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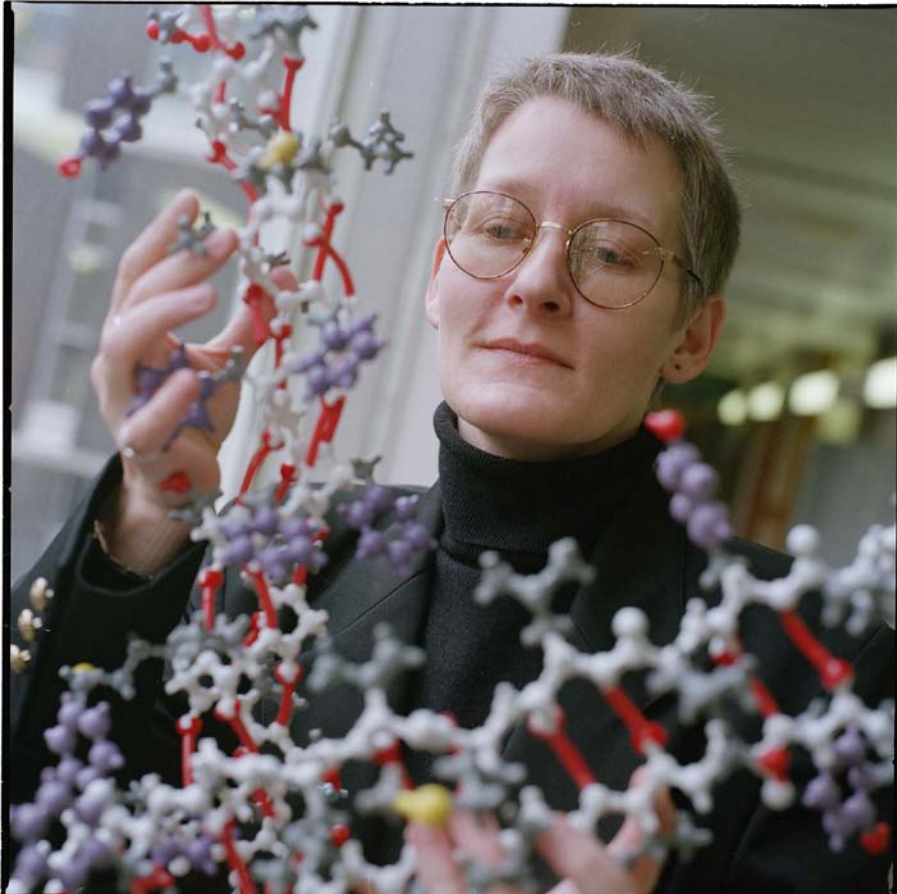


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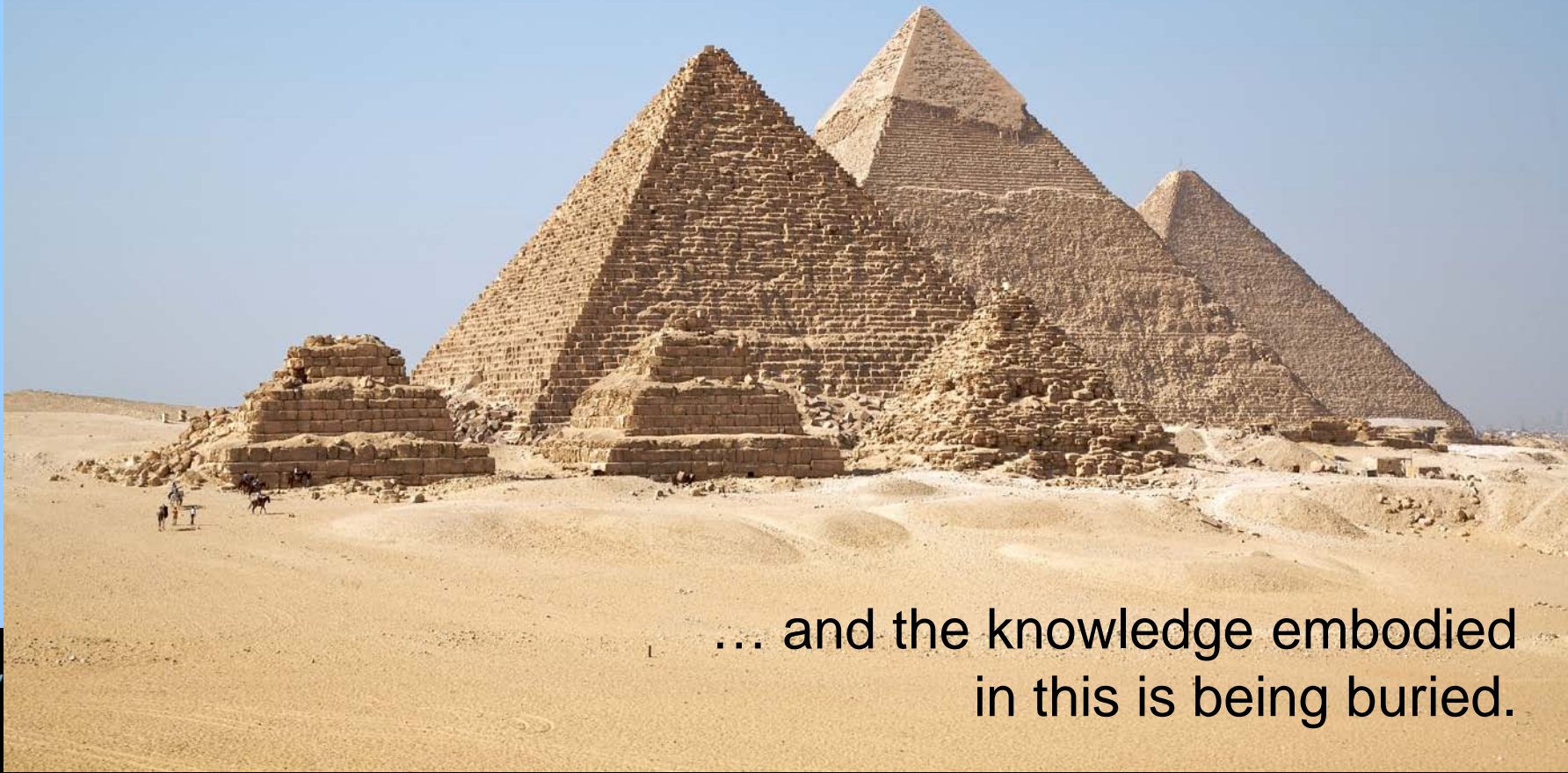
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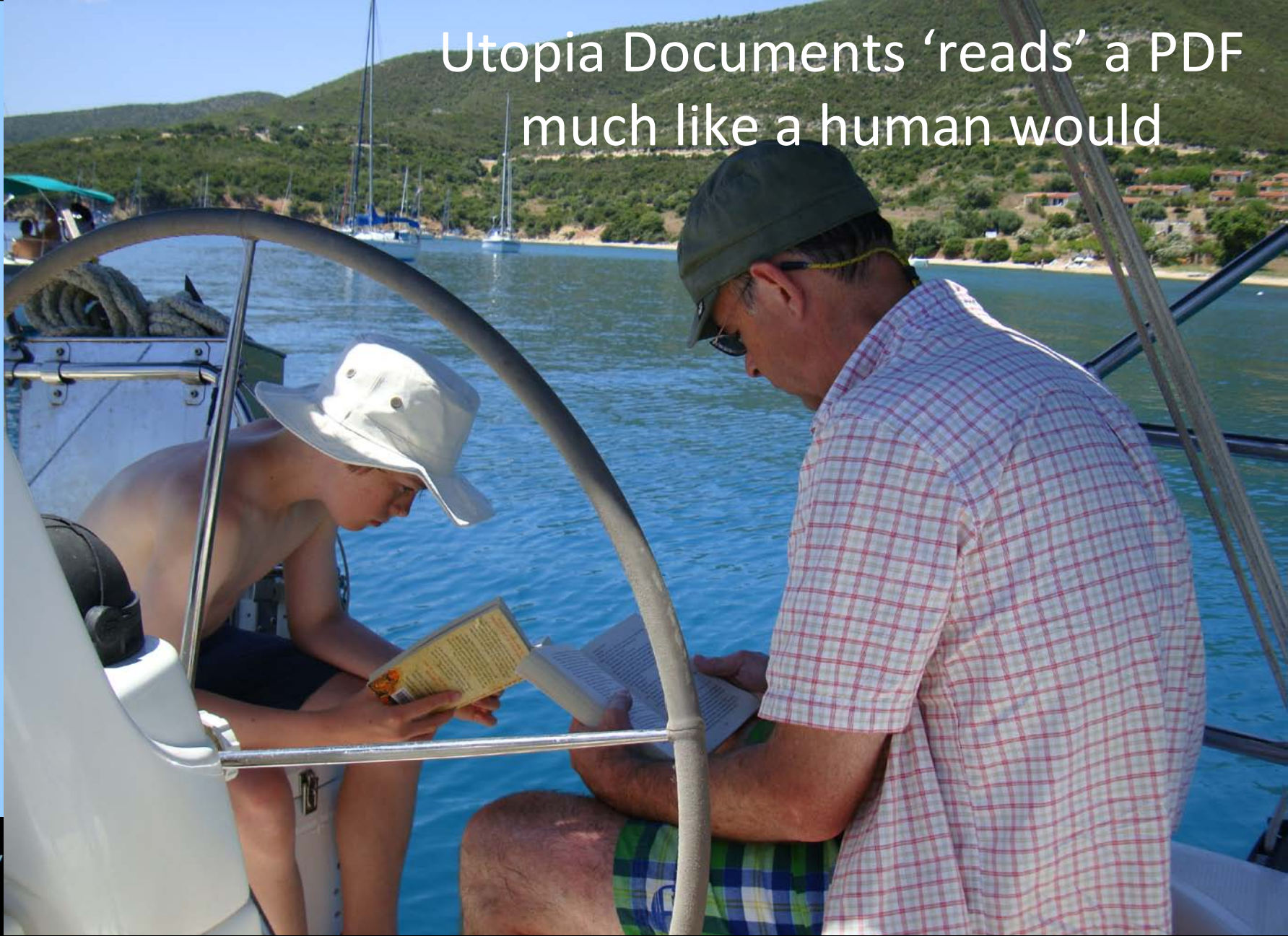


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Compound	A.M. $F_{app}$ ( $\times 10^{-3}$ $\text{cm s}^{-1}$ ) $\pm$ S.D.	PK	$t_{1/2}$ <sup>a</sup>	Caco-2 <sup>b</sup> $F_{app}$ ( $\times 10^{-3}$ $\text{cm s}^{-1}$ )	PAMPA <sup>c</sup> $F_{app}$ ( $\times 10^{-3}$ $\text{cm s}^{-1}$ )	$\text{Log } K_{ow}$ <sup>d</sup>	$\text{Log } D^e$
1. Ethosuximide	0.85 $\pm$ 0.08	99.1	17	0.075	0.13	-0.74	-0.85
2. Aescoprol	0.76 $\pm$ 0.04	99.9	23	0.026	0.00	-1.74	-1.86
3. Mefenol	1.37 $\pm$ 0.03	99.5	37	0.288	0.00	0.71	0.68
4. Mefenol daps	0.32 $\pm$ 0.04	97.1	41	0.025	0.00	1.80	-1.80
5. Atenolol	2.09 $\pm$ 0.10	96.6	52	0.029	0.00	0.15	-1.29
6. Fentanyl	2.15 $\pm$ 0.03	99.9	55	0.049	0.05	0.57	-0.29
7. Metformin	2.27 $\pm$ 0.03	97.3	55	0.558	0.02	1.43	-1.72
8. Furosemide	2.75 $\pm$ 0.02	99.9	90	0.022	0.06	2.07	0.89
9. Fendimetarsulfamide	3.10 $\pm$ 0.06	96.3	70	0.051	0.00	0.07	-0.12
10. Chlorthalidone	3.97 $\pm$ 0.01	99.3	90	2.06	0.17	1.14	1.14
11. Hydrochlorothiazide	4.29 $\pm$ 0.07	99.8	74	1.40	0.14	1.61	1.55
12. Furofyllin	3.74 $\pm$ 0.07	99.2	92	1.67	0.49	1.75	0.29
13. Furosemide	3.97 $\pm$ 0.08	99.8	93	4.39	2.35	1.05	1.25
14. Metoprolol	4.41 $\pm$ 0.08	99.6	95	2.77	0.35	1.88	-0.36
15. Theophylline	5.05 $\pm$ 0.05	99.1	97	2.52	0.88	0.05	0.85
16. Thiametoxim	4.55 $\pm$ 0.09	99.8	97	0.20	0.50	0.91	0.74
17. Naproxen	4.88 $\pm$ 0.02	99.9	96	3.95	1.96	3.19	0.73
18. Verapamil	4.15 $\pm$ 0.03	97.5	98	1.58	0.74	3.79	2.46
19. Amitriptyline	4.91 $\pm$ 0.03	97.8	100	2.82	1.82	0.88	0.31
20. Ketoprofen	4.27 $\pm$ 0.08	99.1	100	2.03	3.67	3.12	-1.51
21. Caffeine	4.13 $\pm$ 0.08	99.3	100	3.98	1.98	-0.07	0.67

<sup>a</sup> Literature  $F_{app}$  values (Chou et al., 2000; Zhu et al., 2000).  
<sup>b</sup> Literature Caco-2  $F_{app}$  values (Alonso and Horiuchi, 2003; Nakkin et al., 1996; Yamashita et al., 2000; Yasudani et al., 2004; Zhu et al., 2000).  
<sup>c</sup> Literature PAMPA  $F_{app}$  values (Bignozzi et al., 2000; Zhu et al., 2003).  
<sup>d</sup> Literature  $\text{Log } K_{ow}$  values (Cragg et al., 2004; Muller et al., 2003; Zhu et al., 2000).  
<sup>e</sup> Literature  $\text{Log } D$  values (Muller et al., 2003; Nishikie et al., 1996; Zhu et al., 2000).

**Figure 9** Lynch imagines being able to toggle between a published table of numerical values and their graphical representation. For readers viewing this article using UDL, from this typical table of data from the *European Journal of Pharmaceutical and Medicinal Sciences* (32), explore the result of clicking on the UDL logo. Reproduced from Corti, G., Maestrelli, F., Cini, M., Zorouk, N. and Mura, P. (2006) Development and evaluation of an *in vitro* method for prediction of human drug absorption II. Demonstration of the method suitability. *European Journal of Pharmaceutical Science* 27, 354-362. Copyright (2006) with permission from Elsevier.

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Lynch, for example, imagines a future in which there exists a wide range of specialized visualization tools for various forms of structured data [37]. It would be useful, he suggests, to be able to toggle between a rendered image and its underlying data-set, or between a published table of numerical values and their graphical representation, perhaps like the scenario shown in Figure 9? In a similar state of reverie, Bourne has a vision in which journals provide software for visualizing and interpreting the published content, obviating the need for specialized knowledge in handling esoteric tools; he envisages such software ultimately

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**Calling International Rescue: knowledge lost in literature and data landslide!**

Altwood, Teresa K.; Kell, Douglas B.; McDermott, Philip; Marsh, James; Pettifer, Steve R.; Thorne, David

Biochem. J. 424 (Pt 3)  
 Pages: 517-523  
 Published: 2009-12-15

**Keywords**  
 dynamic document content; interactive PDF; linking documents with research data; manuscript mark-up; mark-up standards; semantic publishing

**Abbreviations used in the Document**  
 JML: eXtensible Markup Language; CBO: Open Biomedical Centologies; PTM: post-translational modification; DOI: Digital Object Identifier; PLoS: Public Library of Science; UDL: Utopia Documents; CTR: Scientific, Technical and Medical; ITIS: ...

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**Figure 9** Lynch imagines being able to toggle between a published table of numerical values and their graphical representation. For readers viewing this article using UDL, from this typical table of data from the *European Journal of Pharmaceutical and Medicinal Sciences* (32), explore the result of clicking on the UDL logo. Reproduced from Corti, G., Maestrelli, F., Cini, M., Zorouk, N. and Mura, P. (2006) Development and evaluation of an *in vitro* method for prediction of human drug absorption II. Demonstration of the method suitability. *European Journal of Pharmaceutical Science* 27, 354-362. Copyright (2006) with permission from Elsevier.

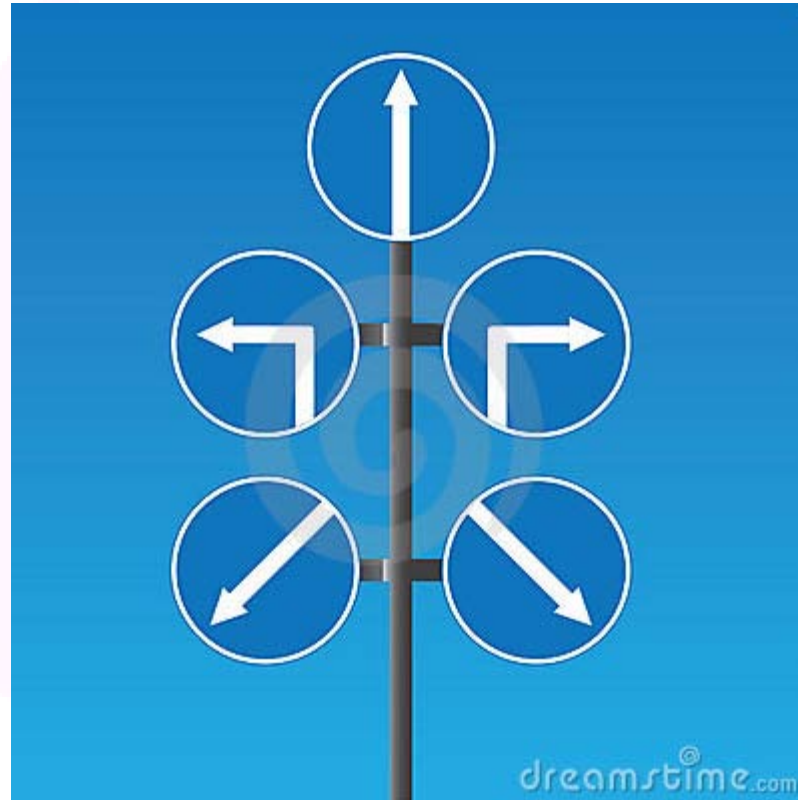
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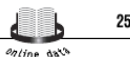
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## Structural contributions of Delta class glutathione transferase active-site residues to catalysis

Jantana WONGSANTICHON\*, Robert C. ROBINSON† and Albert J. KETTERMAN\*<sup>1</sup>

\*Institute of Molecular Biosciences, Mahidol University, Salaya Campus, Nakhon Pathom, 73170, Thailand, and †Institute of Molecular and Cell Biology, Proteos, 138673, Singapore

GST (glutathione transferase) is a dimeric enzyme for biotransformation of xenobiotics and endogenous compounds. In the present study, residues for hydrophobic substrate-binding site (H-site) of a Delta class enzyme were investigated in detail for the first time. Site-directed mutagenesis and crystallographic studies indicate that Tyr<sup>111</sup> indirectly stabilizes GST active-site residues. Kinetics reveal that Tyr<sup>111</sup> indirectly modulates catalysis. Mutations at Tyr<sup>111</sup> also showed evidence for positive co-operativity and 1-chloro-2,4-dinitrobenzene respectively, strongly suggesting a role for these residues in manipulating substrate binding and communication. In the present paper we report crystallographic structures of the wild-type enzyme, and two mutants, in complex with S-hexylglutathione. This study has identified a 'zipper' in the H-site contributing a network of aromatic interactions. Several residues of the cluster directly interact with the hydrophobic substrate, whereas others indirectly

designated k<sub>no</sub> class [25]. Many GST classes have counterparts across different phyla, but some are kingdom-specific, such as Alpha, Mu and Pi are mammal-specific [12,24]; Beta is bacterial-specific [24]; Delta and Epsilon are insect-specific [24]; and Phi and Tau are plant-specific classes [25]. GSTs catalyse CDNB (1-chloro-2,4-dinitrobenzene) as a common substrate [14,26]. Particular GST classes may display substrate selectivity towards other hydrophobic electrophilic compounds. Nevertheless, many GSTs appear to exhibit a degree of cross-specificity for a number of substrates [27]. Amino acids

### INTRODUCTION

GST (glutathione transferase; EC 2.5.1.18) is eminently recognized as a detoxifying enzyme that is widely distributed in all organisms [1]. The enzymatic biotransformation within the active site is generally initiated by conjugation between glutathione and hydrophobic electrophilic toxic substances including drugs, carcinogens, herbicides and insecticides [2]. Amino acid residues forming the G-site (glutathione-binding site) appear to be highly conserved between GST classes and therefore have been studied

designated k<sub>no</sub> class [25]. Many GST classes have counterparts across different phyla, but some are kingdom-specific, such as Alpha, Mu and Pi are mammal-specific [12,24]; Beta is bacterial-specific [24]; Delta and Epsilon are insect-specific [24]; and Phi and Tau are plant-specific classes [25]. GSTs catalyse CDNB (1-chloro-2,4-dinitrobenzene) as a common substrate [14,26]. Particular GST classes may display substrate selectivity towards other hydrophobic electrophilic compounds. Nevertheless, many GSTs appear to exhibit a degree of cross-specificity for a number of substrates [27]. Amino acids

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Wongsantichon, Jantana; Robinson, Robert C.; Ketterman, Albert J.

Biochem. J. 428 (Pt 1)  
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Published: 2010-05-15

**Keywords**  
crystal structure; glutathione transferase (GST); structural motif; structure-function relationship; substrate specificity

**Abbreviations used in the Document**  
shGST: S-hexylglutathione; GST: glutathione transferase; RMSD: root mean square deviation

### Bibliography BJ

(1994) The CCP4 suite: programs for protein crystallography *Acta Crystallogr. Sect. D Biol. Crystallogr.* **50**

Andújar-Sánchez, M.; Clemente-Jiménez, J. M.; Las Heras-Vázquez, F. J.; Rodríguez-Vico, F.; Cámara-Artigas, A.; Jara-Pérez, V. (2003) Thermodynamics of glutathione binding to the tyrosine 7 to phenylalanine mutant of glutathione S-transferase from *Schistosoma japonicum* *Int. J. Biol. Macromol.* **32**

Armougom, F.; Moretti, S.; Poirot, O.; Audic, S.; Dumas, P.; Schaeff, B.; Keduas, V.; Notredame, C. (2006) Espresso: automatic incorporation of structural information in multiple sequence alignments using 3D-Coffee *Nucleic Acids Res.* **34**

Beckett, G. J.; Hayes, J. D. (1993) Glutathione S-transferases: biomedical applications *Adv. Clin. Chem.* **30**

Board, P.; Baker, R. T.; Chelvanayagam, G.; Jermin, L. S. (1997) Zeta, a novel class of glutathione transferases in a range of species from plants to humans *Biochem. J.* **328**

Board, P. G.; Coggan, M.; Chelvanayagam, G.; Eastale, S.; Jermin, L. S.; Schulte, G. K.; Danley, D. E.; Hoth, L. R.; Griffor, M. C.; Kamathi, A. V. (2000) Identification, characterization, and crystal structure of the Omega class glutathione transferases *J. Biol. Chem.* **275**

Caccuri, A. M.; Antonini, G.; Board, P. G.; Parker, M. W.; Nicotra, M.; Lo Bello, M.; Federici, G.; Ricci, G. (1999) Proton release on binding of glutathione to Alpha, Mu and Delta class

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Xenobiotica 38(7-8) 2008 676-708

**Role of transport proteins in drug discovery and development : a pharmaceutical perspective**

A. Ayrton and P. Morgan.

**ABSTRACT**

1. This review will explore, from a pharmaceutical industry perspective, the evidence and consequences of transport protein involvement in pharmacokinetic variability and safety of drugs in humans. With the preclinical and clinical evidence available, the transport proteins that are considered to be the most important in respect of pharmacokinetic variability and safety in humans will be highlighted. 2. A large number of transport proteins have been identified, at both the genetic and the cellular level, which have been suggested to play some role in the absorption, distribution or elimination of endogenous, xenobiotic or drug substrates. 3. The weight of evidence suggests that only a small number of transport proteins need to be routinely considered in the drug discovery setting driven by the magnitude of their impact on tissue distribution, pharmacokinetic variability and drug-drug interactions. 4. For the majority of candidate drugs, an assessment of the role of transporter proteins in their disposition and safety need only be assessed if in vivo properties suggest that active transport is likely to be a significant factor: if transport proteins are implicated in a particular therapeutic target area or if the disposition and safety of a likely candidate are known to be significantly modulated by transport proteins.

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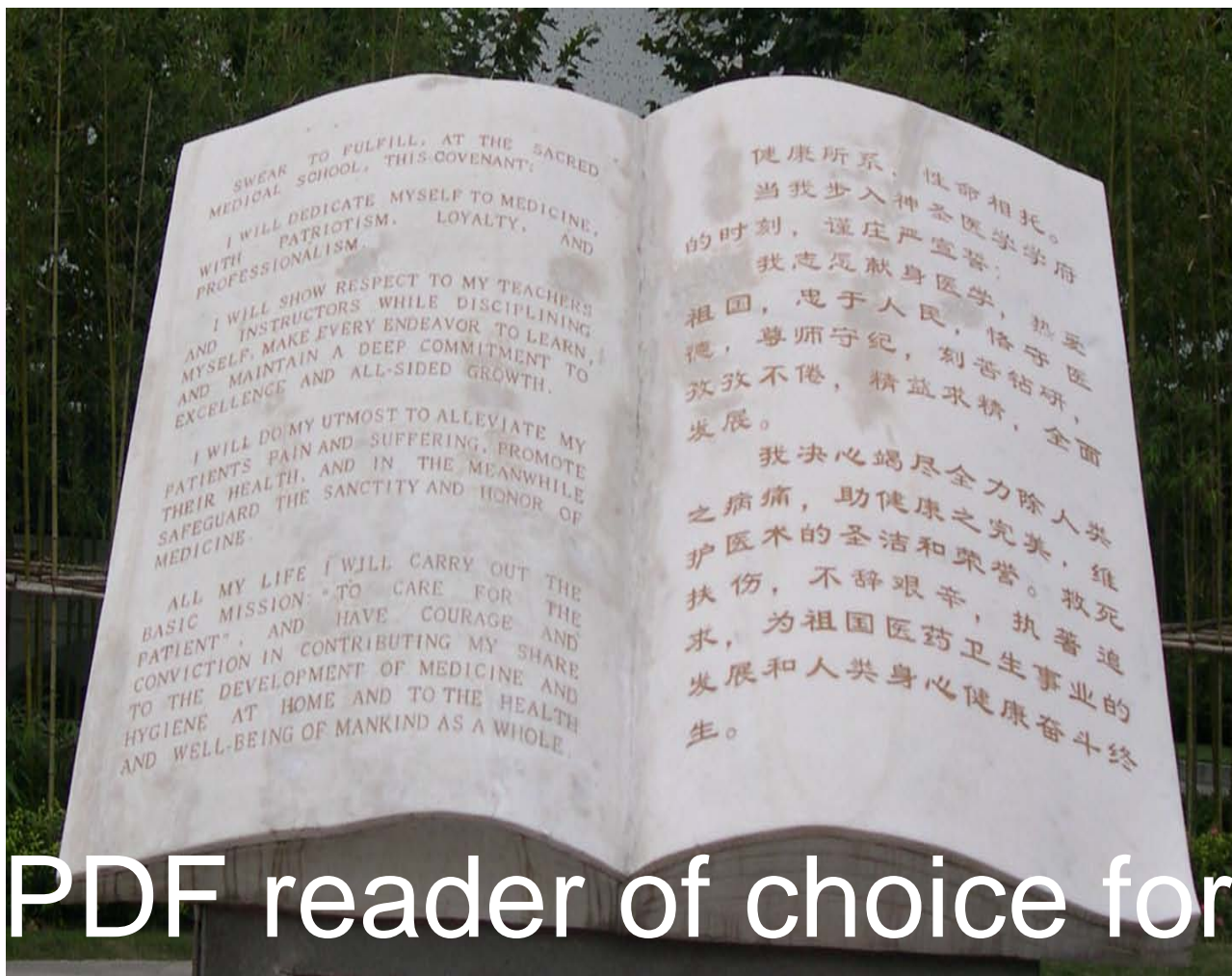
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