INMUNOINFORMATICA

Pedro A Reche, PhD

INDEX

- **IMMUNE SYSTEM**
- **AREAS OF RESEARCH IN IMMUNOINFORMATICS**
- **COMPUTATIONAL VACCINOLOGY**

INMUNOINFORMATICA?

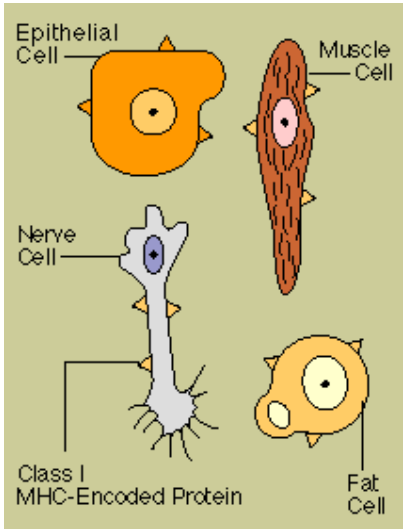
- IMMUNOINFORMATICS: Study of the immune system through the use of computers
  - Existencia masiva de Datos concernientes al sistema inmune
  - Problemas especificos relacionados con el sistema inmune
  - **Complejidad del sistema**

IMMUNE SYSTEM FUNCTION: SELF VS NON SELF RECOGNITION

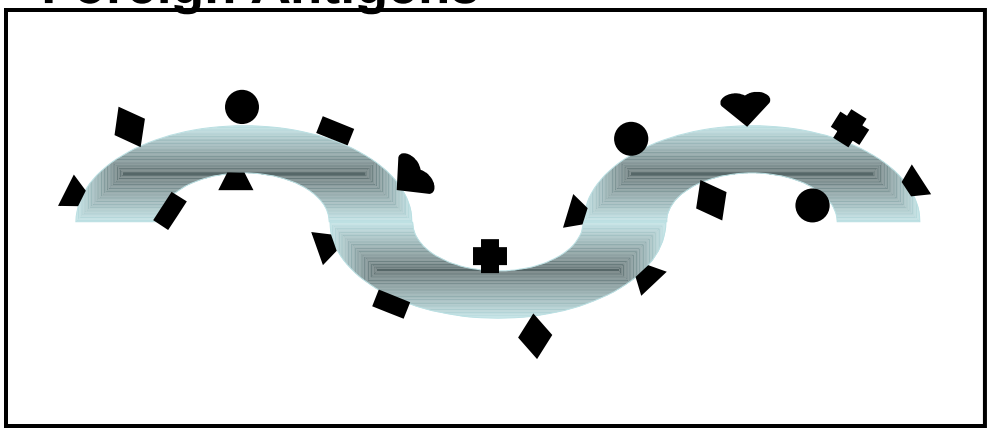
The immune system offer protection against infections

- Immune system function is based on discriminating between self and non-self
- Self and non-self discrimination is achieved through the recognition of small molecular subunits (antigens): self and non-self antigens
- Self antigens confer tolerance and non-self (foreign) antigens activate the immune system

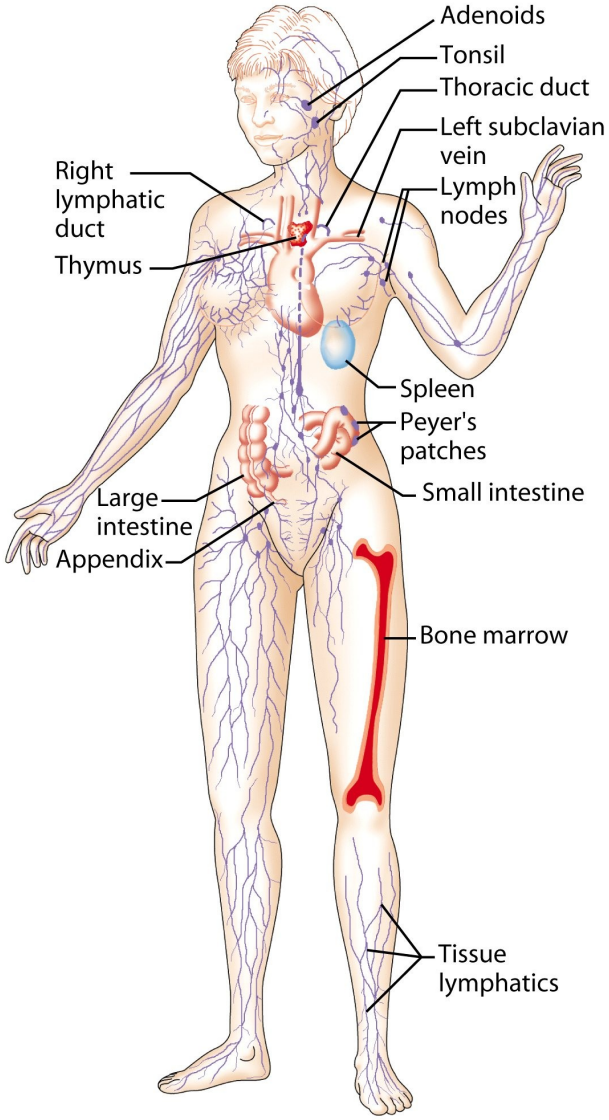
Self Antigens



Foreign Antigens



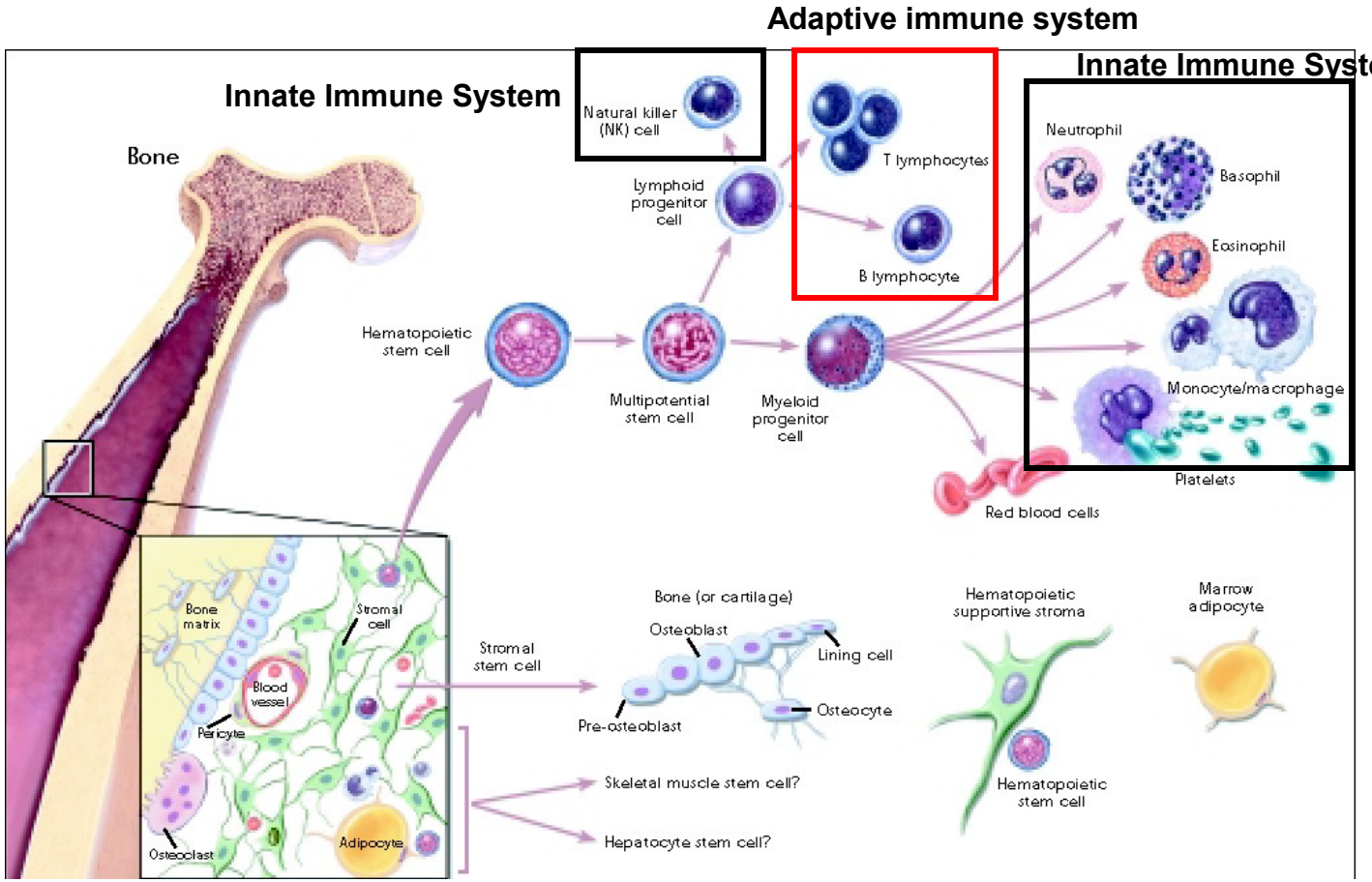
IMMUNE SYSTEM ORGANS



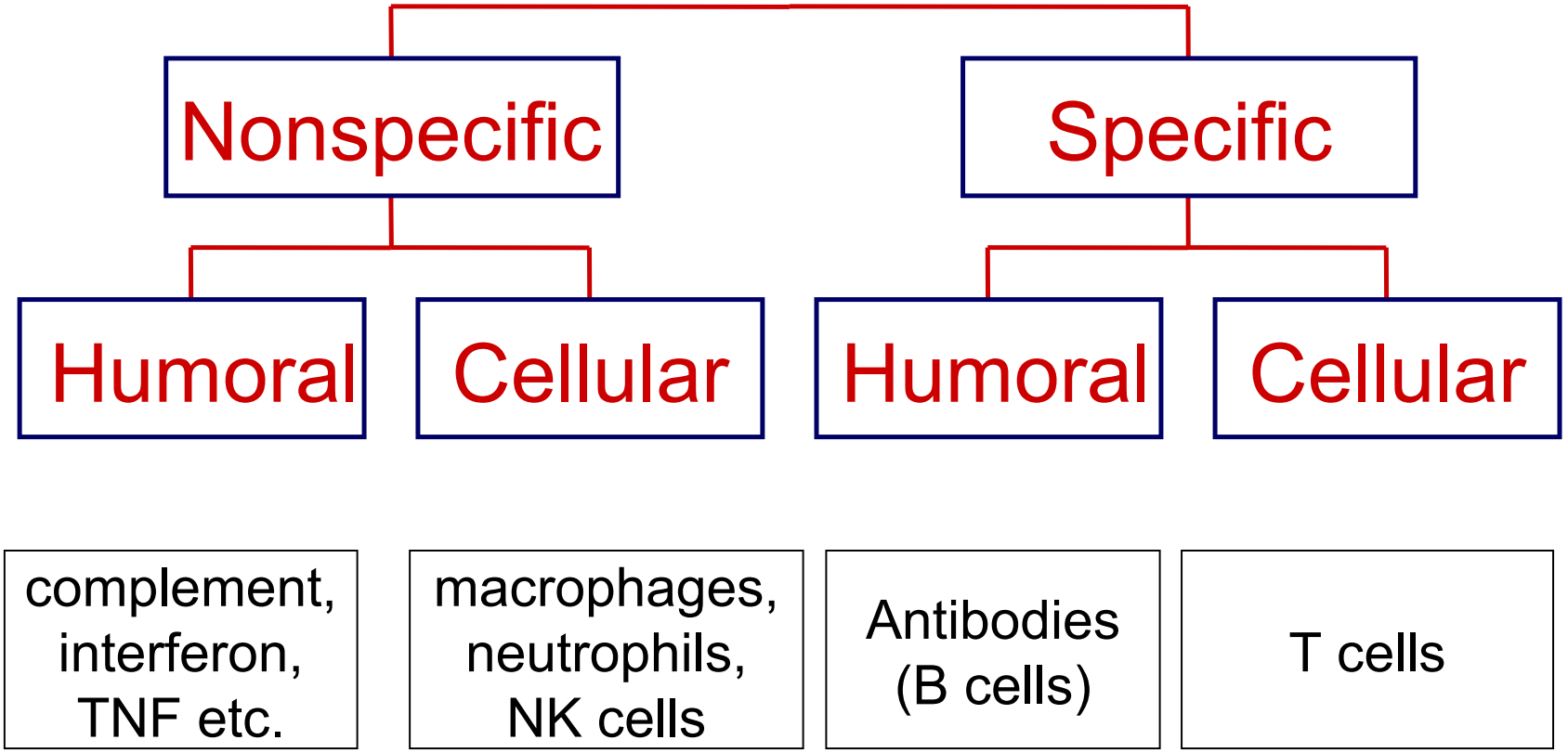
Functions:

- Production of Immune system cells
- Maturacion and education of Immune system cells
- Immune system recognition and activation

IMMUNE SYSTEM CELLS: HEMATOPOYESIS

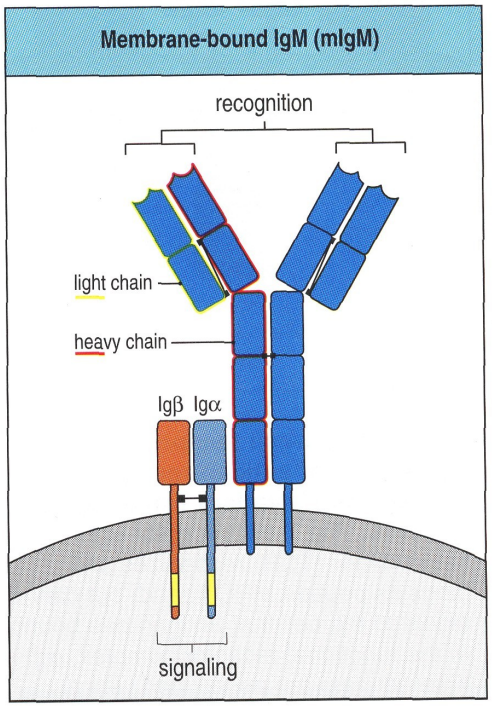


Innate versus Adaptive Immune System



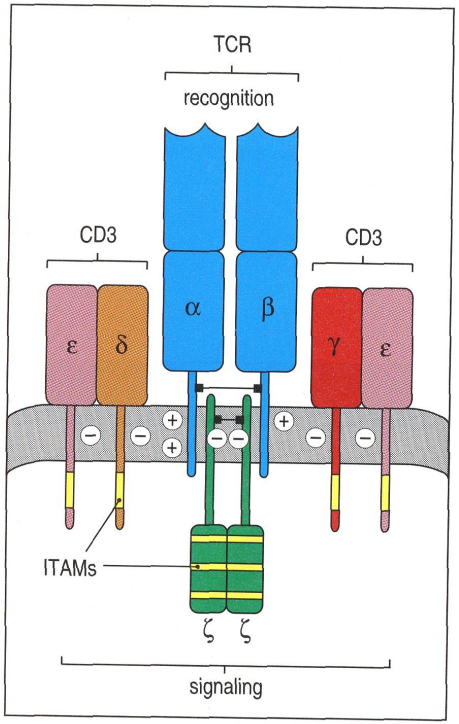
ANTIGEN SPECIFIC RECEPTORS

BCR



10^{20}

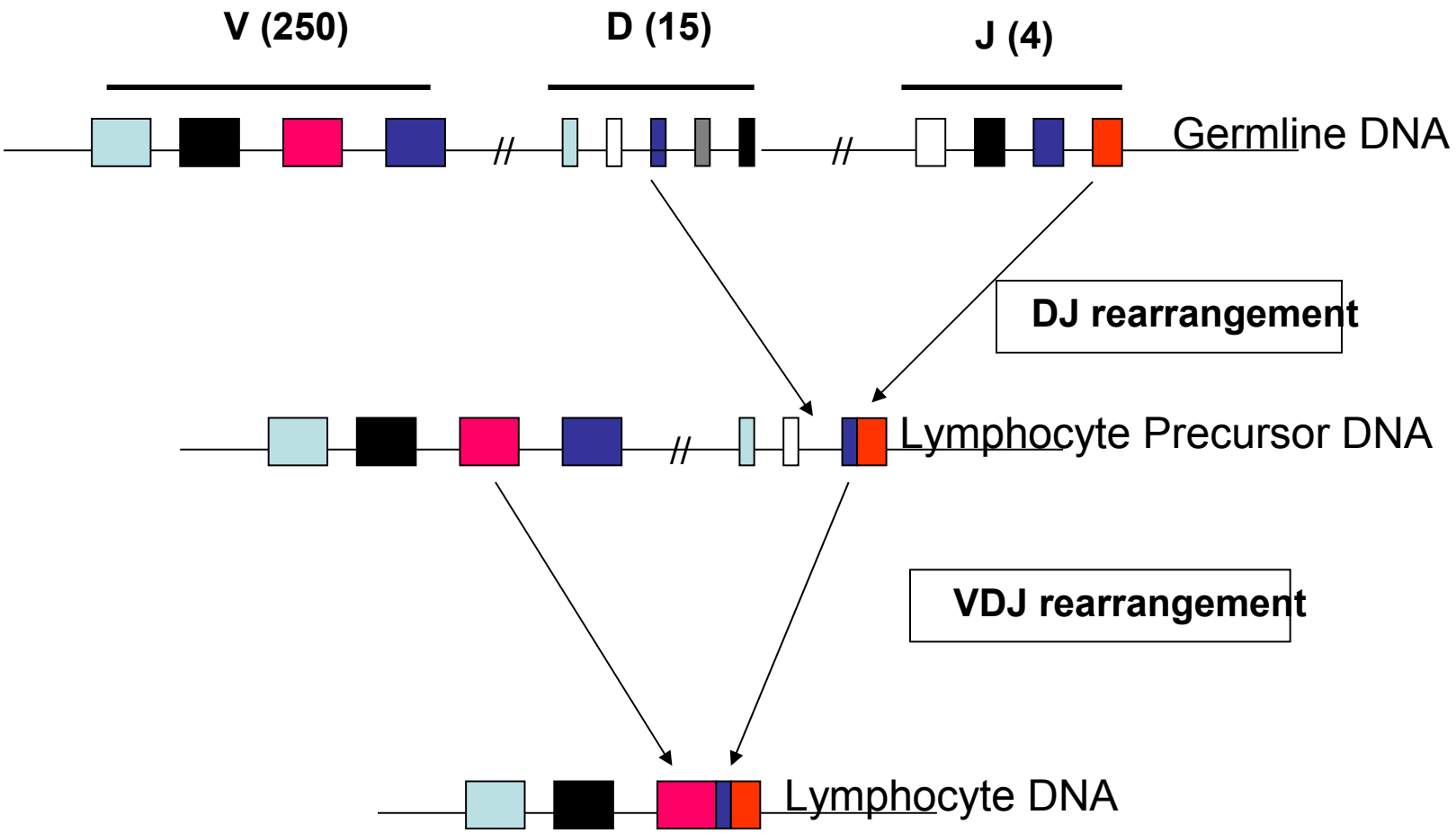
TCR



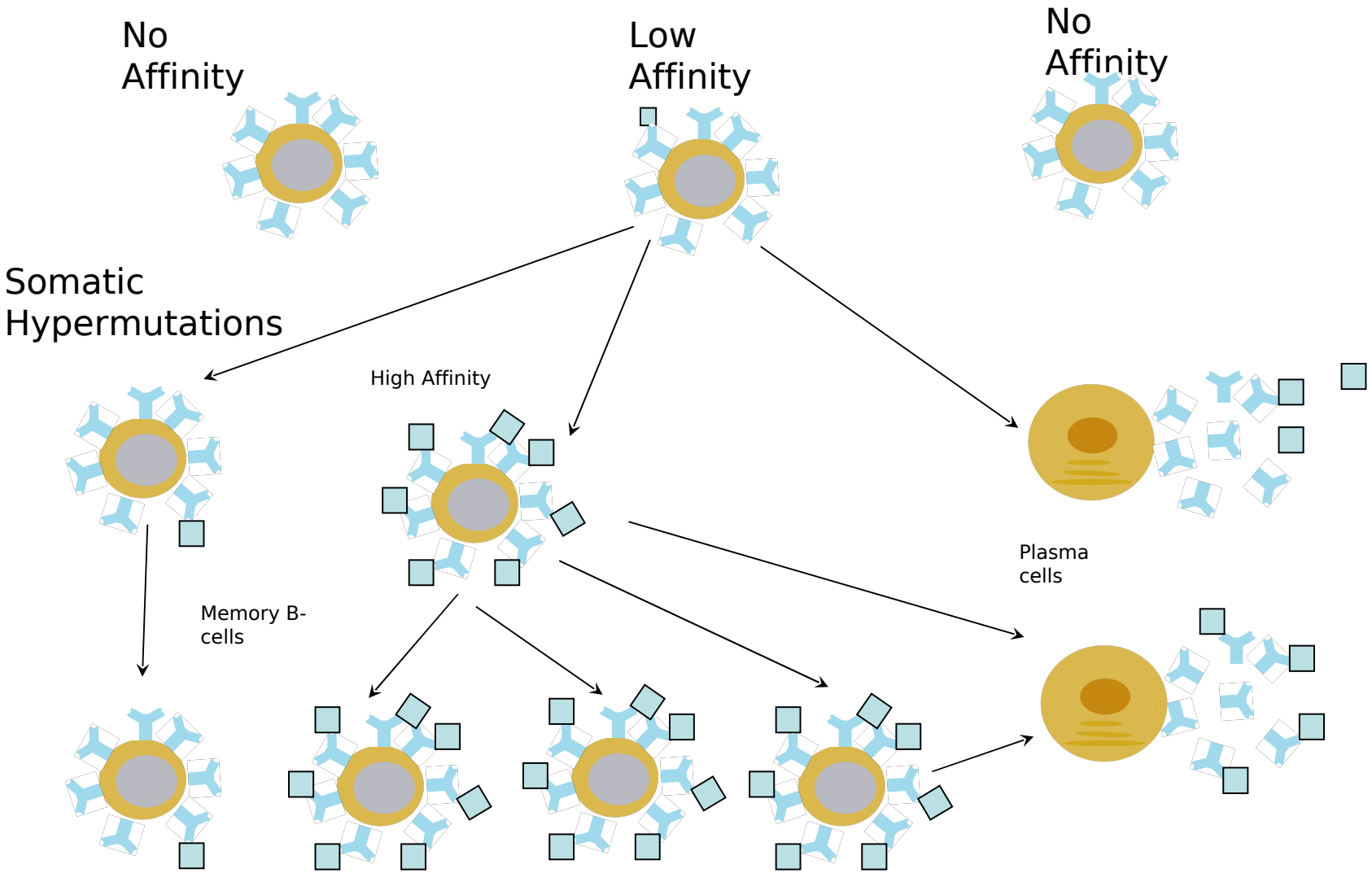
10^{8}

DIVERSITY OF TCR AND BCR REPETOIRES IS GENERATED BY SOMATIC RECOMBINATION

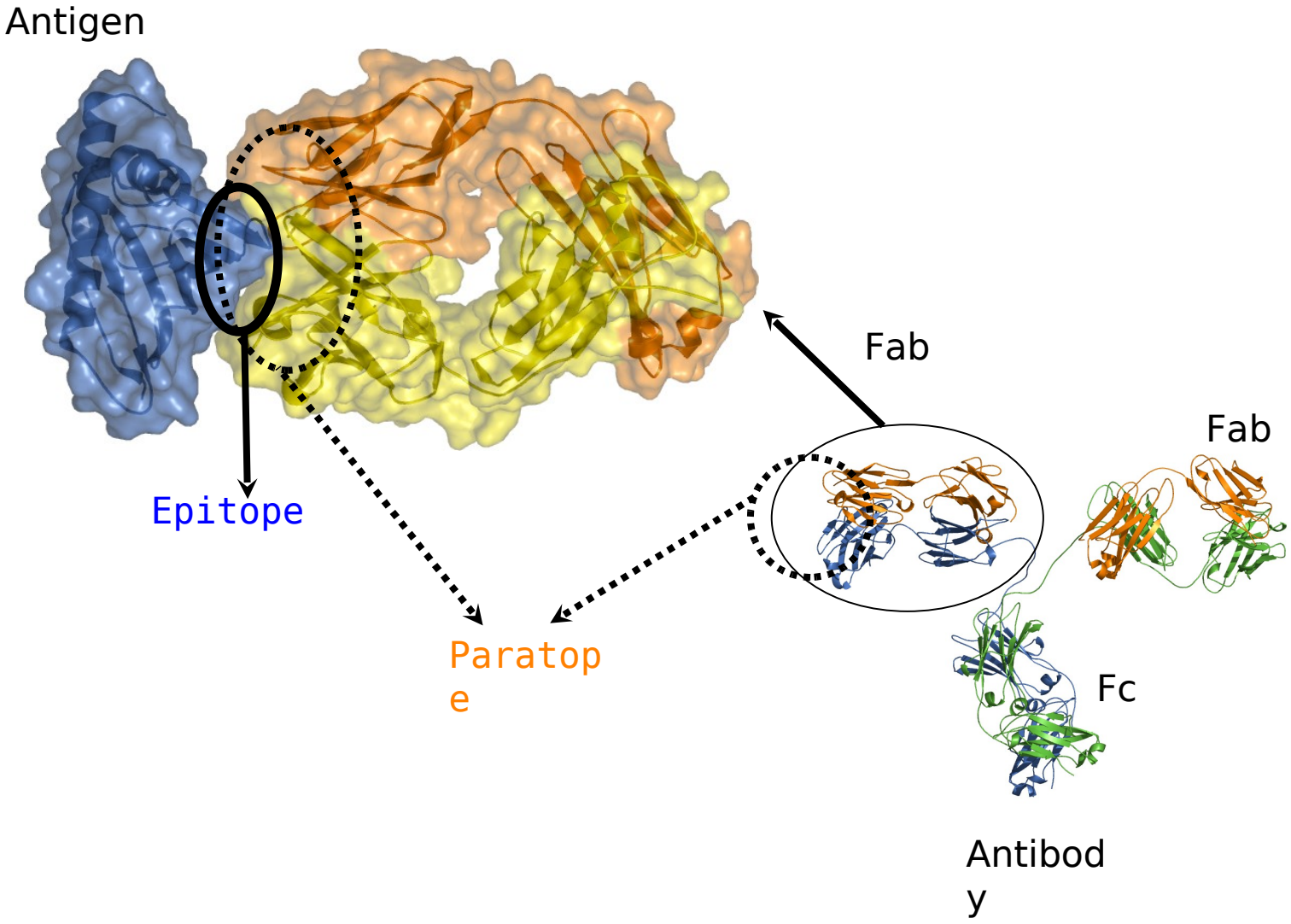
(S. Tonegawa)



B-CELL ACTIVATION: SELECTION AND CLONAL EXPASION



ANTIBODY - ANTIGEN INTERACTION



ANTIGEN RECOGNITION BY T CELLS

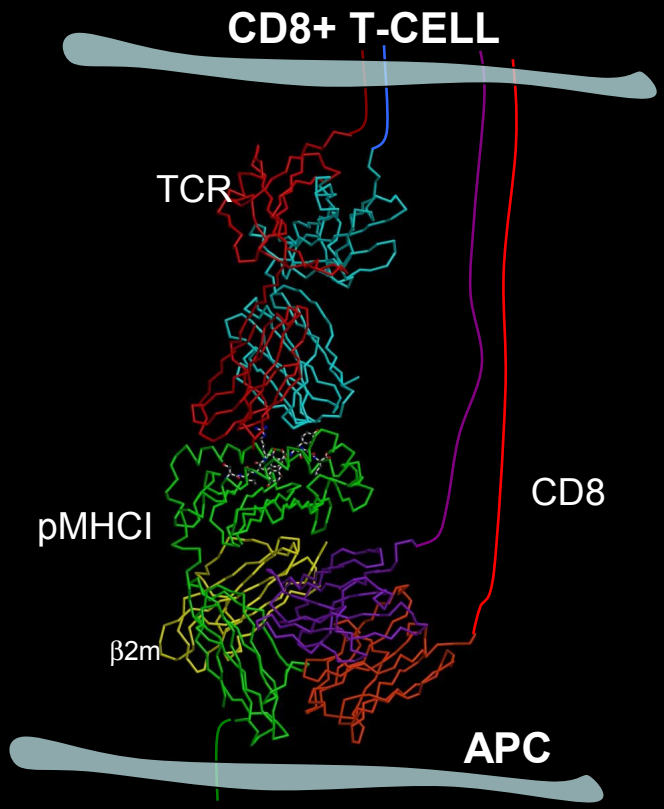
1 : T cells recognize peptides (about 9 amino acids) and not native antigen

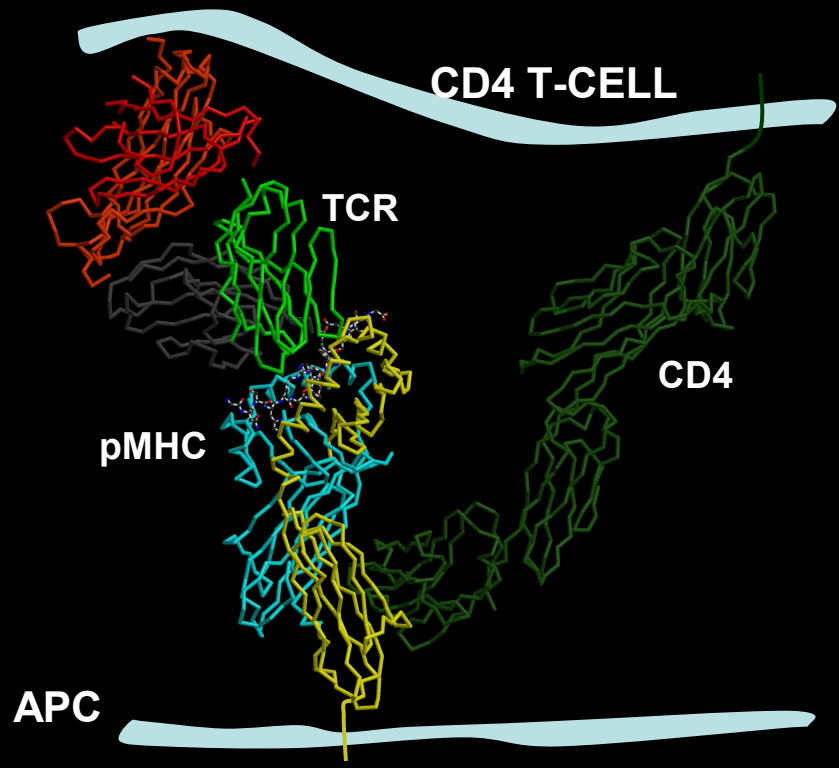
2 : T cells recognize peptides when bound to their own MHC

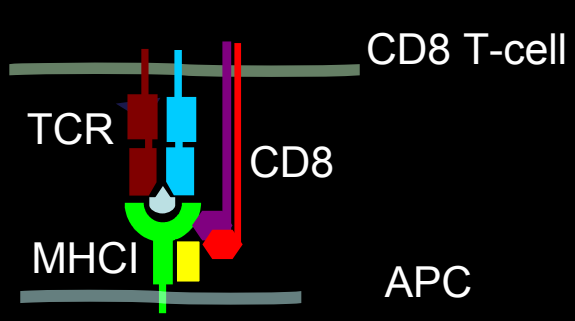
CD4 T cells : MHC-cl II

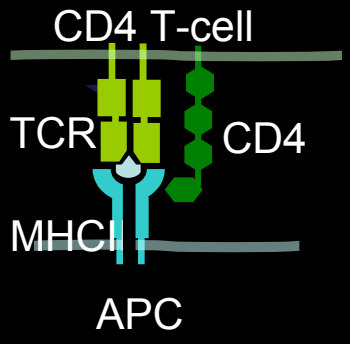
CD8 T cells : MHC-cl I

Structural recognition of peptide-MHCI by TCR

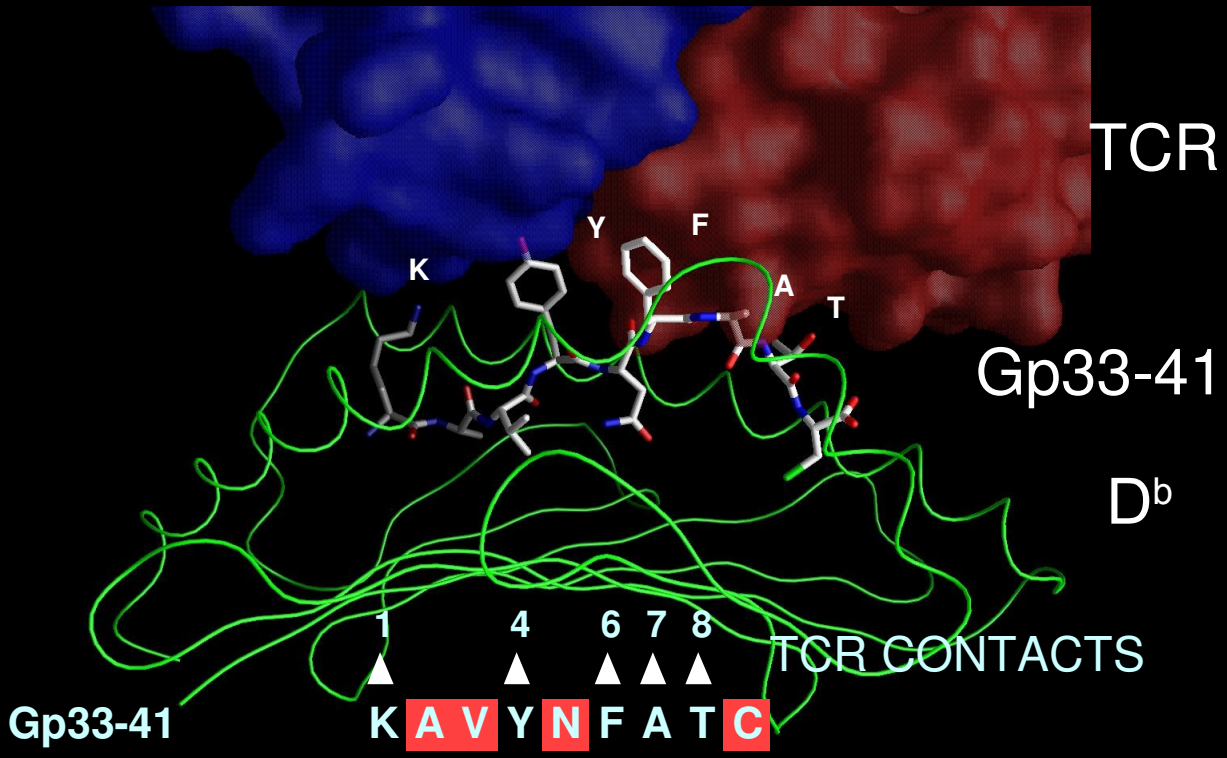




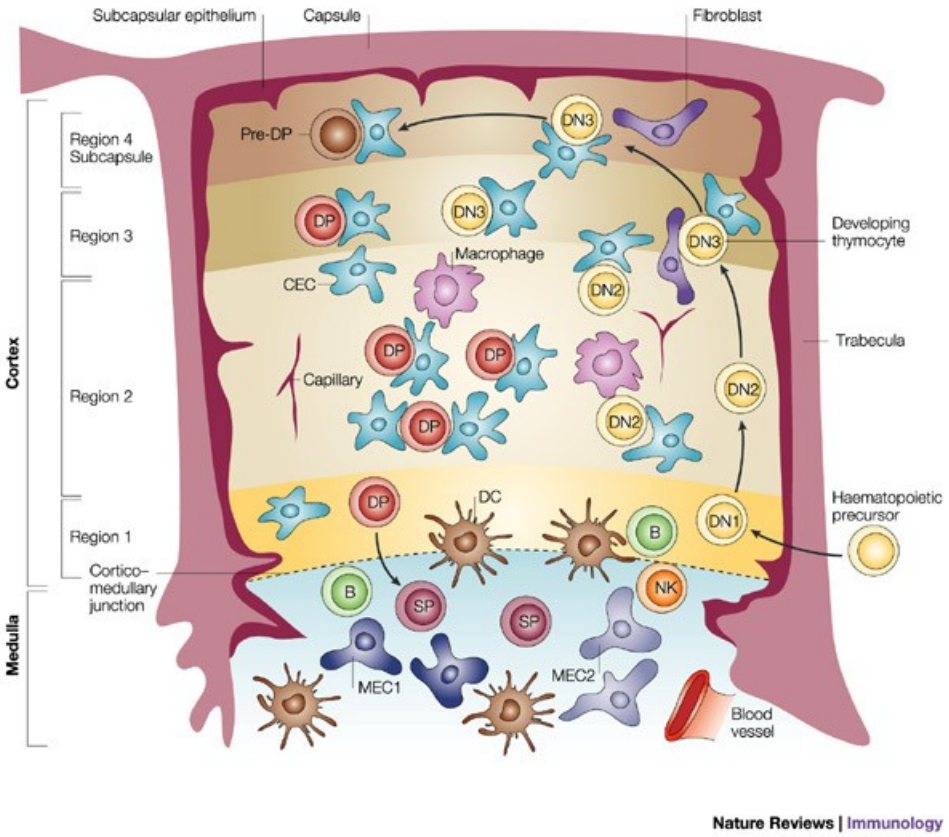




Structural features of TCR Recognition of pMHCI complexes

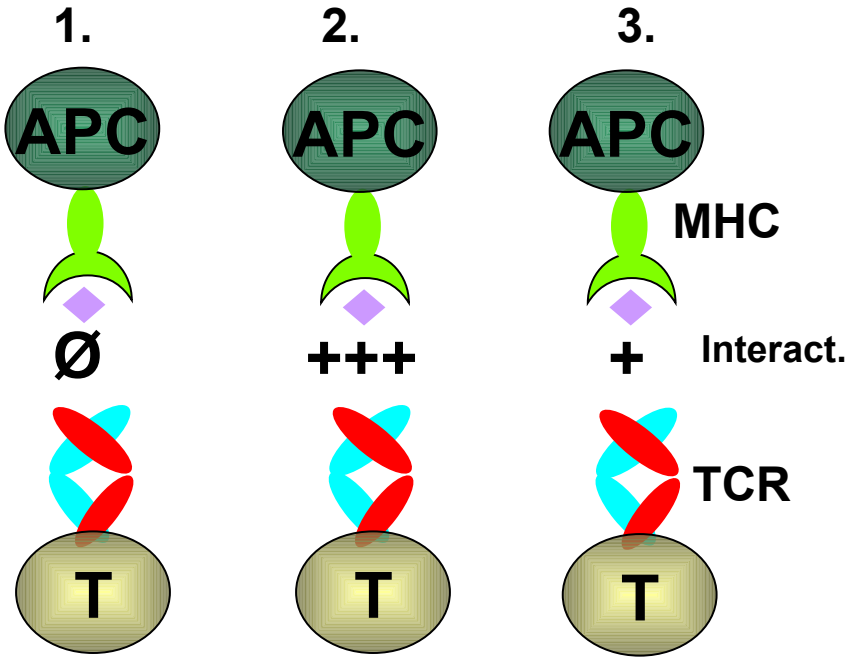


TCR-PMHC FIT AND SELF TOLERANCE OF T-CELLS IS ADQUIRED DURING THYMIC SELECTION

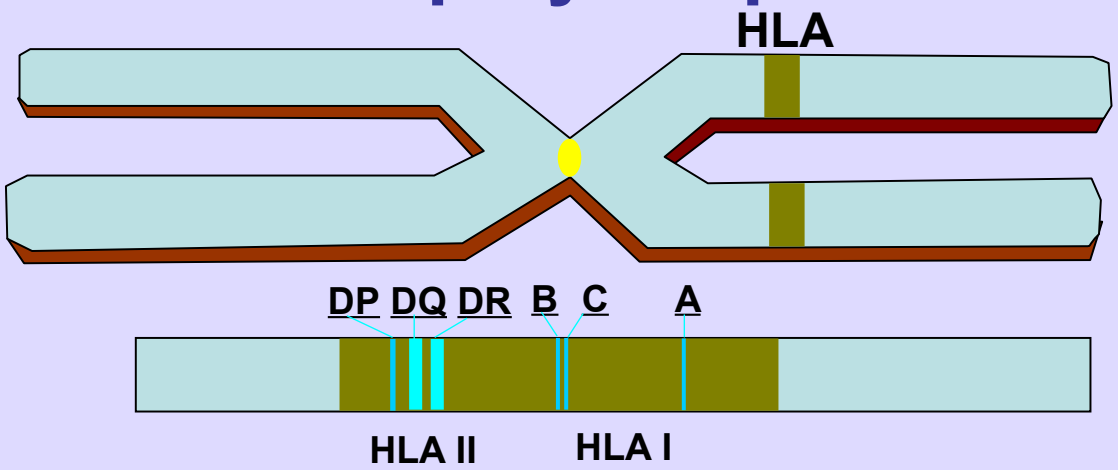


Nature Reviews Immunology 4; 278-289 (2004);

Thymocyte selection is mediated by peptide/MHC/TCR interactions



In humans, MHC molecules are extremely polymorphic



Chr6

HLA MOLECULE	SEQUENCES
CLASS I	
HLA-A	230
HLA-B	447
HLA-C	97
CLASS II	
HLA-DPA	12
HLA-DPB	90
HLA-DQA	17
HLA-DQB	42
HLA-DRA	2
HLA-DRB1	271
HLA-DRB3	30
HLA-DRB4	7
HLA-DRB5	14

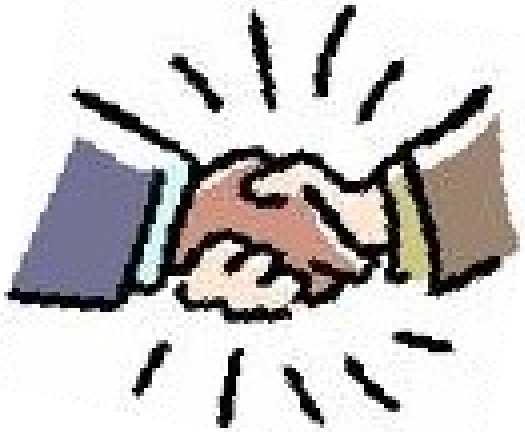
	Black	Caucas.	Hispan.	Nat.Ame	Asian
GF	5.6%	15.1%	6.0%	7.5%	1.5%
PF	10.8%	27.9%	11.6%	14.4%	3.0%

	Black	Caucas.	Hispan.	Nat.Ame	Asian
GF	2.0%	11.75%	6.7%	3.4%	0.7%
PF	3.9 %	22.0 %	12.39%	8.3 %	1.3 %

INNATE AND ADAPTIVE IMMUNE SYSTEM

ANTIGEN PROCESSING AND PRESENTATION

INNATE

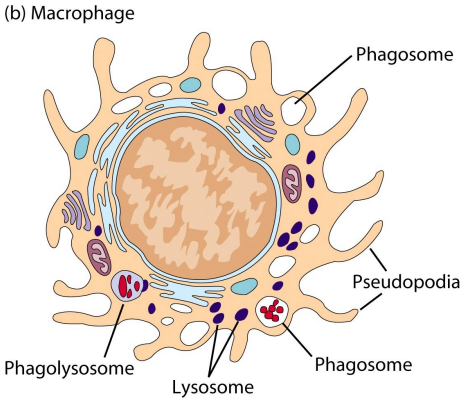


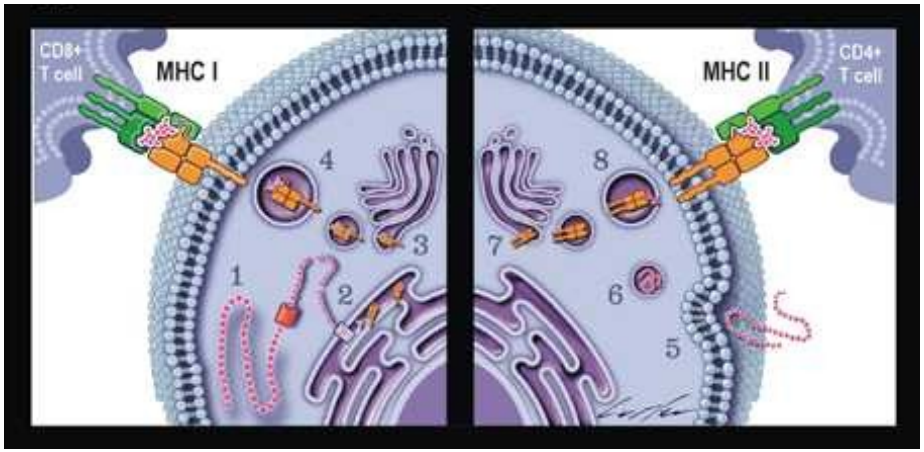
ADAPTIVE

CELLS OF THE INNATE IMMUNE SYSTEM WORK AS ANTIGEN PRESENTIG CELLS

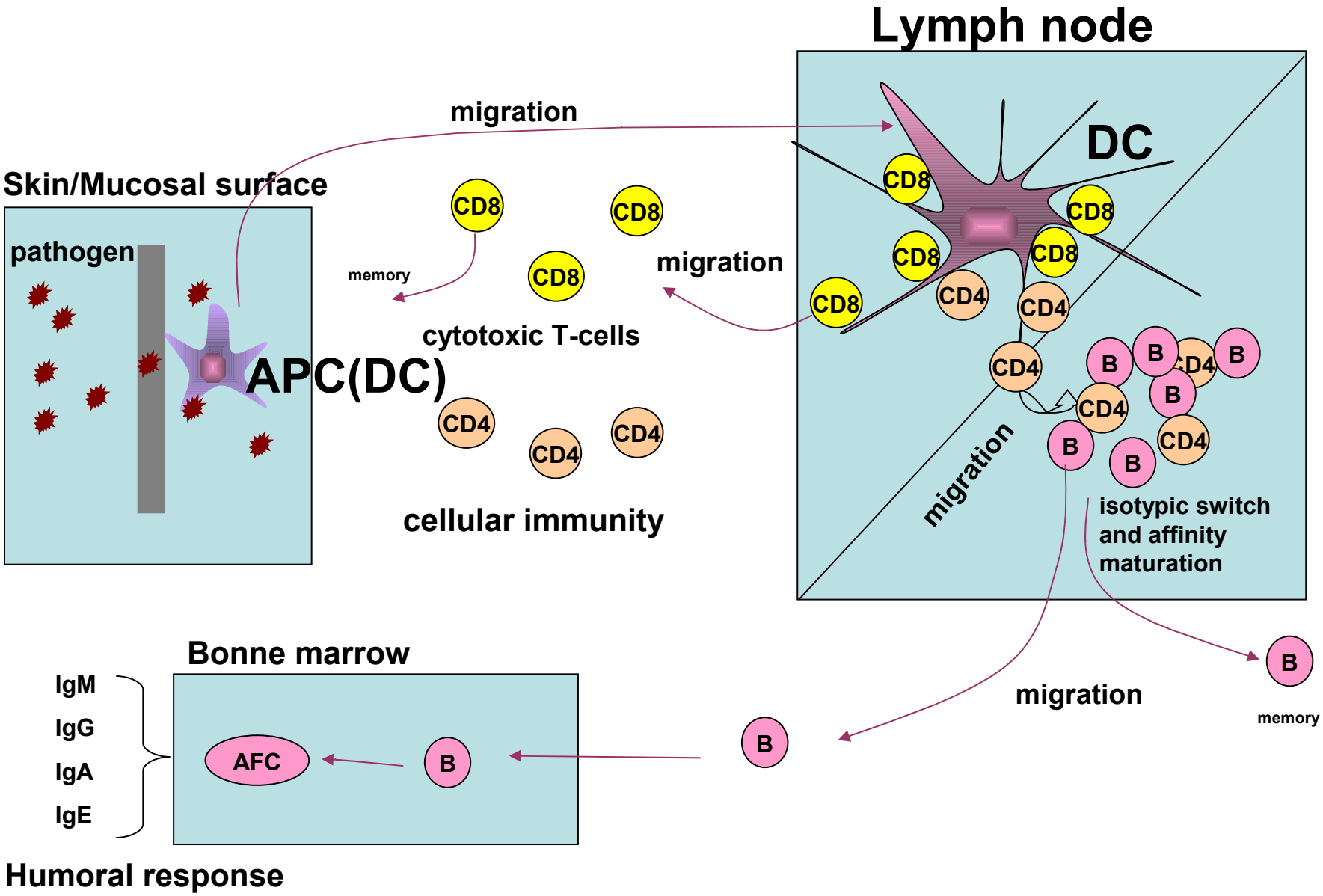
Phagocytic cells:

Granulocytes
Monocytes
Macrophages
Dendritic cells

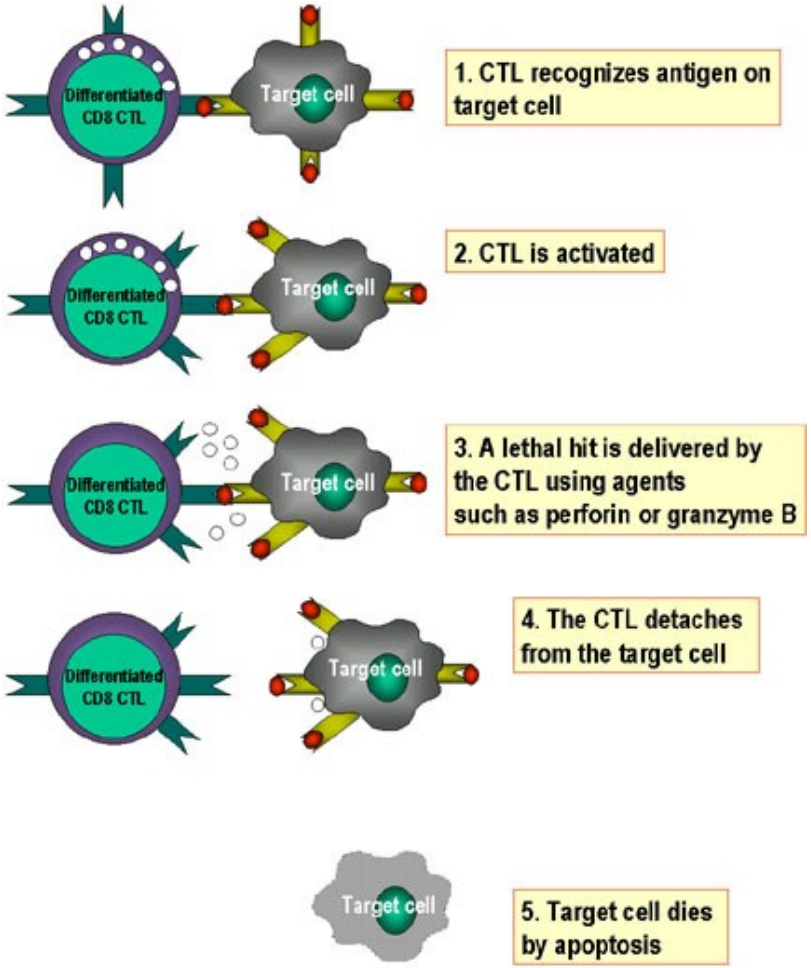




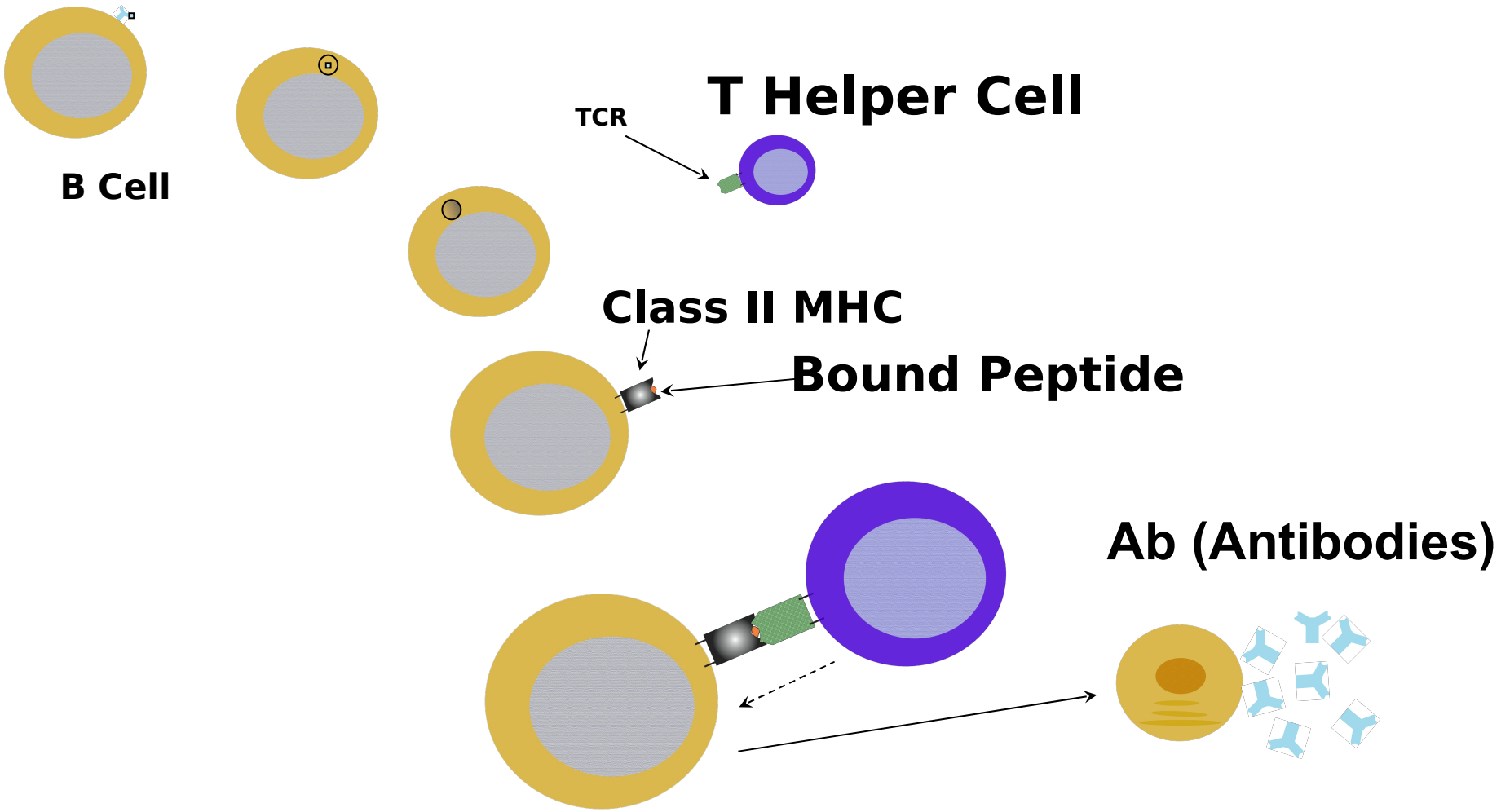
IMMUNE RESPONSE



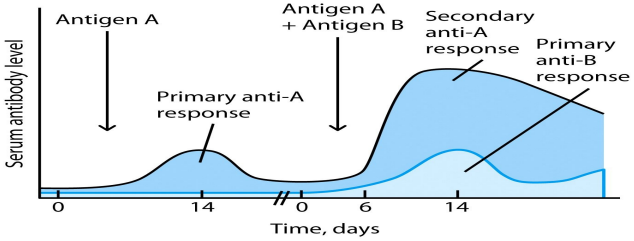
CD8 T cell Efector Function



CD4 T cell Efector Function: B-Cell Activation



B cells – memory cells



IMMUNOINFORMATICS: AREAS OF DEVELOPEMENT

- **Specialized Databases and Resources**

- **System level models describing immune system proceses**

- **Molecular models describing immune system features: Antigen recognition**

IMMUNOINFORMATICS: AREAS OF DEVELOPEMENT

- Generation of Specialized Databases and Resources
  - Databases of immunological sequences: IMGT
  - Databases of epitopes: EPIMHC
  - Database of pathogens: HIV database

IMMUNOINFORMATICS DATABASES: IMGT

http://imgt.cines.fr/

WELCOME !
to the IMGT Home page

THE INTERNATIONAL
IMMUNOGENETICS
INFORMATION SYSTEM®

Im Muno Gene Tics Information system®
http://imgt.cines.fr

IMGT®, the international ImMunoGeneTics information system® http://imgt.cines.fr, is a high-quality integrated knowledge resource specialized in the immunoglobulins (IG), T cell receptors (TR), major histocompatibility complex (MHC), immunoglobulin superfamily (IgSF), major histocompatibility complex superfamily (MhcSF) and related proteins of the immune system (RPI) of human and other vertebrate species, created in 1989 by Marie-Paule Lefranc (Université Montpellier II, CNRS). IMGT, a European project since 1992, works in close collaboration with EBI. IMGT consists of sequence databases (IMGT/LIGM-DB, a comprehensive database of IG and TR from human and other vertebrates, with translation for fully annotated sequences, IMGT/MHC-DB, IMGT/PRIMER-DB), genome database (IMGT/GENE-DB) and structure database (IMGT/3Dstructure-DB), **Web resources** (IMGT Marie-Paule page) and **interactive tools**. The IMGT Home page http://imgt.cines.fr (Montpellier, France) provides a common access to all immunogenetics data.

IMGT founder and director: Marie-Paule Lefranc (Marie-Paule.Lefranc@igh.cnrs.fr), Université Montpellier II, CNRS, LIGM, IGH, IFR3, Montpellier (France)

IMGT® Site Map
Information on IMGT® (creations and updates, references, FAQ, citing IMGT, funding support...)


IMGT Livre d'Or

IMGT databases

- **IMGT/LIGM-DB** (IG and TR from 204 species) (LIGM, Montpellier, France) (**107 367 entries**)
- **IMGT/MHC-DB** (IMGT/MHC-HLA, -NHP, -DLA, -FLA) (ANRI, BPRC, hosted at EBI)
- **IMGT/PRIMER-DB** (IG and TR from 11 species) (LIGM, Montpellier, France) (**1 864 entries**)
- **IMGT/GENE-DB** (IG and TR genes from human and mouse) (LIGM, Montpellier, France) (**1 511 genes, 2 462 alleles**)
- **IMGT/3Dstructure-DB** (IG and TR, MHC and RPI gene and allele identification and IMGT Colliers de Perles) (**1 269 entries**)

IMGT Web resources

- **IMGT Repertoire** (IG and TR, MHC and RPI)
- **IMGT Index** (FactsBook)
- **IMGT Scientific chart** (Sequence description, Numbering, Nomenclature, Representation rules)
- **IMGT Bloc-notes** (Interesting links, PubMed, Meeting announcements, Postdoctoral positions and jobs NEW!, Messages, Search engines...)
- **IMGT Education** (IMGT Lexique, Aide-mémoire, Tutorials, Questions and answers, Enseignements...)
- IMGT Medical page, IMGT Veterinary page, IMGT Biotechnology page
- IMGT Posters and diaporama
- **The IMGT Immunoinformatics page**

IMGT tools

- **IMGT/V-QUEST** (sequence alignment software for IG, TR and HLA)
- **IMGT/JunctionAnalysis** (for human and mouse IG and TR)
- **IMGT/Allele-Align**
- **IMGT/PhyloGene**
- **IMGT/DomainDisplay** (Amino acid sequences)
- **IMGT/LocusView, IMGT/GeneView, IMGT/GeneSearch, IMGT/CloneSearch** (for human IGK, IGL, IGH, TRA/TRD, TRB, TRG, mouse TRA/TRD and human MHC)
- **IMGT/GeneInfo** (TIMC and ICH, Grenoble; LIGM, Montpellier)
- **IMGT/GeneFrequency**
- **IMGT/DomainGapAlign**
- **IMGT/Collier-de-Perles**
- **IMGT/DomainSuperimpose**
- **IMGT/StructuralQuery**

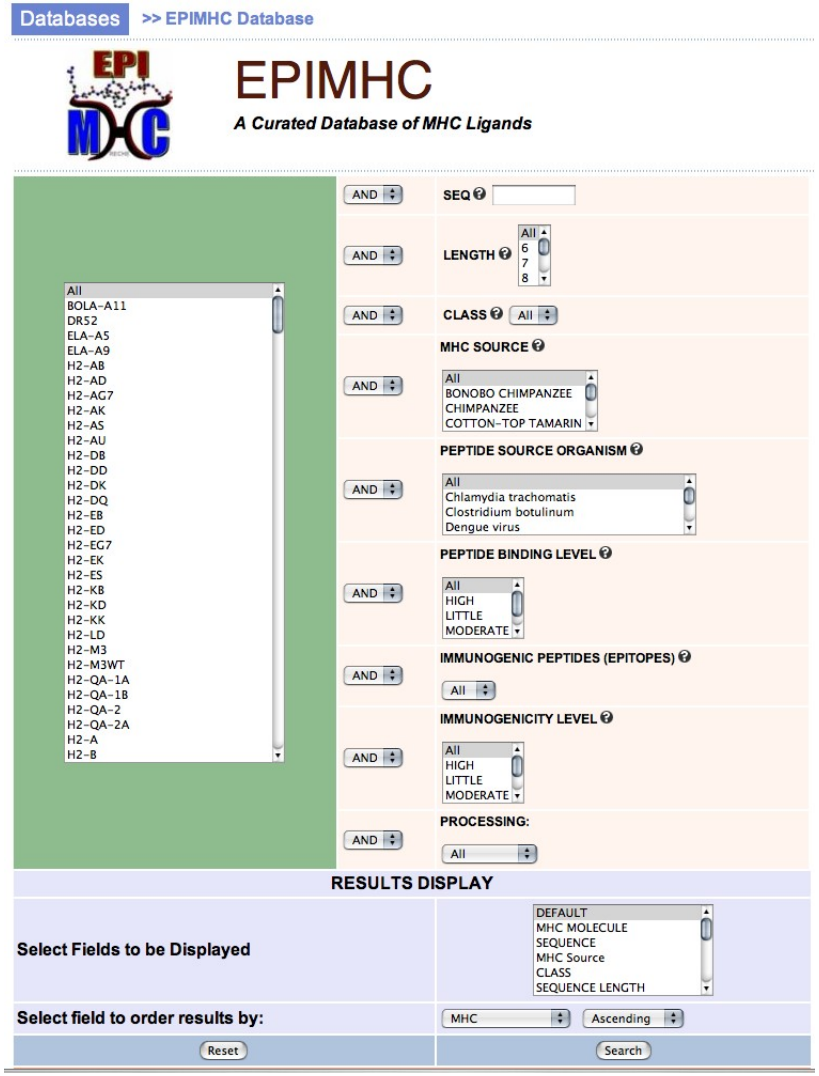
IMGT other accesses

- IMGT Other accesses (SRS, FTP...)
- Compare your sequence against IMGT (BLAST, FASTA)
- IMGT/LIGM-DB Sequence submission
- IMGT flat file release information

Search
Google
WWW IMGT domain

IMMUNOINFORMATICS DATABASES: EPIMHC

http://bio.dfci.harvard.edu/epimhc/



IMMUNOINFORMATICS: SYSTEM LEVEL MODELS

- Symbolic models describing processes at cellular and organ levels:

  - **Immune response to viruses.** Dahari H, Lo A, Ribeiro RM, Perelson AS., Modeling hepatitis C virus dynamics: liver regeneration and critical drug efficacy.J Theor Biol. 2007 Jul 21;247(2):371-81.

  - **Analysis of MHC diversity under host-pathogen coevolution.** Bhattacharya T, et al effects in the assessment of HIV polymorphisms and HLA allele associations.Science. 2007 Mar 16;315(5818):1583-6.

  - **B cell maturation.** Meyer-Hermann et al. An analysis of B cell selection mechanisms in germinal centers. Math Med Biol. 2006 Sep;23(3):255-77

  - **Dynamic models that simulate both cellular and humoral immune responses.** Pappalardo et al simulation of cancer immunoprevention vaccine.Bioinformatics. 2005 Jun 15;21(12):2891-7.

IMMUNOINFORMATICS: MOLECULAR MODELS

- **Use molecular data (sequences, 3D etc)**
  - B cell epitope prediction
  - Modeling of antigen processing events
  - **T cell epitope prediction**
  - **Computer aided design of vaccines: Formulation of vaccines**

WHY BOTHER EPITOPE PREDICTION?

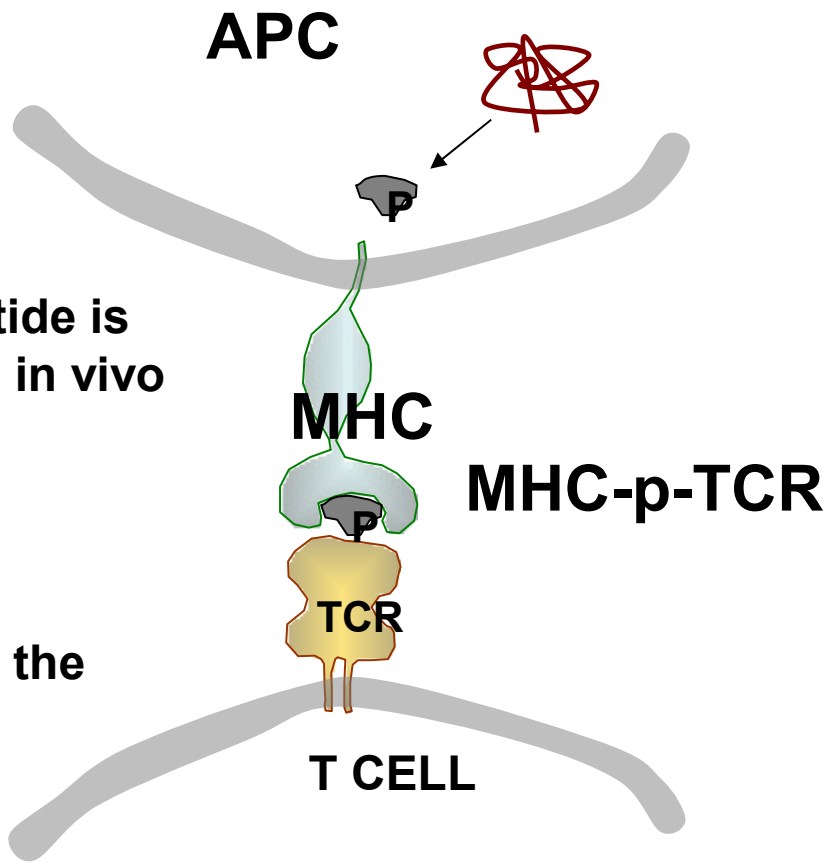
- Predicting the target of the immune system is of practical relevance for:
  - Understanding disease pathogenesis and for making vaccines
  - Understanding the processes selection tolerance, memory and aging of the immune system

Prediction of T cell epitopes

⇨ **T cell epitopes are peptides derived from the processing of proteins that are able to activate T cells in a detectable manner**

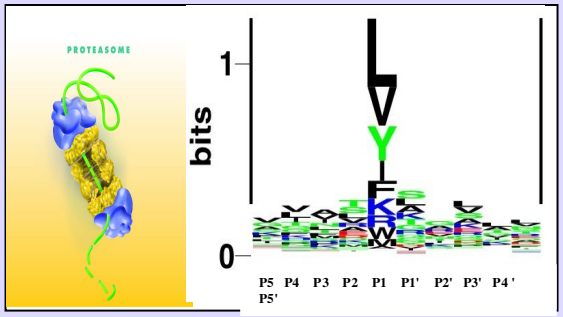
Mechanisms that needs to be modeled

- **Antigen processing. Whether a peptide is processed (released) from a protein in vivo**
- **Binding of the peptide to the MHC molecule**
- **Recognition of the peptide-MHC by the TCR with enough affinity.**

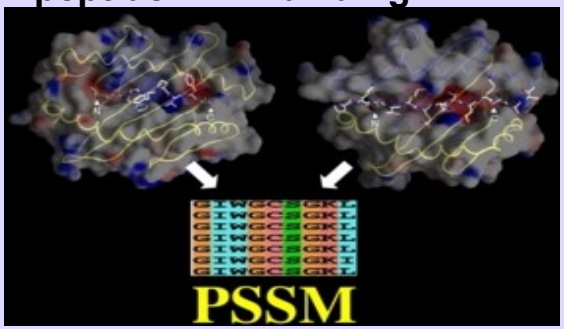


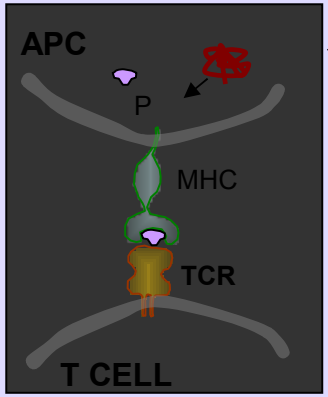
Computer tools for epitope discovery

Antigen Processing

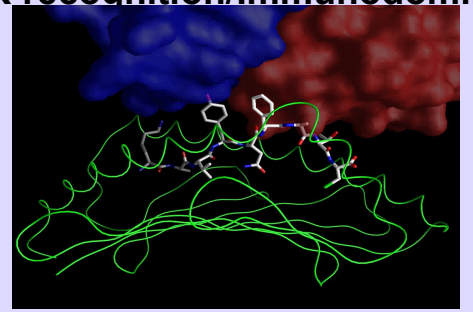


peptide-MHC binding

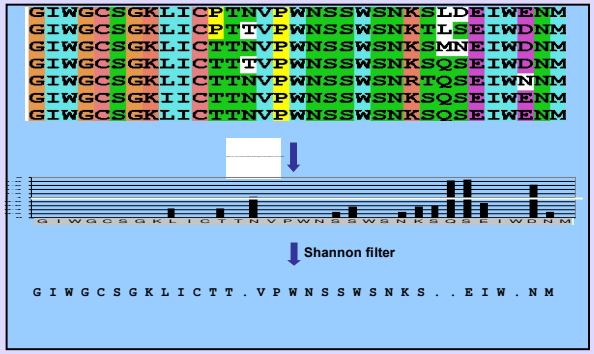




TCR recognition/Immunodominance

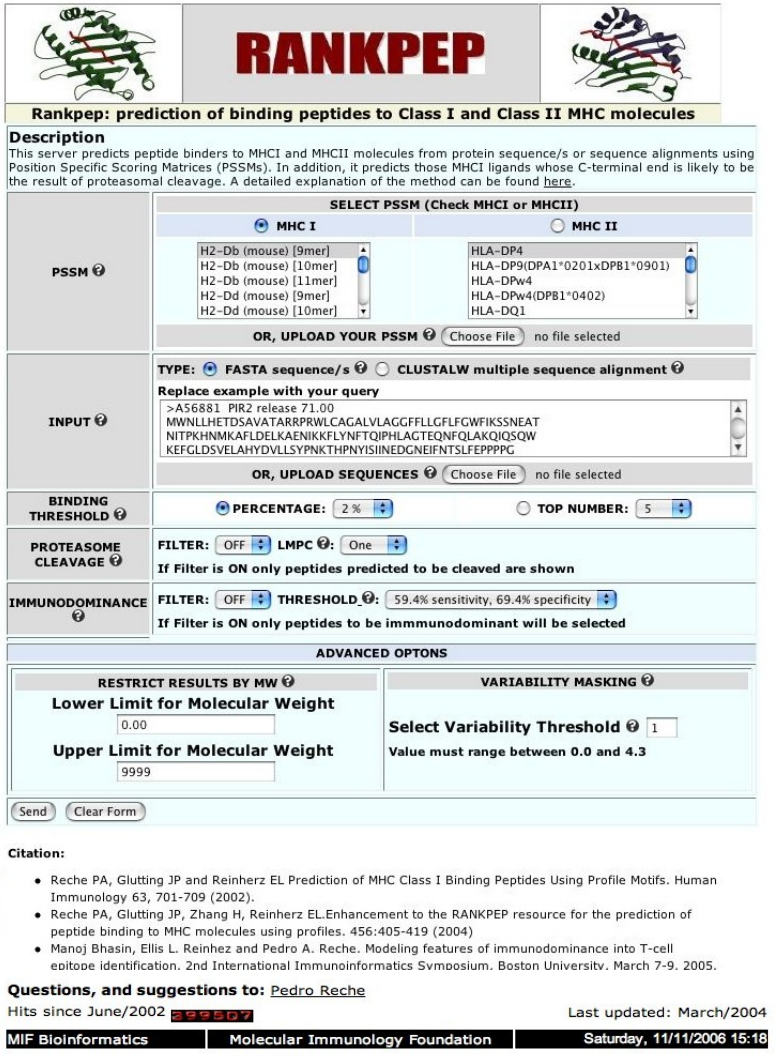


Variability parsing



RANKPEP:SERVIDOR PARA LA PREDICCION DE EPITOPOS

http://bio.dfci.harvard.edu/Tools/rankpep.html



- **RANKPEP es la herramienta mas frecuentemente usada para al predicción de epitopos T (google y 400,000 hits)**
- **Posibilita la predicción de epitopos restringidos por moléculas MHCI y MHCII**
- **Proporciona la colección mas amplia de moléculas de MHC**
- **Predicción del corte por el proteosoma**
- **Es posible predecir cuales son los epitopos inmunodominantes**
- **Flexibilidad y versatilidad:**
  - **INPUT: Proteína/s o alineamientos de proteínas.**
  - **Posibilidad de limitar los resultados de acuerdo a su peso molecular**
  - **Posibilidad de identificar epítopos conservados**

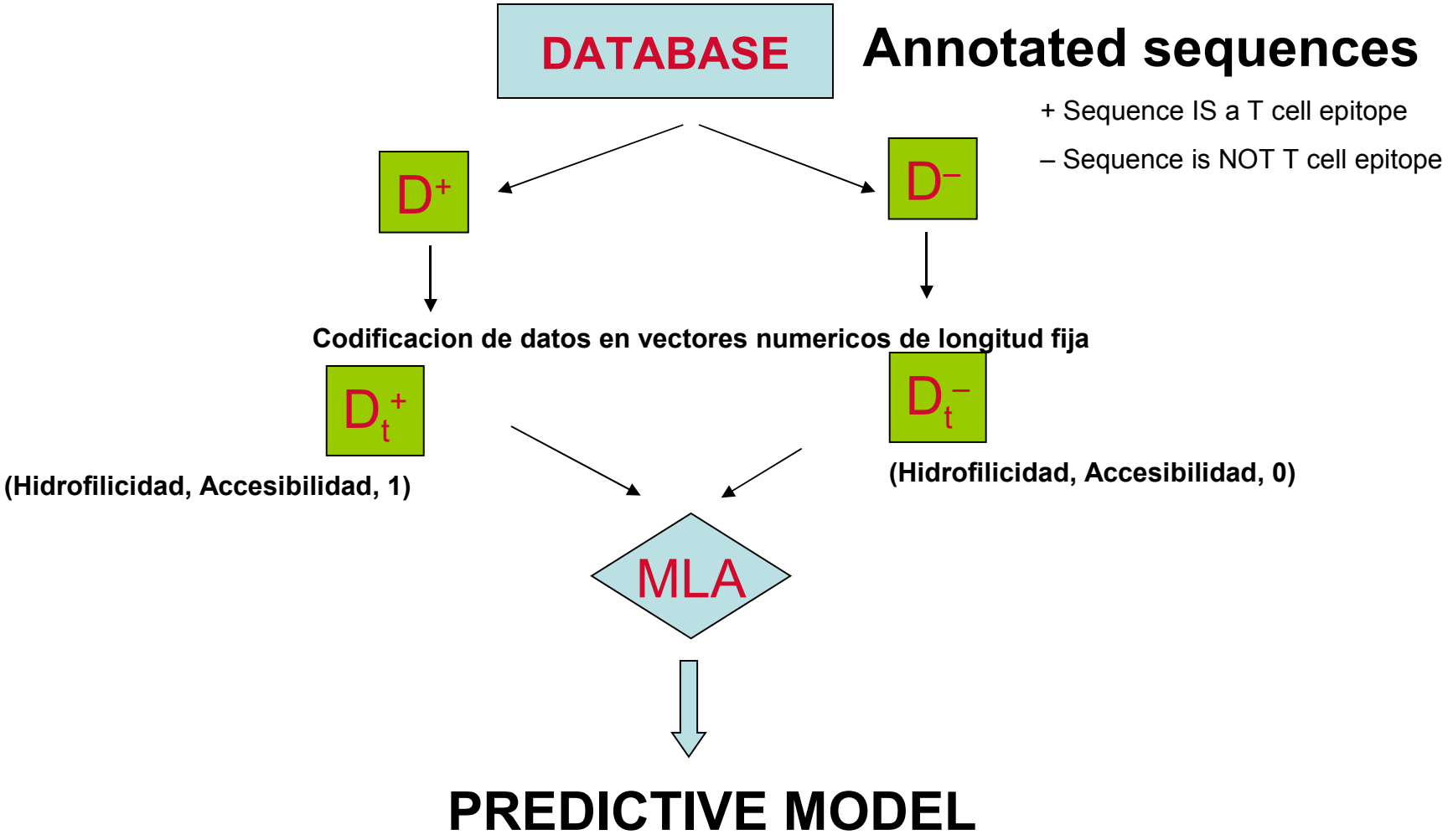
GENERAL PROCEDURE TO DERIVE DATA DRIVEN MODELS

1. **Data Collection.** Eg. Sequences of T cell epitopes
   - Databases Search
   - Text mining

- **Training.** Machine Learning Algorithms

- **Testing and Evaluation**.

GENERATION OF MLA-BASED PREDICTICE MODELS



MLA: WEKA

- Support Vector Machine
- Decision Trees
- Artificial Neural Networks
- K-nearest neighbour learner

EVALUATION

- Select a parameter to quantify the perfomance of model (accuracy, MCC, etc)

- Evaluate performace through x-validation.
  - Train on a subset of the data and test in the remaining dataset

Computer aided design of epitope based vaccines: Computational Vaccinology

MOTIVACION/OBJETIVO

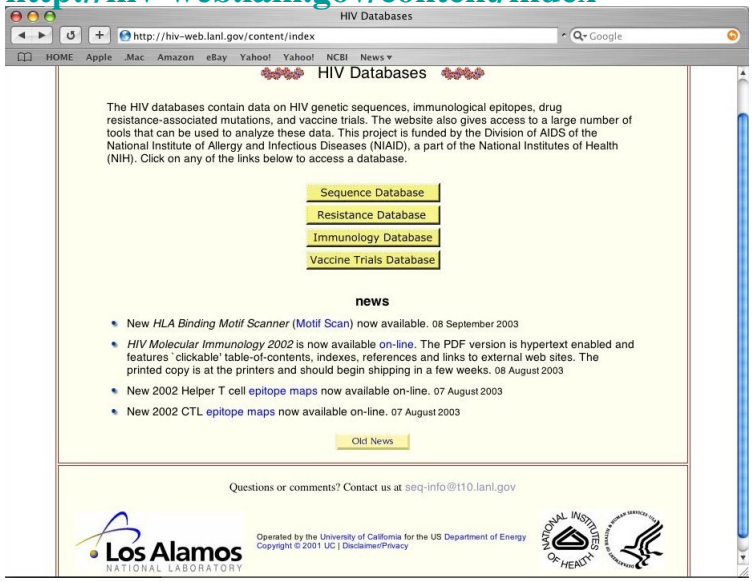
DESARROLLO DE UNA VACUNA DE EPITOPOS T CD8 FRENTE A HIV-1

Pedro A. Reche[§], et al (2006) Elicitation form virus-naive individuals of cytotoxic T lymphocytes directed against conserved HIV-1 epitopes. *Medical Immunology*, 5:1

KNOWN CTL EPITOPES IN HIV-1 INFECTED HUMANS

Los Alamos HIV database is depositary of T-cell epitopes from HIV and SIV

http://hiv-web.lanl.gov/content/index



- **CTL epitope example record**

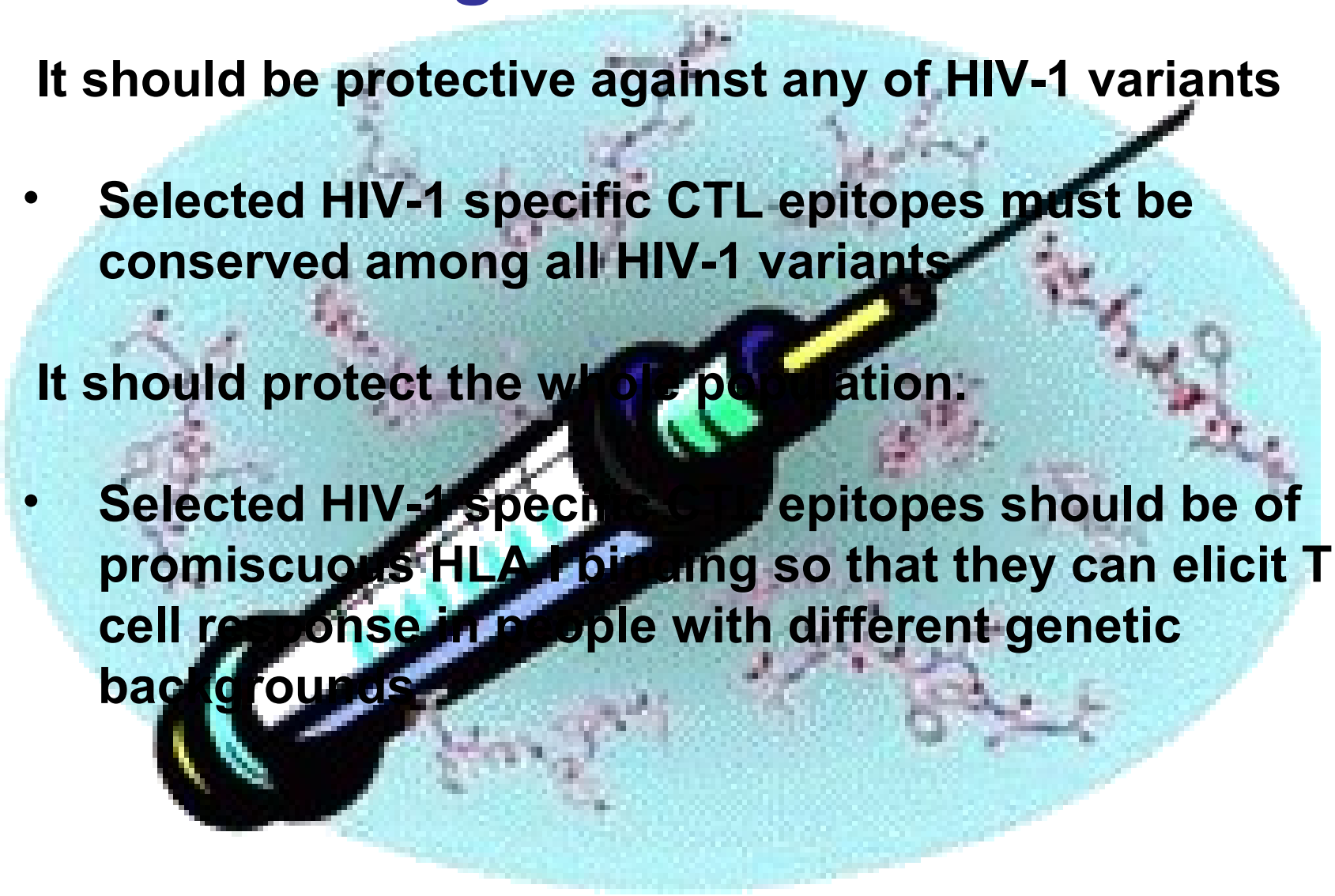
```
Displaying record number 1
HXB2 Location p17(18-26)
Author Location p17(18-26 IIIB)
Sequence KIRLRPGGK
Species(HLA) human (A3)
Immunogen HIV-1 infection
Keywords
Notes
References
```

- **1567 CTL epitope records => 592 unique seq =>195 9mers**

```
Immunogen HIV-1 infection
Species(HLA) human
```

- CTL epitopes from HIV infected patients infected could be used as the basis of a vaccine against HIV1. **How?**

Criteria for a CTL epitope vaccine against HIV-1



1. It should be protective against any of HIV-1 variants
   - Selected HIV-1 specific CTL epitopes must be conserved among all HIV-1 variants
2. It should protect the whole population.
   - Selected HIV-1 specific CTL epitopes should be of promiscuous HLA binding so that they can elicit T cell response in people with different genetic backgrounds

HIV-1 SEQUENCES

Table 1

HIV-1 protein sequences used in this study

	Sequences*																	
GENE	Total	A-A1	B	C	D	F1	F2	G	H	K	O	01	02	04	06	10	11	12	CPZ
GAG	207	10	37	28	5	7	2	4	3	3	5	14	8	3	4	3	4	3	5
POL	204	11	34	26	5	4	3	4	3	2	5	14	12	3	4	3	5	3	5
ENV	408	24	128	51	17	5	5	9	3	2	10	33	16	3	5	3	6	3	5
VIF	427	28	190	40	13	5	5	5	3	2	24	15	12	3	4	3	4	12	5
TAT	219	11	39	29	7	6	3	4	3	2	4	14	14	3	6	3	4	3	5
REV	231	13	39	38	10	6	3	4	3	2	4	17	12	3	4	3	4	3	5
VPU/VPX	333	14	87	50	18	6	3	6	3	2	15	25	14	3	4	3	4	3	5
VPR	368	9	142	44	7	4	3	5	3	2	25	16	12	3	4	3	4	3	5
NEF	449	12	282	44	4	4	3	7	5	2	4	31	12	3	4	3	11	3	4

*HIV-1 sequences were obtained from the HIV database for the indicated clade categories.

Selection of Conserved CTL

HIV1

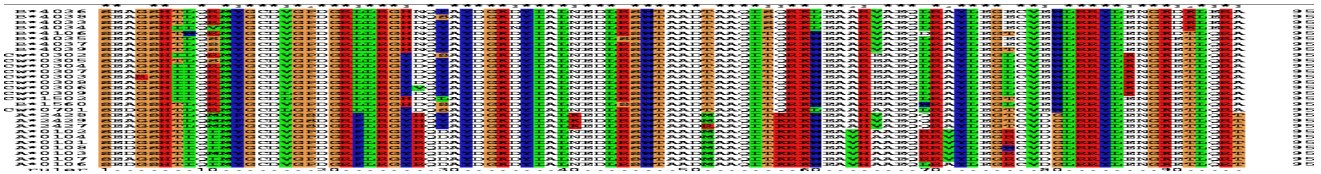
- **GAG**
- **POL**
- **ENV**
- **VIF**
- **TAT**
- **REV**
- **VPU/VPX**
- **VPR**
- **NEF**

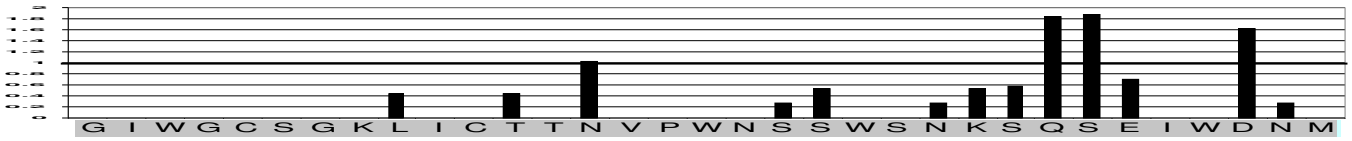
Clustalw →

`GAG.aln`
`POL.aln`
`ENV.aln`
`VIF.aln`
`TAT.aln`
`REV.aln`
`VPU.aln`
`VPR.aln`
`NEF.aln`

Mask variability →

`GAG.seq`
`POL.seq`
`ENV.seq`
`VIF.sea`
`TAT.seq`
`REV.seq`
`VPU.seq`
`VPR.seq`
`NEF.seq`





H=1

Shannon filter

`G I W G C S G K L I C T T . V P W N S S W S N K S . . E I W . N M`

Only HIV-1 specific CTL epitopes that match the consensus sequences are considered for further analysis

Conserved HIV1 CTL Epitopes

H < 1			
HIV CTL	SOURCE	POS	ALLELES (HIVDB)
SPRTLNAWV:	p24	16-24	B0702
AVFIHNFKR:	Integrase	179-187	A0301
MAVFIHNFK:	Integrase	178-186	A0301
TLFCASDAK:	gp160	51-59	A0301
FPVRPQVPL:	Nef	68-76	B3501
RAMASDFNL:	Integrase	20-28	A0201
KLTPLCVTL:	gp160	121-129	A0201
TLNAWVKVI:	p24	19-27	A0201
VIYQYMDDL:	RT	179-187	A0201
LVGPTPVNI:	Protease	76-84	A0201
TVLDVGDAY:	RT	107-115	B3501
PLVKLWYQL:	RT	421-429	A0201
TLNFPISPI:	POL	POL	A0201
NTPVFAIKK:	RT	57-65	A0301
SEGATPQDL:	p24	44-52	
EKEGKISKI:	RT	42-50	B5101
LLWKGEGAV:	Integrase	241-249	A0201
KLVGKLNWA:	RT	259-267	A0201
LTFGWCFKL:	Nef	137-145	A0201
YQYMDDLYV:	RT	181-189	A0201
GPKVKQWPL:	RT	18-26	B0801
WASRELERF:	p17	36-44	B3501
RAIEAQQHL:	gp160	557-565	B5101 B1501 C0304
GLNKIVRMY:	p24	137-145	B1501
KEKGGLEGL:	Nef	92-100	B4002
YFPDWQNYT:	Nef	120-128	A1 B3701 B5701
WYIKIFIMI:	gp160	680-688	A2402
YVDRFFKTL:	p24	164-172	A2601
FVNTPPLVK:	RT	416-424	A1101
DRFFKTLRA:	p24	166-174	B1402
KIQNFRVYY:	Integrase	219-227	A3002
KLNWASQIY:	RT	263-271	A3002
QGWKGSPAI:	RT	151-159	B5101
IRLRPGGKK:	p17	19-27	B2705
DLSHFLKEK:	Nef	86-94	A0301
KIRLRPGGK:	p17	18-26	A0301 B0301
GIPHPAGLK:	RT	93-101	A0301
MTKILEPFR:	RT	164-172	A0301
AETFYVDGA:	RT	437-445	B4501
EEKAFSPEV:	p24	28-36	B4415
CRAPRKKGC:	p2p7p1p6	42-50	B1402
ITLWQRPLV:	Protease	03-11	

Total: 42 peptides

Conser.

H < 0.5			
CTL	SOURCE	POS	ALLELES (HIVDB)
SPRTLNAWV	p24	16-24	B0702 B7
AVFIHNFKR	Integrase	179-187	A0301
MAVFIHNFK	Integrase	178-186	A0301
LVGPTPVNI	Protease	76-84	A0201 A2
TVLDVGDAY	RT	107-115	B3501 B35
GLNKIVRMY	p24	137-145	B1501
SEGATPQDL	p24	44-52	B60
PLVKLWYQL	RT	421-429	A0201
LLWKGEGAV	Integrase	241-249	A0201
FVNTPPLVK	RT	416-424	A1101
KLVGKLNWA	RT	259-267	A0201
YQYMDDLYV	RT	181-189	A0201
QGWKGSPAI	RT	151-159	B5101 B62
GIPHPAGLK	RT	93-101	A0301
LTFGWCFKL	Nef	137-145	A0201
TLNFPISPI	POL		A2
KLNWASQIY	RT	263-271	A3002 A30

Total: 17 peptides

Experimental HLAI binding from HIV database

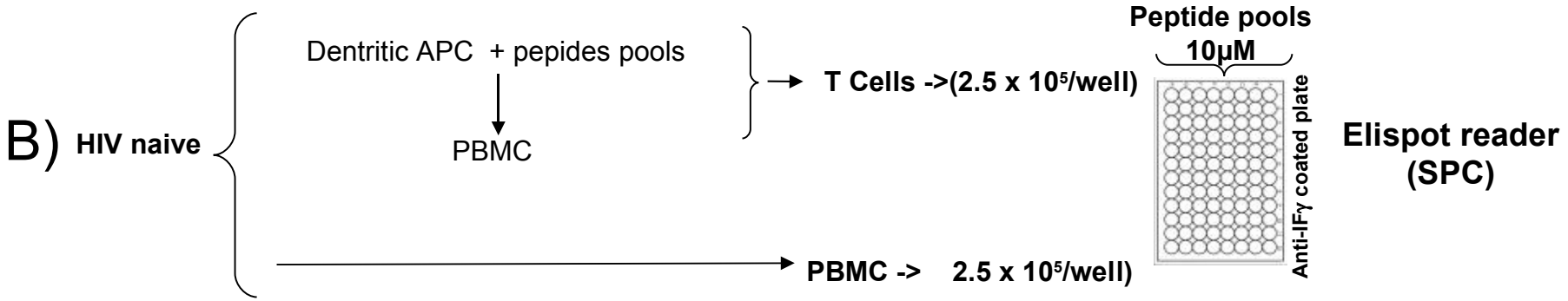
Extended HLAI binding Profile of HIV1 specific CTL Epitopes

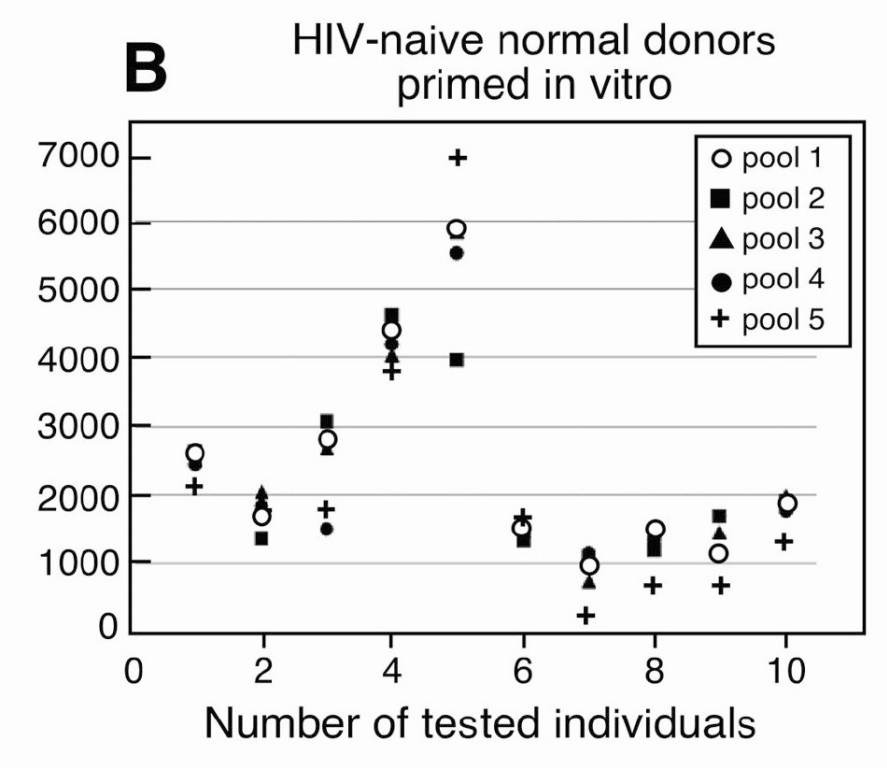
HIV CTL	SOURCE	POS	ALLELES (HIVDB)	ALLELES (HIVDB + PREDICTED)
KLNWASQIY:	RT	263-271	A3002	A1 A3002
TVLDVGDAY:	RT	107-115	B3501	B1501 B3501 B5701 C0304
RAMASDFNL:	Integrase	20-28	A0201	A0201 B2709 C0304
KIRLRPGGK:	p17	18-26	A0301 B0301	A0301 B0301
KEKGGLEGL:	Nef	92-100	B4002	B4002 B4402 B4403
PLVKLWYQL:	RT	421-429	A0201	A0201 A0202 A0203
YVDRFFKTL:	p24	164-172	A2601	A0203 A0204 A0207 A2601 B3801
SEGATPQDL:	p24	44-52		A2902 B39011 B4002 B4402 B4403
LVGPTPVNI:	Protease	76-84	A0201	A0201 A0202 A0205 A0209 B1501 B1516
GLNKIVRMY:	p24	137-145	B1501	A0203 A1 B1501
GPKVKQWPL:	RT	18-26	B0801	B0702 B0801 B3501 B8
DRFFKTLRA:	p24	166-174	B1402	B1402 B2701 B2702 B2703 B2704 B2705 B2709
TLNAWVKVI:	p24	19-27	A0201	A0201 A0202 A0203 A0204 A0206
QGWKGSPAI:	RT	151-159	B5101	B5101
KLVGKLNWA:	RT	259-267	A0201	A0201
LTFGWCFKL:	Nef	137-145	A0201	A0201
YFPDWQNYT:	Nef	120-128	A1 B3701 B5701	A1 B3701 B5701
NTPVFAIKK:	RT	57-65	A0301	A0301 A6601 C0102
AETFYVDGA:	RT	437-445	B4501	B4501
EKEGKISKI:	RT	42-50	B5101	B2701 B3801 B39011 B3909 B4402 B5101 B8
DLSHFLKEK:	Nef	86-94	A0301	A0301 A6601
SPRTLNAWV:	p24	16-24	B0702	B0702 B3501 B5101 B5102 B5103 B5301 B5401 B5502
AVFIHNFKR:	Integrase	179-187	A0301	A0301 A1101 A3101 A3301 A6601 A6801
VIYQYMDDL:	RT	179-187	A0201	A0201 A0205 A0207 A0214
MTKILEPFR:	RT	164-172	A0301	A0301
MAVFIHNFK:	Integrase	178-186	A0301	A0301
ITLWQRPLV:	Protease	03-11		A6802
FVNTPPLVK:	RT	416-424	A1101	A1101
TLFCASDAK:	gp160	51-59	A0301	A0301 A1101 A3101 A3301 A6801
FPVRPQVPL:	Nef	68-76	B3501	A2902 B0702 B3501 B5101 B5102 B5103 B5301 B5401
IRLRPGGKK:	p17	19-27	B2705	B2705
WASRELERF:	p17	36-44	B3501	B3501 B5801
TLNFPISPI:	A2	A2		A0201 A0207
LLWKGEGAV:	Integrase	241-249	A0201	A0201 A0204 A0205 A0209
KLTPLCVTL:	gp160	121-129	A0201	A0201 A0202 A0203 A0206 A0209 B2709
RAIEAQQHL:	gp160	557-565	B5101 B1501 C0304	B1501 B1517 B5101 C0304
EEKAFSPEV:	p24	28-36	B4415	B4415
GIPHPAGLK:	RT	93-101	A0301	A0301
YQYMDDLYV:	RT	181-189	A0201	A0201
WYIKIFIMI:	gp160	680-688	A2402	A0203 A0206 A2402
CRAPRKKGC:	p2p7p1p6	42-50	B1402	B1402
KIQNFRVYY:	Integrase	219-227	A3002	A1 A3002

Apply an algorithm to identify combinations of epitopes providing a population coverage of 95%

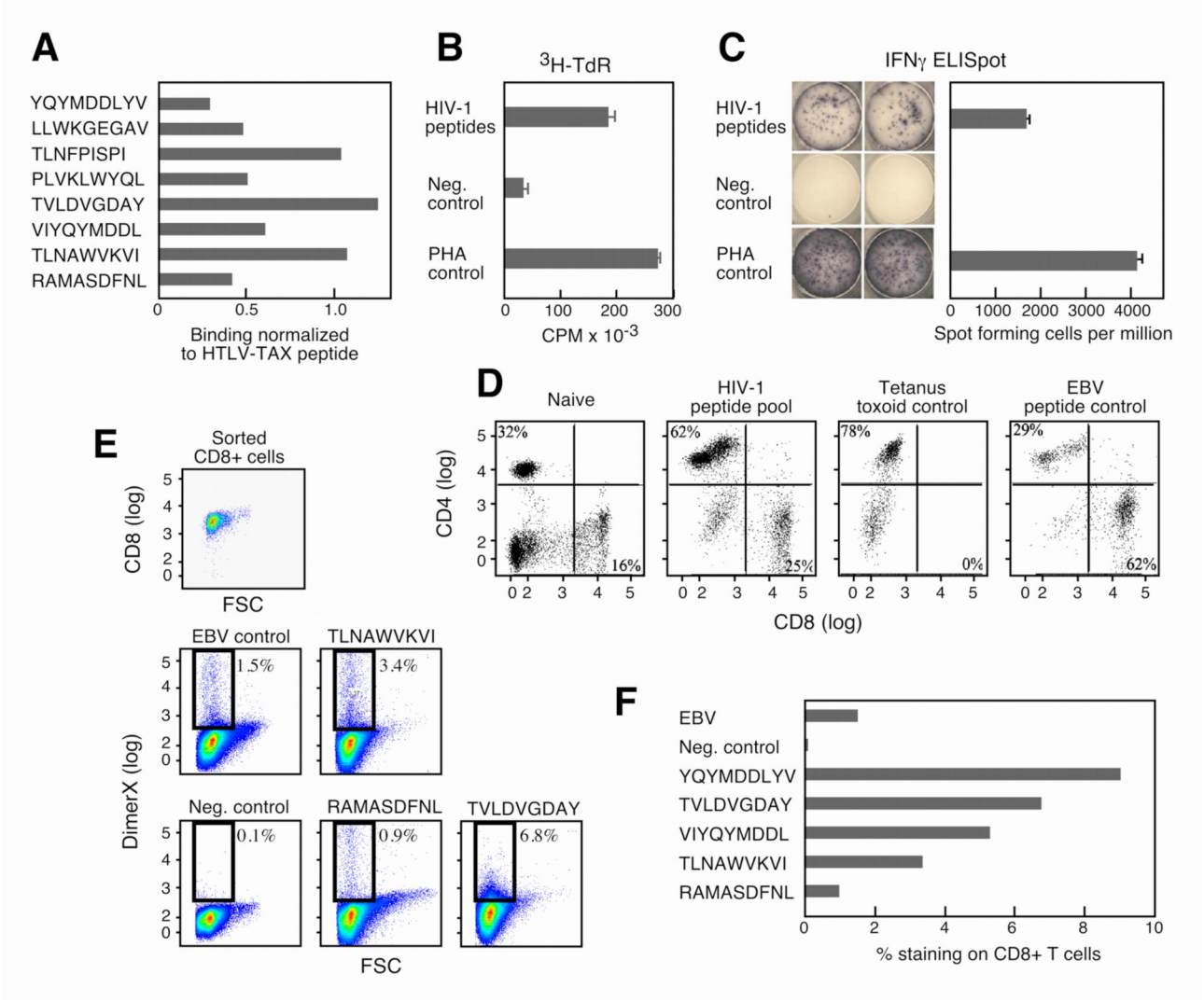
A minimum of 5 peptides are required to cover the whole population

Responses of stimulated T cells from naïve people to CTL pools





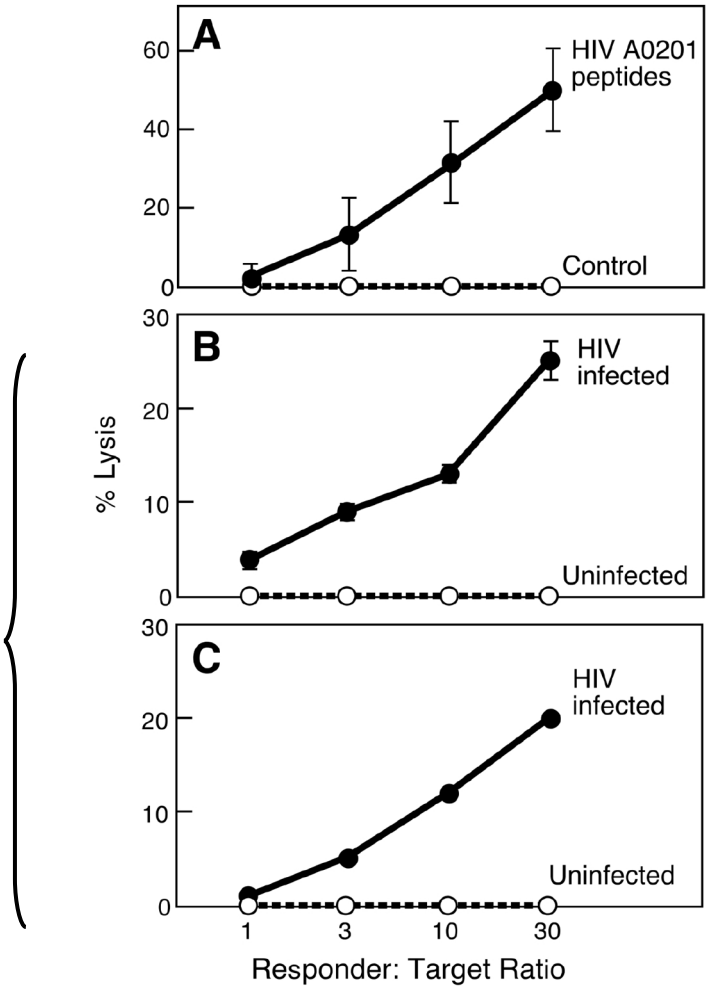
Characterization of HLA-A0201 restricted HIV-1 peptide-specific T cell lines from uninfected individuals



Cytotoxic activity of HIV-1 peptide-specific A0201-restricted T cells from naive donors

T2 cells + peptide +
A0201-restricted HIV-1 specific T cell

T1 cells infected/uninfected with HIV-IIIB



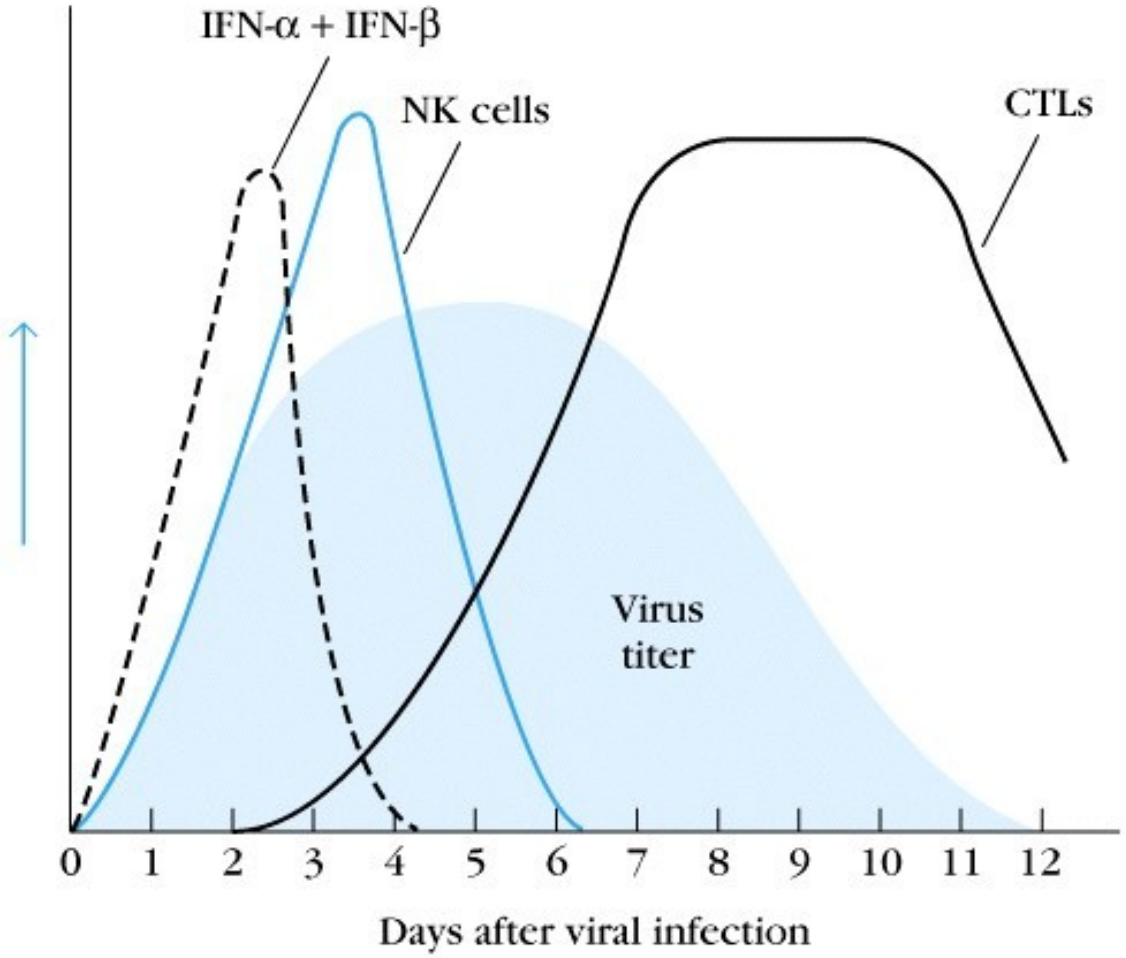
Conclusions

- **Naïve individual have the potential to recognize invariant HIV-1 specific T cell epitopes**

- **Chronic infections and diseases such as cancer may result in the impairment of T cell immune response and therefore epitope vaccine optimization should be carried out from data obtained in naïve healthy patients**

- **Chronic infections and diseases escape the immune system due the emergence of escape mutants that are no longer the target of the immune system and/or by directing the immune response towards antigenic determinants that results in futile pattern of immunodominance. These two issues can be better addressed using epitope-based vaccines that allow to focus the immune response towards the desired regions (strictly conserved epitopes)**

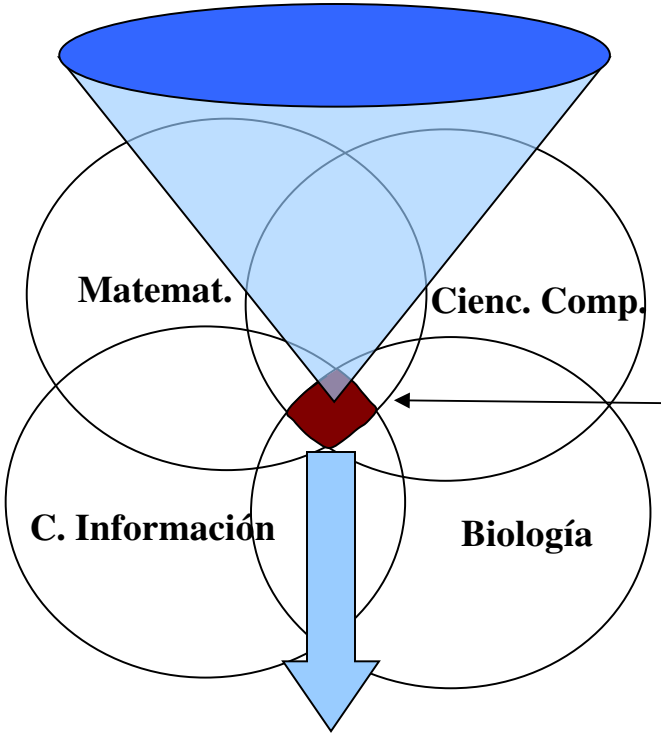
Innate responses to virus infection



BIOINFORMATICA

- **La Bioinformática podría definirse como el campo de la ciencia en el que las Matemáticas, las Ciencias Computacionales y de la Información se encuentran con la Biología para crear un una disciplina nueva.**

DATOS Y INFORMACION/HIPOTESIS



Bioinformática/ Biologia Computac.

Bases de Datos, herramientas de gerencia
Modelos Computacionales para el análisis e interpretacion de datos
Conocimiento Biologico