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New Common Nomenclature for Glycoprotein Genes of Varicella-Zoster Virus and Their Glycosylated Products

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The accumulation of recent data concerning the reactivity of monoclonal antibodies with particular varicella-zoster virus (VZV) glycoproteins and the mapping of several of their respective genes on the VZV genome has led to a unified nomenclature for the glycoprotein genes of VZV and their mature glycosylated products. Homologs to herpes simplex virus glycoprotein genes are noted.

Varicella-zoster virus (VZV), a member of the herpesvirus family, is the causative agent of chicken pox and shingles. Over the last few years, workers studying the glycoproteins of VZV have used different nomenclatures. In toto, this plethora of names has been confusing, particularly to those outside the field. To rectify this problem, six of us (A.J.D., C.M.E., R.W.E., C.G., A.V., and K.Y.) convened at the 1985 Herpesvirus Workshop in Ann Arbor, Mich. Significant information had accumulated from studies of glycoproteins reactive with monoclonal antibodies and from gene mapping to derive a common nomenclature for VZV glycoprotein genes and their multiple products. The nomenclature primarily identifies the VZV glycoprotein genes per se and secondarily identifies their respective glycoprotein products. To avoid confusion with preexisting nomenclatures of either VZV or herpes simplex virus glycoproteins, we named the glycoprotein genes gpI, gpII, gpIII, gpIV, etc. Specific glycoproteins then were identified according to molecular weights ($\times 10^3$) as quantitated in each research group by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), e.g., gpI(92) is the 92-kilodalton (kDa) glycoprotein product of the gpI gene.

A summary of the new common nomenclature is presented in Table 1. Also listed are summaries of old nomenclatures as well as documentation of neutralizing monoclonal antibodies directed against the respective glycoproteins. Gene mapping locations, homologs of herpes simplex virus type 1 (HSV-1) genes, and the predicted size from the DNA sequence of the VZV primary translational product are indicated when known. The salient features of the genes and glycoproteins are as follows.

(i) gpI. The gpI group of glycoproteins, cross-reactive with specific individual monoclonal antibodies, has been resolved in different laboratories as two to four individual species of 45 to 100 kDa by SDS-PAGE (1a, 4, 7, 10–13). These glycoproteins are the most abundant and immunogenic of the VZV envelope glycoproteins (10, 16). They elicit the formation of complement-dependent neutralizing antibodies (1a, 4, 5, 7, 11) and also mediate antibody-dependent cellular cytotoxicity (9). The gpI gene has been mapped to the 70-kDa open reading frame (ORF) at the right-hand end of the VZV U_S region (3) and displays a small degree of sequence homology to HSV-1 gE (A. J. Davison and D. J. McGeoch, submitted for publication).

(ii) gpII. The gpII group of glycoproteins, cross-reactive with specific individual monoclonal antibodies, has been resolved by SDS-PAGE in different laboratories as polypeptides in two size ranges, 115 to 140 kDa and 57 to 66 kDa (1a, 2, 4, 8, 10, 12, 13, 15, 17). These glycoproteins, which elicit the formation of complement-dependent and -independent neutralizing antibodies (1a, 2, 10, 15, 17), are the second most abundant and immunogenic of the VZV envelope glycoproteins (10). The mature viral polypeptides, which migrate as a closely migrating doublet of ca. 60 kDa in reducing SDS-PAGE, migrate as a 120- to 140-kDa single polypeptide in nonreducing SDS-PAGE; hence, gpII has been referred to as a disulfide-linked dimer (8, 15). The gpII gene has been mapped to the 100-kDa ORF in the center of the VZV U_L region (P. M. Keller, A. J. Davison, R. S. Lowe, C. D. Bennett, and R. W. Ellis, submitted for publication) and displays a significant amount of serological cross-reactivity (2) and sequence homology to HSV-1 gB.

(iii) gpIII. The gpIII glycoprotein species migrates in SDS-PAGE as a single 105- to 118-kDa polypeptide (4–7, 10, 14). The glycoprotein, which elicits the formation of complement-independent neutralizing antibodies (5, 7, 10), is the third most abundant and immunogenic of the VZV envelope glycoproteins (10). The gpIII gene has not been mapped yet in the VZV genome.

(iv) gpIV. The gpIV glycoproteins, reactive with antipeptide antibodies, are resolved by SDS-PAGE as 45- and 55-kDa polypeptides (1). The gene for these minor glycoproteins is the 39-kDa ORF at the center of the VZV U_S region (1) which displays a small degree of sequence homology to the HSV-1 U_S7 gene (Davison and McGeoch, submitted).

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TABLE 1. Nomenclature for VZV glycoprotein genes and their mature glycosylated products

New names[a]		Old names of proteins[b]	Neutralizing monoclonal antibodies[c]	Genetic map location[d]	HSV gene homolog[e]	References[f]
Gene	Proteins[g]					
				0.94 (70 kDa)		3
gpI					gE	*h*
	gpI(92), gpI(83), gpI(55), gpI(45)	gC: gp92, gp83, gp55, gp45	+C′			10
	gpI(94), gpI(83), gpI(55), gpI(45)	gp2				12, 13
	gpI(98), gpI(62)	gp98, gp62				7, 9, 11, 16
	gpI(90), gpI(80), gpI(60)	90K, 80K, 60K	+C′			4, 5
	gpI(92), gpI(59), gpI(47)	gp92, gp59, gp47	+C′			1a
gpII				0.47 (100 kDa)	gB	*i*
	gpII(115), gpII(62), gpII(57)	gB: gp115, gp62, gp57	+			10
	gpII(116), gpII(106), gpII(64)	gp3				12, 13
	gpII(140), gpII(66)	gp140, gp66				8
	gpII(130), gpII(125), gpII(62)	gp1, gp3	+			15, 17
	gpII(120), gpII(118), gpII(65)	120K, 118K, 65K				4
	gpII(125), gpII(63)	gp125, gp63	+, +C′			1a, 2
gpIII				?		
	gpIII(105)	gA: gp105	+			10
	gpIII(118)	gp118	+			6, 7
	gpIII(115)	gp1				14
	gpIII(118)	118K	+			4, 5
gpIV					U_S7	*h*
	gpIV(55), gpIV(45)	gp55, gp45		0.92 (39 kDa)		1a
gpV	?	?		?		*j*

[a] New nomenclature for glycoprotein genes and their protein products as proposed in this manuscript.
[b] As referred to in previously published work.
[c] Indicates monoclonal antibodies, reactive with the noted glycoprotein species, shown capable of neutralizing VZV infectivity in vitro. +C′ denotes the dependence upon added complement of the in vitro neutralization activity of these monoclonal antibodies, and + denotes the complement independence of neutralization.
[d] Indicates the map location (in increments of 0.01 on a scale of 0.00 to 1.00) nearest the center of the gene, with the size of the ORF of the gene noted parenthetically.
[e] Denotes that gene in HSV-1 which shares sequence homology with the indicated VZV glycoprotein gene.
[f] The most relevant published work.
[g] Describes the new nomenclature applied to the glycoproteins under "old names," where molecular size in kilodaltons is noted parenthetically.
[h] Davison and McGeoch, submitted.
[i] Keller et al., submitted.
[j] Hypothetical gene (see text).

(v) gpV. The recently completed DNA sequence analysis of the VZV genome (A. J. Davison, unpublished data) has predicted the existence of a total of at least 70 genes. Hydrophobicity analyses of the imputed amino acid sequences of these ORFs suggest the existence of at least five glycoprotein genes (on the basis of their hydrophobic signal or sequences or both). Therefore, a gpV is predicted, although no glycoproteins serologically distinct from gpI through gpIV have been detected yet.

It is noteworthy that three of the VZV glycoprotein genes have sequence homology to HSV-1 genes. While this homology is limited in the cases of VZV gpI-HSV-1 gE and VZV gpIV-HSV-1 U_S7, it is quite extensive in the case of VZV gpII-HSV-1 gB, where there is a 45% homology on the amino acid level and significant serological cross-reactivity between the mature glycosylated products. In the last few years, there have been numerous reports of sequential and functional homologies among genes and proteins of different members of the herpesvirus family. As the complete nucleotide sequences of the many herpesviruses become available, these homologies will be confirmed and extended.

We hope that this simplified and unified nomenclature will be useful to the herpesvirus field in general. It will be used in all publications by the authors of this manuscript.

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