

Immunology II

From MHC and antigen presentation through B/T cell biology, cytokines, inflammation, cytotoxic killing, autoimmunity, hypersensitivity, and how vaccines put it all to use.

MHC & Presentation

B/T Cell Biology

Th1/Th2

Inflammation

CTL/NK/K Cells

Hypersensitivity

Vaccination

Ag Processing

MHC

B-Cell

T-Cell

TD/TI & T-B

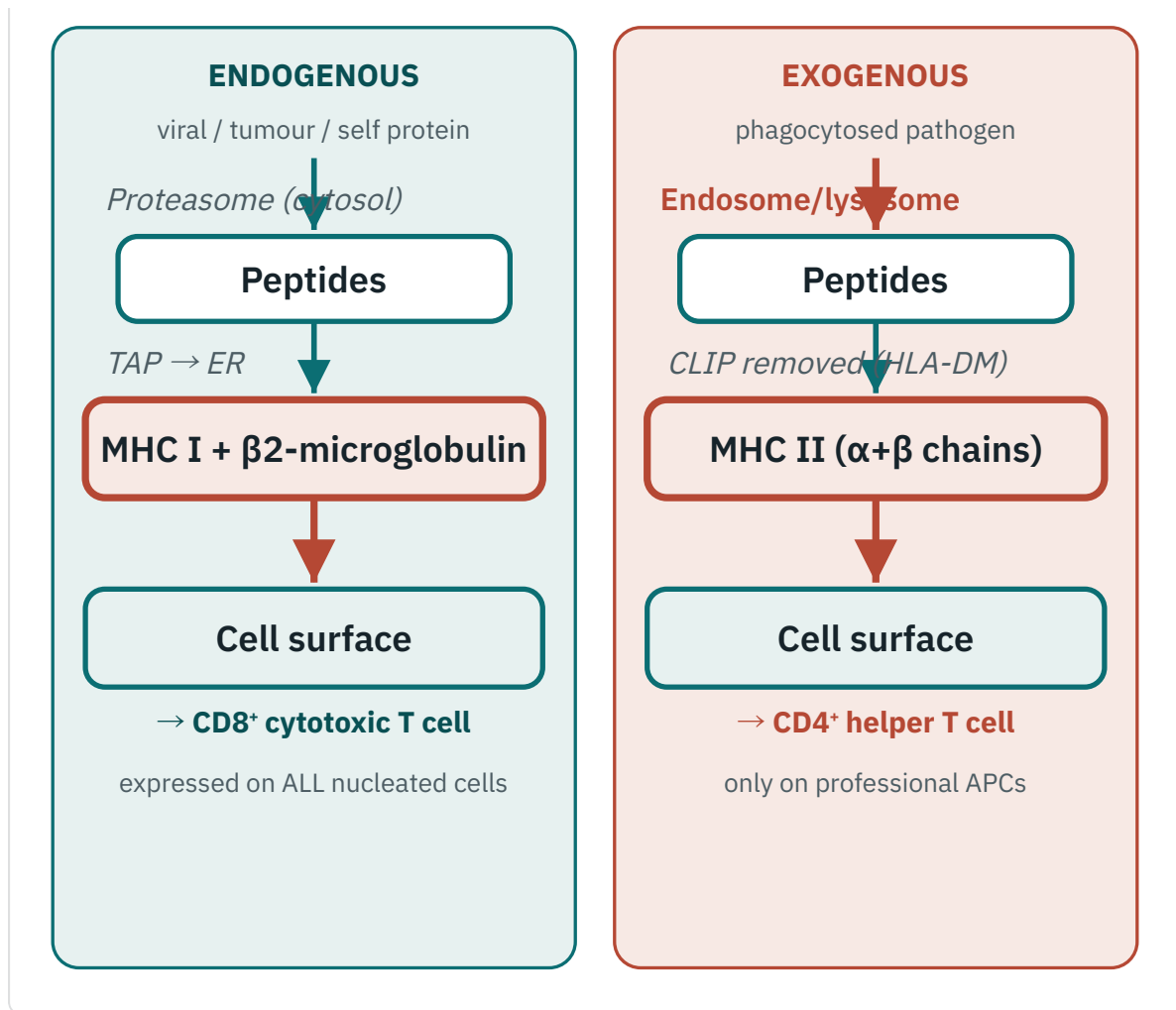
Th1/Th2

Inflammation

1 Antigen Processing & Presentation

Two routes, two T-cell audiences

Endogenous (MHC I) vs. exogenous (MHC II) pathways



CROSS-PRESENTATION

Dendritic cells can divert exogenous antigen onto MHC I as well — essential for generating CTL responses against extracellular pathogens and tumour antigens that were never made inside the presenting cell itself.

2 MHC Molecules

Classification, structure, and where each class is expressed

Feature	MHC Class I	MHC Class II
Human genes	HLA-A, -B, -C	HLA-DP, -DQ, -DR
Chains	1 polymorphic α chain + invariant β2-microglobulin	Polymorphic α + β chains

Peptide groove	Closed-ended ($\alpha 1 + \alpha 2$) — binds short peptides, 8–10 aa	Open-ended ($\alpha 1 + \beta 1$) — binds longer peptides, 13–25 aa
Cellular distribution	All nucleated cells	Dendritic cells, macrophages, B cells, thymic epithelium
Presents to	CD8 ⁺ T cells	CD4 ⁺ T cells

PEPTIDE BINDING, BRIEFLY

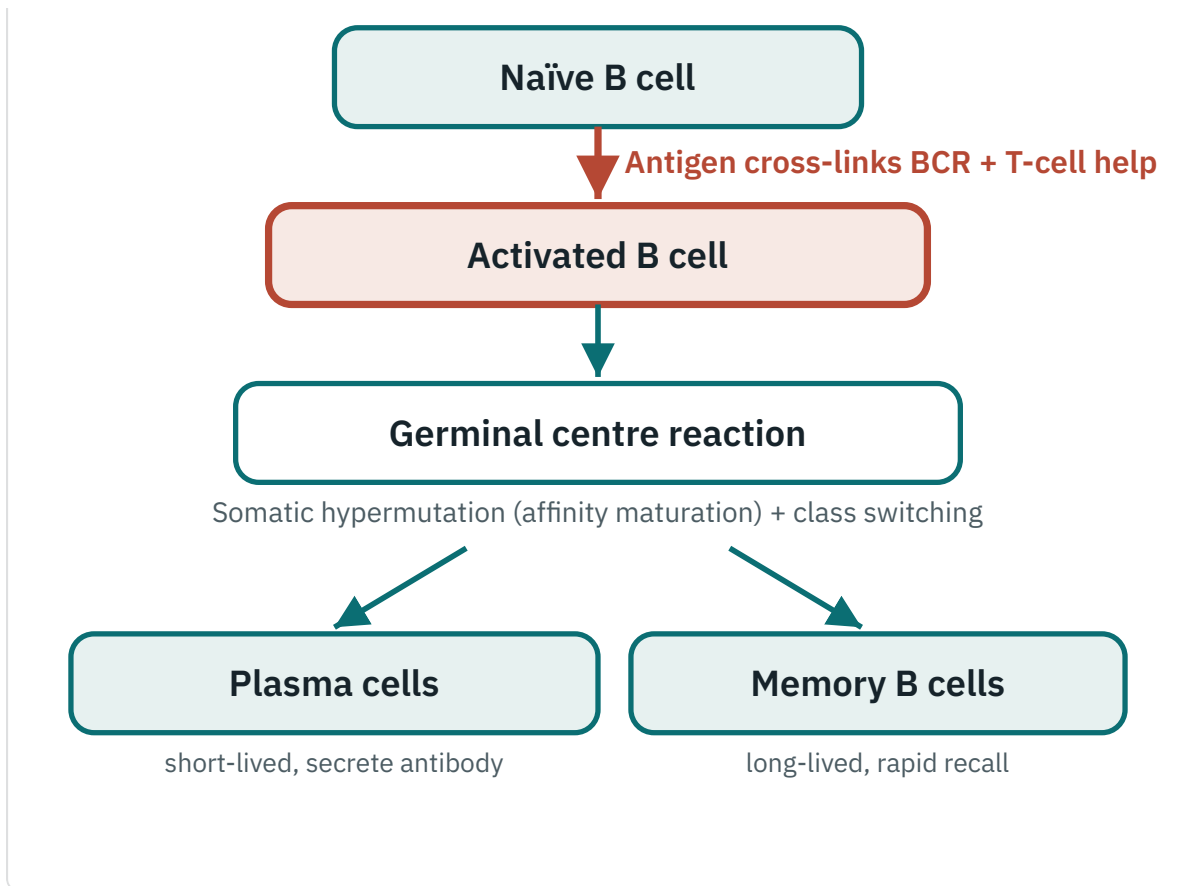
The groove floor has pockets that anchor specific peptide side chains ("anchor residues"), letting one allele bind many different peptides — but with allele-specific preferences. MHC is the most polymorphic region of the human genome, which is exactly why transplant matching is so demanding.

3 B-Cell: Receptor, Activation & Differentiation

From naïve B cell to antibody factory

The **BCR** is a membrane-bound IgM (or IgD) paired with the signalling heterodimer **Ig α /Ig β** (CD79a/CD79b), which carries the ITAMs that transduce the activation signal once antigen cross-links the receptor.

Activation to effector/memory

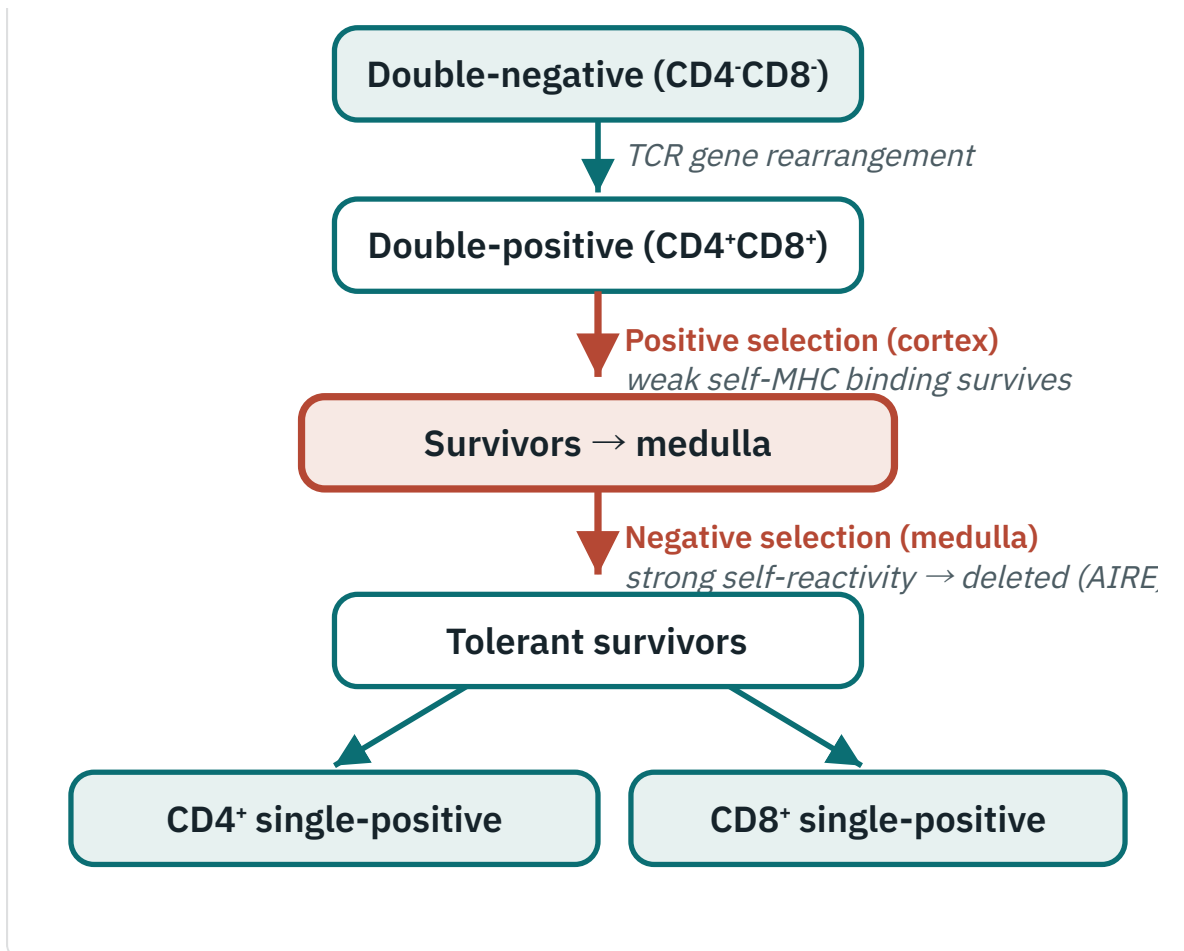


4 T-Cell: Receptor, Maturation & Thymic Selection

Building a repertoire that is useful but not self-destructive

The **TCR** (mostly $\alpha\beta$, a minority $\gamma\delta$) pairs with the invariant **CD3 complex** for signalling, and recognises peptide only in the context of MHC — never free antigen.

Thymic selection



CENTRAL TOLERANCE, IN ONE LINE

Positive selection keeps cells that can see self-MHC (ensuring MHC restriction); negative selection removes cells that see self-MHC + self-peptide too well (preventing autoimmunity). Only cells passing both checkpoints leave the thymus.

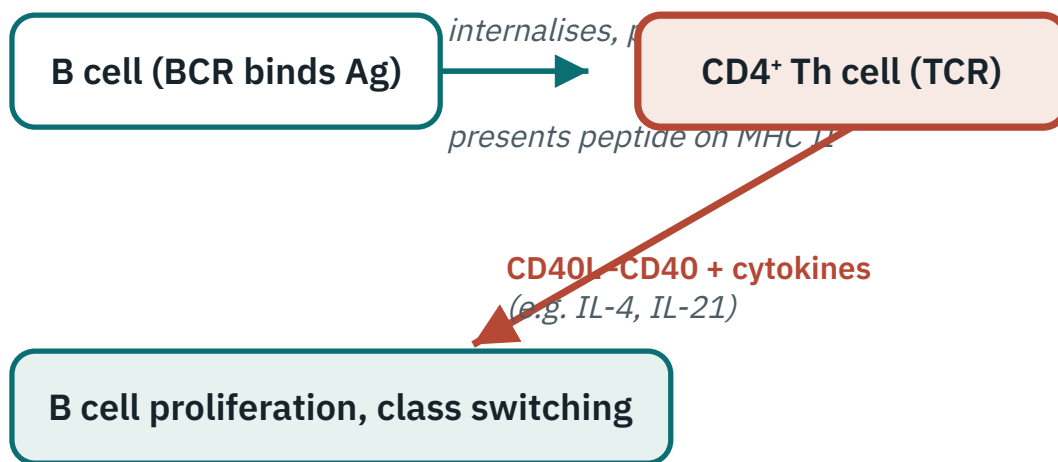
5 Thymus-Dependent/Independent Antigens & T-B Cooperativity

Why some antigens need T-cell help — and some don't

	Thymus-dependent (TD)	Thymus-independent (TI)
Typical antigen	Proteins	TI-1: LPS (mitogenic) · TI-2: repetitive capsular polysaccharide

T-cell help needed?	Yes	No
Class switching / memory	Yes	Minimal / none — IgM predominant
Response in infants	Normal	Poor (TI-2) — basis for conjugate vaccines

Linked recognition – the B-T handshake

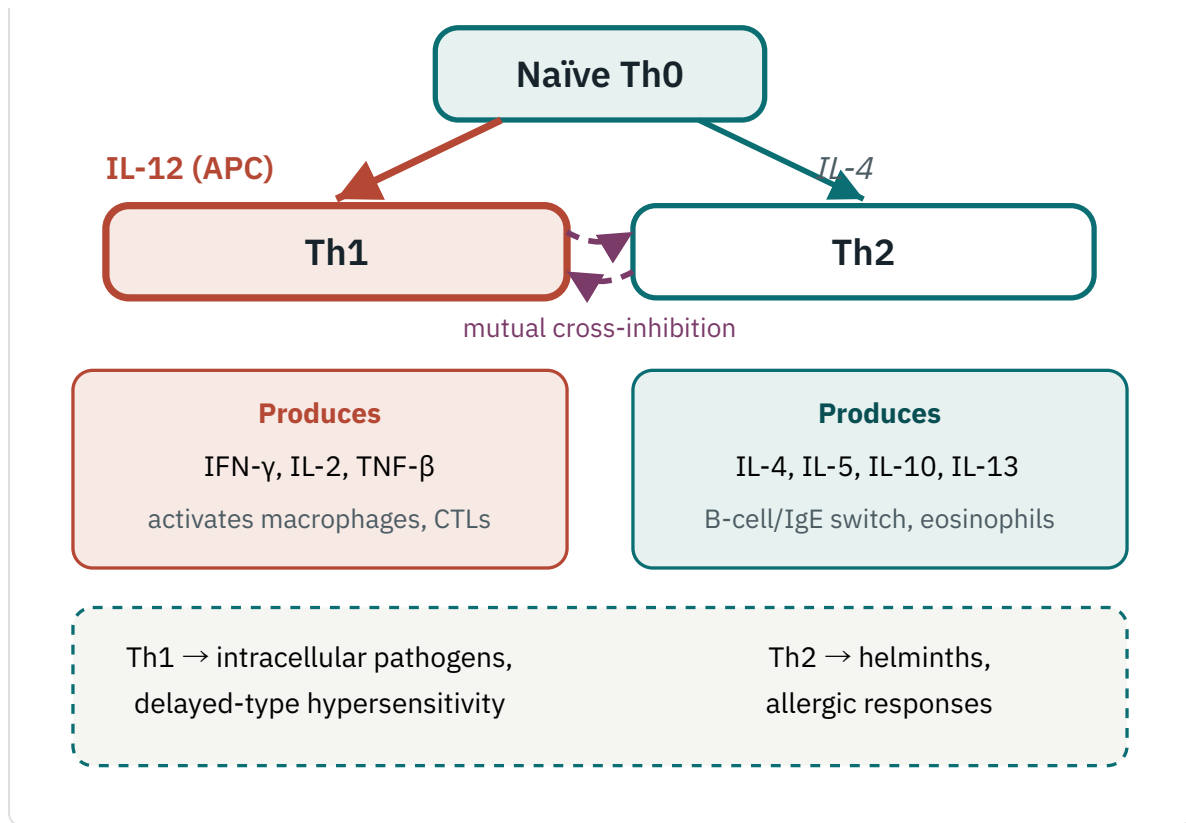


B and T cell must recognise the SAME antigen, different epitopes

6 Cytokines — Th1 and Th2

Two mutually antagonistic helper programmes

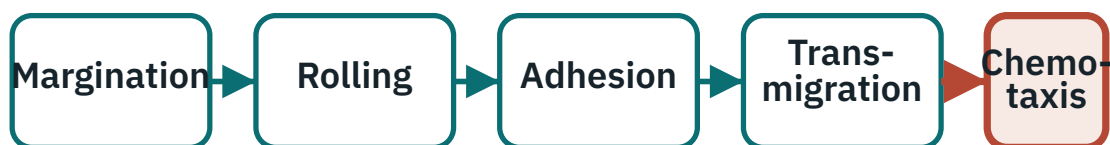
Polarisation of the naïve CD4⁺ T cell



7 Inflammation

The vascular and cellular response to injury or infection

Leukocyte extravasation



Selectins mediate rolling · Integrins/ICAM mediate firm adhesion · C5a, IL-8, LTB₄ drive chemotaxis

Mediator	Main effect
Histamine, serotonin	Early vasodilation, $\uparrow$ permeability
Prostaglandins, leukotrienes	Vasodilation, chemotaxis, pain (arachidonic acid cascade)

IL-1, TNF- α , IL-6	Fever, acute-phase proteins, systemic effects
C3a, C5a	Anaphylatoxins — vasodilation and chemotaxis
Bradykinin	Pain, vasodilation

ACUTE VS. CHRONIC

Acute inflammation (neutrophil-dominated) resolves within days. If the trigger persists, it becomes chronic — macrophages, lymphocytes, and fibroblasts dominate, sometimes forming granulomas (e.g. tuberculosis).

8 Cell-Mediated Effector Responses

CTLs, NK cells, and K cells — three ways to kill a target cell

	CTL (CD8 ⁺)	NK cell	K cell (ADCC)
Recognition	TCR + peptide-MHC I (specific)	Balance of activating/inhibitory receptors — "missing self"	Fc receptor on antibody-coated target
MHC restricted?	Yes	No — triggered by LOW/absent MHC I	No
Killing mechanism	Perforin/granzyme; Fas–FasL	Perforin/granzyme	Perforin/granzyme
Typical target	Virus-infected, tumour cells	Cells that downregulate MHC I to evade CTLs	Antibody-opsonised targets

THE SHARED KILL SWITCH

All three routes converge on the same weapon: perforin punches pores in the target membrane, and granzymes delivered through them trigger apoptosis from inside — a mechanistic thread that ties CTL, NK, and K-cell killing together despite their very different recognition strategies.

9 Autoimmunity & Hypersensitivity

When tolerance fails, or the response overreacts

Autoimmunity is a breakdown of self-tolerance, arising from molecular mimicry, failure of central/peripheral tolerance, epitope spreading, genetic (HLA) susceptibility, or environmental triggers — ranging from organ-specific disease (Type 1 diabetes, Hashimoto's thyroiditis, myasthenia gravis) to systemic disease (SLE, rheumatoid arthritis).

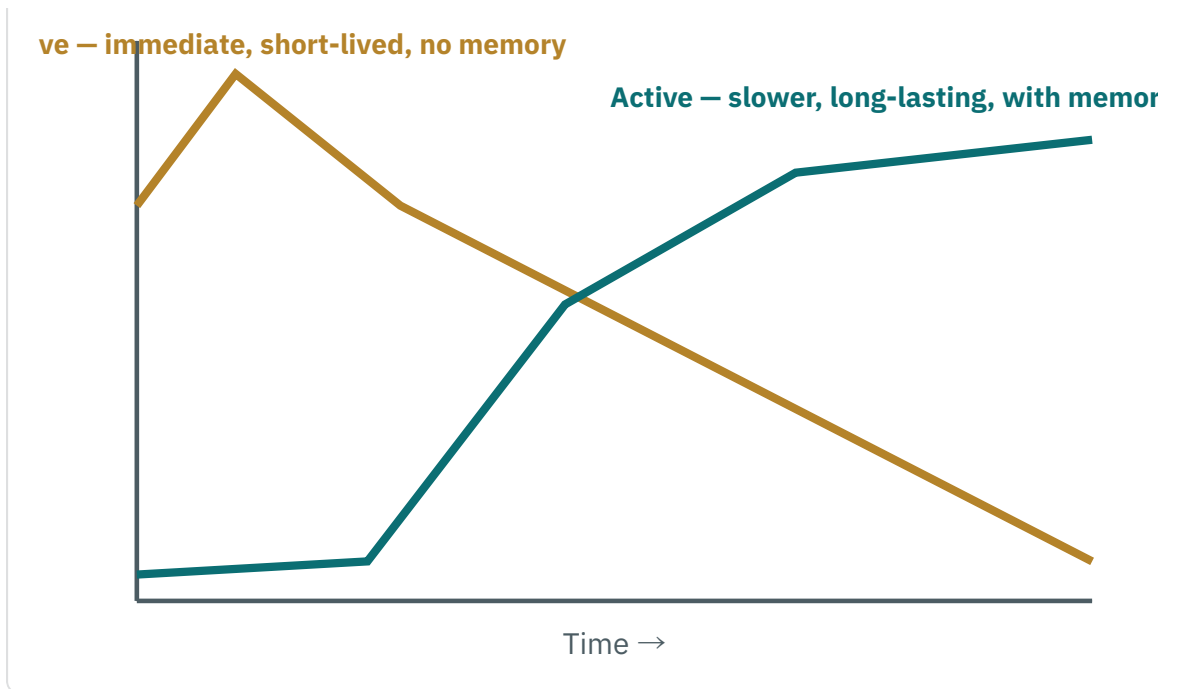
Hypersensitivity — the Gell & Coombs classification

Type	Mechanism	Example
I — Immediate	IgE cross-linked on mast cells/basophils → degranulation	Allergic rhinitis, asthma, anaphylaxis
II — Cytotoxic	IgG/IgM against cell-surface antigen → complement/ADCC	Haemolytic transfusion reaction, Rh disease
III — Immune complex	Ag-Ab complexes deposit in tissue → complement-driven inflammation	Serum sickness, glomerulonephritis, SLE
IV — Delayed (cell-mediated)	T-cell mediated, 24–72 h, no antibody	Tuberculin test, contact dermatitis, graft rejection

10 Vaccination

Passive and active immunisation, vaccine types, toxins & toxoids

Passive vs. active immunisation



Vaccine type	Example	Note
Live attenuated	MMR, BCG, oral polio	Strongest, longest immunity; avoid in immunocompromised
Killed/inactivated	Injectable (Salk) polio, whole-cell pertussis	Safer, weaker — often needs boosters
Subunit / toxoid	Hepatitis B surface antigen; diphtheria/tetanus toxoid	Purified component; very safe
Conjugate	Hib, pneumococcal conjugate	Polysaccharide + carrier protein — converts TI-2 to TD, works in infants
mRNA/DNA	COVID-19 mRNA vaccines	Nucleic acid directs the body's own cells to make antigen

TOXINS AND TOXOIDS

Bacterial exotoxins (e.g. diphtheria, tetanus toxin) are highly immunogenic and can be inactivated with formaldehyde to form **toxoids** — non-toxic but still able to raise protective antibody, the basis of the DPT vaccine. Endotoxin (LPS, gram-negative cell wall) is far less immunogenic and has no toxoid equivalent.

11 Exam Corner

Practice question set — end-semester format

B.Sc. Biochemistry — End-Semester Examination

Paper: Immunology II

Full Marks: 30

Time: 1.5 Hrs

GROUP A — LONG ANSWER (ANSWER ANY TWO)

1. Describe the endogenous and exogenous pathways of antigen processing and presentation, correlating each with the MHC class and T-cell subset involved. **10**
2. Describe thymic selection and explain how positive and negative selection together establish a self-tolerant, MHC-restricted T-cell repertoire. **10**
3. Classify hypersensitivity reactions according to the Gell and Coombs scheme, with mechanism and one example of each type. **10**

GROUP B — SHORT NOTES (ANSWER ANY TWO)

- a. Thymus-dependent vs. thymus-independent antigens **5**
- b. Th1 and Th2 cytokine profiles and their roles **5**
- c. Vaccine types, and the concept of toxoids **5**