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COMMENTARY

GLUTATHIONE TRANSFERASES: NOMENCLATURE

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There has been major recent interest in the glutathione transferases (EC 2.5.1.18), a family of enzymes of overlapping specificity that catalyze the variety of reactions in which glutathione serves as the nucleophile for a wide range of metabolic conversions. This interest has led to the discovery of a number of isoenzymes, for which there is no consistent nomenclature. The confusion which this causes was apparent at a recent Pharmacological Group Meeting of the Biochemical Society and the Glutathione Transferase Workshop‖ that followed. At an informal meeting¶, discussion quickly led to misidentification of the best studied of these enzymes, those isolated from the rat. With the advent of recombinant DNA technology, additional stress has been put upon the existing system. The consensus of the meeting was that a change in nomenclature was necessary and that such nomenclature should be sufficiently flexible to include new isoenzymes as they are identified and characterized. Since the International Union of Biochemstry does not deal directly with isoenzymes in its list of enzymes [1], and since isoenzymes are not uncommon among enzymes metabolizing xenobiotics, we thought it useful to communicate a set of simple ground rules for the rat glutathione transferases that may be applicable generally. The nomenclature of human and mouse enzymes is being considered but is presently in a less defined position.

The meeting agreed that each protein species should be identified by the name of the organism from which it is isolated but not by the tissue from which it is extracted. Since the glutathione transferases are dimers, with each isoenzyme differing with respect to its subunit composition, every different subunit should receive its own number. The identification of each transferase is then based on the numbers given to its two constituent subunits. Thus, a homodimer composed only of subunit 1 would be identified as rat glutathione transferase 1-1, whereas the heterodimer consisting of subunits 1 and 2 would be identified as rat glutathione transferase 1-2, and so on.

In keeping with the guidelines for enzyme nomenclature [2], the burden of proof for the existence of a separate species, in contrast to the possible isolation of a product which is an artifact of the procedure used, is on the investigator. Also adopted was the important principle that each combination of subunits must be characterized by enzymatic properties in order to establish the existence of a distinct enzyme species. Amino acid sequences, deduced from cloned cDNA that represents mRNA for novel subunits, have not been classified since the proteins they represent are not yet characterized with respect to enzymatic activity.

For orientation, Table 1 presents the proposed new nomenclature together with previously used designations for each of the eight isoenzymes that are adequately characterized. The new nomenclature was presented for discussion to the Glutathione

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‖ The meeting, "Developmental, Genetic and Environmental Aspects of Drug Biotransformation and Conjugation" and the "Glutathione Transferase Workshop" were held in Dundee, September 14–17, 1983.

¶ Present were A. M. Benson, P. B. Hulbert, W. B. Jakoby, B. Ketterer, A. Y. H. Lu, B. Mannervik, C-Y. G. Lee, T. J. Mantle, C. B. Pickett and C-P. D. Tu.

Table 1. Nomenclature for the rat glutathione transferase

New nomenclature	Previous nomenclature						
	References						
	[3–5]	[6–9]	[10]	[11]	[3, 11, 12]	[13]	[15–17]
Glutathione transferase 1-1	Ligandin	B	Ligandin	B_1	Y_aY_a	L_2	
Glutathione transferase 1-2	Ligandin	B	B	B_2	Y_aY_a	BL	
Glutathione transferase 2-2		AA		AA	Y_cY_c	B_2	
Glutathione transferase 3-3		A		A	$Y_b^1Y_b^1$	A_2	
Glutathione transferase 3-4		C		C	$Y_b^1Y_b^2$	AC	
Glutathione transferase 4-4		D		"D"	$Y_b^2Y_b^2$	C_2	
Glutathione transferase 5-5		E		E			
Glutathione transferase 6-6							M_T

Transferase Workshop where it received general approval.

The different rat isoenzymes can be distinguished by their characteristic specific activities with a spectrum of test substrates and by use of selective inhibitors [7, 13, 14]. Their subunits also have reproducible relative mobilities on sodium dodecyl sulfate polyacrylamide gel electrophoresis. The estimated M_r values are: 1 = 25,000; 2 = 28,000; 3 = 26,500; 5 = 29,000; and 6 = 26,000. These M_r values are higher than those originally published [3], but are now generally agreed upon. For example, the M_r for subunit 1, determined from amino acid sequences arrived at by recombinant DNA technology, was calculated to be close to 25,500 according to results presented at the meeting by C-P. D. Tu, C. B. Pickett, B. Ketterer and their respective collaborators.

The authors and others will serve as a consulting group for the nomenclature of new species of glutathione transferases and their subunits. W. B. Jakoby (NIH, Building 10/9N-109, Bethesda, MD 20205, U.S.A.) has agreed to serve as a point of contact and to provide a current list of glutathione transferase to all requestors.

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