

CD8 alpha/alpha+ Melan-A/MART-1 specific T-cells in patients with melanoma

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Hallmarks of an effective immune response

- **Immediate immunity:**

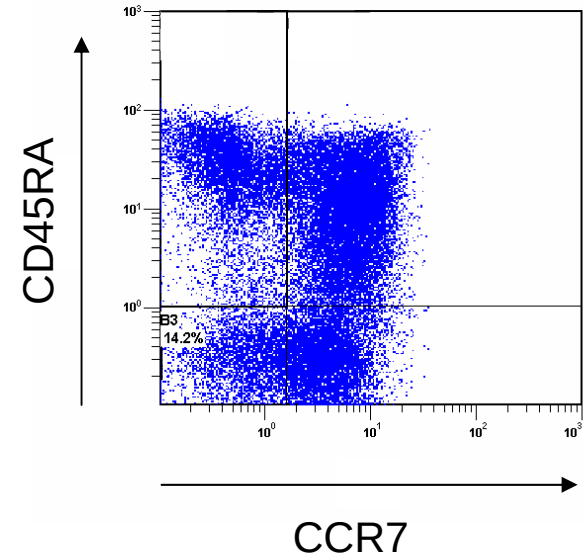
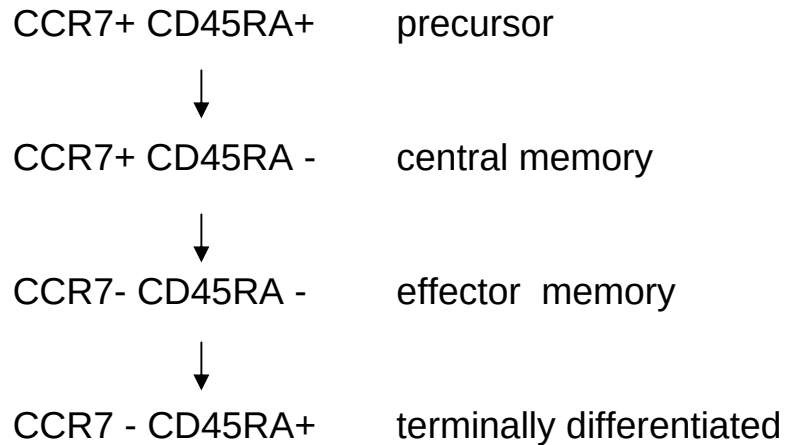
activation of specific CD8⁺ effector cells

- **Establishment of long-term memory:**

differentiation into CD8⁺ memory cells

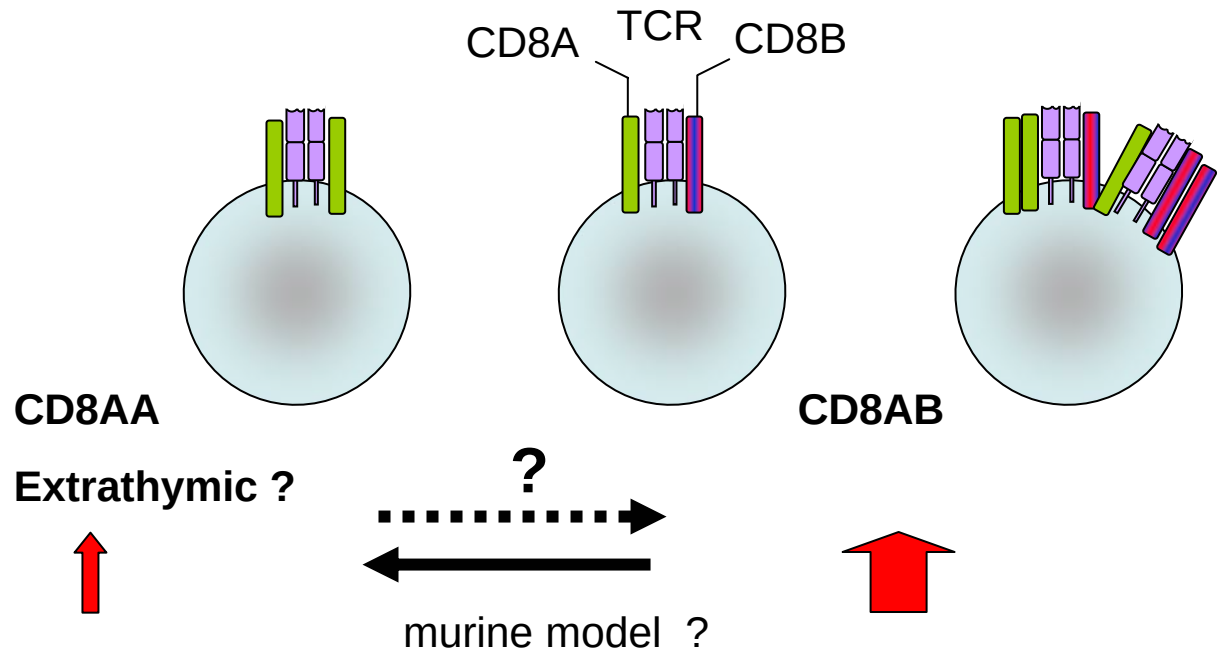
→ Clinical outcome, vaccine

Antigen-induced CD8⁺ T cell maturation



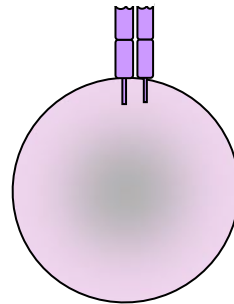
Peripheral circulation:

- Density
- Differentiation
- Memory

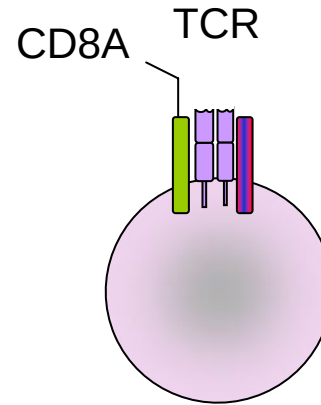


The CD8 coreceptor modulates the avidity

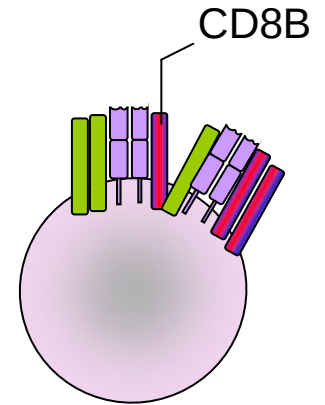
**Proof of principle:
Insect cells**



TCR+

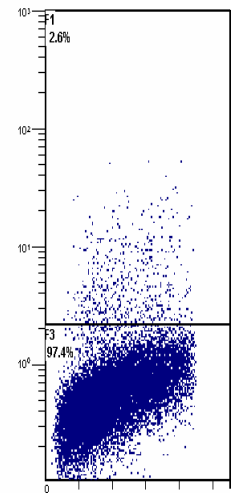
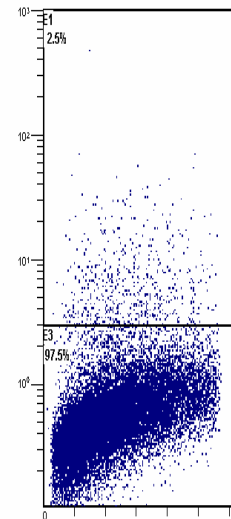
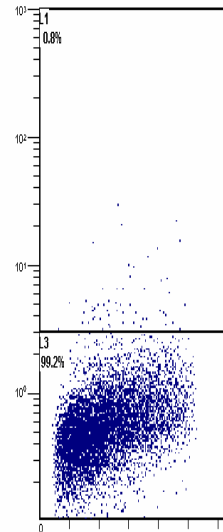


TCR+ CD8AA

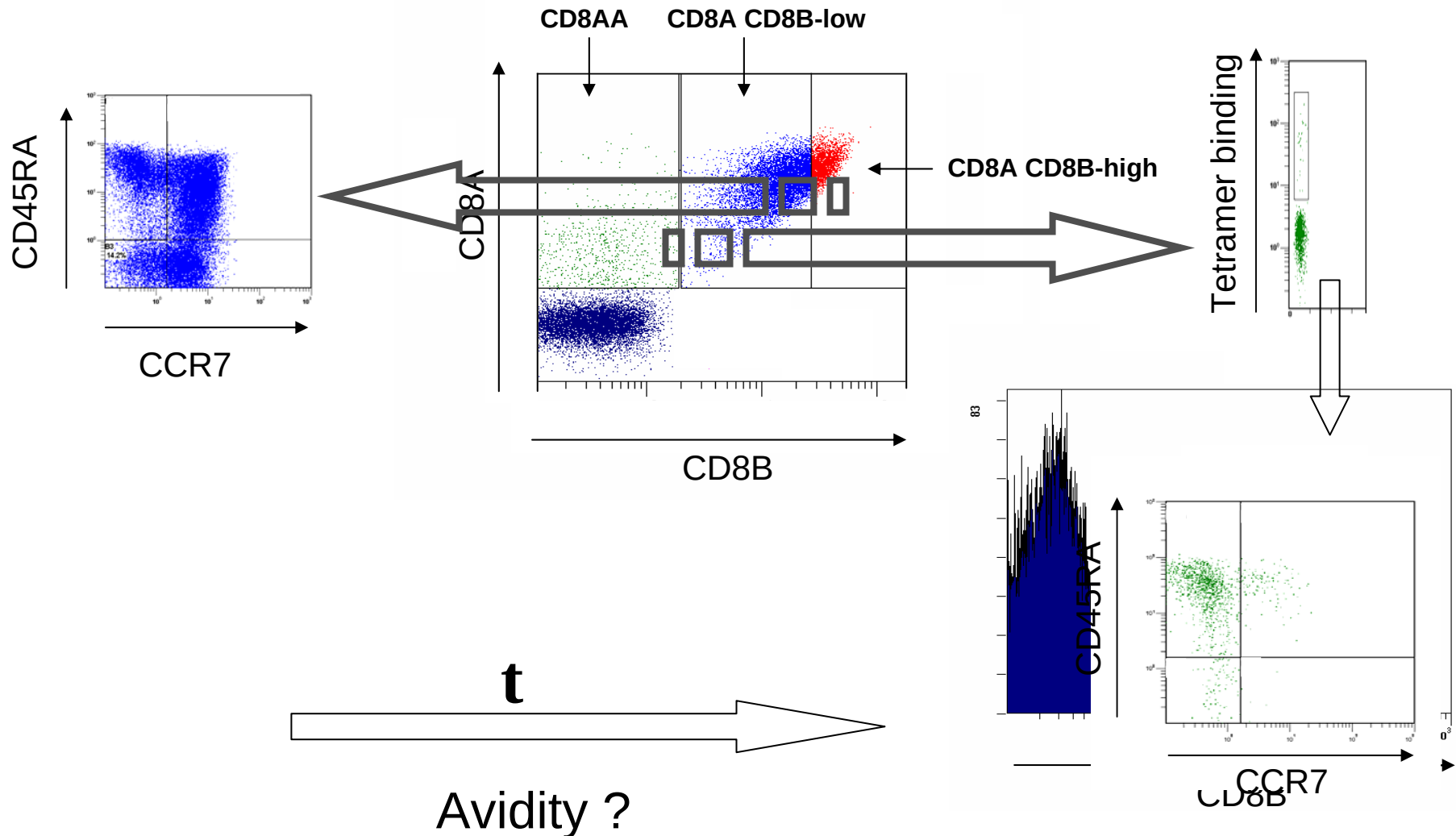


TCR+ CD8A CD8B

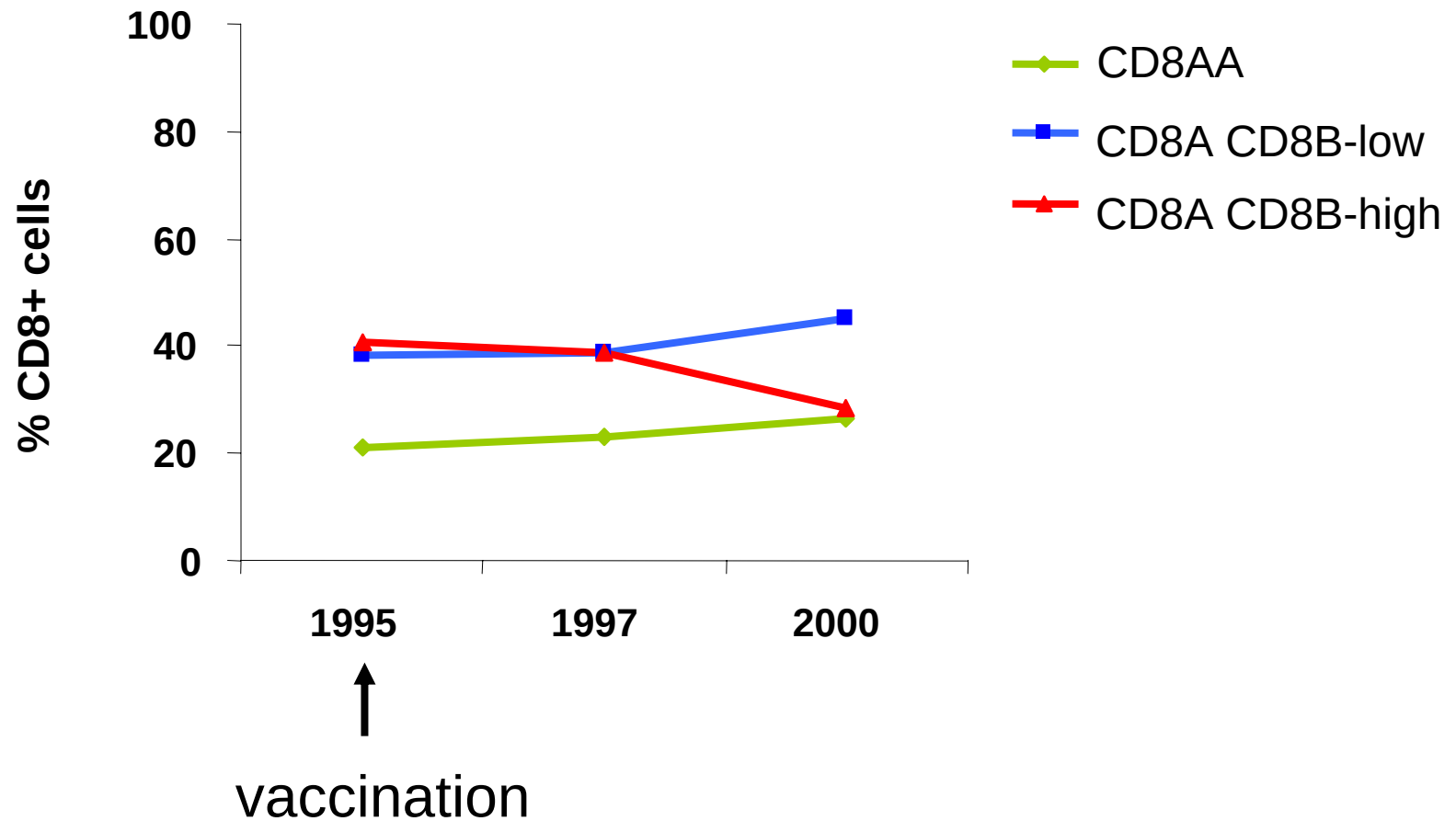
**% tetramer –staining cells
HLA-A2/ELAGIGILTV**



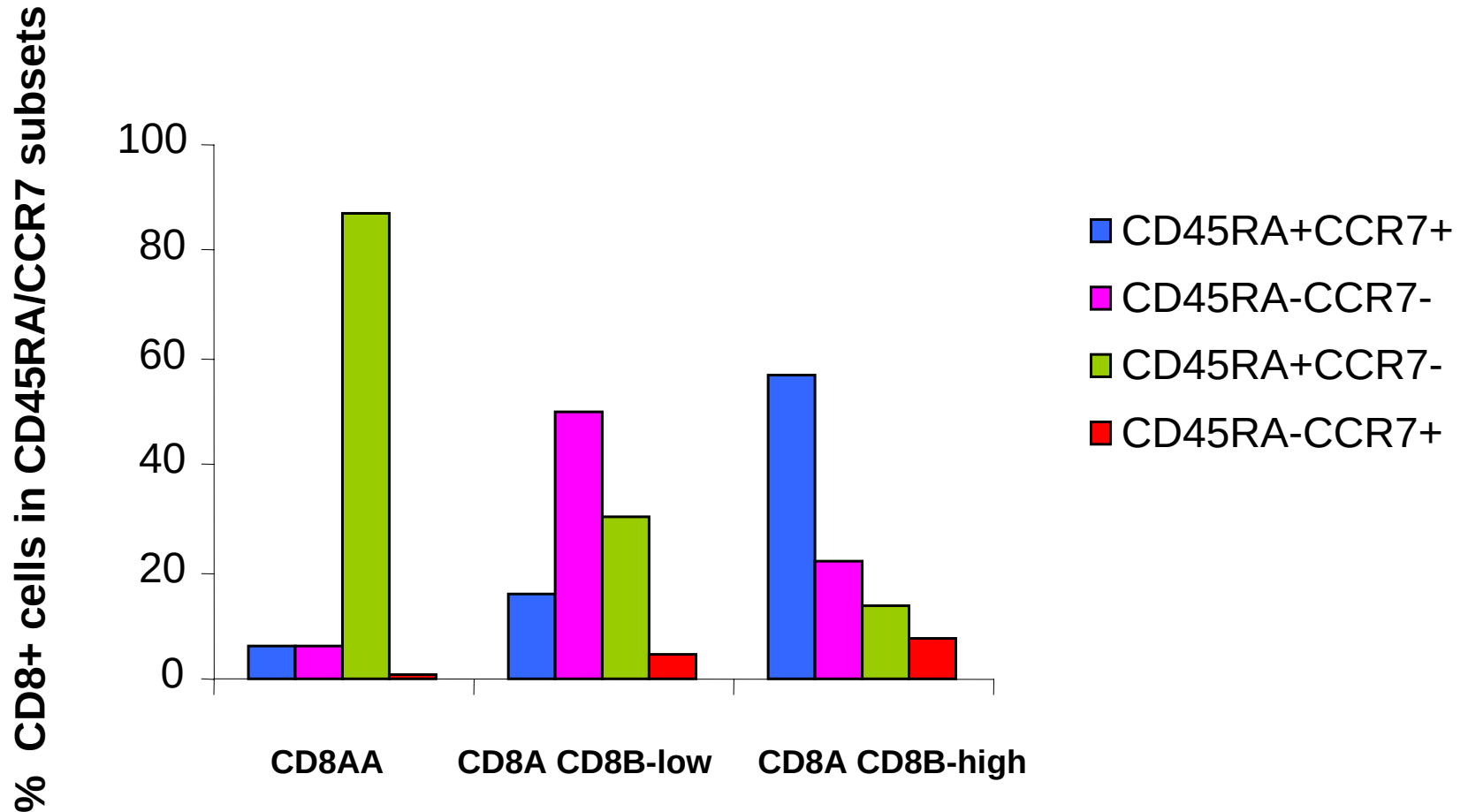
Paradigm: patient with melanoma vaccinated with Melan/MART-1 peptide



CD8AA/CD8A CD8B expression is stable over time



Different maturation in CD8+ T cell subsets

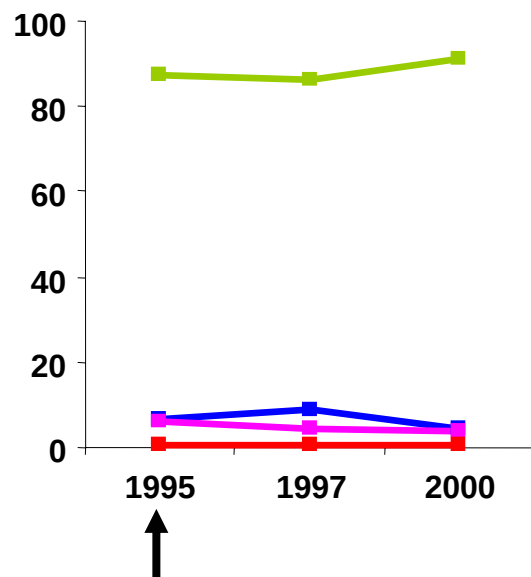


1995 prior to vaccination

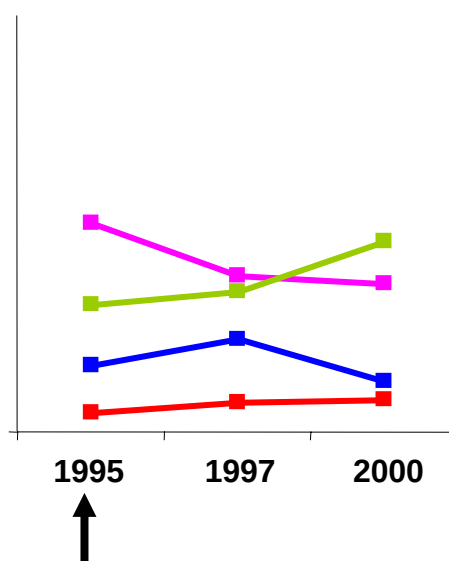
T-cell maturation/homing markers in CD8+ T-cells subsets

% subsets in CD8+ T-cells

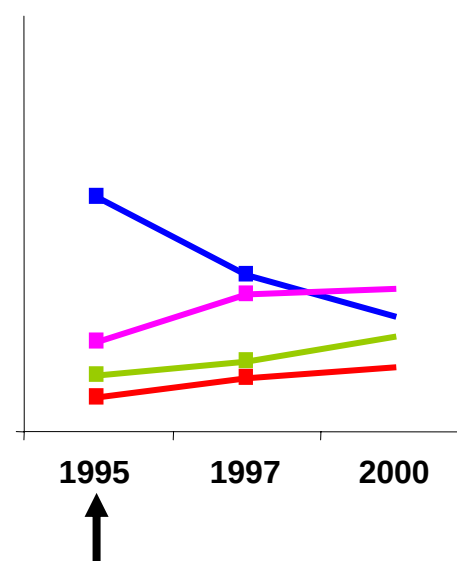
CD8AA



CD8A CD8B-low

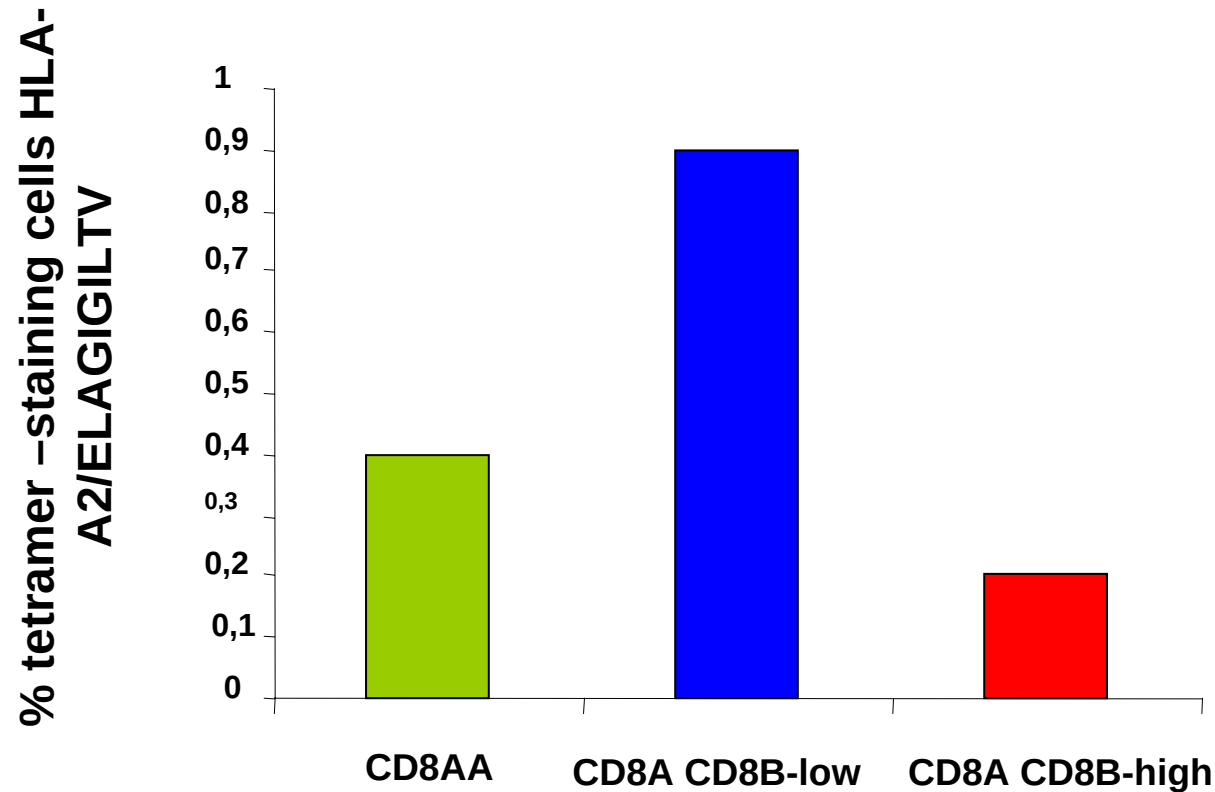


CD8A CD8B-high



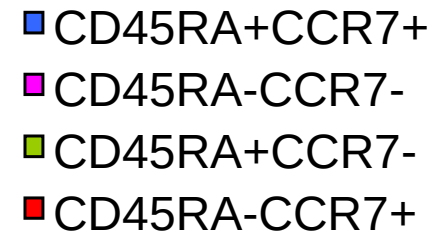
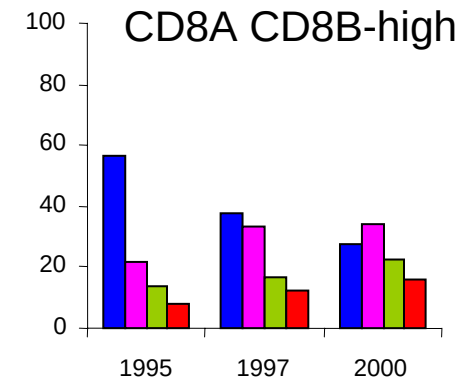
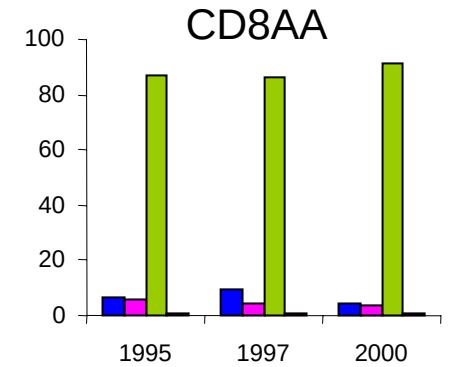
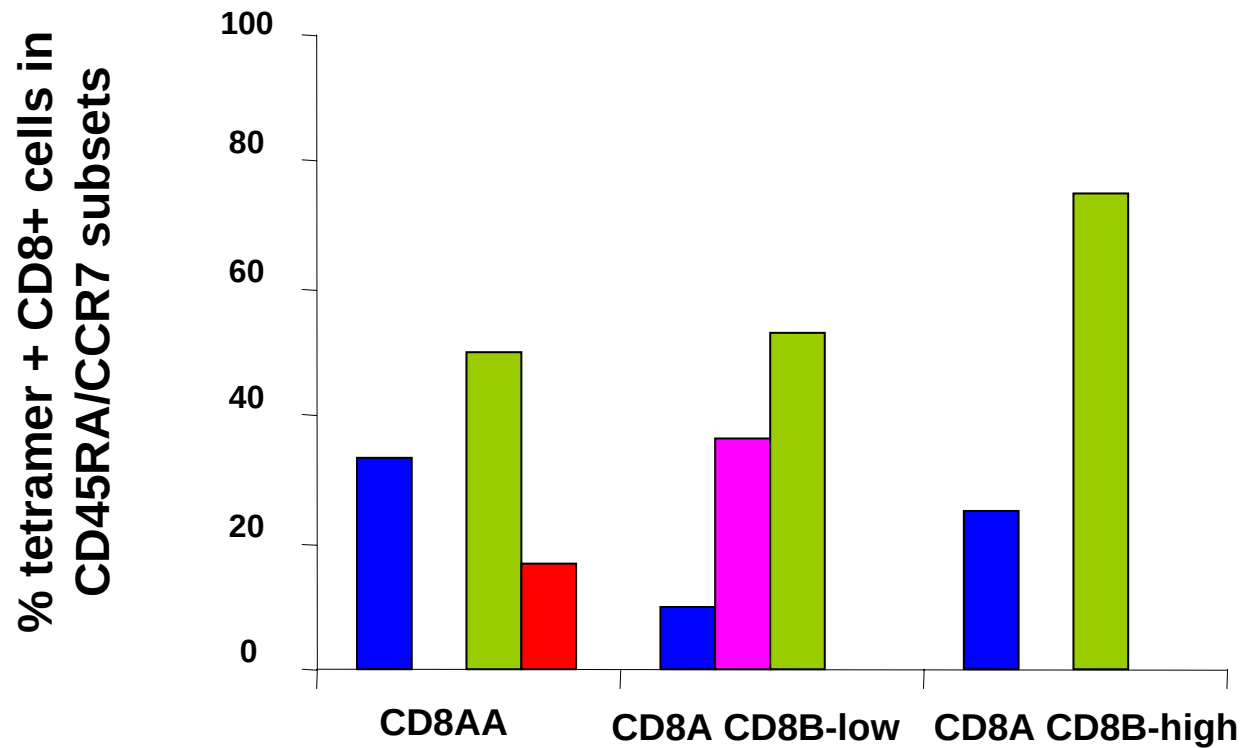
- CD45RA+CCR7+
- CD45RA-CCR7-
- CD45RA+CCR7-
- CD45RA-CCR7+

Differential enrichment of Melan-A/MART-1 in CD8AA / CD8AB + T-cells

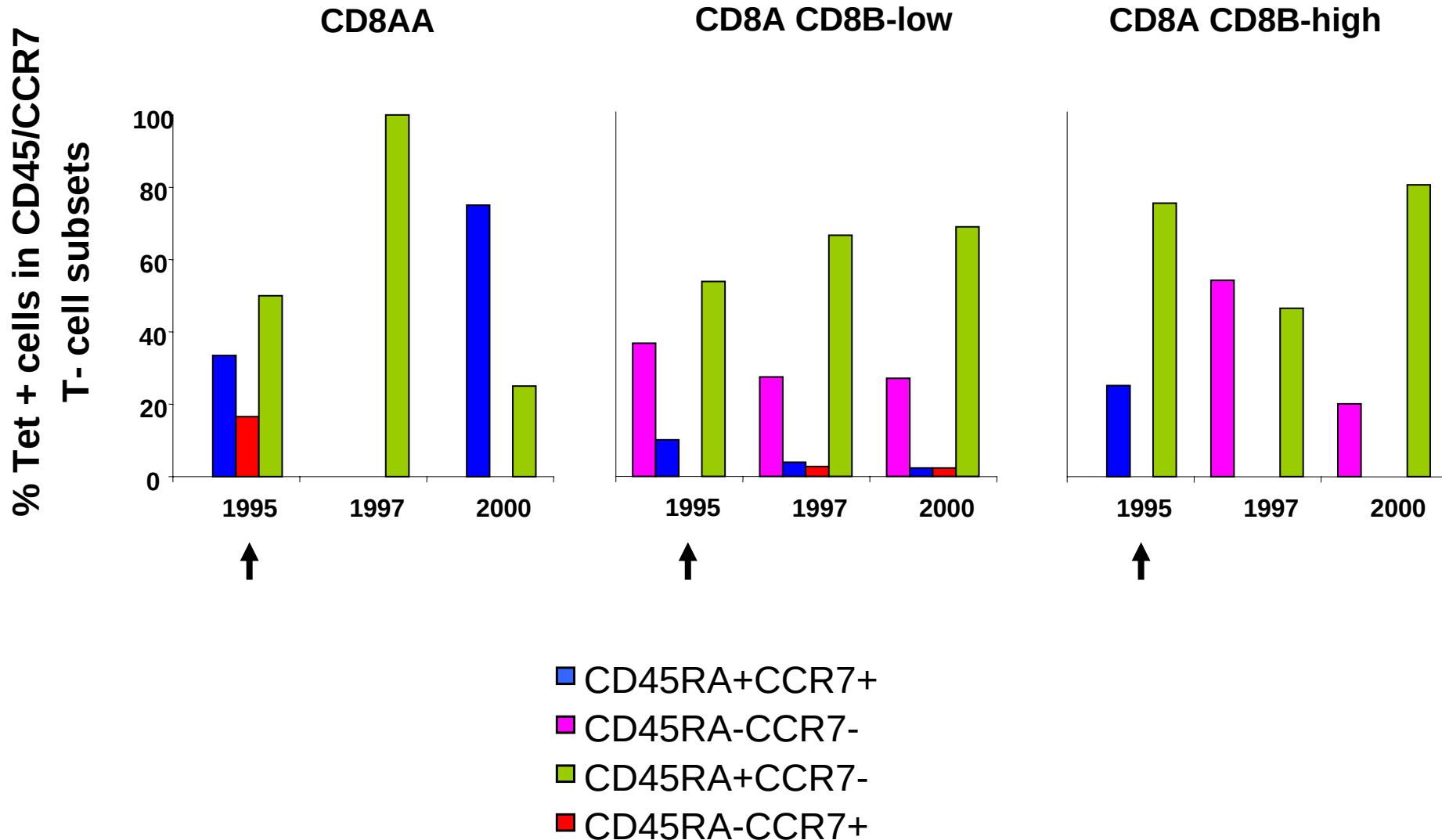


1995 prior to vaccination

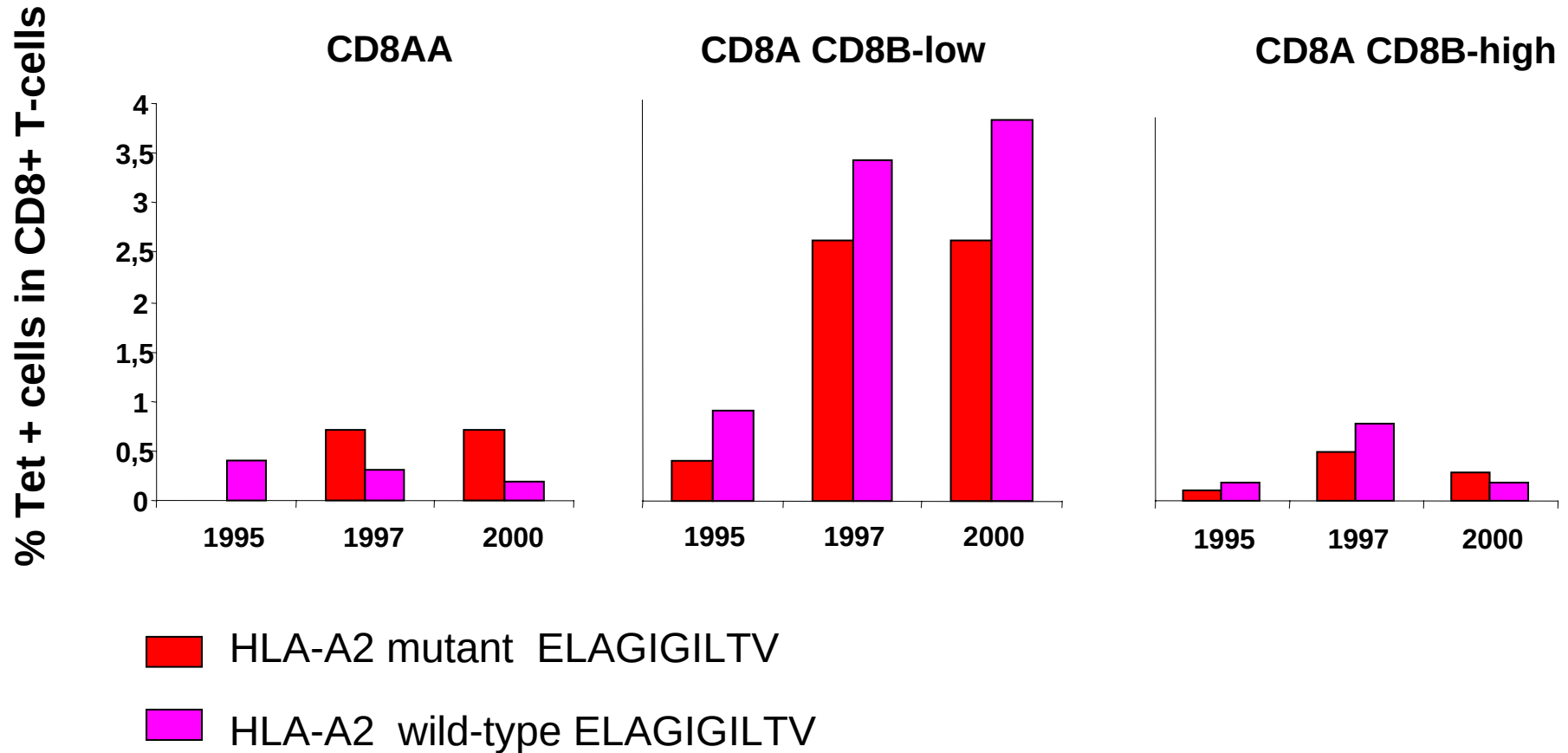
Melan-A/MART-1 specific T-cells reside in the CD45RA+ CCR7- population



Differential dynamics of Tet+ T-cells associated with CD8

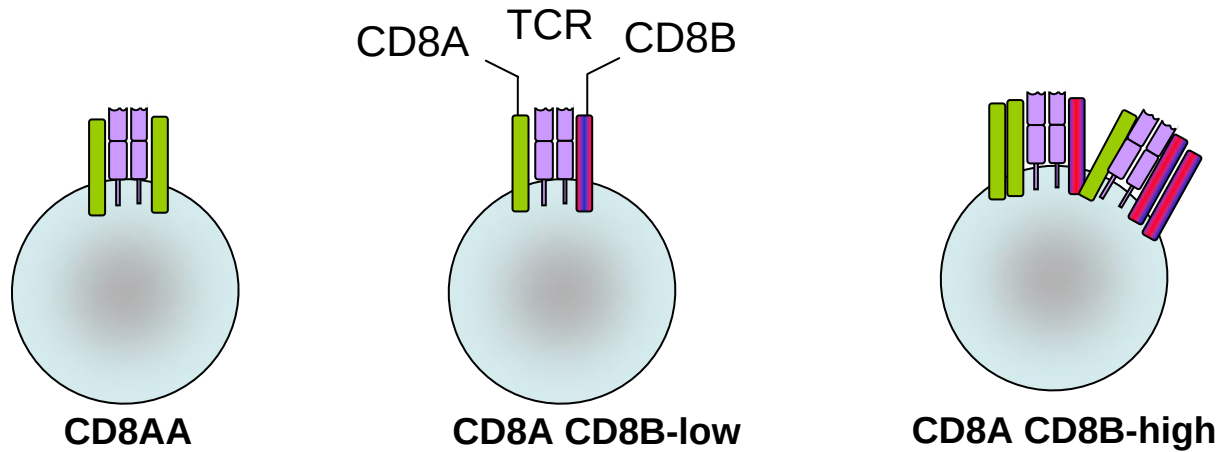


T-cells with different avidity reside in individual CD8 T-cells subsets



, Avidity maturation' of Antigen-specific T-cells over time
in CD8+ T- cell subsets ?

CD8AA tetramer + T-cells are present in patients with melanoma



Presence of
Tet+ T-cells

++

+++

+

Maturation

Terminally differentiated

„Avidity“

++

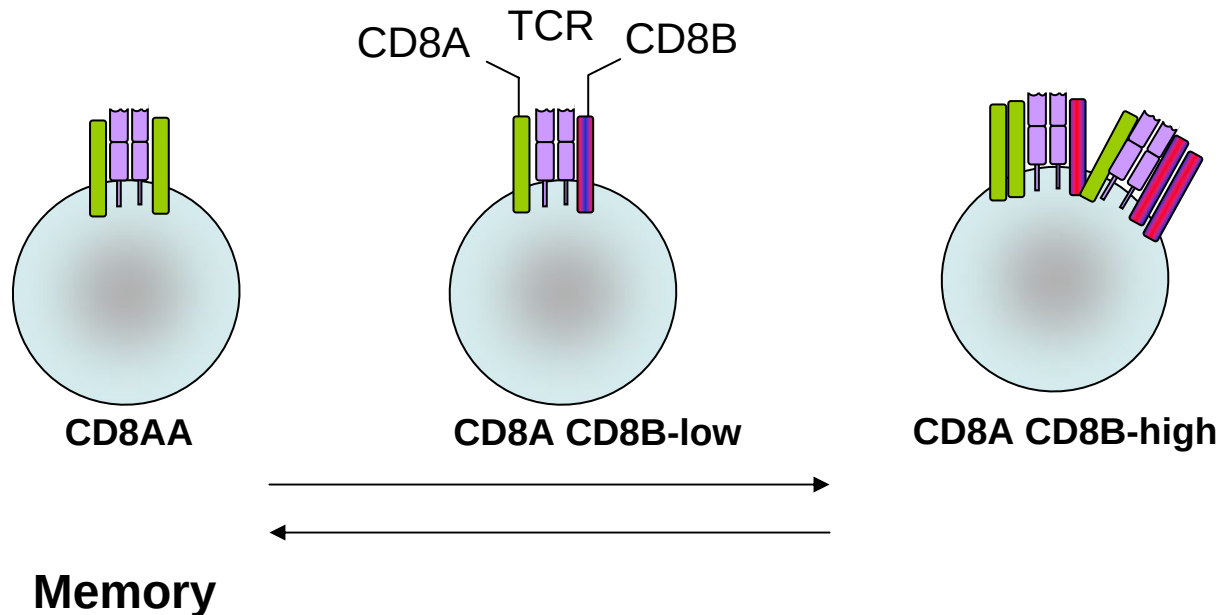
+

+

Clinical
Relevance

Better understanding of CD8+ T-cell biology, immune monitoring in
vaccine trials or development

Hypothesis

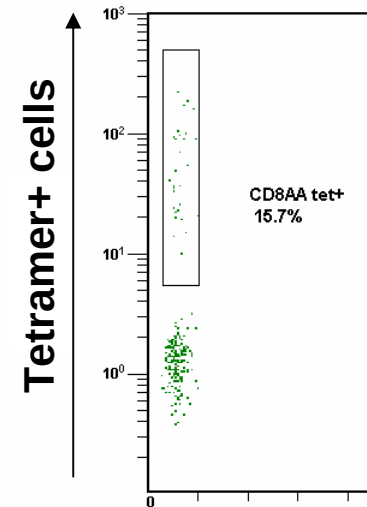
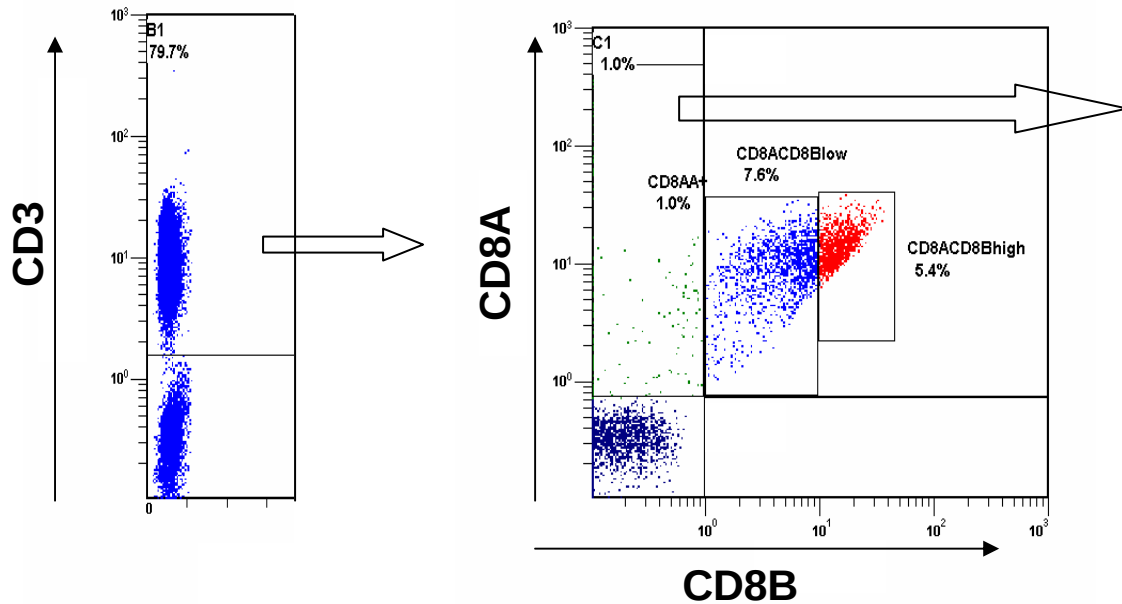
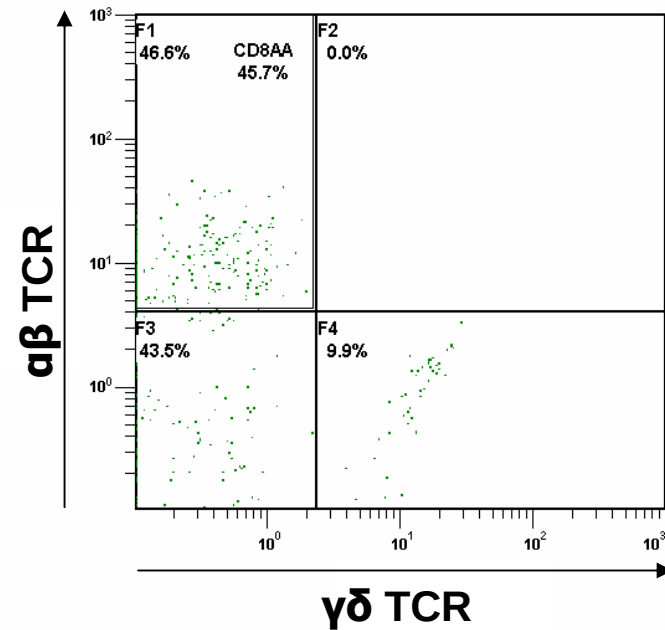


TCR+ CD8AA T-cells represent a unique pool of memory T-cells enriched for high avidity T-cells

Different cells express CD8AA

CD8AA cells:

**T-cells $\alpha\beta$ TCR+, T-cells $\gamma\delta$ TCR+,
NK cells, NKT-cells, dendritic cells**



CD8AA cells show reduced CD107a expression

