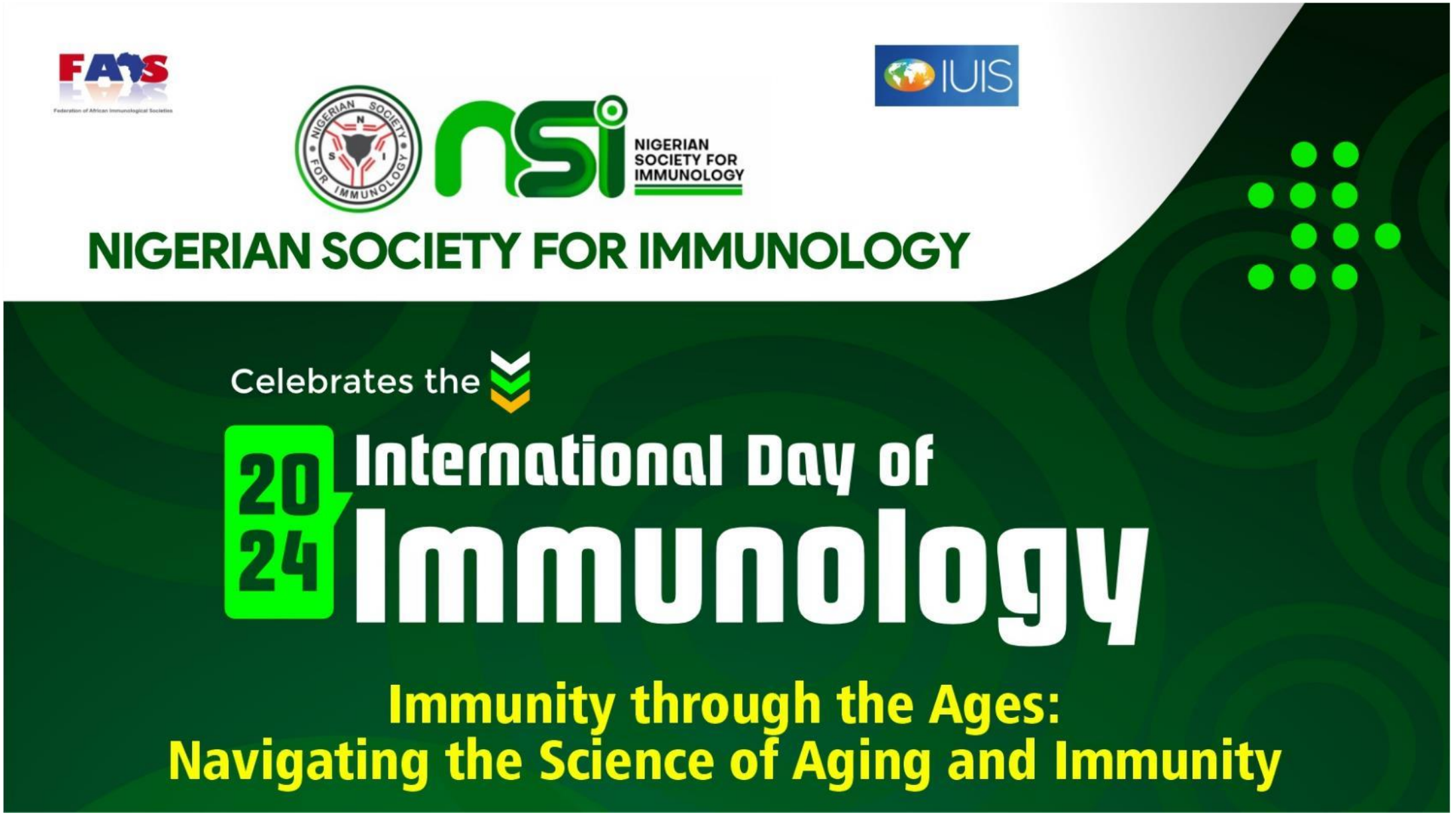
FAIS
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Celebrates the
2024
International Day of
Immunology
Immunity through the Ages:
Navigating the Science of Aging and Immunity

IMMUNITY THROUGH THE AGES: NAVIGATING THE SCIENCE OF AGING AND IMMUNITY

BY

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PRESENTATION OUTLINE

- The Immune System
- Innate And Adaptive Immune Cascade
- Components Of The Immune System
- Origin Of The Immune Cells
- Aging And The Immune System
- Development Of Innate Immune System Through The Ages
- Development Of Adaptive Immune System Through The Ages
- Development Of Immunity In The Foetus
- Development Of Immunity In The Neonate
- Development Of Immunity In The Childhood
- Development Of Immunity In The Adults
- Development Of Immunity In The Aged Population
- Effects Of Aging On The Innate And Adaptive Immunity
- Immune Changes Through The Ages
- Conclusion

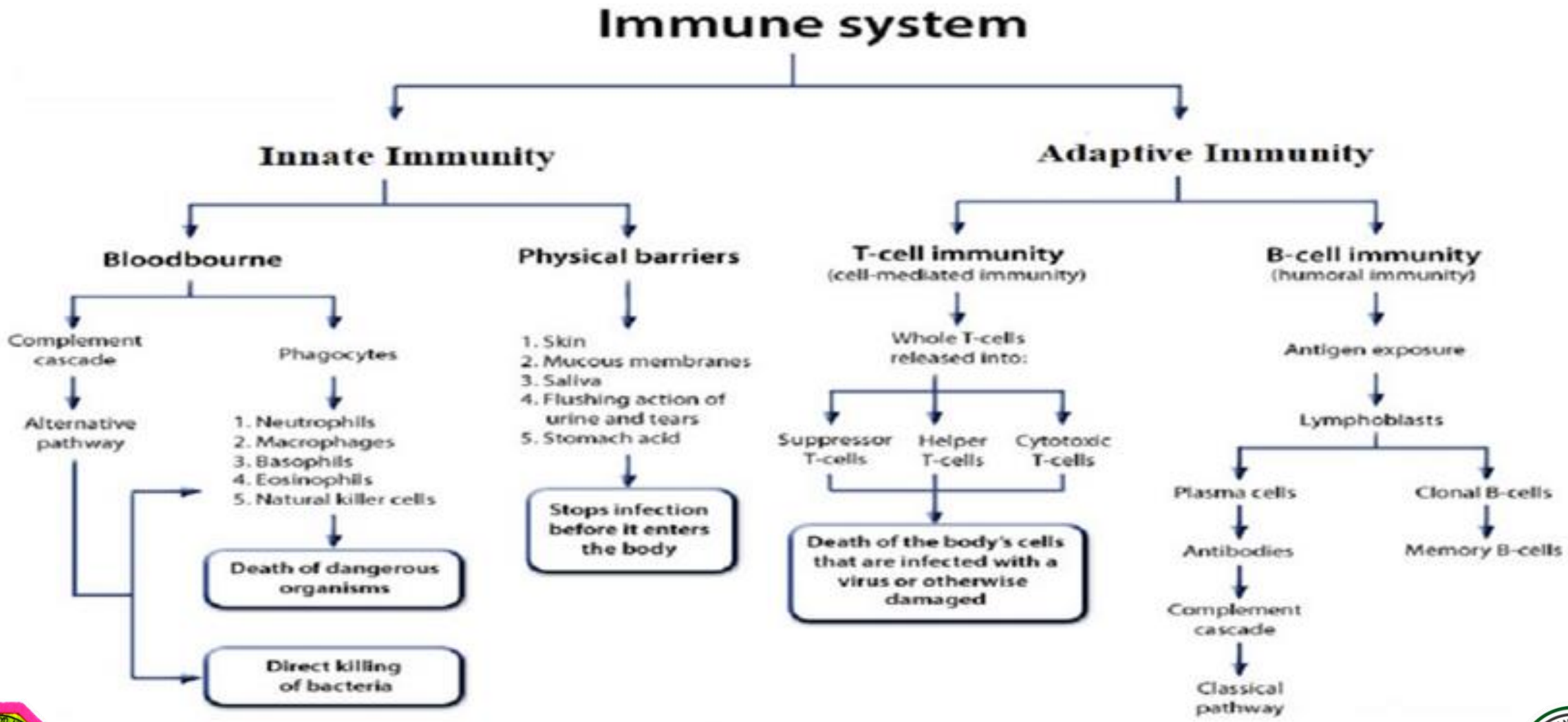
The Immune System

- Immunity is our body's defense mechanism, which works to fight pathogens and prevent diseases.
- The stronger the immune system, the easier it will achieve resistance against disease
- Our immune system is a complex of a specialized cells, and molecules that patrols, recognises and attacks antigens
- Which can be in the forms of bacteria, viruses, fungi, parasites, existing disease or any substances that is capable of eliciting immunological responses.
- Defense against pathogenic infection can occur through the Innate or Adaptive immune system.

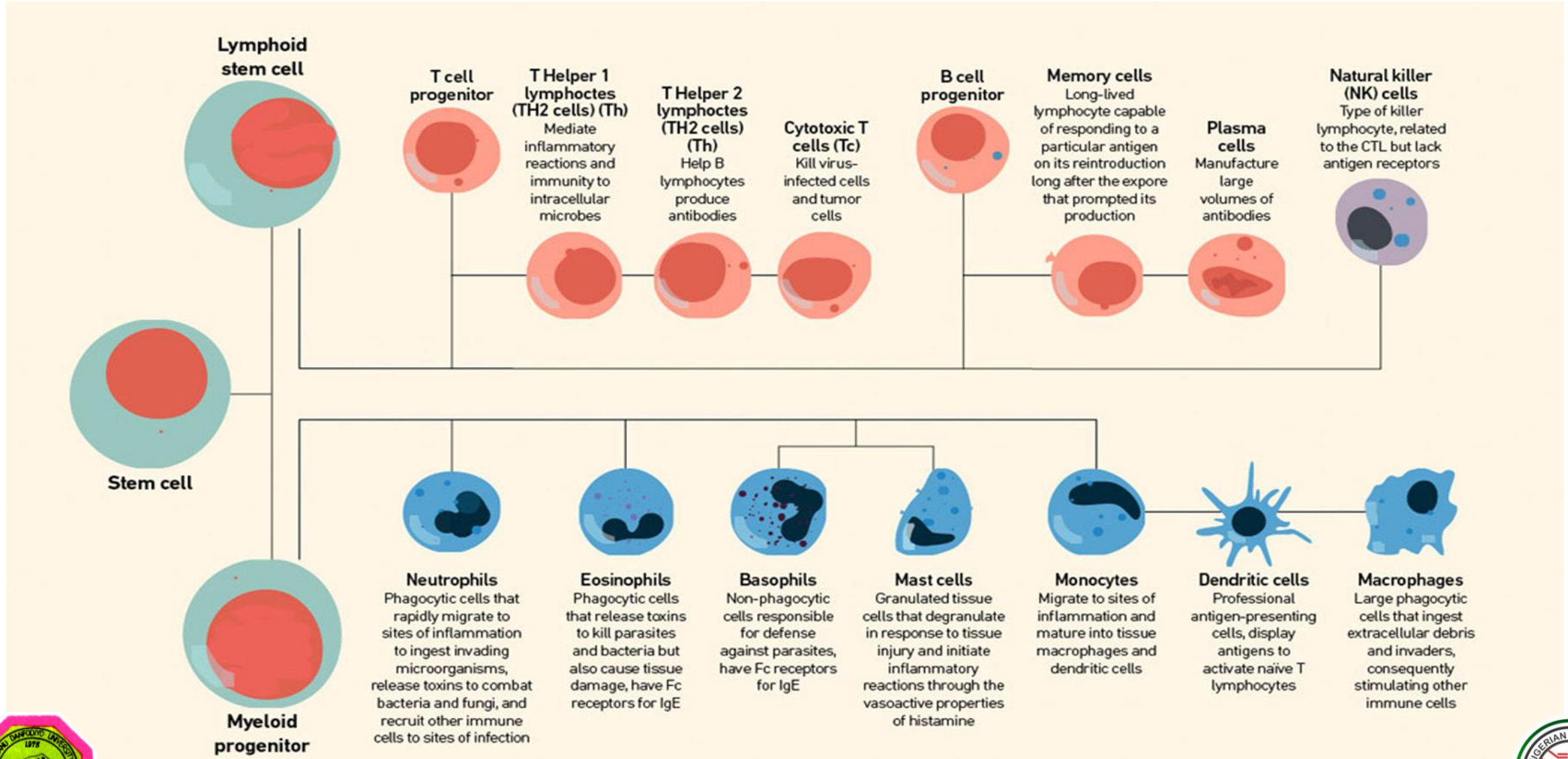
Innate and Adaptive Immune Cascade

- Innate immunity is the first line of defense, it is not specific and can respond immediately or within hours of detecting antigens .
- It does not elicits immunologic memory cells.
- Adaptive immunity is acquired over the lifetime.
- It comes into play when innate immune response can no longer cope with the pathogen.
- It requires specific antigens to produce a specific response.
- It elicits immunologic memory cells of past exposure, which enables a quicker, stronger and more efficient immune response..

Components of the Immune System



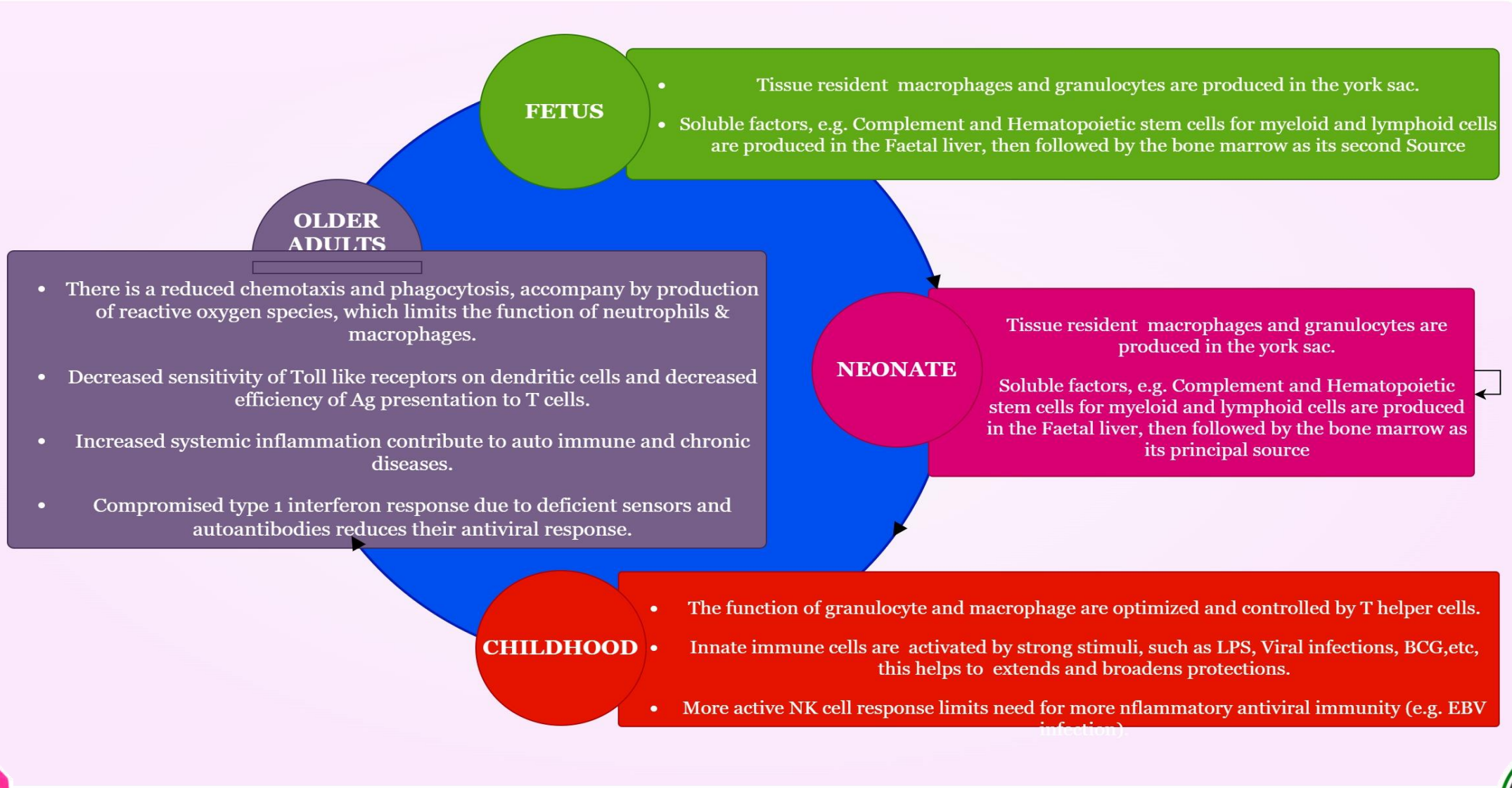
Origin of the Immune Cells



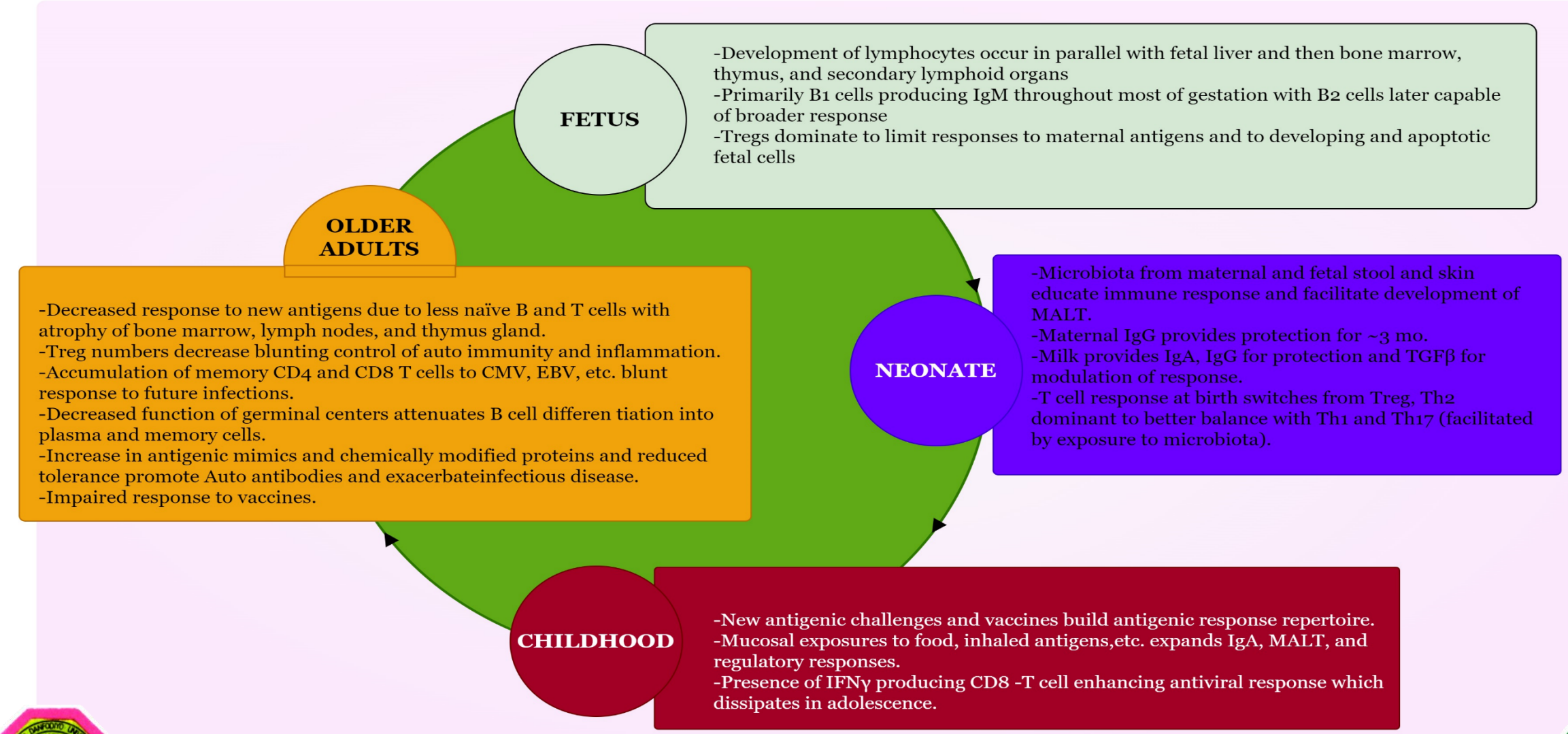
Aging and the Immune System

- The immune system undergoes many changes as individuals age from fetus to older adult.
- The ultimately goal for the immune system is to develop a balance between the effector and the regulatory functions without compromising the protections of the body from microbial attack or tumor Immunosurveillance.
- With aging, the system accumulates immune cells that were dedicated to previously encountered Antigens
- But these cells are less capable of developing immune responses against newly introduced antigens and to control responses to life's challenges, making it more difficult to maintain the balance between effector/inflammatory and regulatory/ suppressive functions.
- This can compromise the system and increase susceptibility to diseases, including inflammatory diseases, and cancers as maybe observed in various aged populations.

Development of the Innate Immune System through the Ages

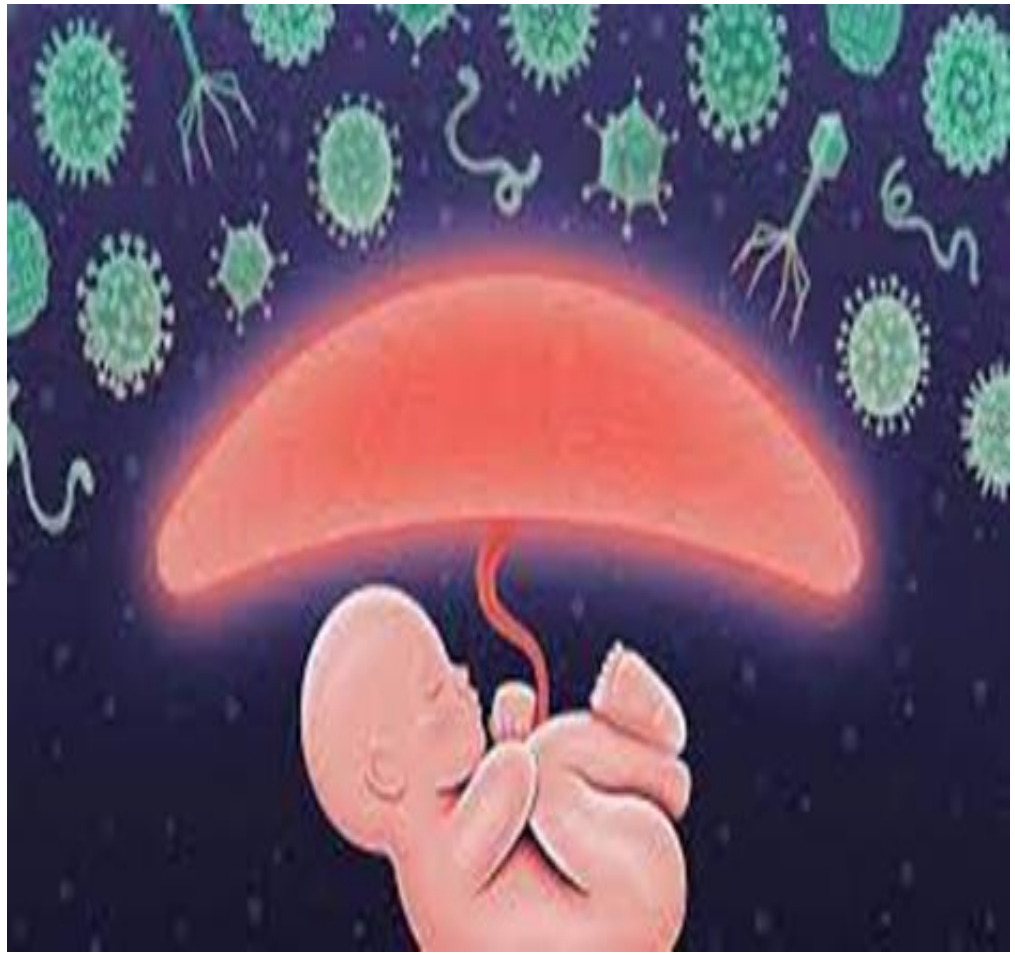


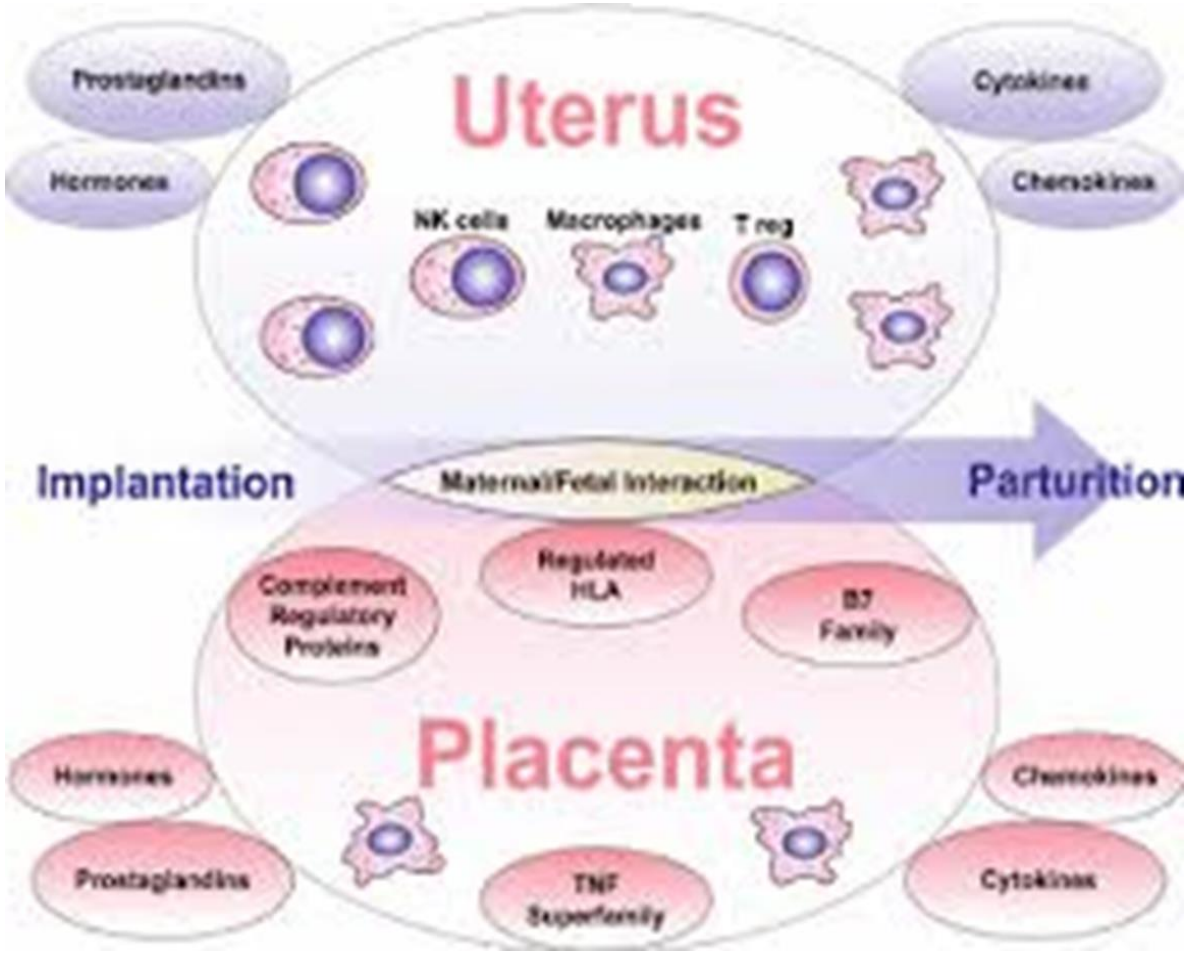
Development of the Adaptive Immune System through the Ages



Development of Immune System in Foetus

- While in the womb, the fetus is protected from infection by the mother's immune system.
- She shares her IgG protections with the fetus but her cell mediated immunity is blunted to prevent rejection of the pregnancy.
- The development of the fetal immune system starts in the yolk sac with the development of tissue resident macrophages and granulocytes.
- Although functional, their responses are weak.
- Hematopoietic stem cells for dendritic cells (DC), other myeloid cells and lymphocytes develop in parallel with the development of the foetal liver and then in the bone marrow, thymus and secondary lymphoid organs.
- Yolk sac and fetal liver generate tissue resident macrophages and DCs, such as Kupffer cells, alveolar macrophages, microglia and Langerhans cells.



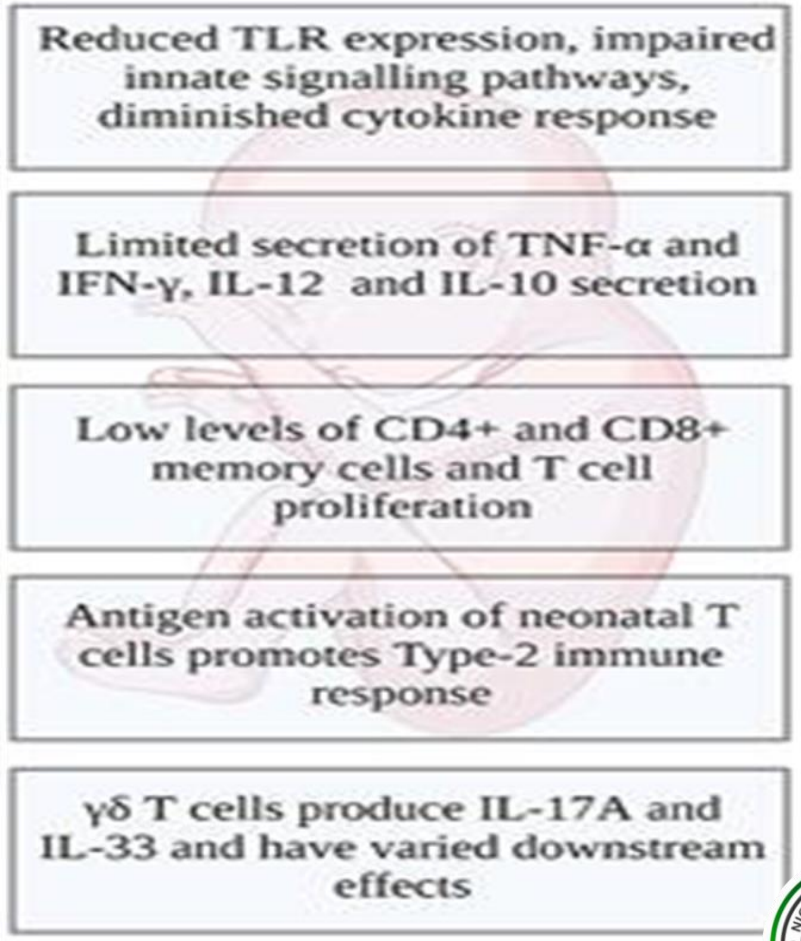

Uterus
Prostaglandins
Cytokines
Hormones
Chemokines
NK cells
Macrophages
T reg
Implantation
Maternal/Fetal Interaction
Parturition
Complement Regulatory Proteins
Regulated HLA
B7 Family
Placenta
Hormones
Chemokines
Prostaglandins
TNF Superfamily
Cytokines

Development of Immunity in the neonate

- While the neonatal immune system develops, the neonate is protected by maternal IgG that crossed the placenta, facilitated by the neonatal Fc receptor .
- The acquired protection lasts for up to 3 months before dissipating due to the normal turnover of IgG..
- After birth, mother's milk supplies IgA and IgG to protect the GI tract and help to select the colonizing microbiota.
- Mother's milk also provides TGFβ and other stimuli of tolerance to promote a regulated, immunotolerant gut immune response.
- Many changes occur upon birth as the system suddenly gets exposed to the microbial world.
- Prior to the development of mature helper T cell responses:.
- Alternative T cells, including
- Invariant Natural Killer (iNKT) cells,
- Mucosal Associated invariant T (MAIT) cells,
- interleukin-8-secreting naïve T cells and
- γδT cells

Development of Immunity in the neonate

- These help to bridge this gap with production of cytokines and chemokines. But despite these, the fetus and neonate remain susceptible to potentially life-threatening intracellular infections, which include:
  - The TORCH (toxoplasma, other, rubella (measles), cytomegalovirus, herpes simplex virus, hepatitis and HIV) infections.
- As well as others infections like
  - Herpesviruses, paramyxoviruses, influenza, malaria, tuberculosis and listeria .
- Untill the cell-mediated immune response is fully developed.



Development of Immunity in Childhood

- Immunity continues to develop through childhood with constant exposure to new antigenic challenges through infections and vaccines.
- Immunizations that elicit antibody can be initiated in the first 6 months
- but those that require replication of live attenuated viruses and induction of cell mediated protective responses (MMRV) are deferred until after 12 months of age.
- Innate immune memory is induced by exposure to strong activators, such as LPS, viral infections, or BCG, which encourage opening of chromosomal sequences to promote effector gene expression and
- Innate stem cell differentiation to increase protections against a broad range of pathogens for extended periods .
- Innate immune memory provides children with a more generic protection system as the antigen specific immunity develops its repertoire.

Immunity in an Adult population

Higher levels of all circulating immune components, adequate innate and adaptive response

High levels of IFN-γ, IL-6, IL-12 to fight infection

Memory T and B cells accumulate and hasten future immune response

Increased use of Type-1 immune response and CD8 T-cell proliferation

NK cells are regulated by inhibitory receptors and are highly active

Immunity in the Aged Population

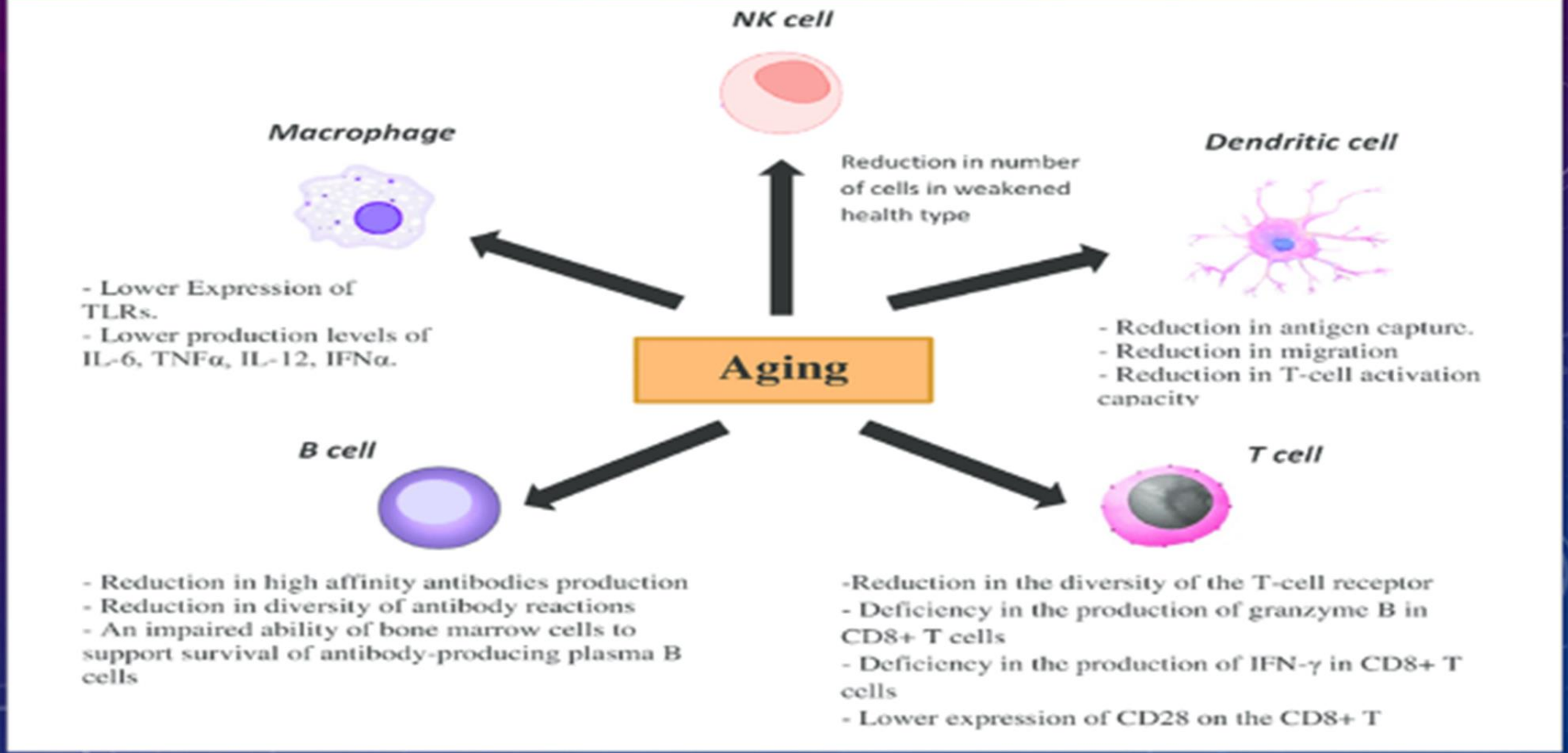
- As people age, the immune system becomes less effective in the following ways:
- The immune system becomes less able to distinguish self from nonself, As a result, autoimmune disorders become more common.
- Macrophages (which ingest bacteria and other foreign cells) destroy bacteria, cancer cells, and other antigens more slowly.
- This slowdown may be one reason that cancer is more common among older people.
- T cells respond less quickly to the antigens.
- There are fewer white blood cells capable of responding to new antigens. Thus, when older adults encounter a new antigen, the body is less able to remember and defend against it.
- Older adults have smaller amounts of complement proteins and do not produce as many of these proteins as younger people do in response to bacterial infections.

Immunity in the Aged Population

- Although the amount of antibody produced in response to an antigen remains about the same overall, the antibodies become less able to attach to the antigen.
- This change may partly explain why pneumonia, influenza, infective endocarditis, and tetanus are more common among older adults and result in death more often
- These changes may also partly explain why vaccines are less effective in older adults and thus why it is important for older adults to get booster shots (which are available for some vaccines).

These changes in immune function may contribute to the greater susceptibility of older adults to some infections and cancers.

Immunity in the Aged Population



Effects of Aging on the Innate Immune System

Natural killer cells

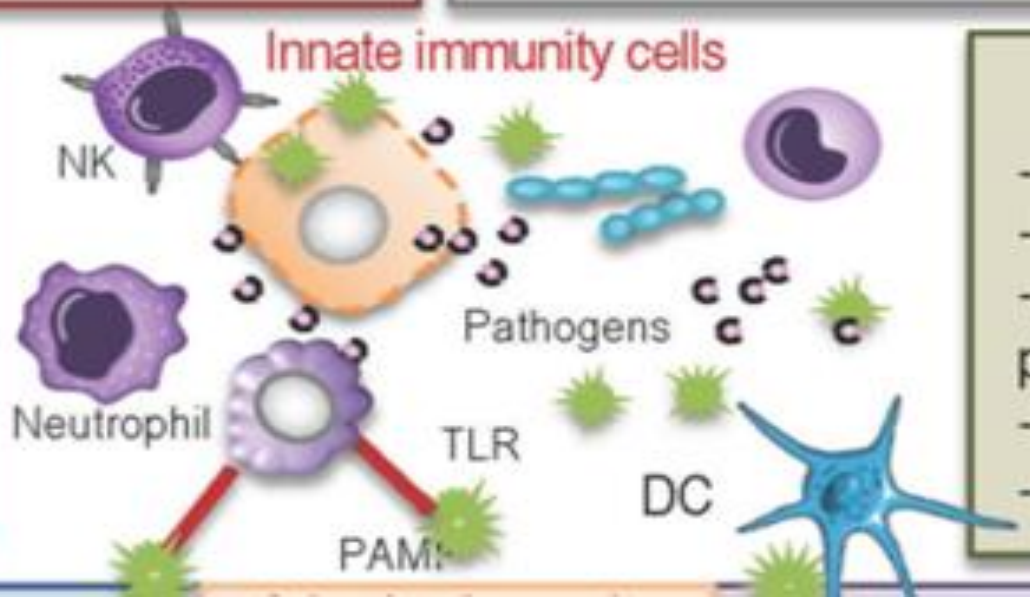
-Compensatory increase in cell numbers
-Reduced per-cell cytotoxicity
-Decreased signal transduction
-Reduced response to cytokines
-Impaired cytokine production

Monocytes and macrophages

-Reduced expression and function of TLR
-reduced killing capacity
-Reduced chemotaxis and phagocytosis
-Decreased cytokine production
-Reduced MHC-expression and signalling

Neutrophils

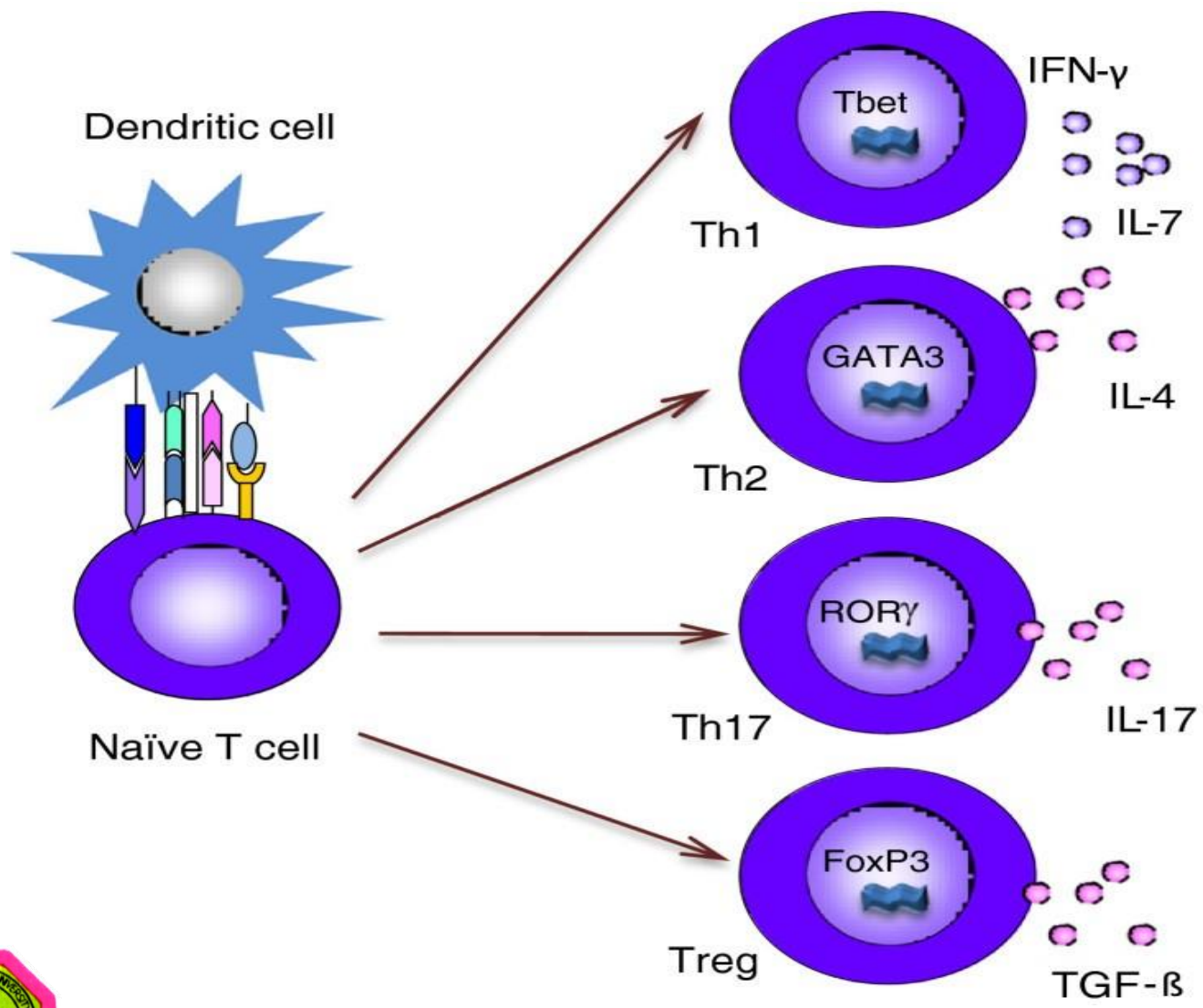
-Reduced chemotaxis
-Dysfunction of TLR
-Decreased MHC
-Impaired signalling
-Impaired cytokine production



Dendritic cells

-Reduced numbers
-Impaired function
-Altered cytokine production
-Failure to stimulate
-Impaired signalling

Effects of Aging on the Adaptive Immune System



- Alterations to TCR-structure
- Compromised assembly into signalosome
- Altered signal transduction pathways
- Alterations to co-stimulatory receptor

Age-related defects in T-cell activation

Immune Changes through the Ages

Adaptive Immunity

B cell function
Ab production

B cells

CD4 T cells
CD8 T cells
Memory T cells

T cells

T Cells

Thymus Involution

Aging

Innate Immunity

Neutrophil

Decreased function

Macrophage

TLR activity decreases
IL-6, 12, TNF-α, IFNα increases
No Phagocytosis

DC

No stimulation of T cells
IFN, ICAM-1 production

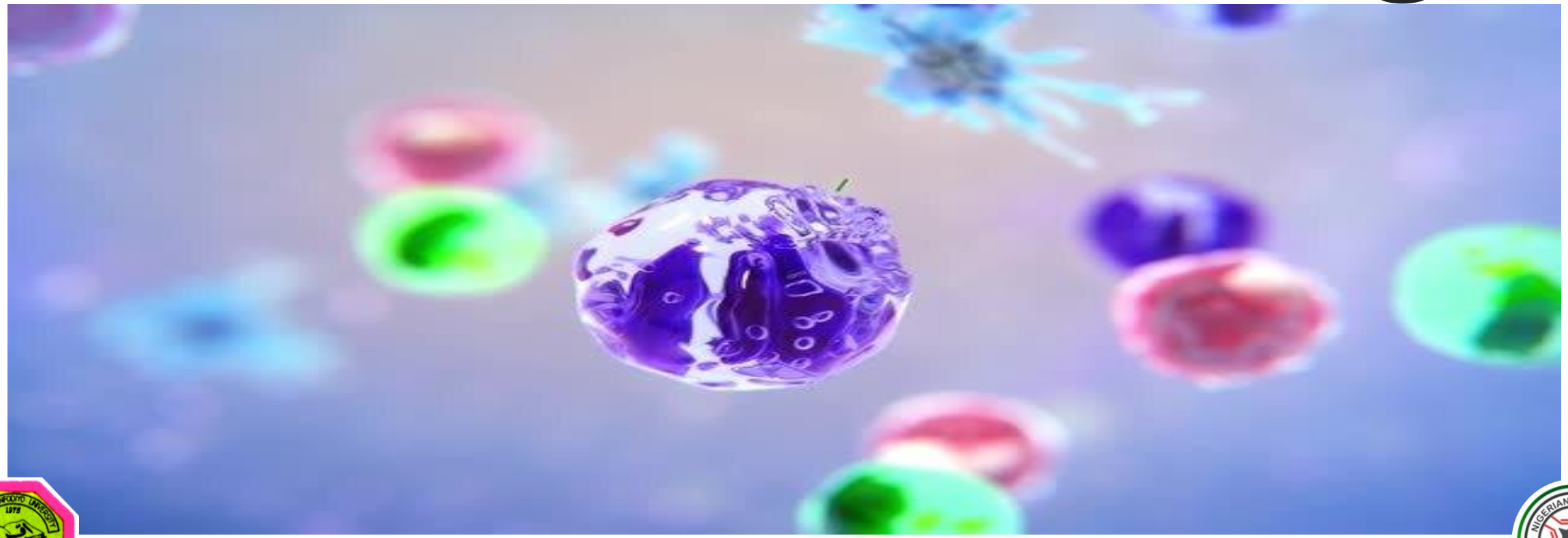
NKT

Decreased numbers and
Decreased cytotoxic activity

Conclusion

- The immune system is the body's defense against foreign or dangerous invaders.
- The immune system changes throughout life.
- ✓At birth, acquired (specific) immunity is not fully developed.
- ✓However, newborns have some antibodies, which crossed the placenta from the mother during pregnancy. These antibodies protect newborns against infections until their own immune system fully develops.
- ✓Breastfed newborns also receive antibodies from the mother in breast milk.
- As people age, the immune system becomes less able to distinguish self from nonself.
- As a result, autoimmune disorders , Diabetes, CVD, Cancers and other inflammatory diseases become more common and prevalent amongst the aged population.

Thanks for Listening



Naïve CD4 cells
Th2 & Th17 cells
Regulatory T cells
B1 cells
CD56+ natural killer cells

Th1 & Tfh cells
Memory T cells
Memory B cells
CD16+ natural killer cells
Antigen-presenting cells

Many components of the immune system undergo significant changes between infancy and adulthood.

THE END