

Contents

1	Introduction	13
	Background.....	13
	<i>HIV-infection and treatment</i>	13
	<i>Drug pressure</i>	13
	<i>Immune response and pressure</i>	13
	<i>The human leukocyte antigen system</i>	14
	<i>CTL escape mutants</i>	15
	<i>Preliminary data</i>	16
	Research problem, hypothesis, objective and experimental approach ...	16
	Relevance	17
2	Materials and Methods	19
	Patients	19
	Cells and Culture Media	20
	Scanning sequences for CTL restricted epitopes	21
	Design of peptides	21
	Generation of T cell clones	21
	Gamma interferon (IFN- γ) ELISPOT assays	22
	Restriction assay	22
	Blocking assay	23
	Additional HLA-B and -C typing.....	24
	Evaluation of data and statistical analysis	25
3	Results and Discussion	27
	3.1 Peptide Design	27
	<i>Results of the epitope prediction systems</i>	27
	<i>Results of the anchor position search</i>	28
	3.2 Results of ELISPOT assays using WT peptides / Confirmation of potential epitopes	31

	<i>Peptides covering amino acid 33 (protease)</i>	31
	<i>Peptides covering amino acid 46 (protease)</i>	33
	<i>Peptides covering amino acid 75 (reverse transcriptase)</i>	35
	<i>Peptides covering amino acid 103 (reverse transcriptase)</i>	35
	<i>Peptides covering amino acid 118 (reverse transcriptase)</i>	36
	<i>Peptides covering amino acid 210 (reverse transcriptase)</i>	37
3.3	Results of ELISPOT assays using variant peptides / The effect of mutations within newly found epitopes	37
	<i>Peptides covering amino acid 46 (protease)</i>	37
	<i>Peptides covering amino acid 75 (reverse transcriptase)</i>	40
	<i>Peptides covering amino acid 118 (reverse transcriptase)</i>	41
	<i>Peptides covering amino acid 210 (reverse transcriptase)</i>	42
4	Conclusion and Synthesis	45
5	References	49