SIV and SHIV CTL Epitopes Identified in Macaques

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There is accumulating evidence to suggest a key role for CTL in the containment of HIV and SIV infections. As such, there is considerable interest in developing vaccines designed to induce virus-specific CTL responses. Various macaque species, most notably the rhesus macaque, have been used extensively to study AIDS virus pathogenesis and vaccine efficacy. As a result of these studies a number of SIV and SHIV CTL epitopes, and their restricting MHC class I molecules, have been identified. Accurate definition of these CTL epitopes, however, is critical both to the development of vaccines as well as to the construction of MHC class I tetrameric complexes which have revolutionized our ability to measure CTL responses to individual CTL epitopes. In the list provided below, only the Mamu-A*01 restricted CTL epitopes have been optimally defined through the use of peptide dilutions and knowledge of Mamu-A*01's peptide binding motif. The other epitopes listed in Table I have been identified through the use of overlapping peptides, however, their optimal lengths have yet to be determined. In Table II additional CTL epitopes are listed for which the restricting MHC class I molecules have yet to be identified. Furthermore, the majority of these epitopes have only been mapped using overlapping 20mer peptides. It will be important to define both the restricting MHC class I molecule of these epitopes and their optimal length if they are to be considered for use in vaccination trials or tetramer construction. The expansion of this list will be very important to studies designed to examine the role of CTL in AIDS virus infections and the effectiveness of CTL-based vaccines. Please contact us with any additional contributions to this list.

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Table 1 Defined CTL Epitopes with Known Restricting MHC class I Molecules

Virus	Protein	Epitope	Restricting MHC Class I Allele[1]	Genbank Acc. No.	Reference
SIVmac251	Gag	CTPYDINQM	Mamu-A*01	U50836	Miller, et al. 1991 Allen, et al. 1998
SHIV	Env	YAPPISGQI	Mamu-A*01	U50836	Egan, et al. 1999
SHIV	Pol	STPPLVRLV	Mamu-A*01	U50836	Egan, et al. 1999
SIVmac251	Env	YNLTMKCR	Mamu-A*02	U50837	Watanabe, et al. 1994
HIV-1	Env	KPCVKLTP	Mamu-A*08		Voss, et al. 1996
SIVmac251	Env	EITPIGLAP[2]	Mamu-B*01	U42837	Yasutomi, et al. 1995
HIV-1	Env	NNLLRAIEA	Mamu-B*12		Voss, et al. 1996
SIVmac32H-J5	Gag	SVDEQIQWM	Mafa -A*02		Geretti, at al. 1997

[1]MHC Class I allele designations: Rhesus macaque (*Macaca mulatta*) Mamu; cynomolgus macaque (*Macaca fascicularis*) Mafa

[2]Note: We have been unable to detect responses to this CTL epitope in Mamu-B*01 defined, SIV infected rhesus macaques (Allen, et al. unpublished observations)

Table 2 CTL Epitopes without Defined Restricting MHC class I Molecules

Virus	Protein	Epitope	Restricting MHC Class I Allele	Reference
SIVmac251	Nef	GLEGIYYSAR	unknown	Mortara, et al. 1998
SIVmac239	Env	CNKSETDRW	unknown	Erickson, et al. 1994
SIVmac251	Nef	DWQDYTSGPGIRYPK	unknown	Bourgault, et al. 1992
SIVmac251	Nef	LRAMTYKLAIDMSHFI	unknown	Bourgault, et al. 1992
SIVmac251	Nef	GIRYPKTFGWLWKLV	unknown	Bourgault, et al. 1992
SIV	Gag	SYVDRFYKSLRAEQTD-AAYK	unknown	Gotch, et al. 1993
SIVmac251	Env	YCTLYVTVFY	unknown	Allen, et al. unpublished
	Env	SCTRMMETQTSTWFGF-NGTR	unknown	Allen, et al. unpublished
	Env	GRDNRTIISL	unknown	Allen, et al. unpublished
	Env	RRPGNKTVLPVTIMSG-LVFH	unknown	Allen, et al. unpublished

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                10        20        30        40        50        60        70        80        90
Gag 251  MGARNSVLSGKKADELEKIRLRPGGKKKYMLKHVVWAANELDRFGLAESLLENKEGCQKILSVLAPLVPTGSENLKSLYNTVCVIWCIHA
Gag 239  --V-------------------N-------------------------------------------------------------------

               100       110       120       130       140       150       160       170       180
Gag 251  EEKVKHTEEAKQIVQRHLVVETGTAETMPKTSRPTAPSSGRGGNYPVQQIGGNYVHLPLSPRTLNAWVKLIEEKKFGAEVVPGFQALSEG
Gag 239  ----------------------T-------------------------------------------------------------------

               190       200       210       220       230       240       250       260       270
Gag 251  CTPYDINQMLNCVGDHQAAMQIIRDIINEEAADWDLQHPQPAPQQGQLREPSGSDIAGTTSSVDEQIQWMYRQQNPIPVGNIYRRWIQLG
Gag 239  ---------------------------------------------------------------------------------------

               280       290       300       310       320       330       340       350       360
Gag 251  LQKCVRMYNPTNILDVKQGPKEPFQSYVDRFYKSLRAEQTDAAVKNWMTQTLLIQNANPDCKLVLKGLGVNPTLEEMLTACQGVGGPGQK
Gag 239  ------------------------------------------------------------------------------------------

               370       380       390       400       410       420       430       440       450
Gag 251  ARLMAEALKEALAPVPIPFAAAQKRGPRKPIKCWNCGKEGHSARQCRAPRRQGCWKCGKMDHVMAKCPDRQAGFLGLGPWGKKPRNFPMA
Gag 239  ----------------------Q-------------------------------------------------------------------

               460       470           480       490       500
Gag 251  QVHQGLTPTAPPEDPAVDLLKNYMQLG....KQQRESREKPYKEVTEDLLHLNSLFGGDQ
Gag239   ------M-------------------REKQ---------------------------
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Figure 1a. Gag CTL Epitopes

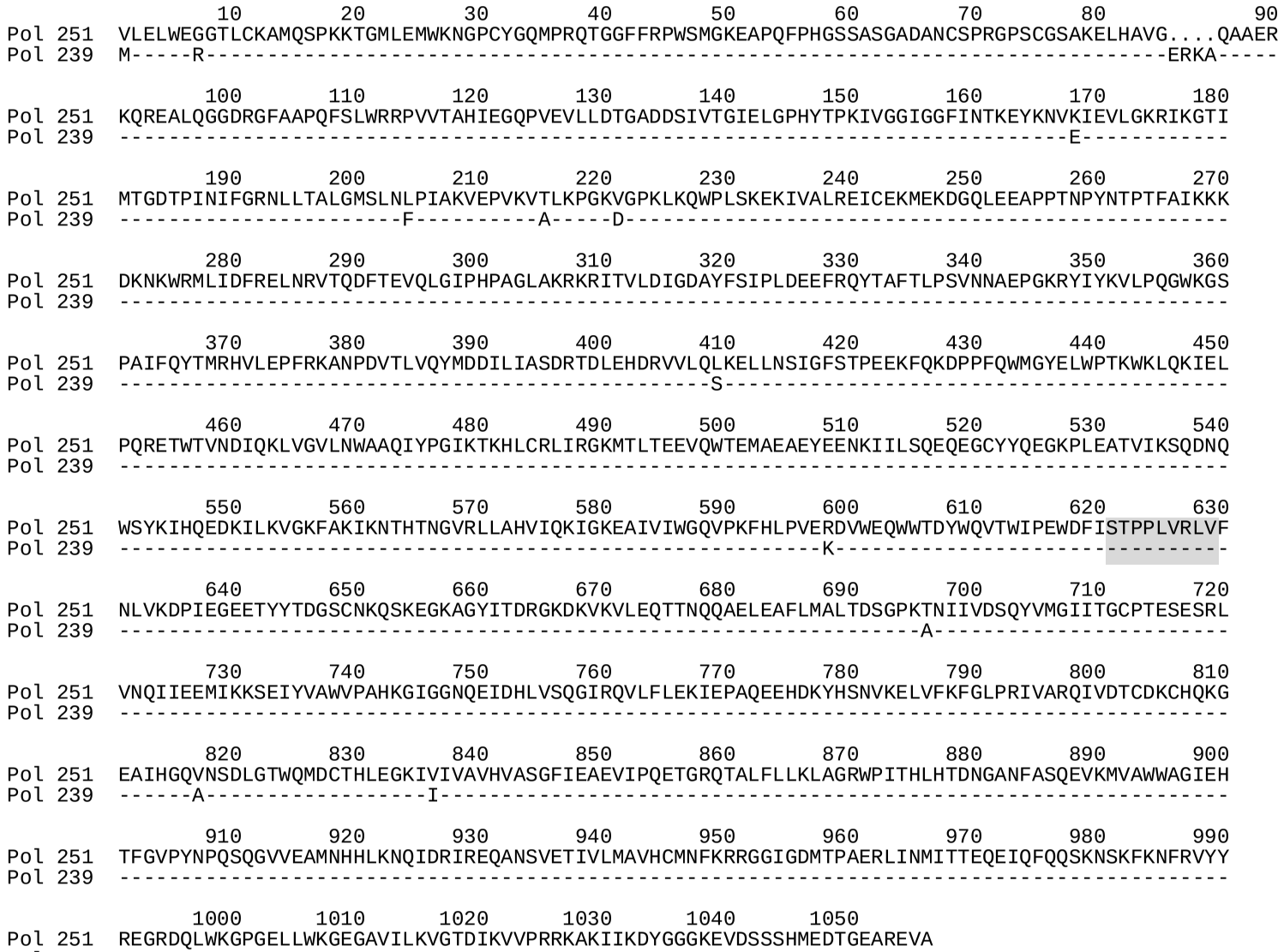

Figure 1b. Pol CTL Epitopes

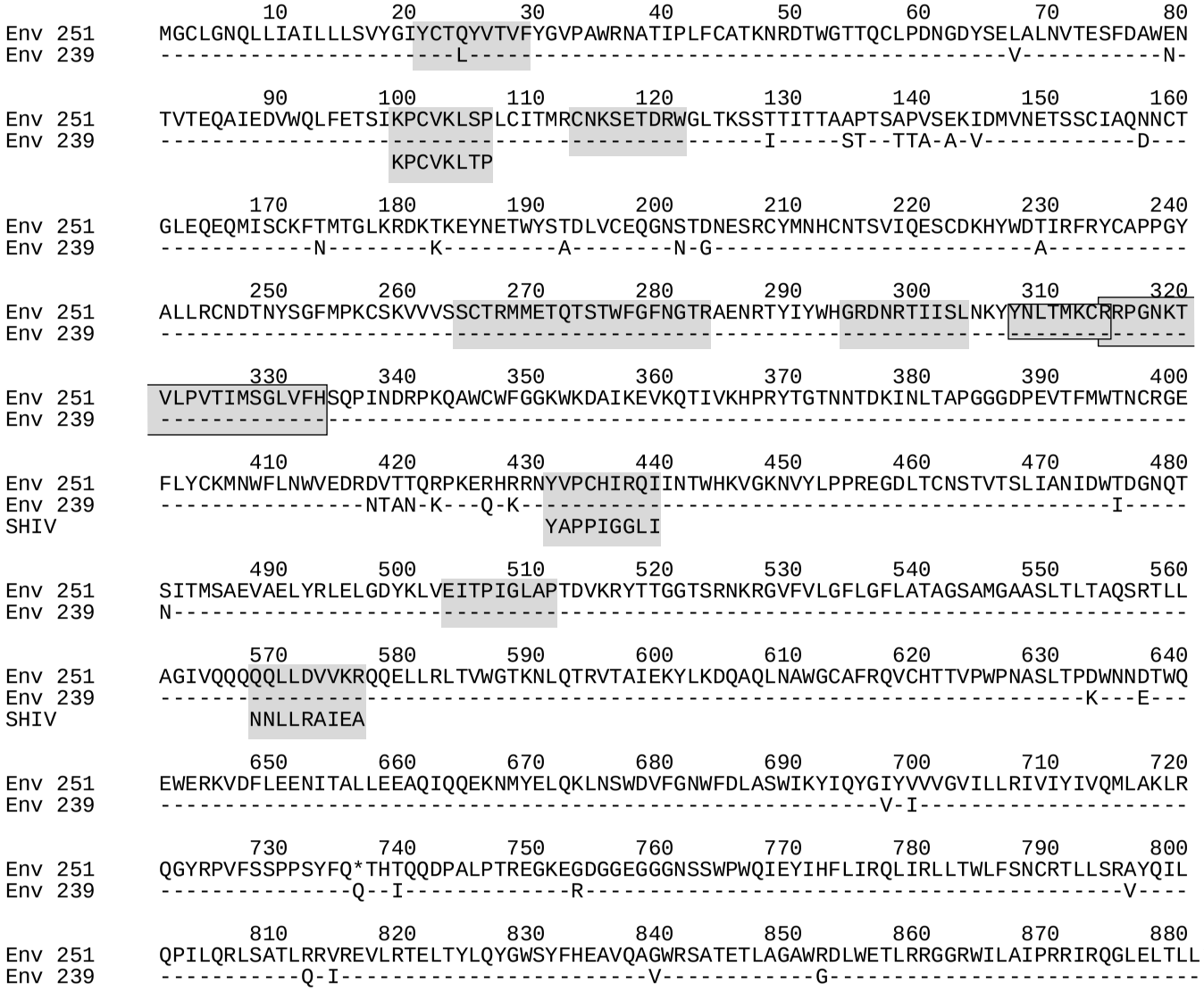

Figure 1c. Env CTL Epitopes

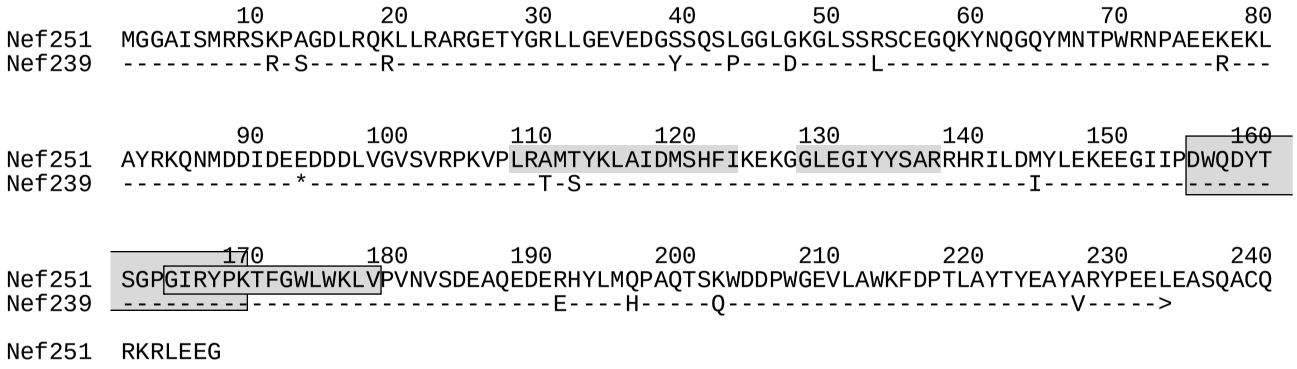

Figure 1d. Nef CTL Epitopes

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