protection of the cells against the effects of the reactive oxygen species. In addition, it functions in the reduction of the disulfide linkages of proteins and other molecules and the synthesis of the deoxyribonucleotide precursors of DNA [14]. The intracellular

glutathione is the source of its content in plasma and it is a substrate of the membrane-bound GGT by acting as a  $\gamma$ -glutamyl donor to different acceptors [13]. Accordingly, glutathione is also involved in liver diseases in addition to hepatotoxicity [13].

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