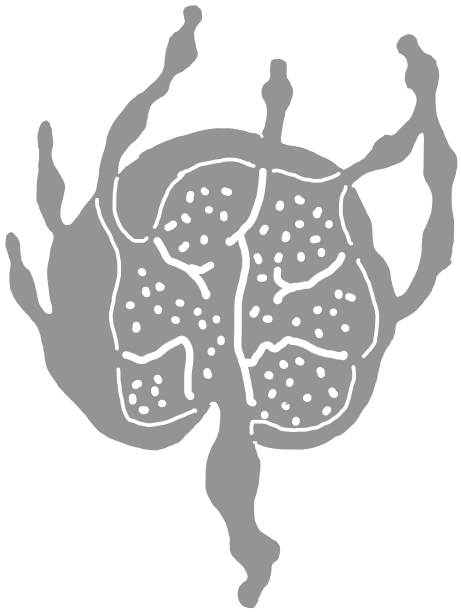

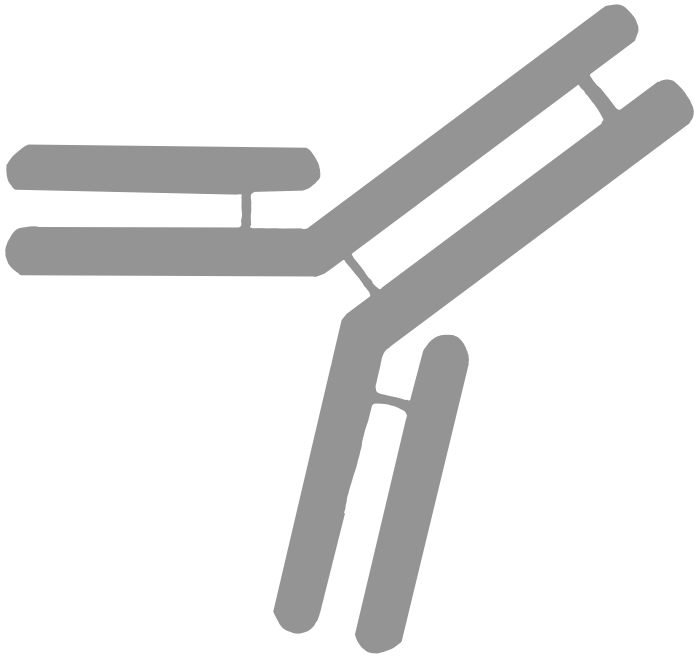

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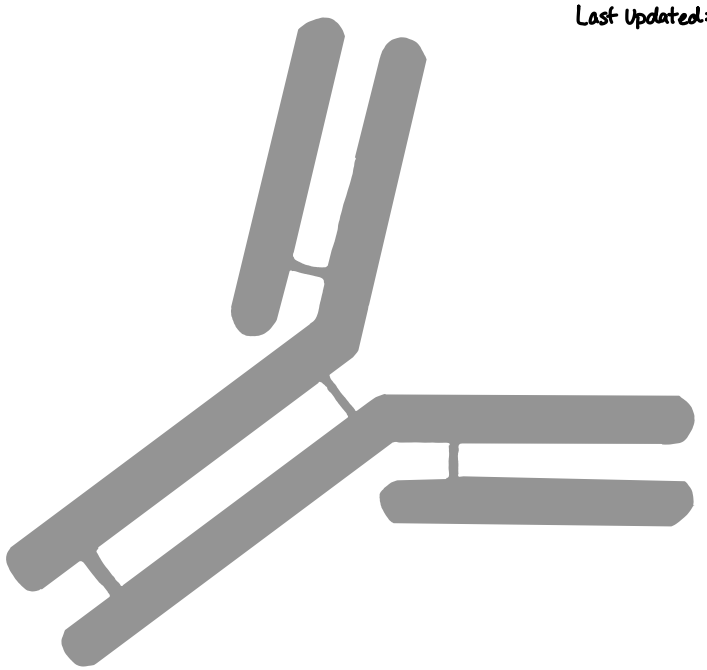
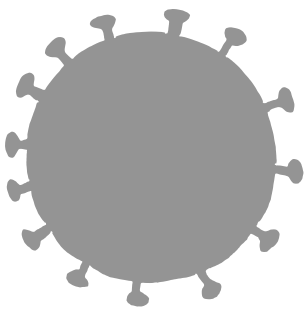
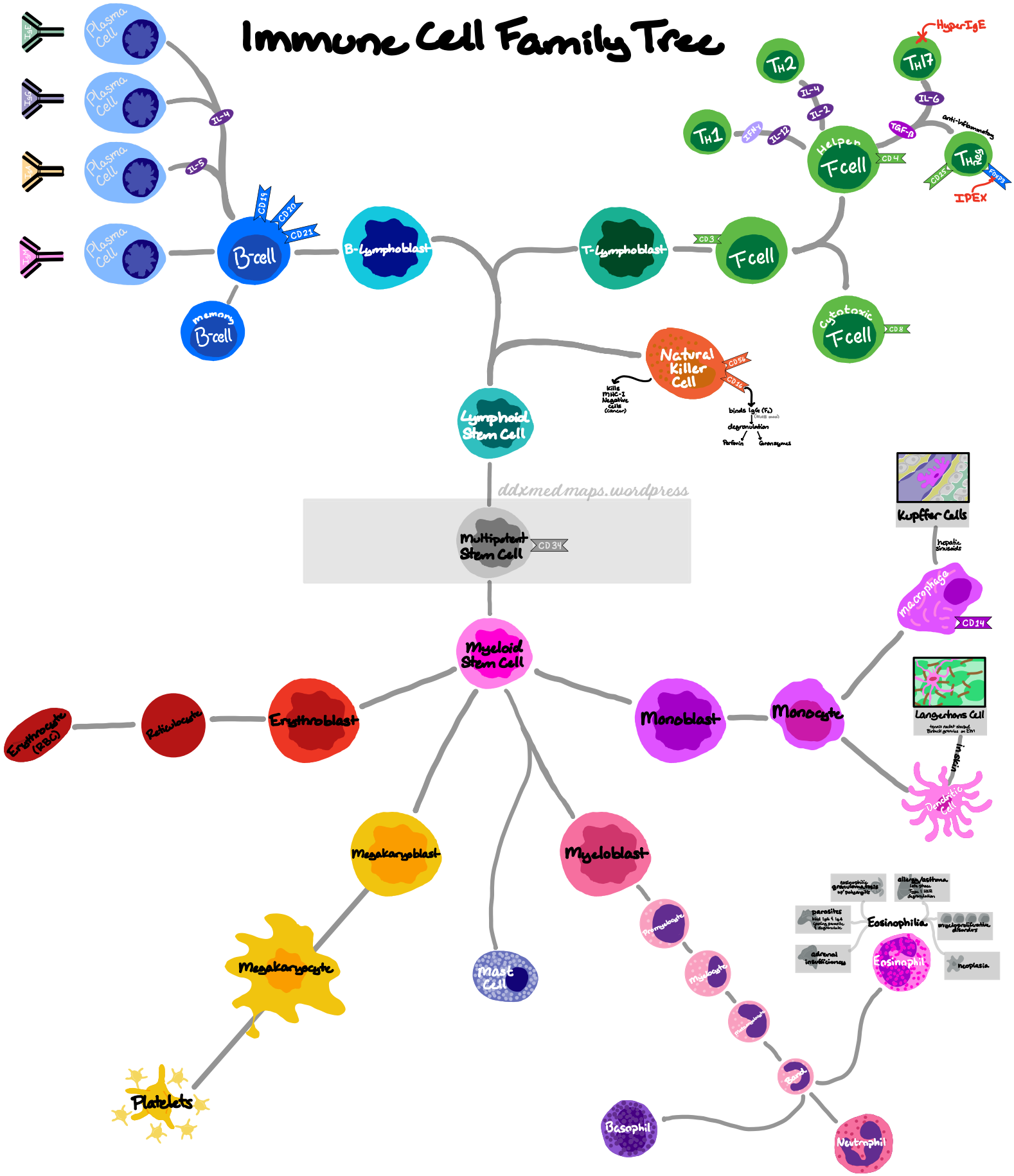
Immunology

First Draft: April 3rd 2021

Last Updated: December 21, 2021






Immune Cell Family Tree
Plasma Cell
IL-4
IL-5
B-cell
CD19
CD20
CD21
B-lymphoblast
memory B-cell
Lymphoid Stem Cell
T-lymphoblast
CD3
T-cell
Helper T-cell
CD4
TH2
IL-4
IL-2
TH1
IFN-γ
IL-12
TH17
IL-6
HyperIgE
TGF-β
anti-inflammatory
TReg
CD25
FOXP3
IPEX
cytotoxic T-cell
CD8
Natural Killer Cell
CD56
CD16
kills MHC-I Negative Cells (cancer)
binds IgG (Fc)
degranulation
Perforin
Granzymes
ddxmedmaps.wordpress
Multipotent Stem Cell
CD34
Myeloid Stem Cell
Kupffer Cells
hepatic sinusoids
macrophage
CD14
Langerhans Cell
in skin
Dendritic Cell
Monoblast
Monocyte
Erythroblast
Reticulocyte
Erythrocyte (RBC)
Megakaryoblast
Megakaryocyte
Platelets
Myeloblast
Promyelocyte
Myelocyte
Metamyelocyte
Band
Neutrophil
Basophil
Mast Cell
Eosinophilia
allergy/asthma
parasites
myeloproliferative disorders
adrenal insufficiency
neoplasia
Eosinophil

Human Leukocyte Antigen Genes

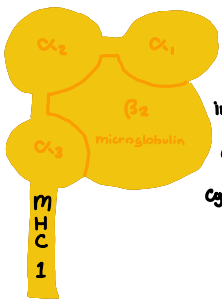
haplotype - cluster of genes on single chromosome
low rate of crossover
25% chance of sibling being identical HLA match
better match = ↓ risk of transplant rejection

HLA-A | HLA-B | HLA-C | HLA-DP | HLA-DQ | HLA-DR

1 letter = MHC I

2 letters = MHC II

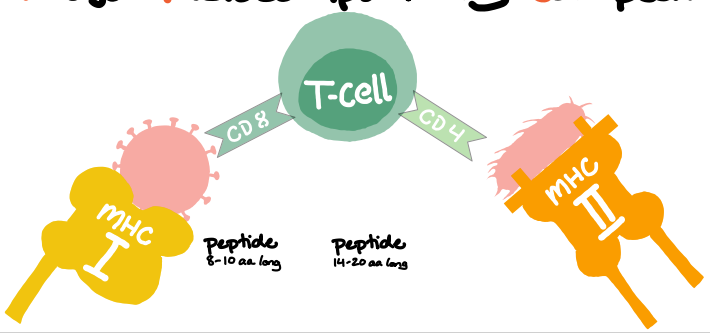
MHC Class I



any nucleated cell presents an intracellular antigen to Cytotoxic T-cells

CD8+ T-cell

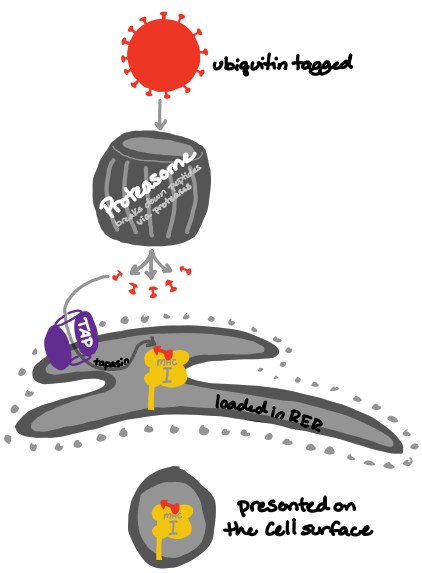
Major Histocompatibility Complex

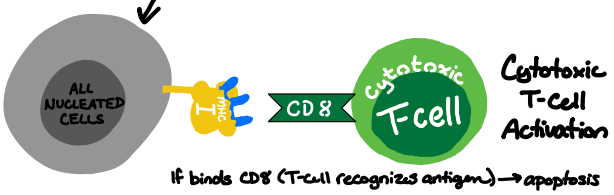


MHC Class II

Endogenous Pathway

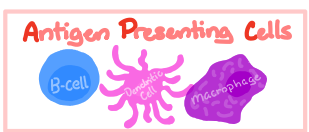
Intracellular Pathogen





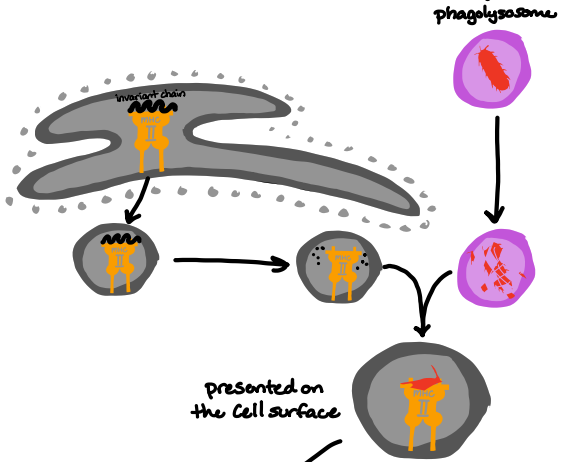
If binds CD8 (T-cell recognizes antigen) → apoptosis

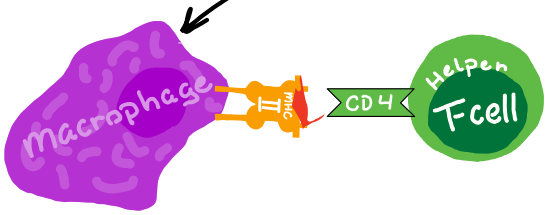
Antigen Presenting Cells



Exogenous Pathway

phagocytose (eat) extracellular pathogen





1° Lymphoid Structures

Bone Marrow

Thymus

2° Lymphoid Structures

Spleen

Lymph Nodes

The Lymph Node

Lymph flows through Lymphatic vessels carrying Lymphocytes (T-Cells & B-Cells) around the body.

Lymph Nodes are like army bases where the lymphocytes can train to fight an infection.

Capsule

mantle

Germinal Center

2° Follicle

Trabecula

Afferent Lymphatic Vessel

2° pale germinal center

+follicular dendritic cells

1° dense, dormant

1° Follicle

B-cell

T-cell

Plasma Cell

Medulla

Efferent Lymphatic Vessel

Medullary Sinuses

Medullary Cords

Paracortex

Antigen Presenting Cells

Dendritic Cell

↑Cellular immune response (viral infection)

Hyperplasia

Lymphadenopathy (LAD)

Underdeveloped:

DiGeorge Syndrome

Outer Cortex

B-cell

Agammaglobulinemia

T-cell

Dendritic Cell

Lymphocyte Maturation

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Class Material
see following pages for VDJ & Ig explanations

(too detailed for Step 1)

Early Pro-B

RAG 1 & 2 Genes
$D_H + J_H$ Chromosome 1
$D_H + J_H$ Chromosome 2

Late Pro-B

Allelic Exclusion
$V_H + D_H J_H$
first successful chromosome inhibits second

Large Pre-B

no success → apoptosis
Heavy Chain Complete!

Allelic Exclusion Part 2
$V_L + J_L$ Kappa & Lambda?
AIRE: autoimmune regulator gene

Small Pre-B | Small Pre-B

Light Chain Complete!

Multipotent Stem Cell

Bone Marrow

B-Lymphoblast

Lymphoid Stem Cell

T-Lymphoblast

VDJ Recombination
(See next page)

Immature B-cell

"Alternative Splicing"
μ (IgM) & δ (IgD) heavy chains expressed

mature naive B-cell

allows access to lymph where it searches for antigens

enters lymph
- forms 1° Follicle in lymph nodes
- searches for antigens
  - lymphoid organs
  - peripheral tissues

mature naive B-cell
exposed to antigen

T-cell independent

Plasma Cell

IgM

CD4 | immature T-cell | CD8

⊕Selection
can you bind MHCs?

⊖Selection
Central Tolerance via AIRE
will you attack self?
yes? die or Treg

CD4 | mature naive T-cell

mature naive T-cell | CD8

Cortex Thymus Medulla

naive T-cell
TCR
CD3
CD4
CD28

APC
MHC II
B7
CD86
CD80

mature naive B-cell
MHC II
CD40

Activation
TCR
CD3
CD4
activated T-cell
CD40L

medulla

memory B-cell

activated B-cell

2° Follicle

Germinal Centers

B-cell

Isotype (Class) Switching
IL-4
IL-5

Plasma Cell | Plasma Cell | Plasma Cell | Plasma Cell

IgM | IgG | IgG | IgA

Affinity Maturation
via Somatic Hypermutation

CD4 | Helper T-cell

Cytotoxic T-cell | CD8
contain granules w/ perforin & granzymes

Paracortex

IL-12 IFNγ

IL-4 IL-2

TGF-β

IL-6

IFNγ
IL-10
IL-4
IL-1
IL-2

T_H1
IL-2
IFNγ
Cell Mediated Type IV HSR

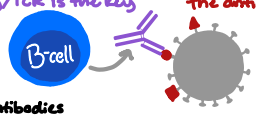
T_H2
IL-13
IL-5
IL-6
Allergy/Asthma Type I HSR

T_H17
IL-17
IL-21
IL-21

T_{reg}
TGF-β
IL-10
IL-35

How do lymphocytes recognize the enemy?

Anatomy of the **B-Cell Antibody** & **T-cell Receptor** & how it binds antigens
- the Ig/TCR is the key
- the antigen is the lock
- be it pieces of bacteria, viruses, or our own bodies in the case of autoimmunity



The B-cell shuffles the genes for the hypervariable region & if it encounters an antigen that it binds it matures & makes more antibodies

Generation of Antibody Diversity (before antigen is seen)
- VJ (light chain) & VDJ (heavy chain) Recombination
- Terminal deoxynucleotide Transferase adds random nucleotides
- light chain & heavy chain randomly paired up

Specificity (after antigen is seen)
- Affinity Maturation via Somatic Hypermutation → Variable Region (antigen specific)
- Isotype Switching → Constant Region (isotype specific)

Affinity: Binding strength

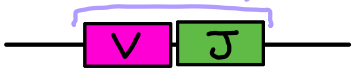
Rearrangement cuts out unused genes & shortens DNA

B-Cell Receptor
Immunoglobulin/Antibody

Hypervariable (VDJ) Region

Heavy Chain

Light Chain

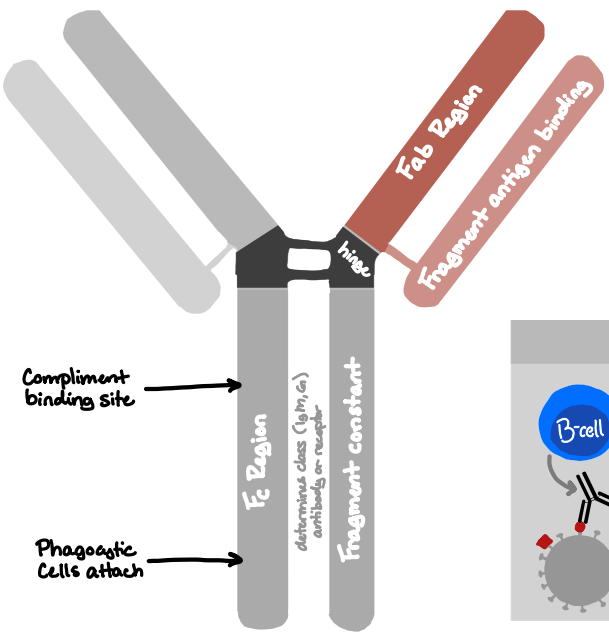


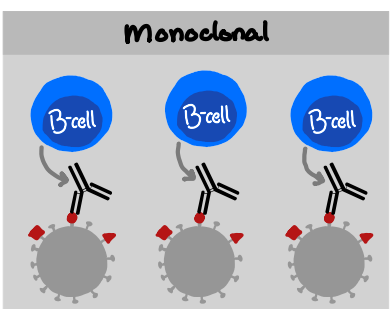
T-Cell Receptor

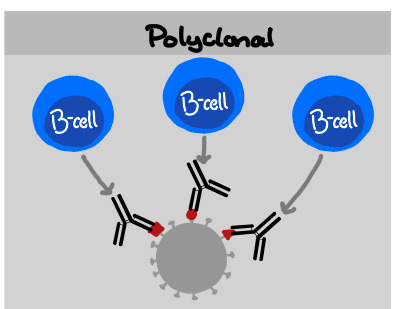
Hypervariable (VDJ) Region

Beta

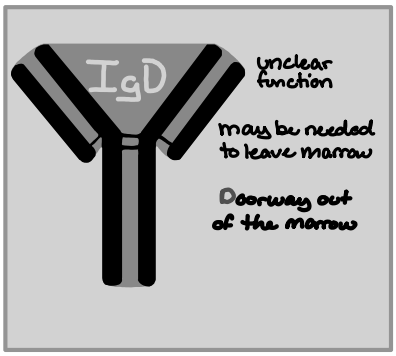
Alpha

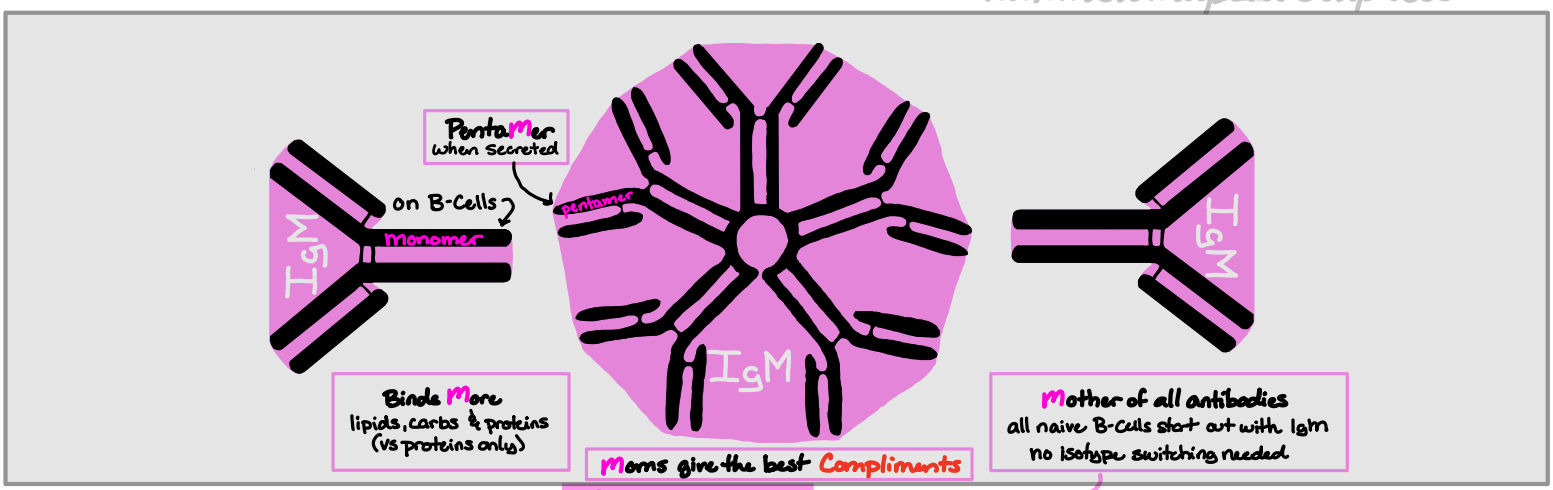






Immunoglobulins

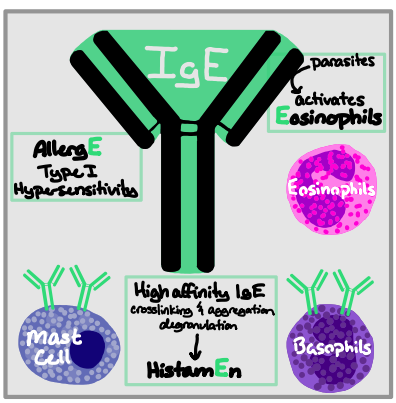


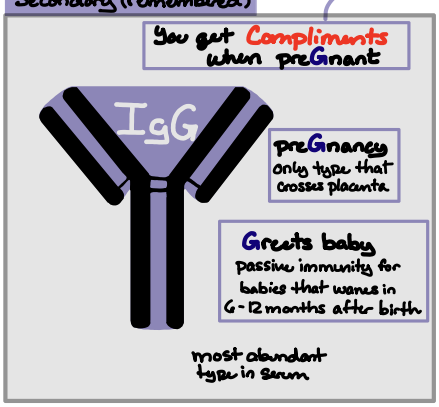


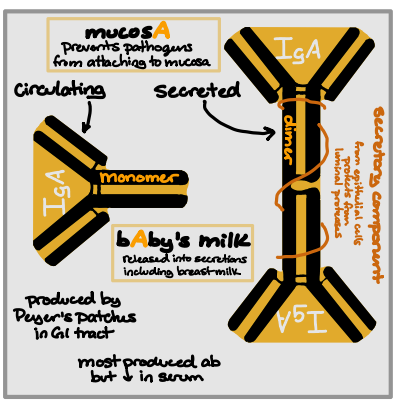
Primary (immediate)

Antigen Response → Secondary (remembered)

Fixes Compliment







Cytokines

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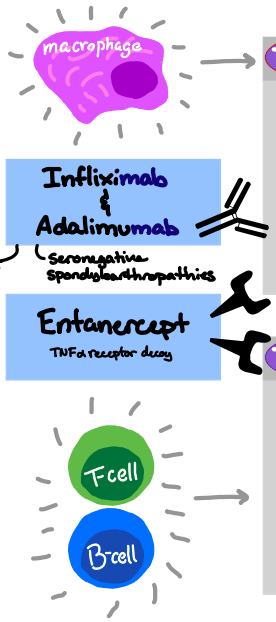
Tumor Necrosis Factor



TNFα "Cachectin"

part of the fever & sepsis triad

recruits WBCs

activates endothelium → leaky vessels

"tumors make things leaky"

maintain granulomas → TB

malignancy cachexia

fever & sepsis triad | hot cockeria | IL-1 + TNF-α

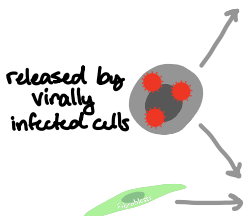
TNFβ "Lymphotoxin Alpha"

cytotoxic → ↑carcinogenesis

↑ Colony Stimulating Factor Synthesis

↳ ↑ fibroblast → wound healing

InterFeroNs



IFN-α & **IFN-β**

α & β interfere with viruses

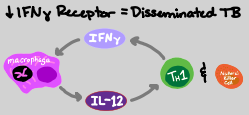
innate & antitumor immunity

tell neighbor cells to ↓protein synthesis but ↑ MHC I expression

MHC I

IFNγ

↓IFNγ Receptor = Disseminated TB



gamma = granuloma activator

granuloma formation

↑ MHC II expression

MHC II

allows macrophages to kill intracellular bacteria

Transforming Growth Factor-β

TGF-β

↑Fibroblast & fibrosis

Tissue Regeneration

Proliferation phase of wound repair

↓

Overexpression = Keloids

(also ↑ IGF-1 & PDGF, ↓ MMP)

Fibrillin-1 → TGF-β

↑ matrix metalloproteinase production

↓

cleave ECM

myxomatous mitral degeneration in Marfan Syndrome

growing the breaks of the immune system when you turn 17

attenuates inflammation

InterLeukins

Basiliximab & Daclizumab ⊣ IL-2R

Tocilizumab ⊣ IL-6
IL-6 levels correlate with severity of Giant Cell Arteritis

Ustekinumab ⊣ IL-12/IL-23

Tralokinumab (asthma) ⊣ IL-13

Ixekizumab & Secukinumab ⊣ IL-17A
Seronegative Spondyloarthropathies
Psoriasis

Ustekinumab ⊣ IL-12/IL-23
Psoriasis

1. **IL-1** hot - part of the fever & sepsis triad
2. **IL-2** T-cells & Natural Killer Cell produced in response to calcineurin — Th2 — "two" cell activation
3. **IL-3** bone marrow like GM-CSF — 3-some if you wanna bone (hematopoiesis)
4. **IL-4** ↑atopy — Plasma Cell IgE & IgG Antibody production — Th2 — ain't 2 proud to BEG 4 help
   B cell → Class Switching — asthma
5. **IL-5** Plasma Cell IgA & eosinophils — 5 fingers = 11:5 or eosin is 5 letters
6. **IL-6** aKute phase reactants — part of the fever & sepsis triad — Th17
   induces RBC rouleaux formation → sinks faster ↑ESR (Erythrocyte Sedimentation Rate)
7. **IL-7** ↑lymphocytes
8. **IL-8** Chemotaxis — Neutrophils — bacterial infections — Clean up on aisle 8! (clear infection)
9. **IL-9** regulates hematopoiesis
10. **IL-10** released by Th2 & macrophage — prevents autoimmunity & maintains tolerance — attenuates inflammation
    necessary for granulation tissue to form
    impaired by ↑blood glucose → nonhealing wounds in Diabetes Mellitus
11. **IL-11** stimulates platelet production
12. **IL-12** Th1 — IFNγ — macrophage — IL-12 — Th1 & Natural Killer Cell
13. **IL-13** B cell class switching → Plasma Cell IgE — ↑VCAM1 (CD106)
    atopy
14.
15.
16.
17. **IL-17** ↑TNFα & prostaglandins → Δ bony erosions & regrowth
18.
19. released by Th17
20. & recruits Neutrophils to site of inflammation
21. **IL-21**
22. **IL-22** Psoriasis
23. **IL-23** (Similar to IL-12)
24. **IL-24**
25.
26.
27.
28. **IL-28** released by macrophage & promote antiviral immunity
29. **IL-29**
30.
31.
32. induces apoptosis & fever & sepsis triad
33.
34.
35. **IL-35** released by Th2 — prevents autoimmunity & maintains tolerance

hot T-bone steak

fever & sepsis triad — hot cockeria — IL-1 + TNF-α

"two" cell activation

3-some if you wanna bone (hematopoiesis)

ain't 2 proud to BEG 4 help

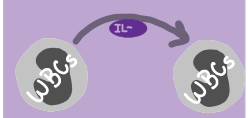
5 fingers = 11:5 or eosin is 5 letters

fever & sepsis triad

clean up on aisle 8! (clear infection)

attenuates inflammation

InterLeukins



some are **Chemokines**
↓
do Chemotaxis (attract other cells)

Cell Surface Markers

KEY
- CD = in First Aid or UWorld
- CD = monocyte/macrophage
- CD = T-cell
- CD = B-cell
- CD = B-cell tumor
- CD = NK cell

From wikipedia & research papers = may be too low yield

1. **CD1a** & CD207 — Langerhan Cell histiocytosis; Birbeck granules "Tennis Rackets"; S-100 = mesodermal origin
2. T-Cell adhesion
3. **CD3** — +TCR; binds antigen MHC complex; signal transduction
4. **CD4** — Helper T-cells — **CD4**
5. **CD5** — +CD23 Chronic lymphoblastic Leukemia; −CD23 Mantle Cell Lymphoma

Tiny T-cells 2-8

6. T-Cell activation + not sensitive/specific to T-cells
7. **CD7** — T-cells
8. **CD8** — Cytotoxic T-cells
9. Cell trafficking

TdT — ALL Pre-B & T cell marker

FcR

C3bR

Chemokine Receptors

CCR5

CXCR4

HIV coreceptors allows viral fusion

10. **CD10** — Pre-B cell marker; Acute lymphoblastic Leukemia; "Neprilysin"

Middle Myelocytes (monocytes, granulocytes) 11-18

11. **CD11a** (α subunit) + **CD18** (β-2 integrin) = LFA-1 on PMN → binds ICAM-1 (CD54) — Leukocyte Extravasation (leaving blood vessels)
    CD11b → ↑ expression in eosinophils
    CD11c — Hairy Cell Leukemia
12. Doesn't exist
13. Zinc binding metalloproteinase – Myeloid Cells

14→M

14. **CD14** — most specific to monocyte/macrophage → PAMPs (LPS)
15. **CD15** — granulocytes & Reed-Sternberg Cells (Hodgkin Lymphoma)

NK cells are Gangster from age 16-56

16. **CD16** — binds Fc of bound IgG; activates NK cell; also on other myelocytes
17. variety of cells

18→ multi lobe nucleus PMN

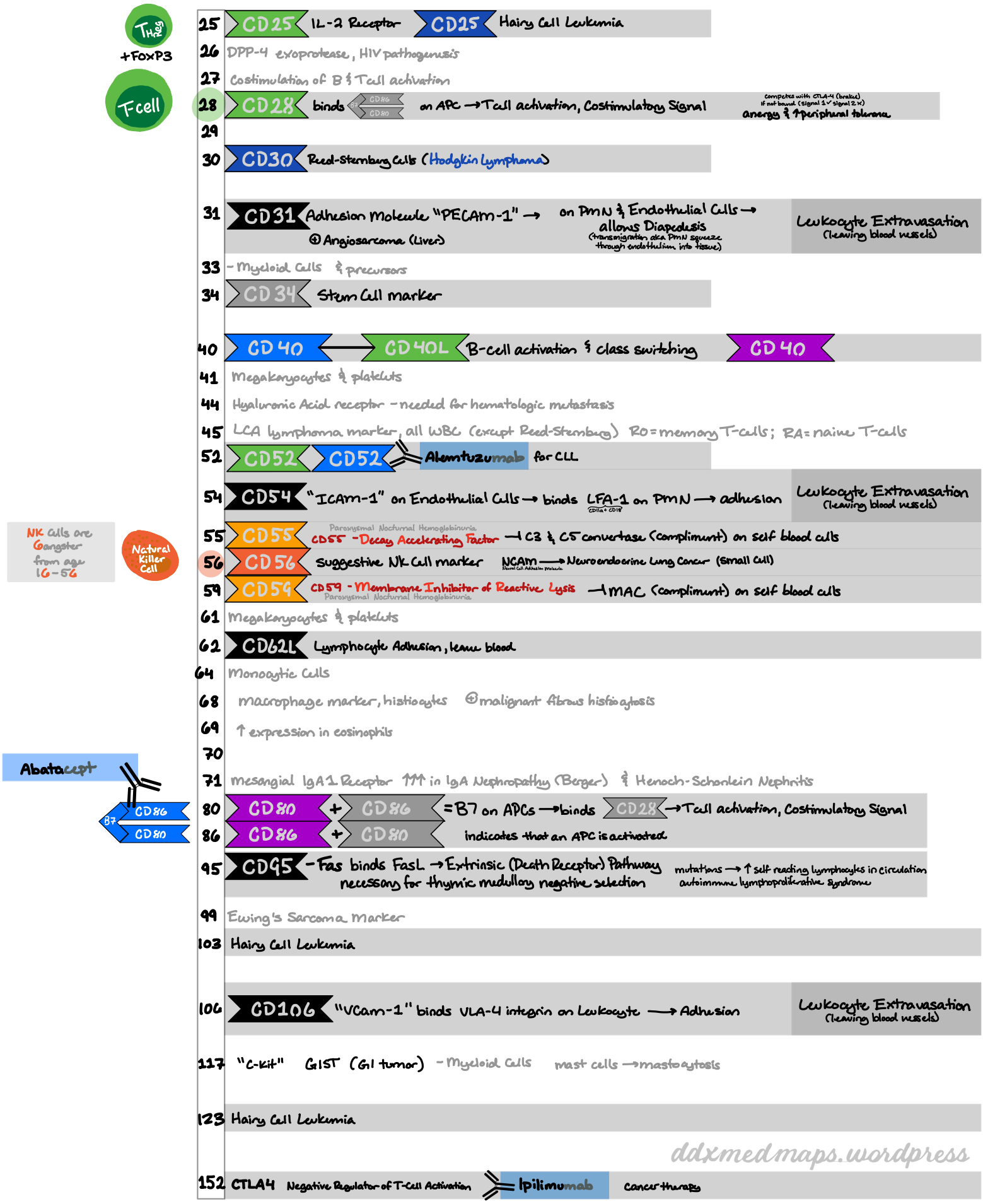
18. **CD18** (β-2 integrin) + **CD11a** (α subunit) = LFA-1 on PMN → binds ICAM-1 (CD54) → Leukocyte Adhesion (Deficiency) on neutrophils — Leukocyte Extravasation (leaving blood vessels)

Big B-cells *19 & 20* (& 21-24)

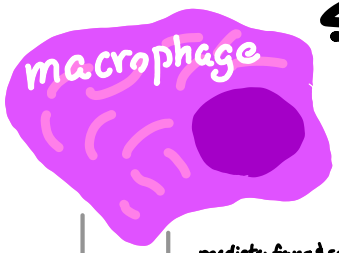
19. **CD19** — B-cells
20. **CD20** — B-cells — **Rituximab** monoclonal antibody — autoimmune diseases & B-cell cancers

21. **CD21** — EBV receptor → Epstein Barr Virus binds to enter B-Cells — must be 21 to drink at the bar
22. mature B-Cells — **CD22** — Hairy Cell Leukemia
23. mature B-Cells — **CD23** — Chronic lymphoblastic Leukemia
24. B-Cell regulation

more spread out version on ddxmedmaps.wordpress


T Reg
+FoxP3
T-cell
25 CD25 IL-2 Receptor CD25 Hairy Cell Leukemia
26 DPP-4 exoprotease, HIV pathogenesis
27 Costimulation of B & T cell activation
28 CD28 binds CD86 CD80 on APC → T cell activation, Costimulatory Signal
competes with CTLA-4 (brake). If not bound (signal 1 ✓ signal 2 ✗)
anergy & ↑ peripheral tolerance
29
30 CD30 Reed-Sternberg cells (Hodgkin lymphoma)
31 CD31 Adhesion Molecule "PECAM-1" → on PMN & Endothelial Cells → allows Diapedesis (transmigration aka PMN squeeze through endothelium into tissue)
Leukocyte Extravasation (leaving blood vessels)
⊕ Angiosarcoma (Liver)
33 - Myeloid cells & precursors
34 CD34 Stem cell marker
40 CD40 — CD40L B-cell activation & class switching CD40
41 Megakaryocytes & platelets
44 Hyaluronic Acid receptor - needed for hematologic metastasis
45 LCA lymphoma marker, all WBC (except Reed-Sternberg) RO = memory T-cells; RA = naive T-cells
52 CD52 CD52 Alemtuzumab for CLL
54 CD54 "ICAM-1" on Endothelial Cells → binds LFA-1 (CD11a+CD18) on PMN → adhesion
Leukocyte Extravasation (leaving blood vessels)
NK cells are Gangster from age 16-56
Natural Killer Cell
55 CD55 Paroxysmal Nocturnal Hemoglobinuria CD55 - Decay Accelerating Factor → C3 & C5 convertase (complimunt) on self blood cells
56 CD56 Suggestive NK cell marker NCAM (Neural Cell Adhesion Molecule) → Neuroendocrine Lung Cancer (small cell)
59 CD59 Paroxysmal Nocturnal Hemoglobinuria CD59 - Membrane Inhibitor of Reactive Lysis → MAC (complimunt) on self blood cells
61 Megakaryocytes & platelets
62 CD62L Lymphocyte Adhesion, leave blood
64 Monocytic cells
68 Macrophage marker, histiocytes ⊕ malignant fibrous histiocytosis
69 ↑ expression in eosinophils
70
Abatacept
71 Mesangial IgA1 Receptor ↑↑↑ in IgA Nephropathy (Berger) & Henoch-Schonlein Nephritis
B7 CD86 CD80
80 CD80 + CD86 = B7 on APCs → binds CD28 → T cell activation, Costimulatory Signal
86 CD86 + CD80 indicates that an APC is activated
95 CD95 - Fas binds FasL → Extrinsic (Death Receptor) Pathway necessary for thymic medullary negative selection
mutations → ↑ self reacting lymphocytes in circulation autoimmune lymphoproliferative syndrome
99 Ewing's Sarcoma Marker
103 Hairy Cell Leukemia
106 CD106 "VCAM-1" binds VLA-4 integrin on Leukocyte → Adhesion
Leukocyte Extravasation (leaving blood vessels)
117 "C-kit" GIST (GI tumor) - Myeloid cells mast cells → mastocytosis
123 Hairy Cell Leukemia
ddxmedmaps.wordpress
152 CTLA4 Negative Regulator of T-Cell Activation Ipilimumab Cancer therapy

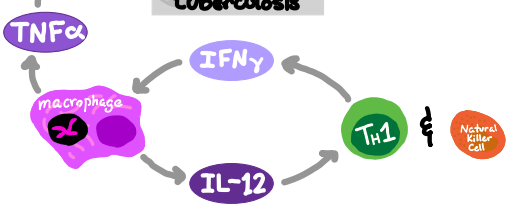
Some Random Cytokine Relationships



First acute
- mediate fever & sepsis
- "Osteoclast Activating Factor"
- IL-1 → express adhesion molecules; Chemokine secretion
- IL-6 → acute phase protein production
- TNFα → malignancy cachexia; OBCs → maintain granulomas (TB)

then recruit
- IL-8 → Clean up on aisle 8 (pls eat this bug for us) → neutrophils
- IL-12 → CD4+ T-cell → T_H1

Mycobacterium tuberculosis



T_H1
- IL-2 → CD4+ T-cell → T_H1
- IFNγ → macrophage; good job now eat it!!
- IFNγ → macrophage → granuloma formation (γ = gamma = granuloma activator)
- "I've got something!" → Natural Killer Cell → get 'em

T_H2
- IL-4 → B-cell → Plasma Cell
- IL-4 → B-cell growth
- IL-5 → B-cell → Plasma Cell
- IL-5 → eosinophils

T_{H2}

$T_{H1/2}$
- IL-10 → "attenuate"
  - inflammation
  - MHC II
  - T_H1 cytokines

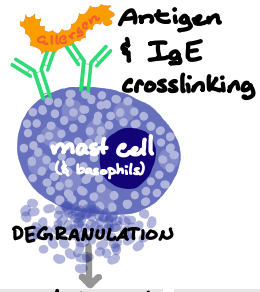
T-cell
- Helper
  - CD4+ T-cell → regulatory
  - IL-2 → cell growth → CD8+ T-cell → Cytotoxic
- IL-3 → like GM-CSF → bone marrow growth & differentiation

Hypersensitivity Reactions

ddxmedmaps.wordpress

Mast Cells

A TYPE I



immediate (min)
histamine, tryptase → vasodilation & inflammation

Late (hours)
chemokines, Leukotrienes → inflammation

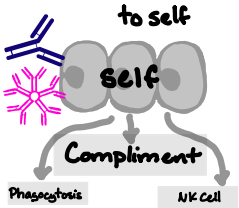
→ mucus production → Seen in nasal secretions, etc

- Allergic Rhinitis
- Asthma
- Anaphylaxis
- Atopy

Cytotoxic Antibody

B TYPE II

IgG/IgM AntiBodies to self



Cell Destruction
- Autoimmune Hemolytic Anemia
- ITP
- Transfusion Reactions
- Hemolytic Disease of the Newborn

Inflammation
- Goodpasture's Syndrome (Biopsy → smooth GBM with linear antibody deposition)
- Rheumatic Fever
- Hyperacute Transplant Rejection

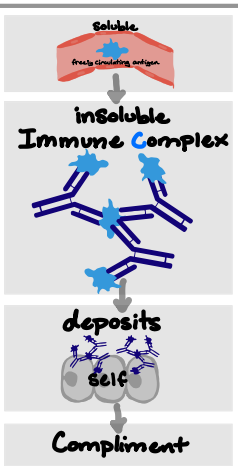
Cell Dysfunction (Autoreceptor)
- Myasthenia Gravis
- Grave's Disease
- Pemphigus Vulgaris

II & III Type I Diabetes Mellitus

II & III Multiple Sclerosis

Immune Complex

C TYPE III



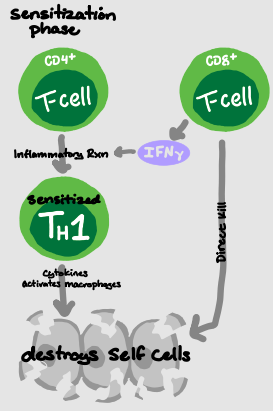
Fibrinoid Necrosis

- Post-Streptococcal Glomerulonephritis (Biopsy → Lumpy Bumpy: globular or thick antibody deposition, Lumps of complexes)
- Systemic Lupus Erythematosus
- Rheumatoid Arthritis
- Polyarteritis Nodosa
- Serum Sickness: drugs (penicillin, mabs), infections (Hep B) → 1-2 weeks → immune complexes (if phagocytes can't keep up they deposit in tissues.) → fever, urticaria, arthralgias, +/- proteinuria, +/- LAD
- Tests: Arthrus Rxn

Delayed Cell Mediated

D TYPE IV

Delayed Cell Mediated

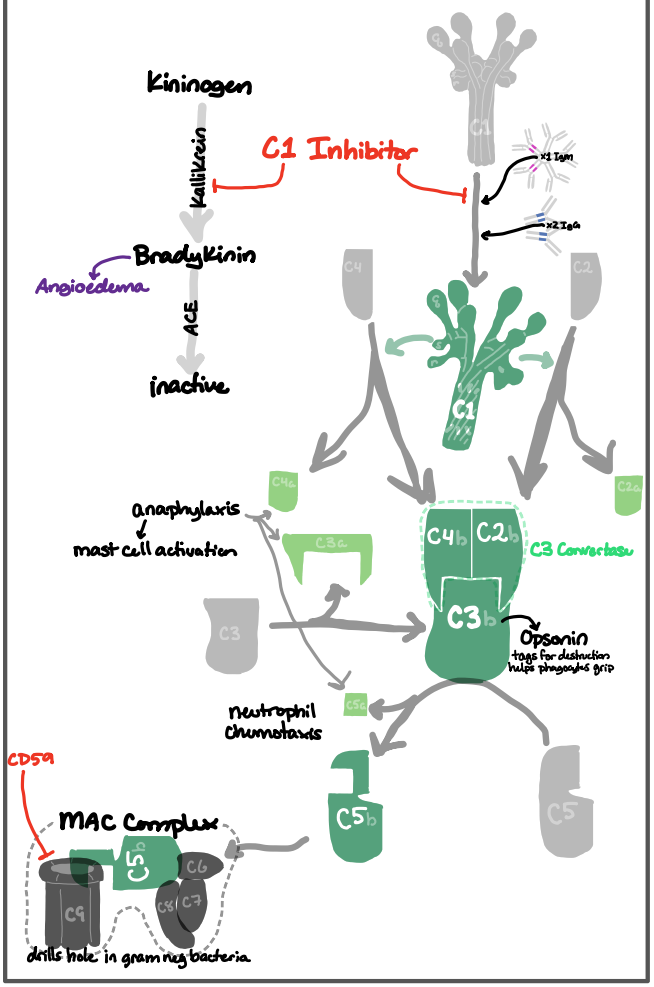


- Urushiol (hair dye), Poison Ivy, Nickel → Contact Dermatitis
- Diabetes Mellitus (Type 1)
- Diagnose TB — PPD takes 48 hours
- Graft vs Host (see next page)
- Granuloma Formation

Complement Cascade

3 ways to activate:

Classical	Alternative	Lectin
C-Reactive Protein on IgG/IgM binds antigen	molecules on microbe surface, C3b cleaves slowly on own	mannose/sugars on microbe surface diff C1



activates → Compliment deposits

ACEi → Angioedema

vasodilation, leaky vessels → Edema

C1 Inhibitor Deficiency

Hereditary Angioedema (without Urticaria)

↓ Serum C4

bradykinin buildup

Transplant Rejection

ddxmedmaps.wordpress

Chronic Allograft Nephropathy

Bronchiolitis Obliterans (lymphocytes & granulation tissue infiltrate, small airway obstruction, lung disease)

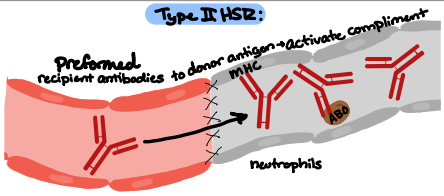
Vanishing Bile Duct Syndrome

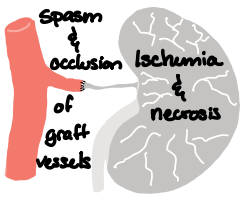
Accelerated Atherosclerosis

minutes → hours | weeks → months | months → years

Hyperacute

Type II HSR:





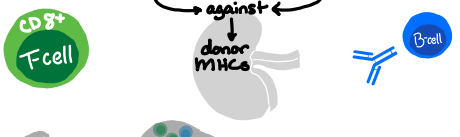
Prevent w/ crossmatch
rare, not treatable
remove graft

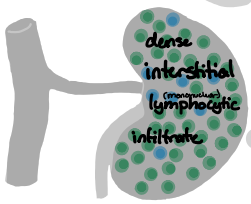
Acute

Cellular → Type IV HSR > humoral → Type II HSR

recipient T-cells activated against donor MHCs

recipient B-cells produce antibodies



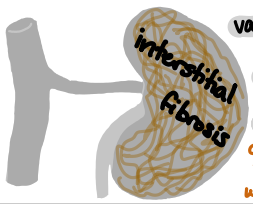


prevent/reverse w/ immunosuppressants

vasculitis of graft cells

Chronic

Cellular → Type IV HSR & humoral → Type II HSR



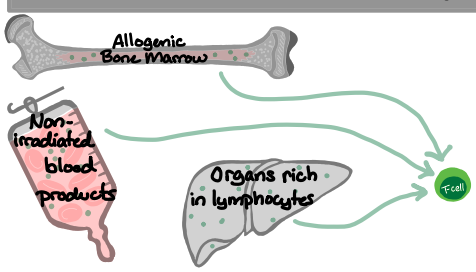
vascular smooth muscle proliferation
parenchymal atrophy
dominated by arteriosclerosis

occurs to some degree in most transplants which eventually fail

Host immune system attacks donor tissue → Graft Failure (no systemic involvement)

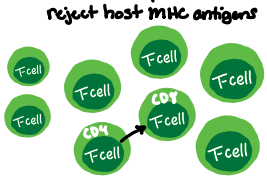
Immune cells within donor tissue attack immunocompromised host → Multiorgan Failure

Graft-Versus-Host Disease



donor immunocompetant T-cells proliferate in immunocompromised host & reject host MHC antigens

timing: variable



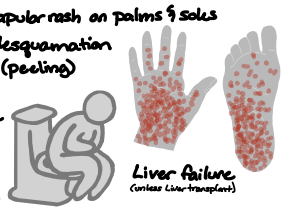
Cellular → Type IV HSR

maculopapular rash on palms & soles +/- desquamation (peeling)

diarrhea

GI bleed

abdominal pain

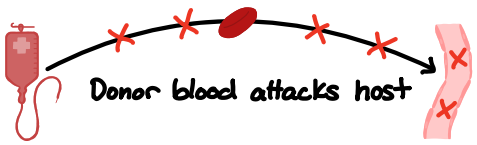


Liver failure (unless Liver-transplant)

severe organ dysfunction

Post Transfusion Purpura
delayed response to platelet antigens
5-10 days after transfusion:
petechiae, purpura +tx: IVIG

Blood Transfusion Reactions



Hemolytic

Type II HSR: host preformed antibodies → donor RBC antigen

usually: ABO Incompatibility

usually: Rh Incompatibility
reaction to previously encountered blood antigen

Acute
during to 24 hours

Intravascular
tachypnea
tachycardia
fever chills
hypotension
nausea
flushing
flank pain
hemoglobinuria
reddish urine
alkalinize urine
vasopressors diuretics
hyperkalemia
DIC bleeding from all sites
Renal Failure

Extravascular
mild fever generally self limited & asymptomatic
jaundice
hyperbilirubinemia

Delayed
24 hours to 2 weeks

anti-RBC antibodies
⊕ Direct Coombs Test (DAT)

Usually within 1 hour

#1 Adverse Transfusion Reaction
benign

prevention: leukoreduction of blood products (filtering out WBC before storage)
headaches
chills
flushing
fever
more common in children

preformed Cytokines that accumulate in storage
previously thought: host antibodies to donor HLA & WBC

Acetaminophen for fever

1-6 hours

Febrile Nonhemolytic

Usually within 2-10 days

Type II Hypersensitivity

(acute) hypotensive
normotensive (⊘ BP)

Usually within 1-6 hours

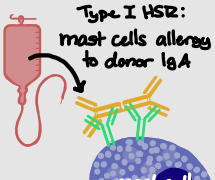
fever
chills
flushing

Usually within minutes

during → 2 hours

Allergic/Anaphylactic

Type I HSR:
mast cells allergy to donor IgA

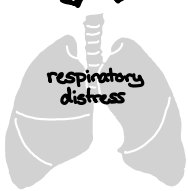


release of preformed inflammatory mediators

IgA Deficiency

Allergy:
urticaria
pruritus

Anaphylaxis:
wheezing
shock
fever
hypotension



minutes to 6 hours

Transfusion Related Acute Lung Injury

1st hit: risk factors (smoking, alcohol, etc.)
make neutrophils build up in the lungs

noncardiogenic pulmonary edema
ARDS mimic
fever
hypotension

2nd hit:
Donor anti-leukocyte IgG activates neutrophils & causes inflammatory mediator release

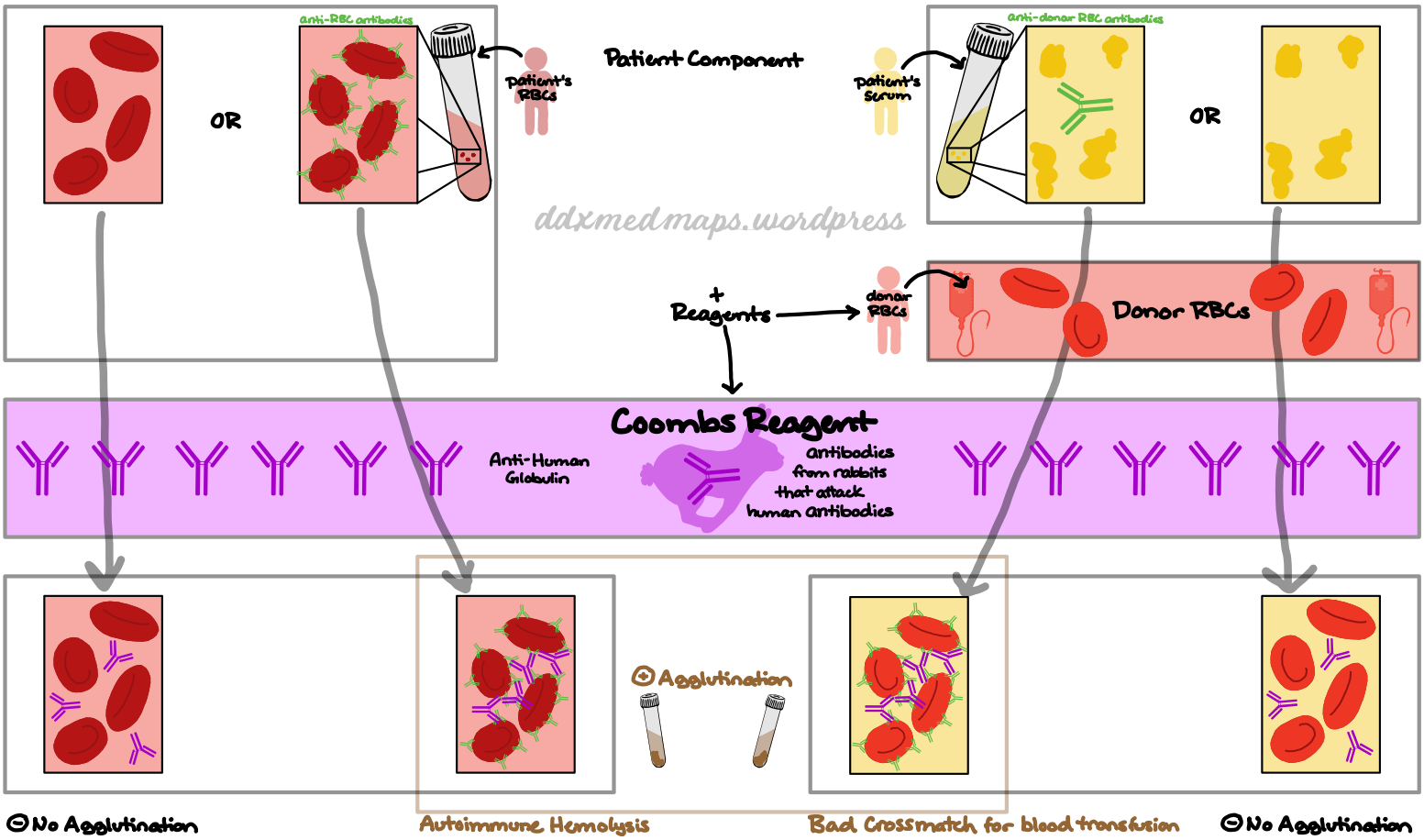
Coombs Test

DIRECT (DAT)

Detects antibodies bound to patient's RBCs

INDIRECT

Detects antibodies in patient's serum that react to donor RBCs



Genetic Immunodeficiency Disorders

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Thymic Aplastia

22q11 microdeletion
→ 3rd & 4th pharyngeal pouches
majority have Conotruncal Cardiac Defects
ToF, TA, Interrupted Aortic Arch

Velocardiofacial Syndrome

Craniofacial, Abnormal facies, Cleft palate

DiGeorge Syndrome

↓T-cells → recurrent viral & fungal infections
Thymic aplasia
no parathyroids → Hypocalcemia → tetany
Hypopituitarism?

depleted paracortical areas

↓ or absent thymic shadow (CXR)
↓ T-cell (flow cytometry)

Chronic Mucocutaneous Candidiasis

AIRE (classic) → T-cell dysfunction
→ cell mediated immunity against Candida
recurrent skin & mucosal Candida infections
persistent but noninvasive

Persistent mucosal candidiasis → thrush

#1 Primary Immunodeficiency

Isolated IgA Deficiency

unknown cause
Asymptomatic (majority)
+/- Airway & GI infections esp giardiasis
+/- Autoimmune disease
+/- Atopy
Anaphylaxis to blood w/ IgA
false ⊕ β-hCG test

normal or ↑

IgA Deficiency

IgA elevation

Severe Combined ImmunoDeficiency

- HLA match retroviral gene therapy
Treatment
+ HLA match marrow transplant
↓T-Cell Receptor Excision Circles ↓ T-cell

Failure to thrive
Chronic diarrhea
Infections
- Recurrent
- Opportunistic
- all types

Autosomal Recessive #2 ADA (Adenosine Deaminase)
RAG (↓VDJ recombination)

#1 IL-2R γ chain XR

Hyper-IgM Syndrome

B cell — CD40 — CD40L — T cell
class switching

Severe Pyogenic infections (early in life)
Opportunistic Pneumocystis Cryptosporidium CMV

#1 CD40L XR

absent germinal centers (biopsy)

Ataxia-Telangiectasia

AR
Autosomal Recessive ATM
→ detect DNA damage & halt cell cycle mutations accumulate
↑risk of Lymphoma & Leukemia
Cerebellar Atrophy → Ataxia
Spider Angiomas (Telangiectasias)
↓ B cell ↓ T cell Lymphopenia
↑AFP
↑sensitivity to radiation limit x-ray exposure

Wiskott Aldrich Syndrome

WBC & platelets can't recognize actin cytoskeleton
→ antigen presentation
Recurrent (pyogenic) Infections worsen w/ age
Thrombocytopenia & smaller platelets
↑bleeding petechiae
Eczema
↑risk of autoimmune disease & malignancy

WAS XR

IgE elevation & Eczema

↓Immunoglobulin

X-Linked (Bruton) Agammaglobulinemia

BTK defect XR
→ tyrosine kinase → B-Cell Maturation
@ 6mo (maternal IgG wanes)
↓CD19 B-cells
B cell absent in blood
live vaccines contraindicated
recurrent bacterial & enteroviral infections (meningitis)
↓lymph nodes & tonsils
absent germinal centers & 1° follicles

Common Variable ImmunoDeficiency

unknown cause → B-cell differentiation
usually diagnosed after puberty
↑risk of Lymphoma, autoimmune disease
bronchiectasis, sinopulmonary infections
↓ Plasma cell

NADPH Oxidase XR

Chronic Granulomatous Disease

↓ROS → ↓respiratory burst
Dysfunctional neutrophils
↑susceptibility to catalase positive organisms
Abnormal dihydrorhodamine (flow cytometry) test
↓green fluorescence
nitroblue tetrazolium dye reduction test (obsolete)
fails to turn blue

neutrophils

Leukocyte Adhesion Deficiency Type 1

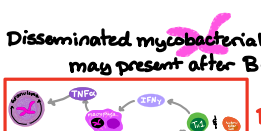
CD18 (LFA-1 Integrin)
→ migration & chemotaxis
Autosomal Recessive CD18
Late (>30d) umbilical cord separation
Absent pus
Dysfunctional neutrophils
recurrent skin & mucosal bacterial infections
↑neutrophils in blood BUT absent in wounds
impaired wound healing
↑WBC#

AD Hyper-IgE (Job) Syndrome

→ neutrophil recruitment
↓TH17 Cells
Cold (non inflamed) Abscesses (Staph)
Baby teeth retained
Autosomal Dominant STAT3
Coarse facies
Derm (eczema)
↑IgE & Eosinophils
minor trauma → Fractured bones
recurrent sinopulmonary infections

IL-12 Receptor Deficiency

Disseminated mycobacterial & fungal infections
may present after BCG vaccine



Autosomal Recessive
Defect in Pathway
↓IFNγ
↓TH1 response
#1 cause of Mendelian Susceptibility to Mycobacterial Diseases
Mycobacterium tuberculosis

Chediak-Higashi Syndrome

(lysosomal trafficking regulator)
microtubule dysfunction
→ phagosome-lysosome fusion
giant granules in granulocytes & platelets
Progressive neurodegeneration
Lymphohistiocytosis
Nystagmus
Albinism (partial)
recurrent Infections (pyogenic)
peripheral Neuropathy
mild coagulation defects
pancytopenia
Autosomal Recessive LYST

IPEX Syndrome

Immune Dysregulation
Polyendocrinopathy
Enteropathy
X-Linked
nail dystrophy
dermatitis
assc diabetes in ♂ infants
FOXP3 Deficiency → autoimmunity
→ expressed by Tregs
↑Ig Production