

EVOLUTION OF MICROSOMAL GSTs

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Glutathione S-transferases (GSTs) are an ancient superfamily of catalytic and binding proteins ubiquitously distributed in highly diverse aerobic organisms, with crucial biological roles in the detoxification of both endogenous and exogenous toxic compounds and in cell protection from oxidative insults. GSTs fall into two distinct families: the soluble or cytosolic GSTs (cGSTs) and the membrane-bound microsomal GSTs (mGSTs). Cytosolic GSTs are by far the most numerous, with tens of members in all aerobic organisms. From an evolutionary point of view, they seem to derive from an ancestral glutathione-binding protein, although the great family expansion took place independently in the different phyla following their separation. On the contrary, microsomal GSTs are less numerous and, with the exception of mammalian ones, very little characterized. Mammalian mGSTs belong to the MAPEG protein family, which also includes members from plants, fungi and bacteria. Their evolution is still unclear: they might have common ancestors with the cGSTs or have an independent origin. Here we present the first data concerning microsomal GSTs from a wide range of organisms, and a preliminary phylogenetic analysis.

Over 100 putative microsomal GSTs, spanning many taxa from bacteria to mammals, were isolated through BLAST screening of EST sequences databases, using the rice microsomal GST as query. Hydrophathy profiling confirmed the presence in all sequences of 3 or 4 transmembrane domains, as expected for mGSTs.

Phylogenetic trees were generated starting from different GST gene sets: 1) selected microsomal and cytosolic GSTs from all organisms; 2) all mGSTs isolated; 3) only plant mGSTs. The results can be summarized as follows: 1) Cytosolic and microsomal GSTs separate in two totally distinct branches, indicating either an independent origin or a very ancient separation and subsequent independent evolution. 2) Microsomal GSTs form 3 distinct groups (class 1, 2 and 3), each one including sequences from different organisms. A fourth group, consisting of only bacterial sequences, is less defined. Mammals, fishes, echinoderms and birds have representatives of different groups, while insects, plants, fungi and algae have just one class. 3) Plants microsomal GSTs form a subgroup within class 3. Furthermore, monocots and dicots are clearly separated, as already seen for cytosolic GSTs.