

# 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		Reference
		Class I Allele <sup>1</sup>	Acc. No.	
SIVmac251	Gag CTPYDINQM	Mamu-A*01	U50836	Miller, et al. 1991
SHIV	Env YAPPSGQI	Mamu-A*01	U50836	Allen, et al. 1998
SHIV	Pol STPPLVRLV	Mamu-A*01	U50836	Egan, et al. 1999
SIVmac251	Env YNLTKCR	Mamu-A*02	U50837	Watnabe, et al. 1994
HIV-1	Env KPCVKLTP	Mamu-A*08		Voss, et al. 1996
SIVmac251	Env EHTPIGLAP <sup>2</sup>	Mamu-B*01	U42837	Yasutomi, et al. 1995
HIV-1	Env NNLLRAIFA	Mamu-B*12		Voss, et al. 1996
SIVmac32H-15	Gag SVDEQIQWM	Mafa-A*02		Geretti, et al. 1997

<sup>1</sup>MHC Class I allele designations: Rhesus macaque (*Macaca mulatta*) Mamu; cynomolgus macaque (*Macaca fascicularis*) Mafa

<sup>2</sup>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 GLEGIYYVSAR	unknown	Mortara, et al. 1998
SIVmac239	Env CNKSETDRW	unknown	Erickson, et al. 1994
SIVmac251	NeF DWQDYTSGPGRYPK	unknown	Bourgault, et al. 1992
SIVmac251	NeF LRAMTYKLAIDMSHF	unknown	Bourgault, et al. 1992
SIVmac251	NeF GIRYPKTFGWLWKLIV	unknown	Bourgault, et al. 1992
SIV	Gag SYVDRFYKSLRAEQTD	unknown	Gotch, et al. 1993
	AAVK		
SIVmac251	Env YCTLYVTVFY	unknown	Allen, et al. unpublished
	Env SCTRMMETQTSTWFGF	unknown	Allen, et al. unpublished
	Env NGTR		
	Env GRDNRTIISL	unknown	Allen, et al. unpublished
	Env RRPGNKTVLPVTIMSG	unknown	Allen, et al. unpublished
	Env LVFH		

	10	20	30	40	50	60	70	80	90
Gag 251	MGARNNSVLSGKKADELLEKIRLRPGGKKKYYMLKHVWVAANLEDRFGLAE SILHNEKGCQKILSVLAPLVPPTGSENLIKSLYMTVCVIWCIIHA								
Gag 239	--V-----N-----								
Gag 251	100	110	120	130	140	150	160	170	180
Gag 239	-----T-----								
Gag 251	EKKVKHTEFAKQIVQRHLVVEETGTAETMPKTSRPTAPSSSGGGNYPVQQIGGNVYHLPLSPRRLNAWKLIIEKKFGAEVYVDFGQALLSEG								
Gag 239	-----								
Gag 251	190	200	210	220	230	240	250	260	270
Gag 239	-----								
Gag 251	CTPYDINQMLNCVGDHQAAMQIIRDIINEEADWDLQHPQAPQQGQLREPSGSDIAGTTSVYDEQIQMWRQONPIPVGNITYRRWIQLG								
Gag 239	-----								
Gag 251	280	290	300	310	320	330	340	350	360
Gag 239	-----								
Gag 251	LQKCVRMVNPITNIIDVKQGPEKPFQSYVDRFYKSLRAEQTDAAVKNMWTQTLLIQNANPDCKLVLKGLGVNPTLLEMLTACQGVGGPGQK								
Gag 239	-----								
Gag 251	370	380	390	400	410	420	430	440	450
Gag 239	-----Q-----								
Gag 251	ARLMAEALKEALIAVPVIPFAAAQKRGRPKRIKWNCGKEGHSARQCRAPRRQGCWKCGKMDHVMACPDROAGFLGLGPMGKKPRNFPMA								
Gag 239	-----								
Gag 251	460	470	480	490	500				
Gag 239	-----M-----								
Gag 251	QVHQGLTPTAPDEPDAVDLILKNYMQLG...KQQRESREKPYKEVTEEDLILHINSLFGGDQ								
Gag 239	-----REKQ-----								

Figure 1a. Gag CTL Epitopes

SIV and SHIV Epitopes

Pol 251	VLELWEGTLCKAMQSPKKTGMLMWMKNGPCYGQMPRQGTGFRFRPWSMGKARQFPHGSSASGADANCSPRGSSAKELHAVG...QAAR	10	20	30	40	50	60	70	80	90
Pol 239	M-----R-----									ERKA-----
Pol 251	KQREALQGGDRGFAPQFSLMRRPVVTAHIEGQPVVELLDTGADDSIVTGETLGPHTYTPKIVGGIGGFINTKEYKNVKEIYLGKRIKGTI	100	110	120	130	140	150	160	170	180
Pol 239	-----									-----F-----
Pol 251	MTGDTPIINIFGRNLLTALGMSLNP IAKVVEPKVTLKPGKVPKIQWPLSEK EIVALREICEKMEKDGLLEAPPTNPVPTFAIKKK	190	200	210	220	230	240	250	260	270
Pol 239	-----F-----A-----D-----									-----
Pol 251	DKNKWRMLIDFRRLNRVTQDFTFVQLGIPHEBAGLAKRKRITVLDIGDAYFSIPLDEFRQYTAFTLP SVNNAEPGRYIYKVLPRQGWKGS	280	290	300	310	320	330	340	350	360
Pol 239	-----									-----
Pol 251	PAIFQYTMRHVLEPERFKANPDTLVQYMDLILIASDRTDLEHDRVVLQLKELLNSIGFSTPEEKFOKDDPFQWMMGYELWPTKWLQKIEL	370	380	390	400	410	420	430	440	450
Pol 239	-----S-----									-----
Pol 251	PQRETWTVNDIQKLVGLINWMAQIYPGIKTKHLQRLIRGKMLTTEEVQWTMAEAEYEENKILLSQEQEGCYQEGKPLEAFVIKSQDNQ	460	470	480	490	500	510	520	530	540
Pol 239	-----									-----
Pol 251	WSYKIHQEDKILKVGKFAKIKNTHNTNGVRLAHVYIQIGKRAIVIWGQVPRFHLPERDVWEQWTTDYWQVTWIPEWDFISTPPLVRLVLF	550	560	570	580	590	600	610	620	630
Pol 239	-----K-----									-----
Pol 251	NLVKDP IEGEFTYYTDGSCNKSQSEKAGAYITDRGKDKVKYKLEQTNNQDALEAFIMALTDSGPKTNIIVDSQYVMGIITGCPTESESR L	640	650	660	670	680	690	700	710	720
Pol 239	-----A-----									-----
Pol 251	VNQIIEEMIKKSEIYVAVWVPAHKGIGGNQETDHLVVSQGIROVLFLEKIEPAQEEHDKYHSNVKELVLFKGLPRIVARQIYVDTCDKCHQKG	730	740	750	760	770	780	790	800	810
Pol 239	-----									-----
Pol 251	EAIHGQVNSDLGTWQMDCTHIEGKIVIVAIVAVASGFI EAEVLPQETGRQFTALFLKLLAGRMPITHLHTDNGANFASQEVKVAWMAWAGIEH	820	830	840	850	860	870	880	890	900
Pol 239	-----A-----I-----									-----
Pol 251	TFGVPRYNPQSQGVVEAMNHKKNQIDRIRREQANSVETIVLMAVHCMNFKRRGGIGDMTPARLLINMITTEQEIQFQQSKNSKFKNFRVYY	910	920	930	940	950	960	970	980	990
Pol 239	-----									-----
Pol 251	REGRDQLWKGEGELLWKGEGAVILKVGTDIKVPPRRKAKIKDYGGGKEVDSSSHMEDTGEAREVA	1000	1010	1020	1030	1040	1050			
Pol 239	-----									-----

Figure 1b. Pol CTL Epitopes

IV-10  
DEC 98



**SIV and SHIV Epitopes**

Nef251 10 20 30 40 50 60 70 80  
 MGGAI SMRRSKPAGDLRÖKILRARGETTYGRLLGEVEDGSSOSLGGIGKGLSSRSCEGÖKYNOGQYMTTPWRNPAEKEKTL  
 Nef239 -----R-S-----R-----Y---P--D-----L-----R-----  
 Nef251 90 100 110 120 130 140 150 160  
 AYRKÖNMDDIDEEDDDL VGVSVRPKVP LRAMTYKLAIDMSHFTKEKGGLEGT YYSARRHRILDMYLEKEKEGIIPDWÖDYT  
 Nef239 -----\*-----T-S-----I-----I----->  
 Nef251 170 180 190 200 210 220 230 240  
 SGRGIRYPKTFGWLWKLVPVNVSDDEAÖEDERHYLMÖPAÖT SKWDDPWGEVLAWKFDPTTLA YTYEA YARYPELEEA SÖACÖ  
 Nef239 -----E---H---Q-----V----->  
 Nef251 RKRLEEG

Figure 1d. Nef CTL Epitopes

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