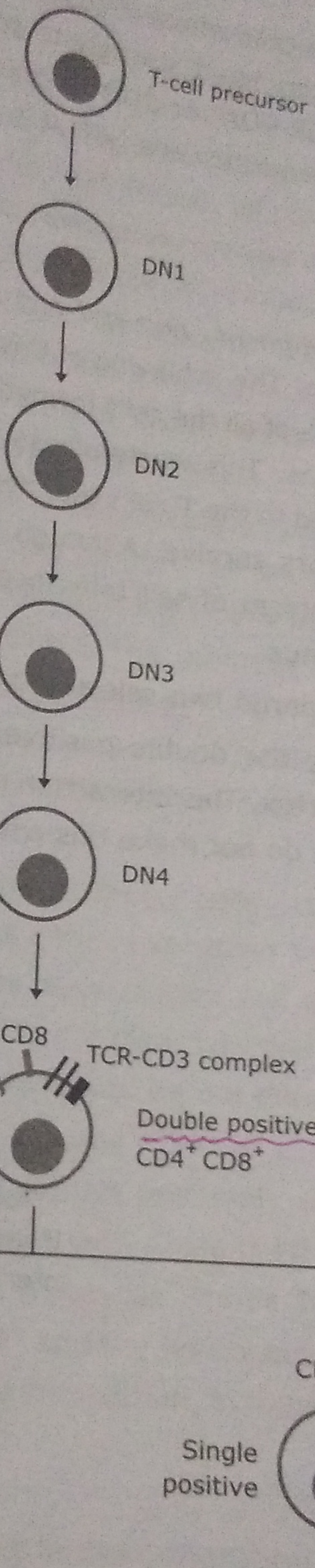
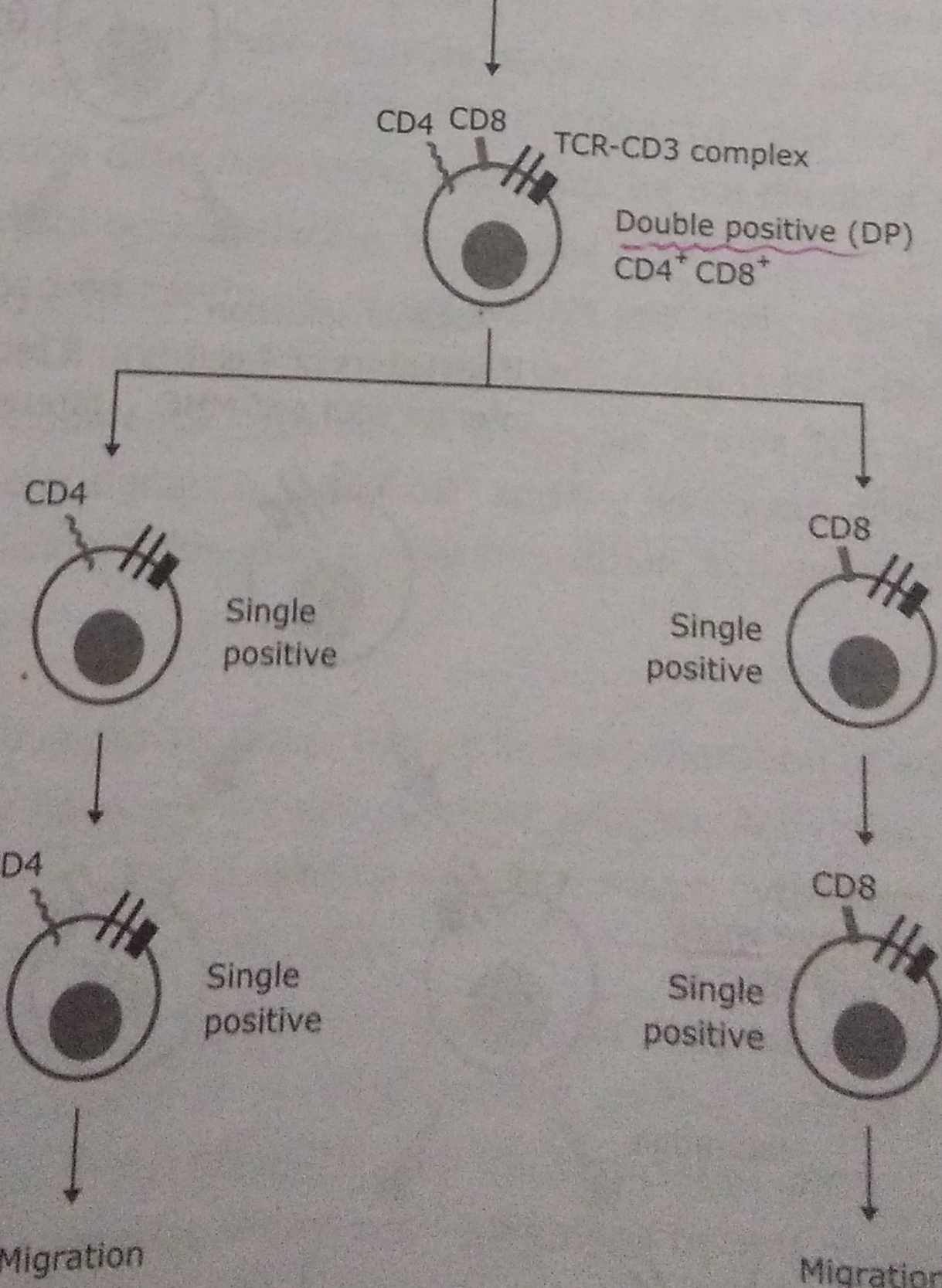
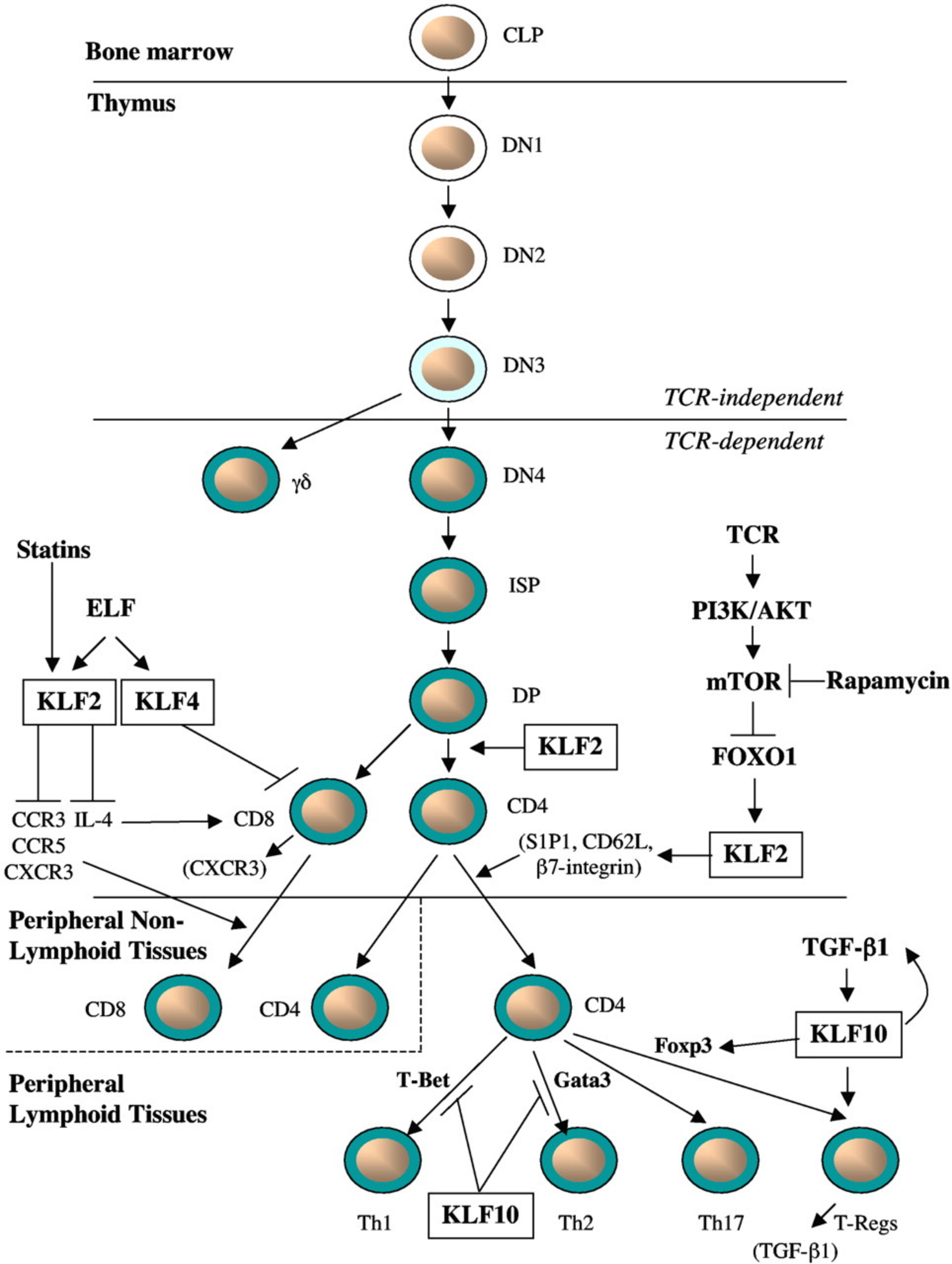
Early thymocyte development
Double negative (DN)
$CD4^-$ $CD8^-$
(Thymic cortex)




Positive and
negative selection
(Thymic cortex)




Negative selection
(Thymic medulla)


Bone marrow
CLP
Thymus
DN1
DN2
DN3
TCR-independent
TCR-dependent
γδ
DN4
Statins
ISP
TCR
PI3K/AKT
ELF
mTOR
Rapamycin
KLF2
KLF4
DP
KLF2
FOXO1
CCR3
IL-4
CD8
CD4
CCR5
CXCR3
(CXCR3)
(S1P1, CD62L,
β7-integrin)
KLF2
Peripheral Non-
Lymphoid Tissues
TGF-β1
CD8
CD4
CD4
KLF10
Foxp3
T-Bet
Gata3
Peripheral
Lymphoid Tissues
Th1
KLF10
Th2
Th17
T-Regs
(TGF-β1)

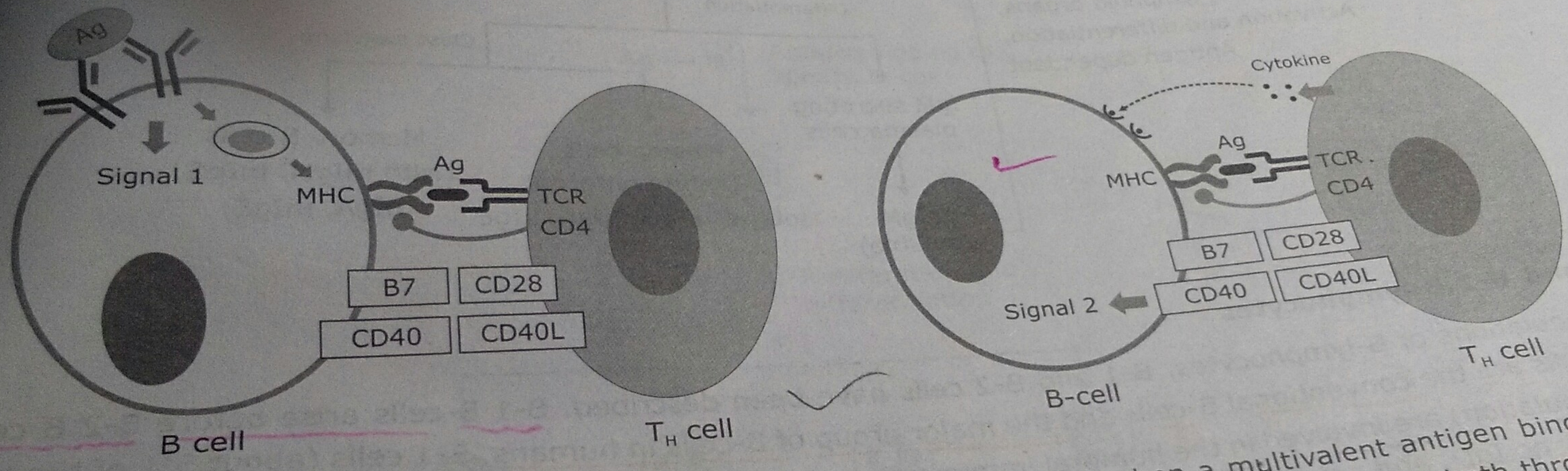


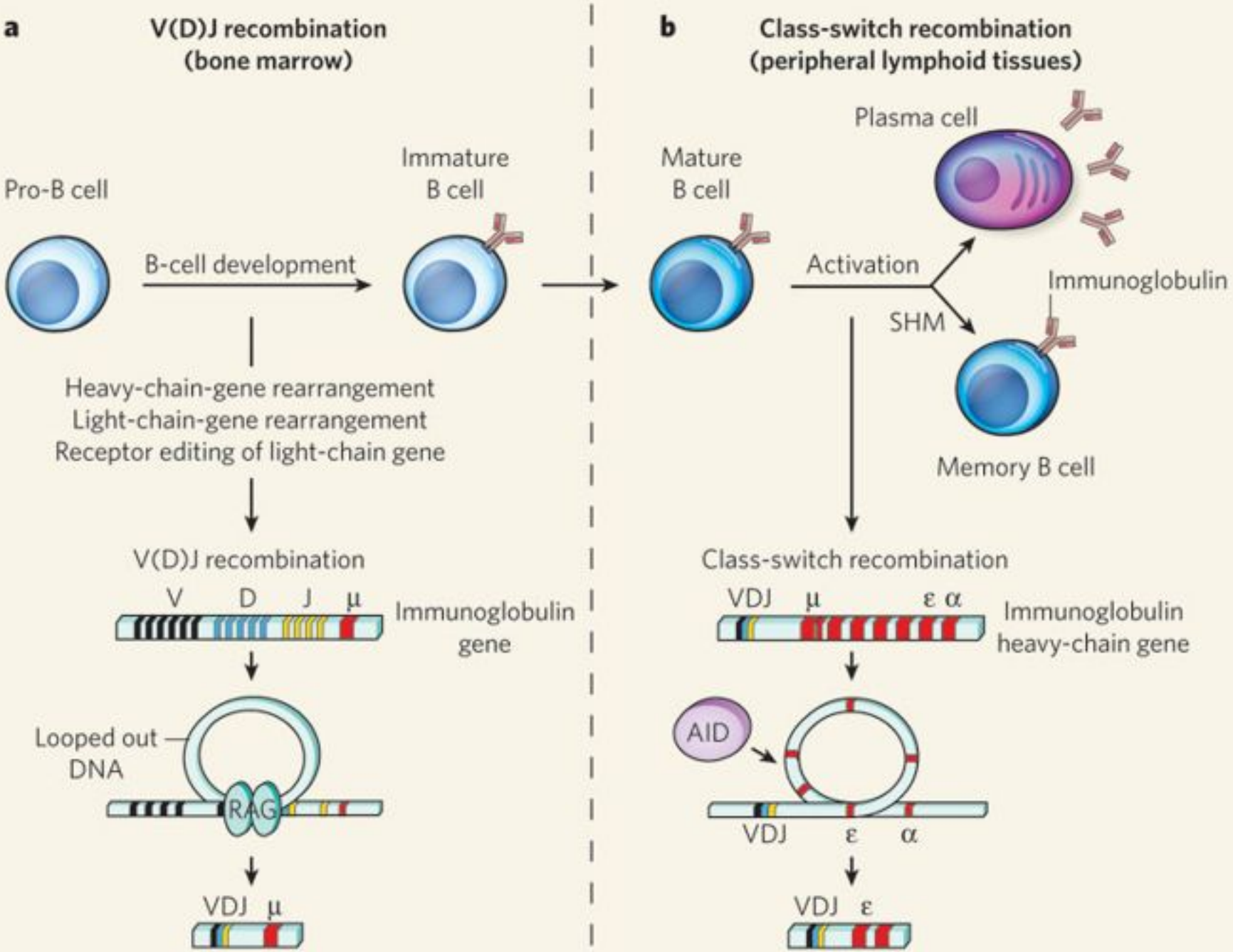

**Figure 5.22** Two signals that activate a B-cell. The first is generated when a multivalent antigen binds and cross-links mIg. The second signal is provided by an activated T-cell, which binds to the B-cell both through its antigen receptor and via a separate interaction between CD40 on the B-cell and CD40L on the activated $T_H$ cell. The bound T-cell then delivers cytokines and other signals to its partner B-cell to complete the activation process.

The B-cells after receiving the activating signals move into specialized regions of the lymph node or spleen to begin the process of differentiation into an antibody secreting **plasma cells** and **memory B-cells**. Some of these cells die after the initial primary response is completed, whereas others take up long-term residence in the long-lived plasma cells. Some antigen-stimulated B-cells migrate into the differentiate. As the follicle fills with proliferating class switching,

Facing Ag into body leads to activation of

① APC to MHC I → $T_c$ or $T_{H1}$ for endogenous Ag → leads to CMI.

② APC to MHC II → $T_{H2}$ for exo. Ag → leads to humoral immunity.


a
V(D)J recombination
(bone marrow)
Pro-B cell
B-cell development
Immature
B cell
Heavy-chain-gene rearrangement
Light-chain-gene rearrangement
Receptor editing of light-chain gene
V(D)J recombination
V D J μ
Immunoglobulin
gene
Looped out
DNA
RAG
VDJ μ
b
Class-switch recombination
(peripheral lymphoid tissues)
Plasma cell
Mature
B cell
Activation
Immunoglobulin
SHM
Memory B cell
Class-switch recombination
VDJ μ ε α
Immunoglobulin
heavy-chain gene
AID
VDJ ε α
VDJ ε