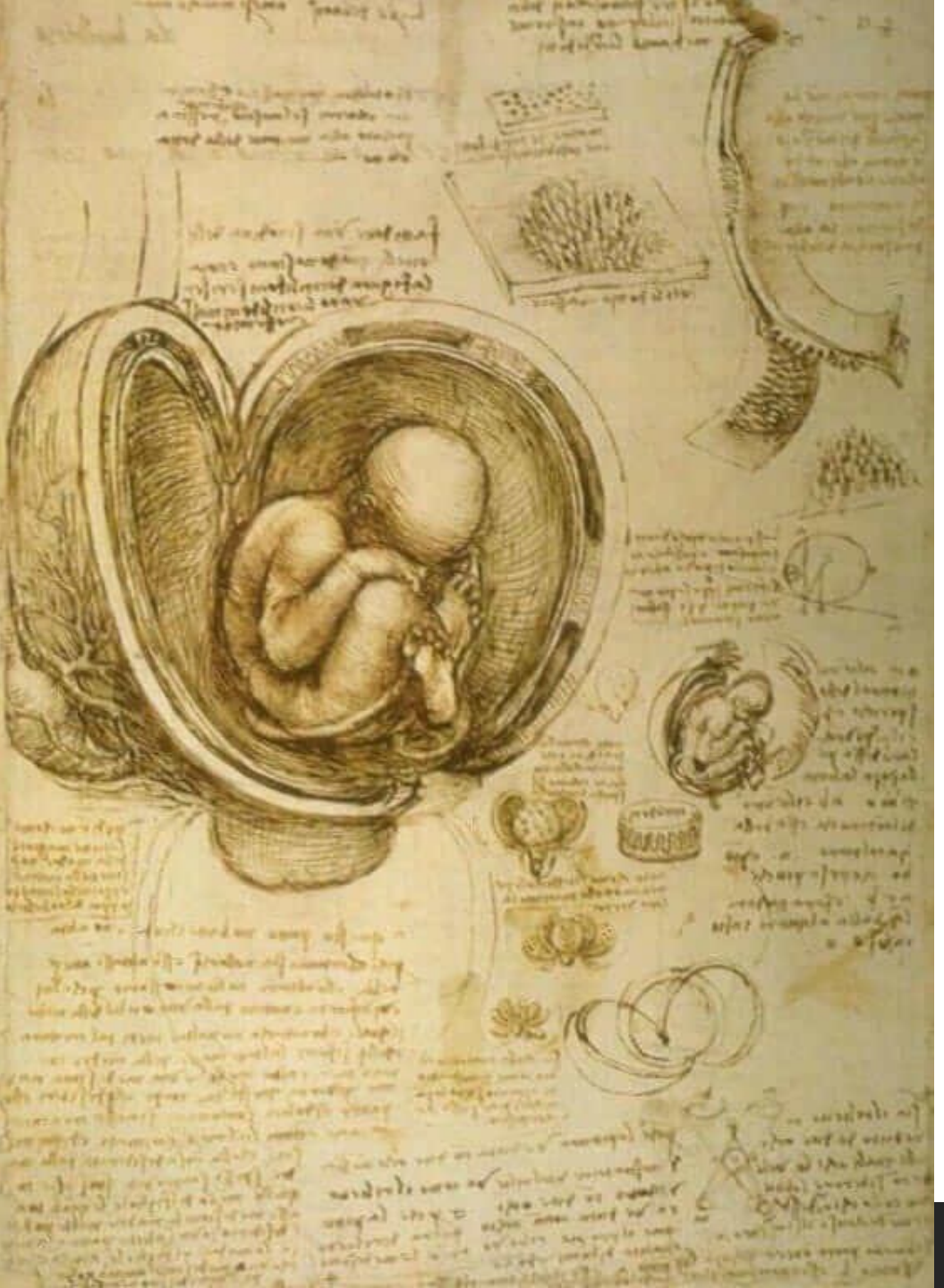


Modulation of immune development and maturation in the offspring by maternal environment

ILHEM MESSAOUDI, PHD

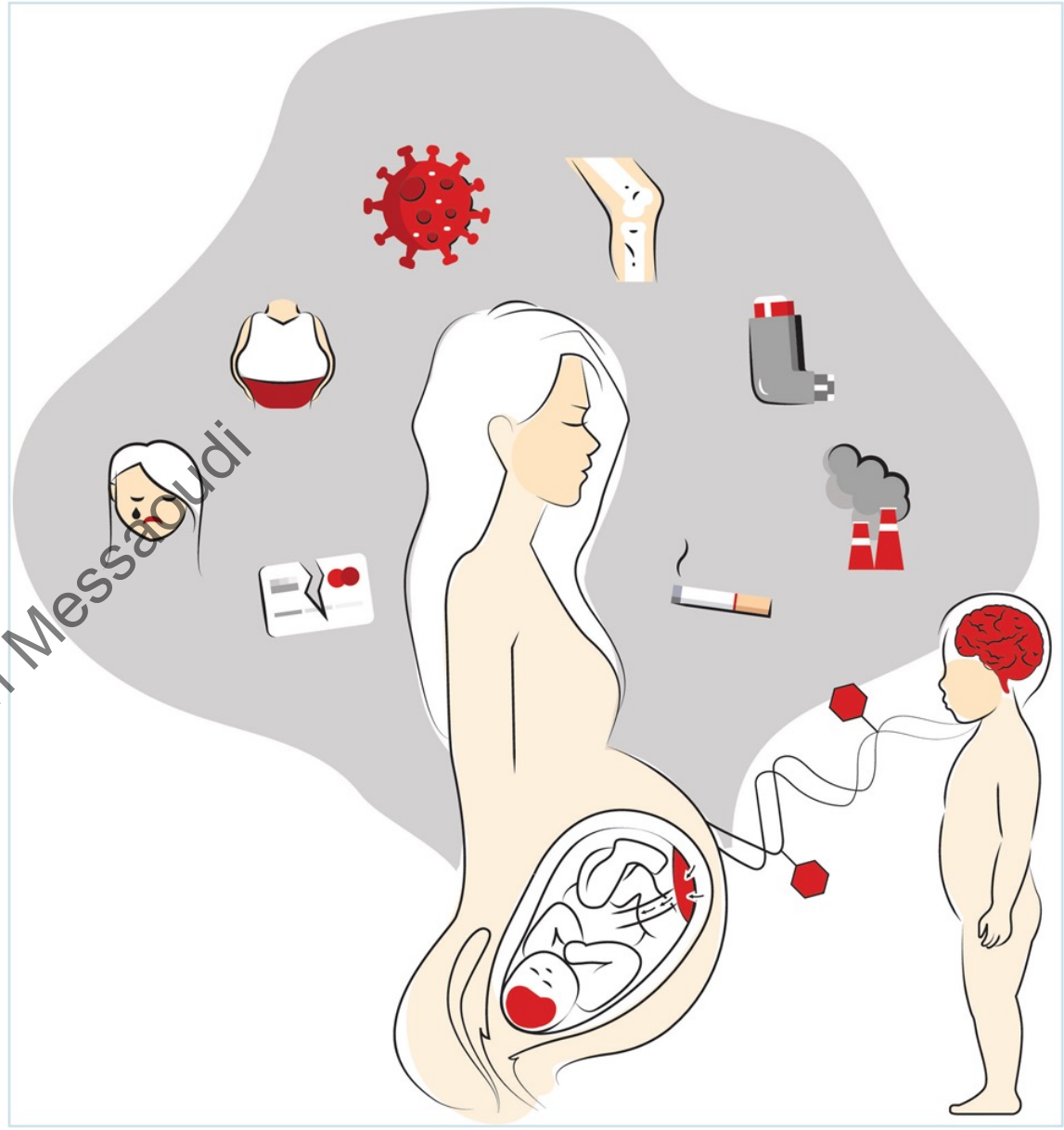
UNIVERSITY OF CALIFORNIA IRVINE, SCHOOL OF BIOLOGICAL SCIENCES

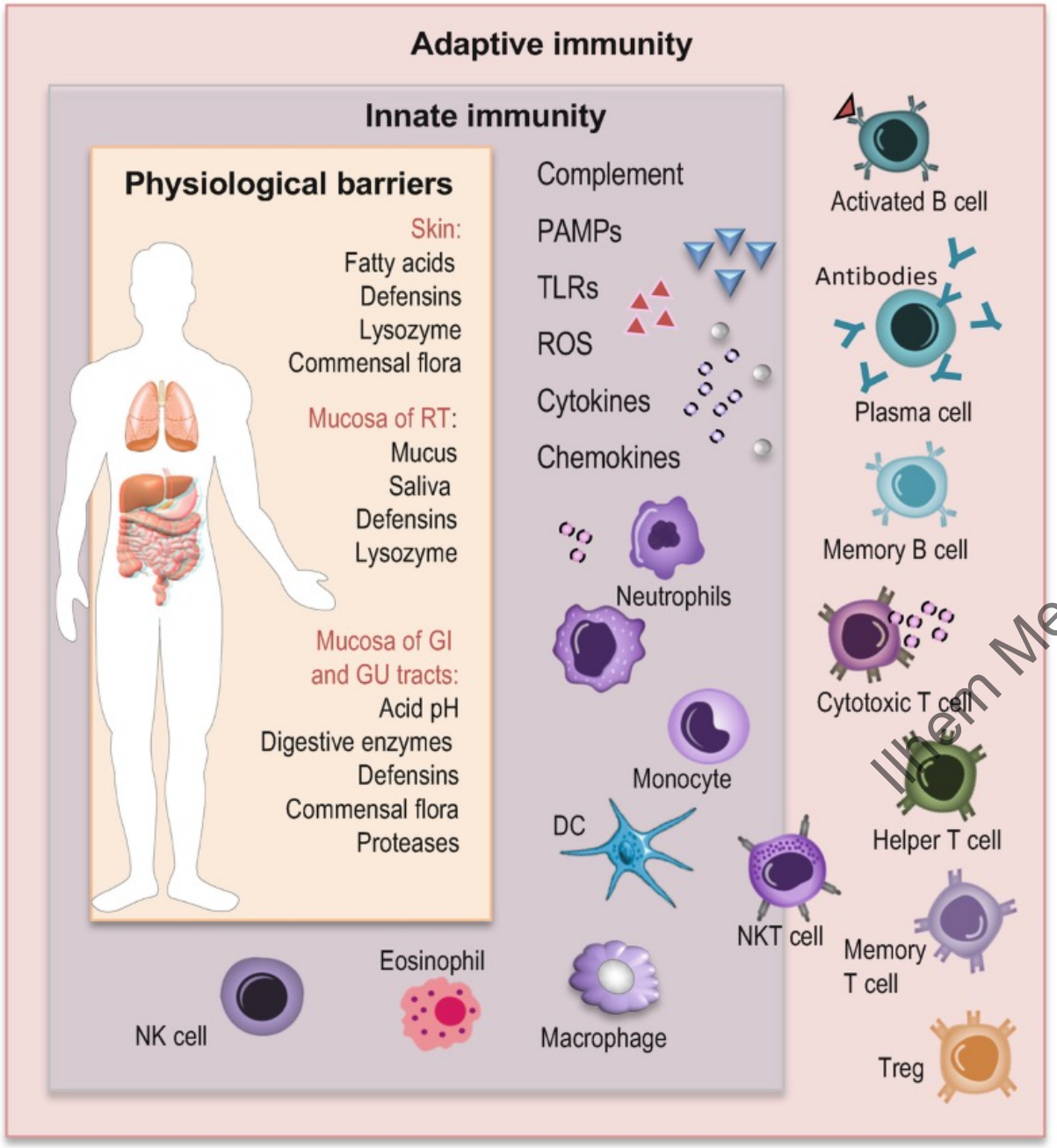
(SOON TO BE UNIVERSITY OF KENTUCKY COLLEGE OF MEDICINE)

fetus in womb by Leonardo da Vinci, circa 1511

Developmental origins of health and disease

Nutritional or other environmental stimuli during critical periods of growth and development have the potential to permanently "program" the structure and/or function of cell populations, emerging organ systems, or homeostatic pathways

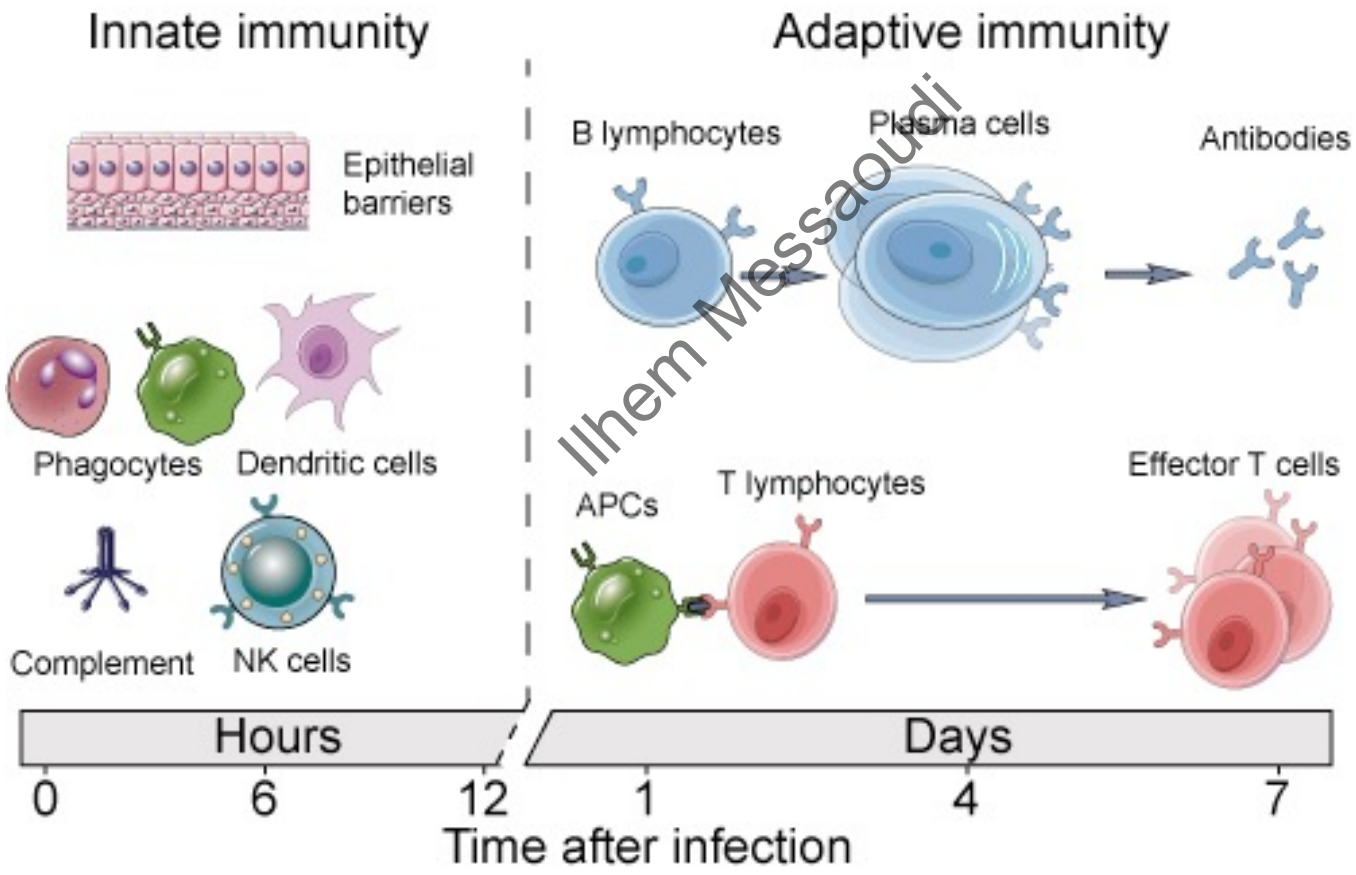




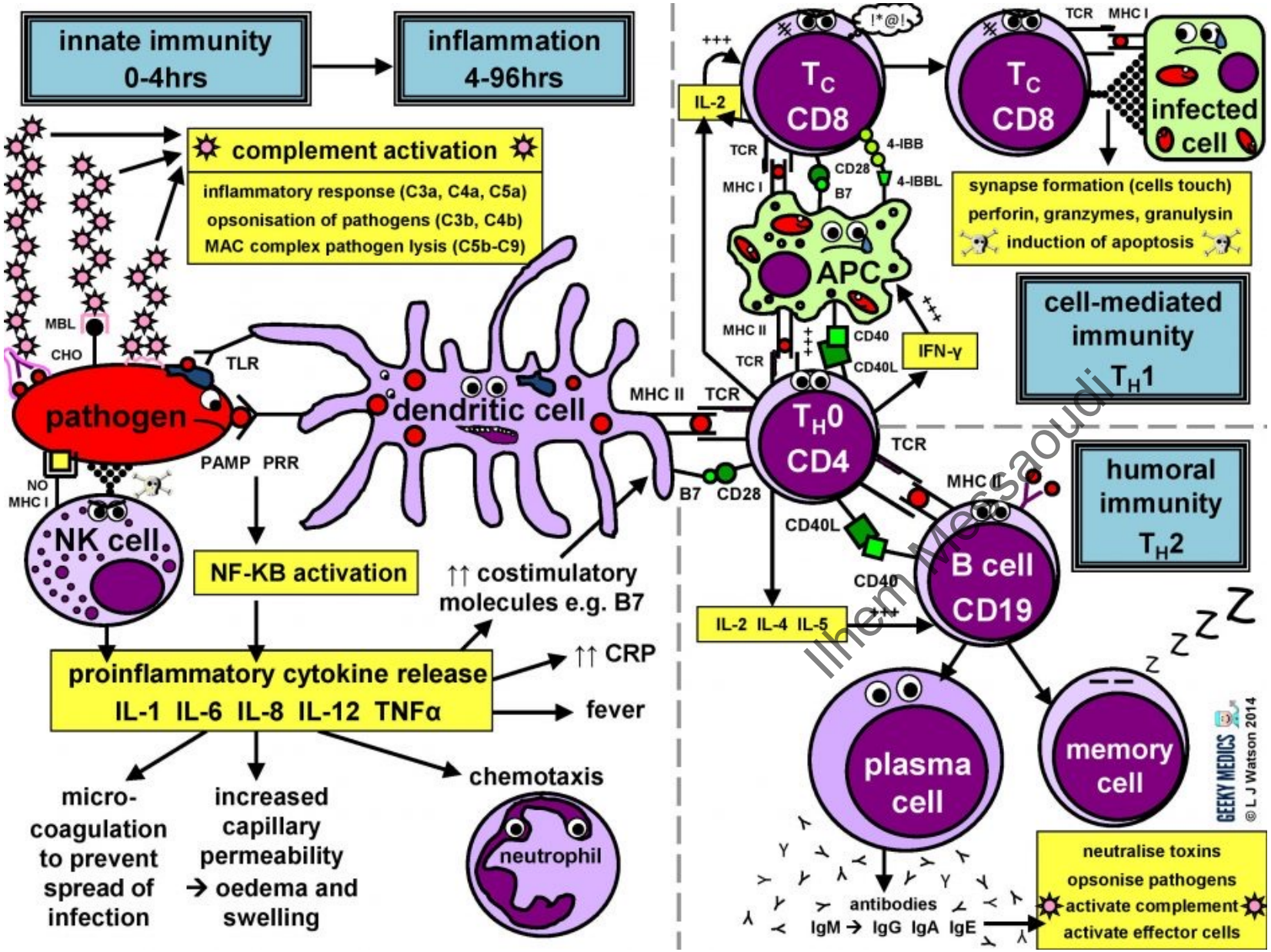
Overview of the immune system

Muller L. et al., 2019
Biochemistry and Cell Biology of Ageing: Part II Clinical Science

Innate versus adaptive immuntiy

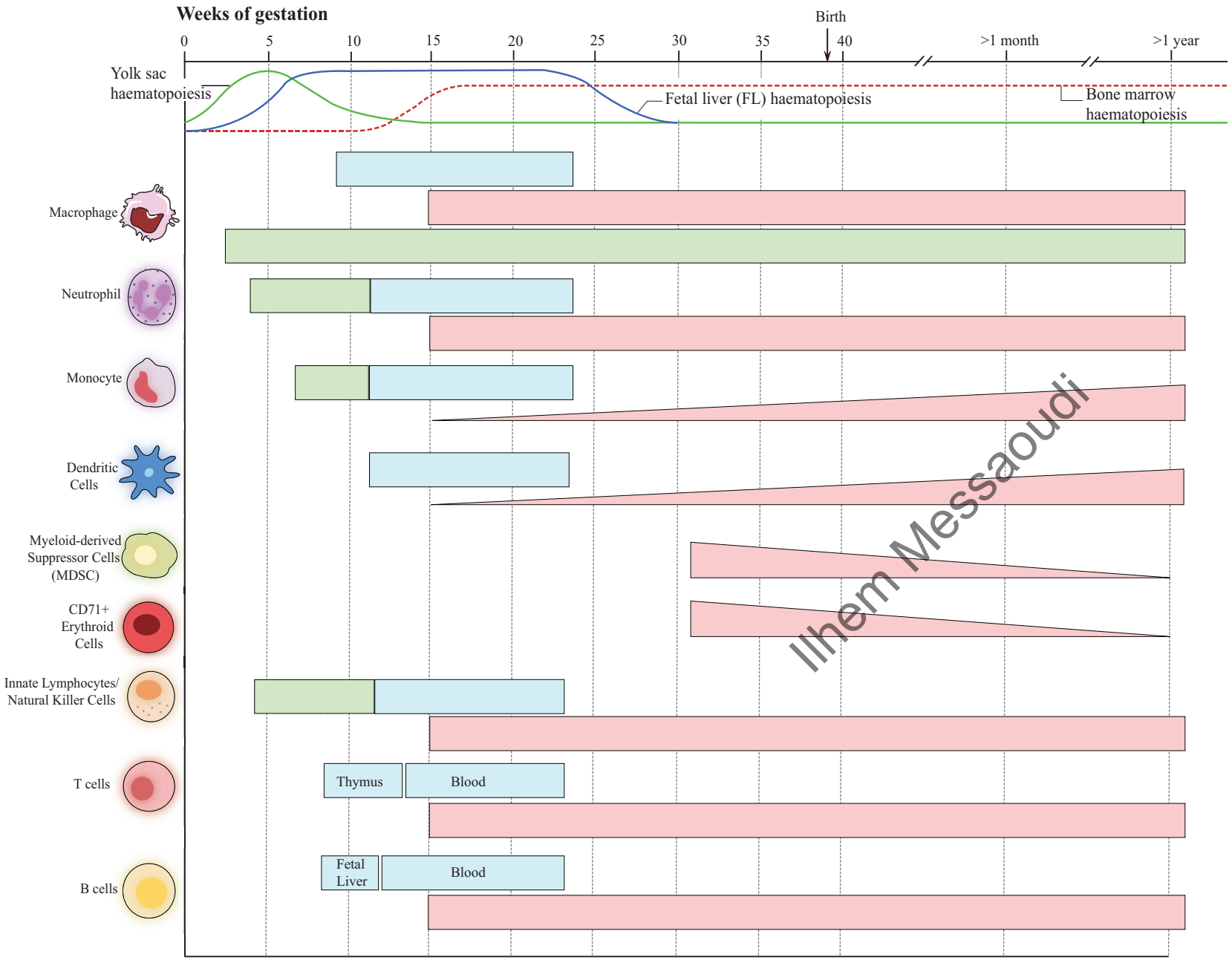


https://www.creative-diagnostics.com/innate-and-adaptive-immunity.htm



Immune response to pathogens

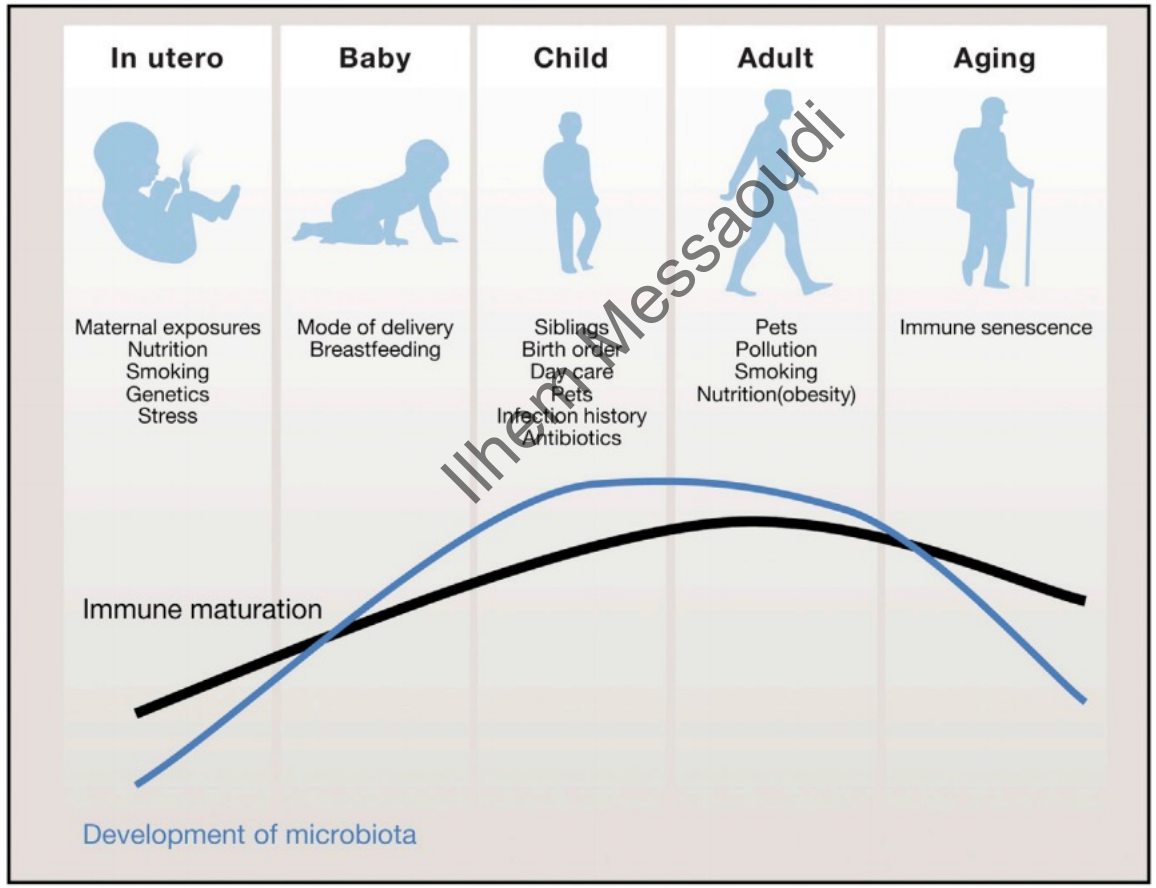
https://geekymedics.com/immune-response/



Immune ontogeny

https://doi.org/10.1002/JLB.3RI0619-181R

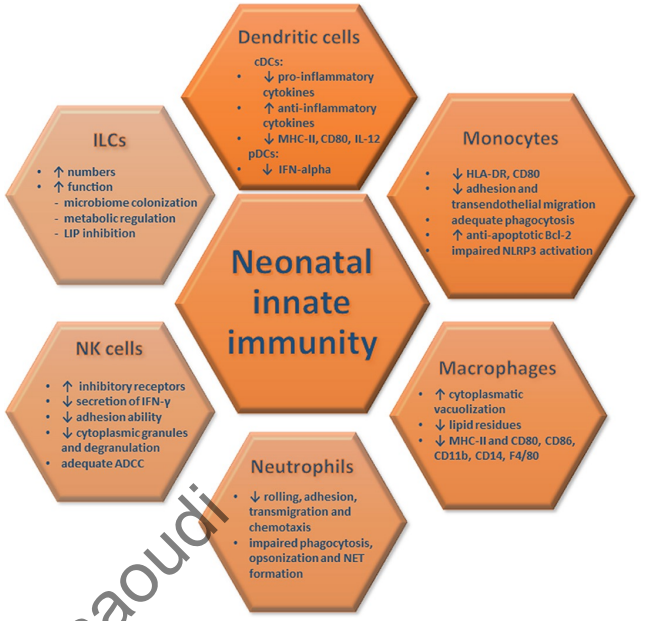
Immunity changes across the life span

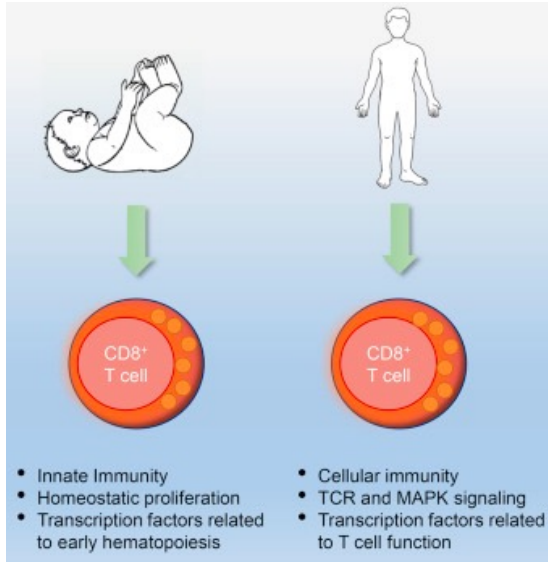


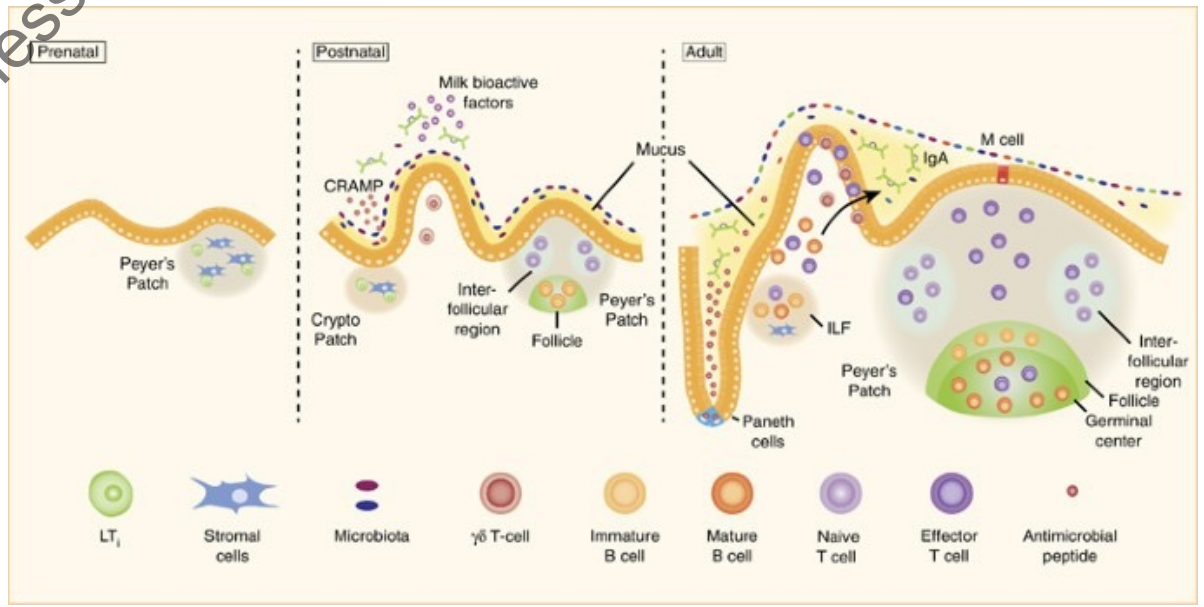
http://dx.doi.org/10.1016/j.immuni.2017.04.005

Neonatal immune system is immature, but functional

- Neonates rely more heavily on the innate immune branch
- Adaptive branch is sluggish and biased towards Th2 responses
- Mucosal sites do not yet have a fully developed local immune system

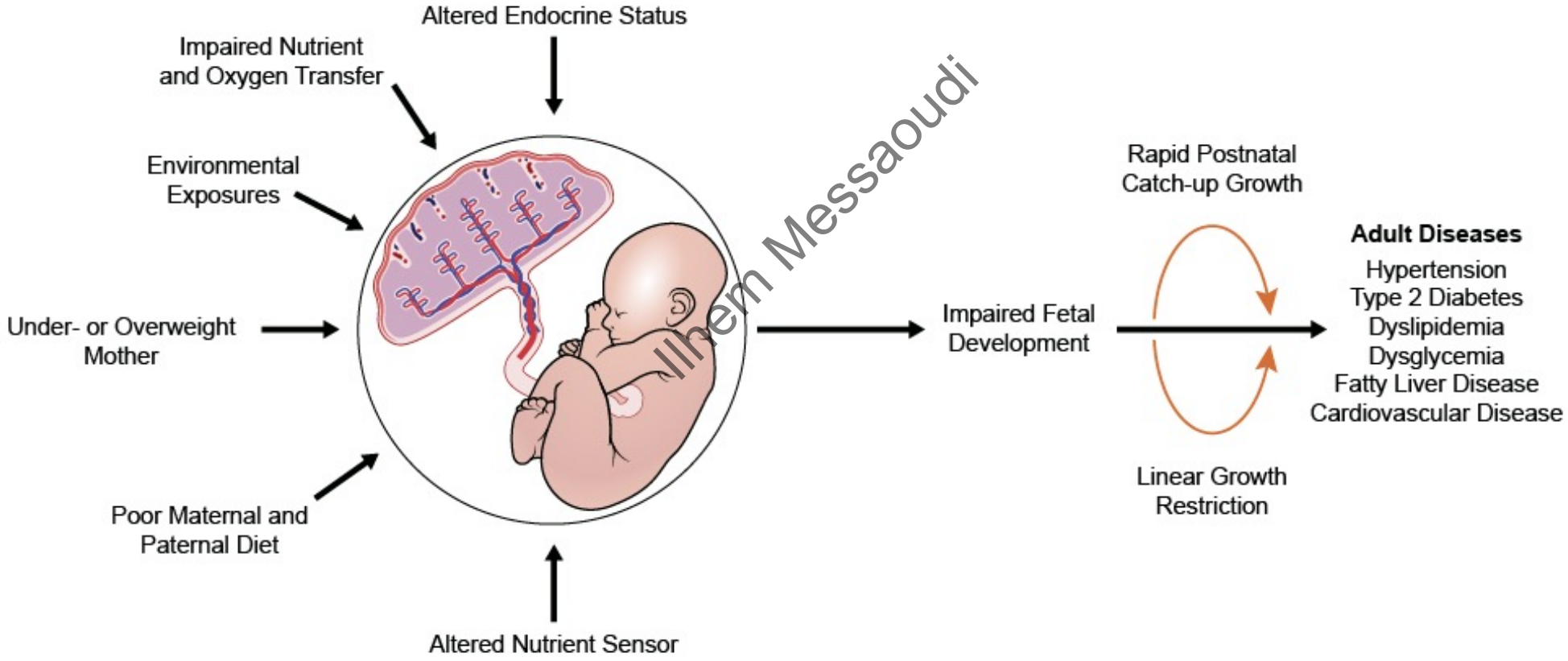






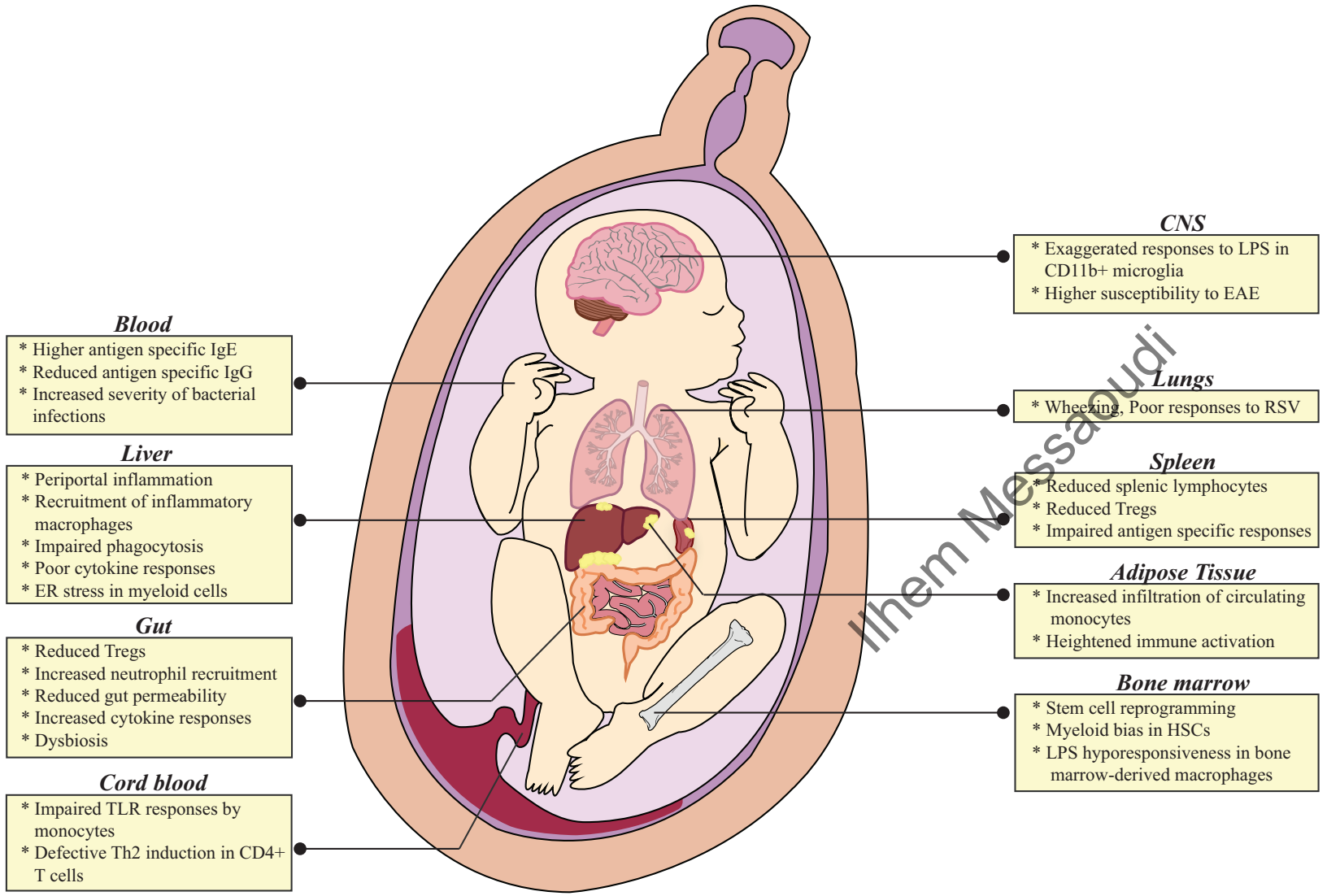
https://doi.org/10.1016/j.celrep.2016.10.056
https://www.nature.com/articles/mi201681
https://doi.org/10.3389/fped.2020.00005

Maternal health and immunological outcomes in the offspring



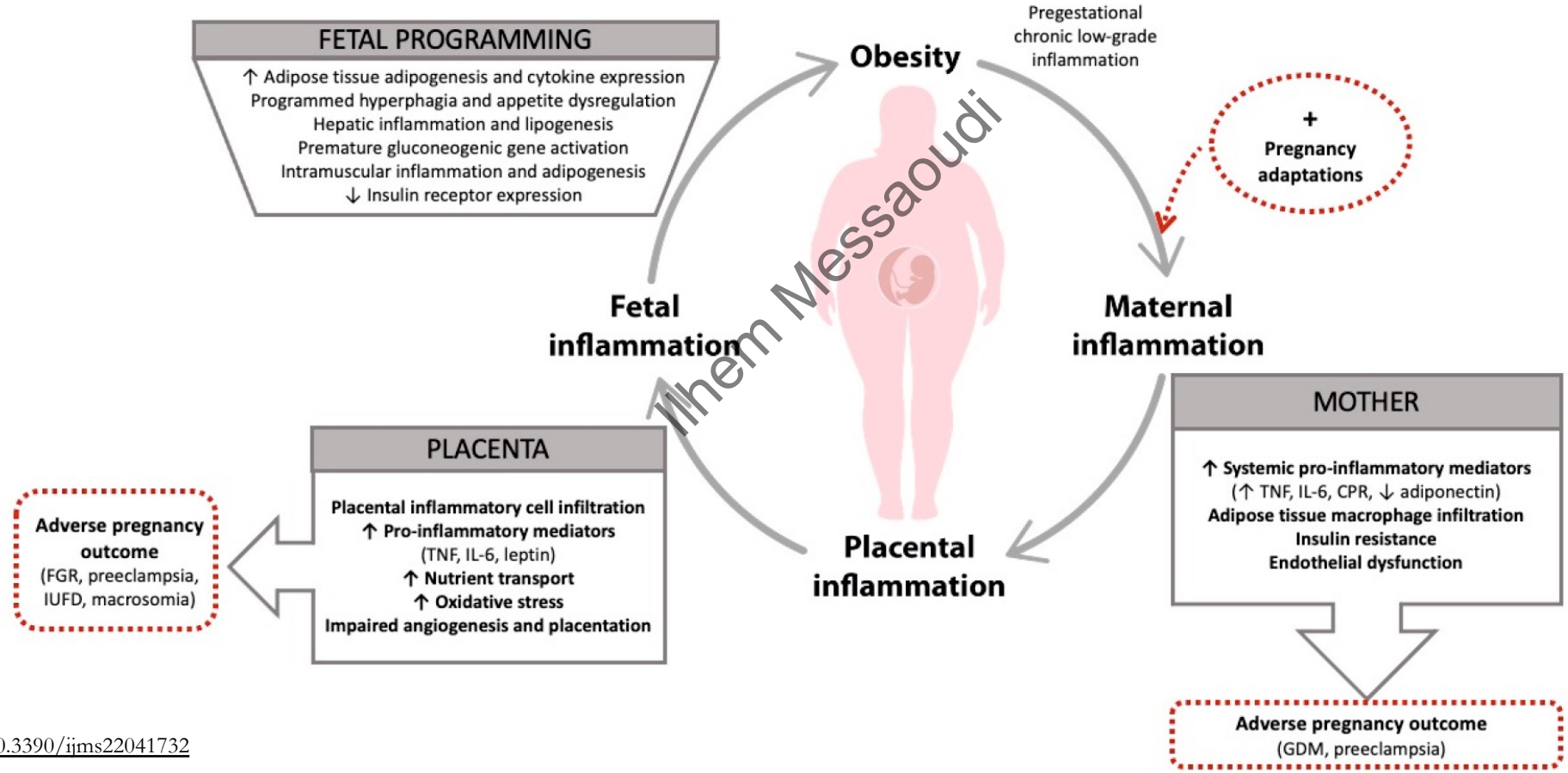
Hoffman D.J. et al.,
https://doi.org/10.1152/physrev.00002.2020

Pregravid obesity and immune outcomes in the infant



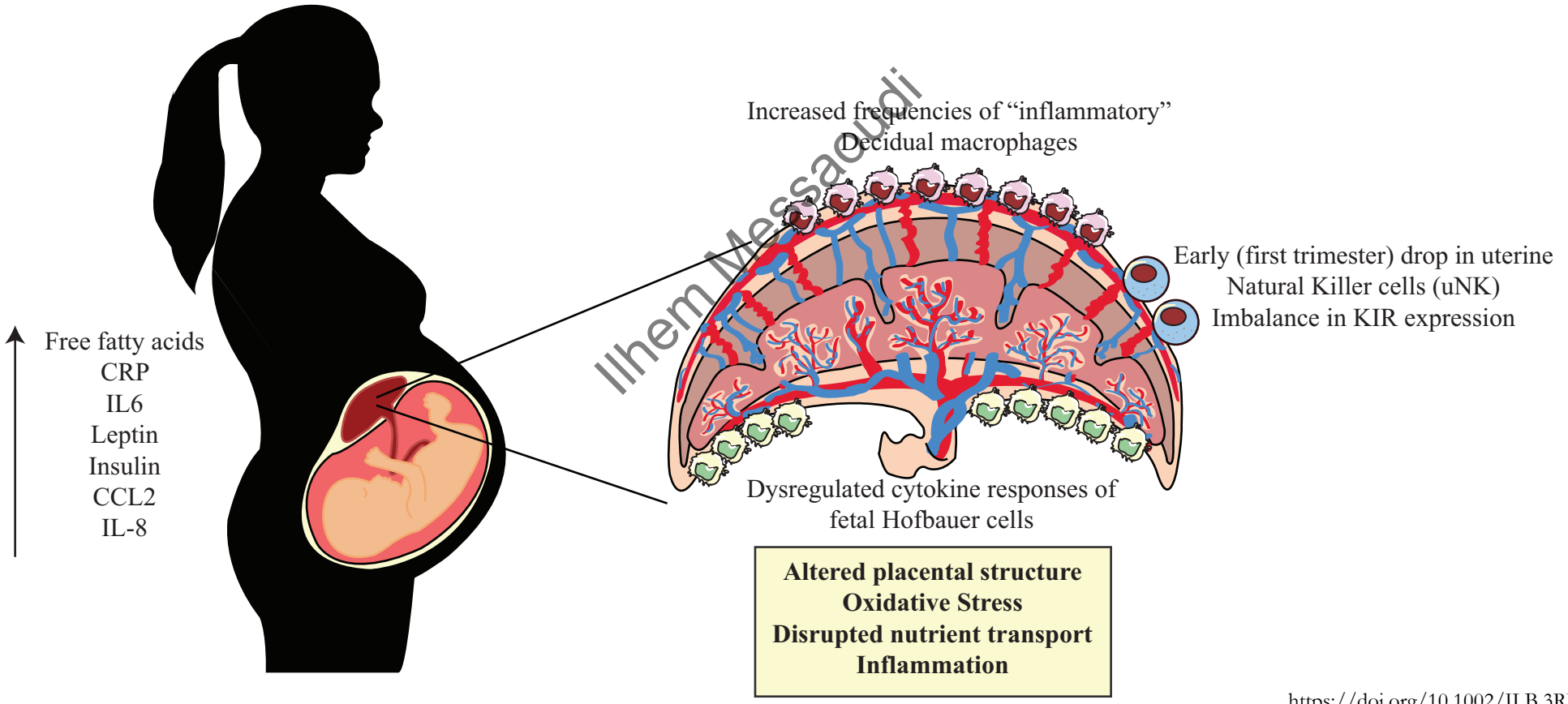
https://doi.org/10.1002/JLB.3RI0619-181R

Mechanisms of offspring immune reprogramming by maternal obesity



https://doi.org/10.3390/ijms22041732

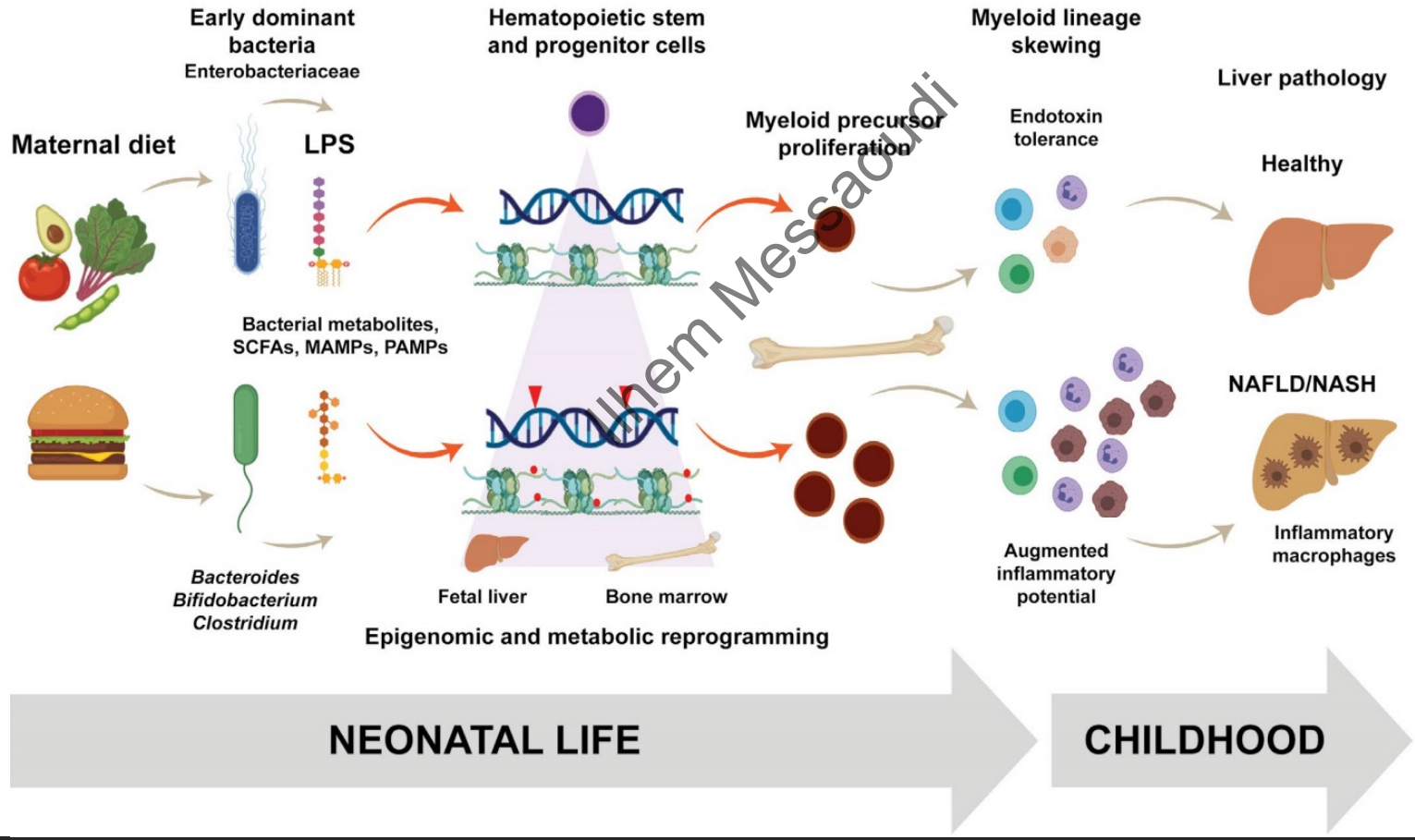
The gate keeper - placenta



Altered placental structure
Oxidative Stress
Disrupted nutrient transport
Inflammation

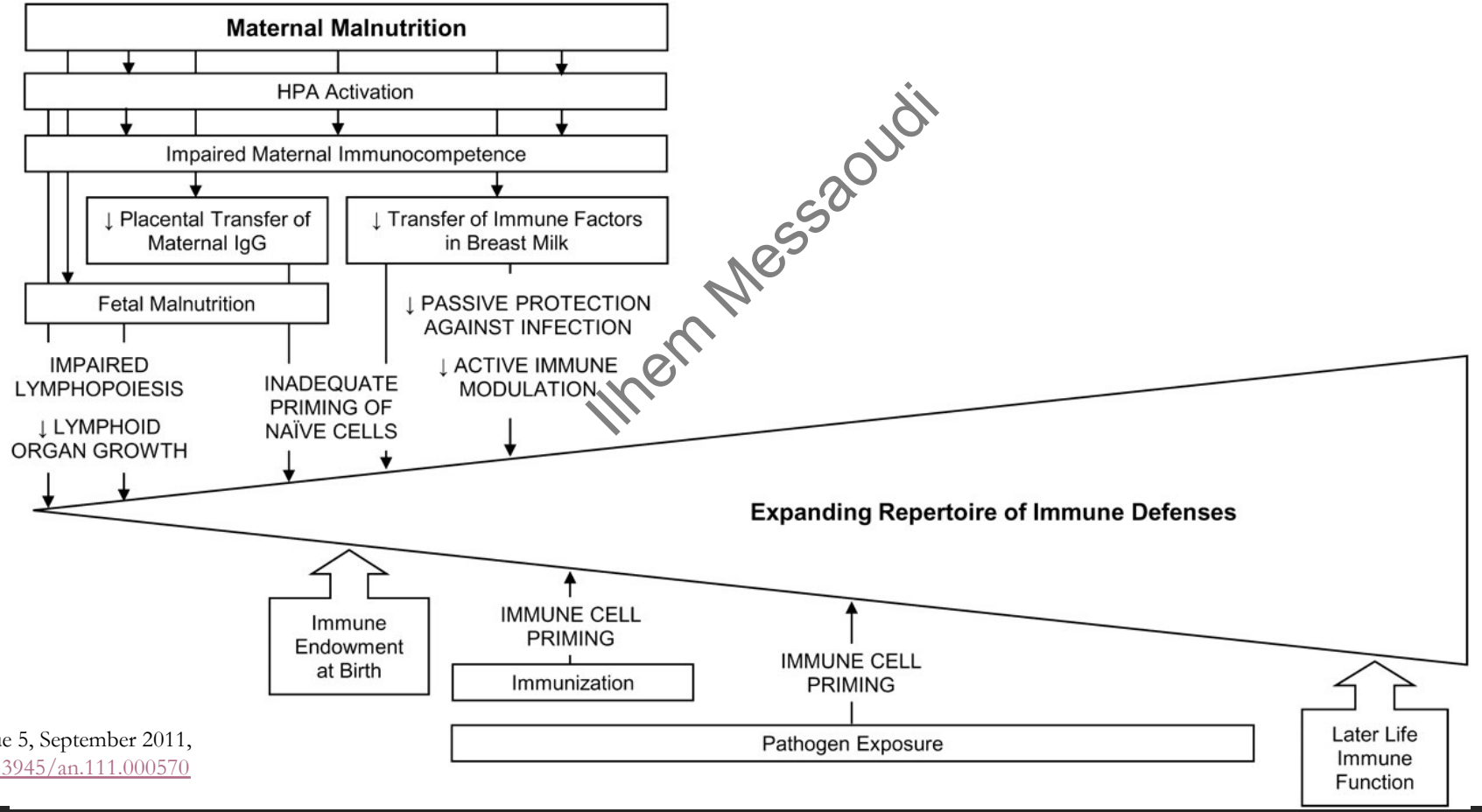
https://doi.org/10.1002/JLB.3RI0619-181R

Epigenetic rewiring of fetal immune cells by maternal microbiota

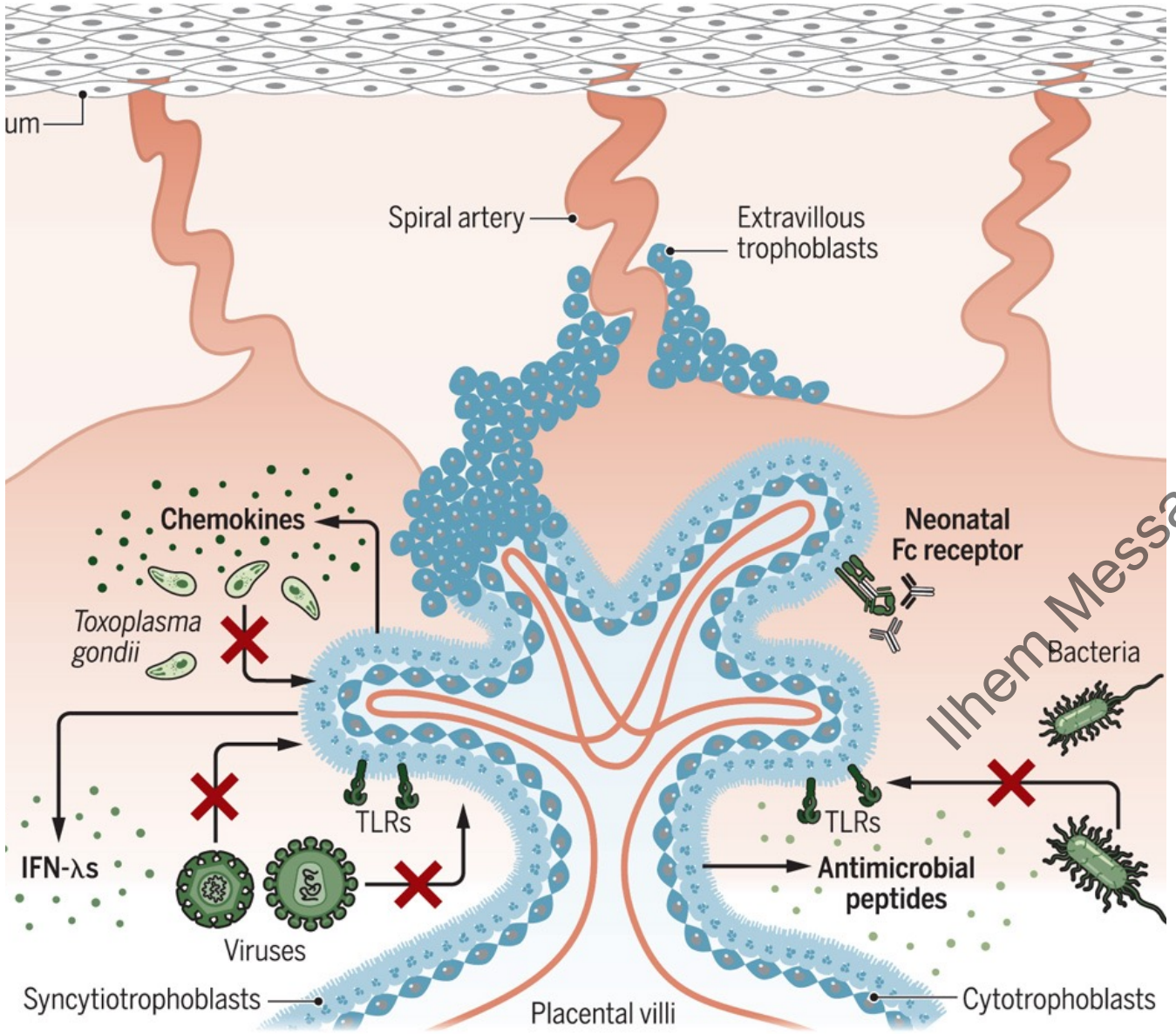


Jonscher K.R. et al., J. Cell Immun 2020

Maternal malnutrition disrupts development of fetal immune system



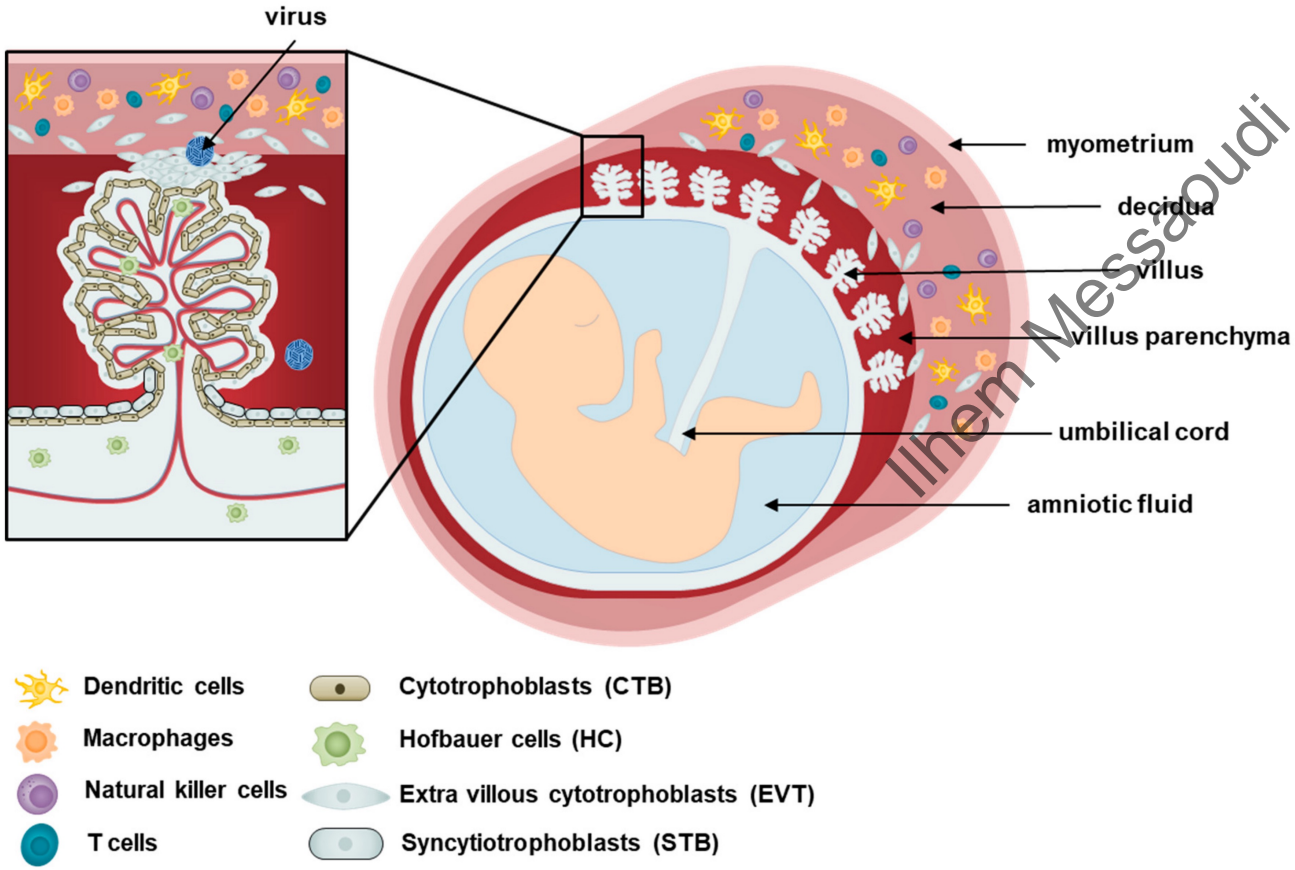
Amanda C. Palmer
Advances in Nutrition, Volume 2, Issue 5, September 2011, Pages 377–395, https://doi.org/10.3945/an.111.000570

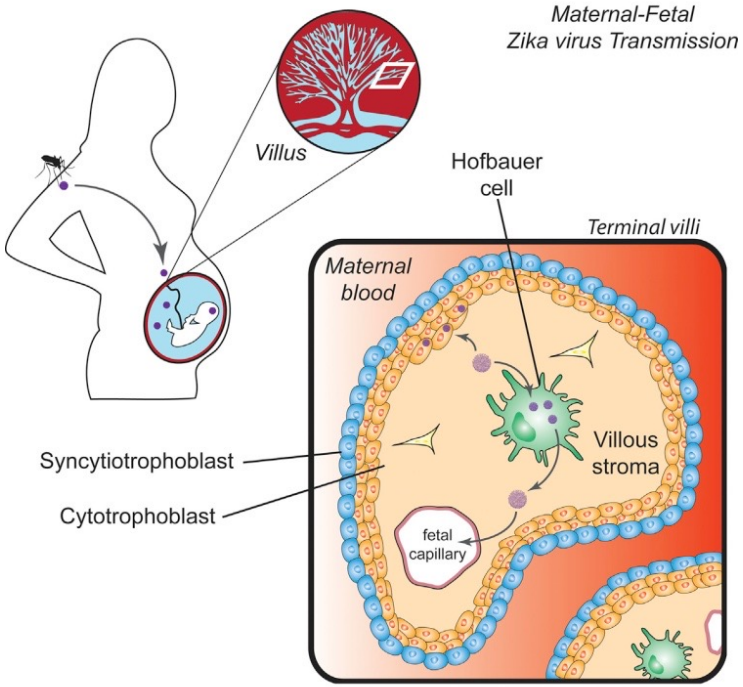


Mechanisms of placental immune defenses

Ander S. E., et al.,
DOI: 10.1126/sciimmunol.aat6114

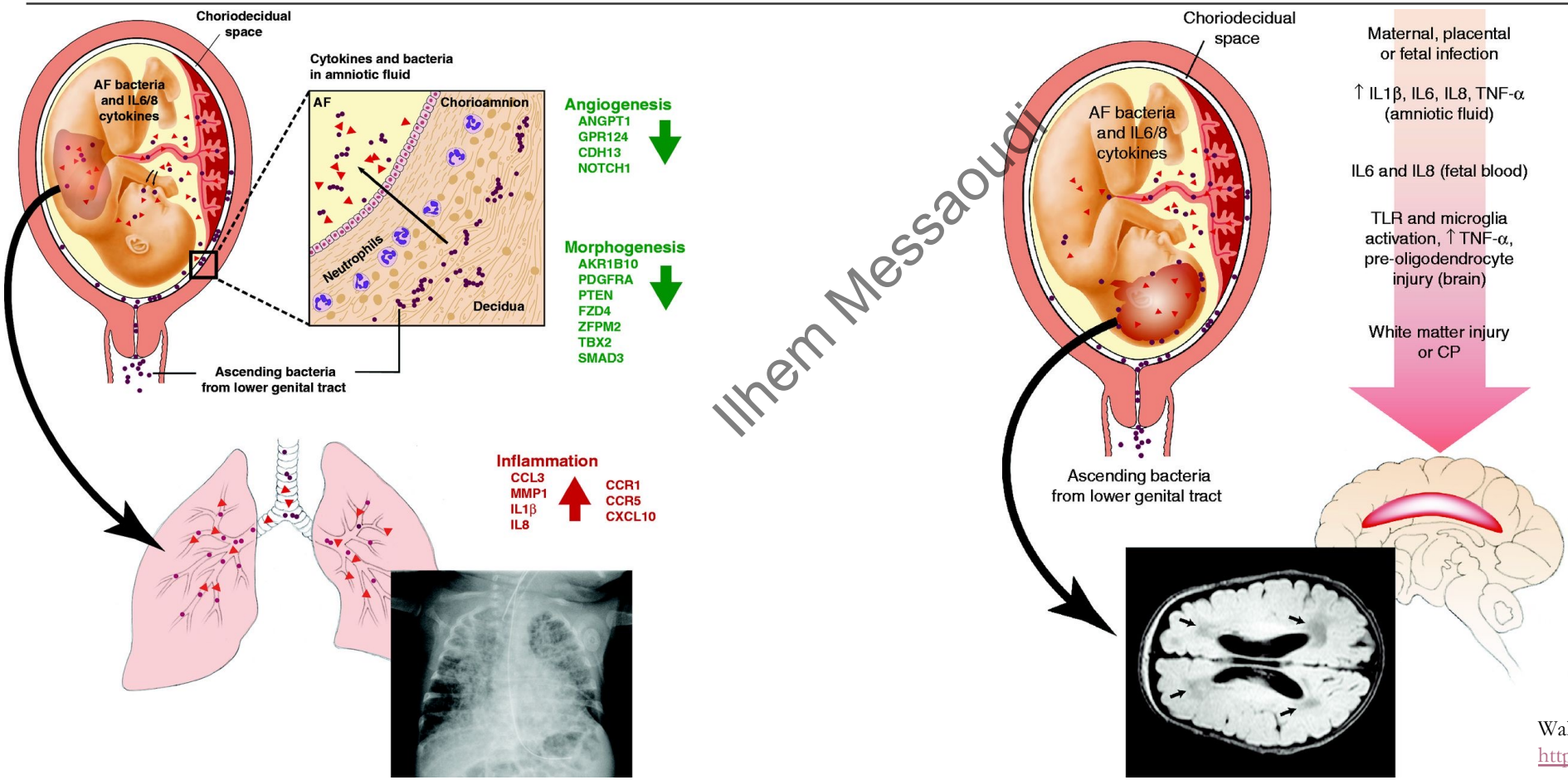
But some pathogens get across…



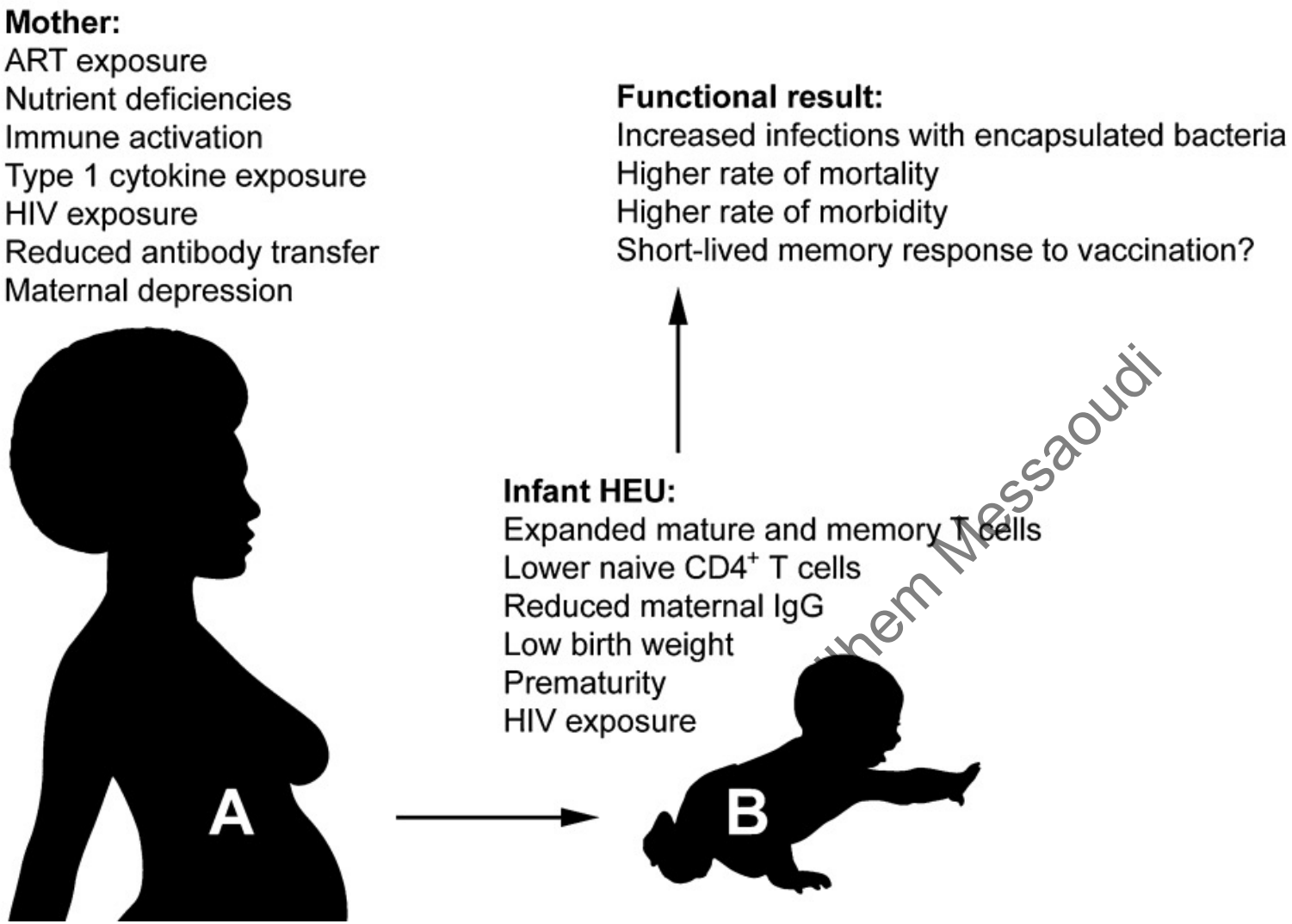


Lee J.K., et al.,
https://doi.org/10.3390/v12010005
Quicke K. M., et al.,
10.1016/j.chom.2016.05.015.

Impact of maternal infection on fetal development

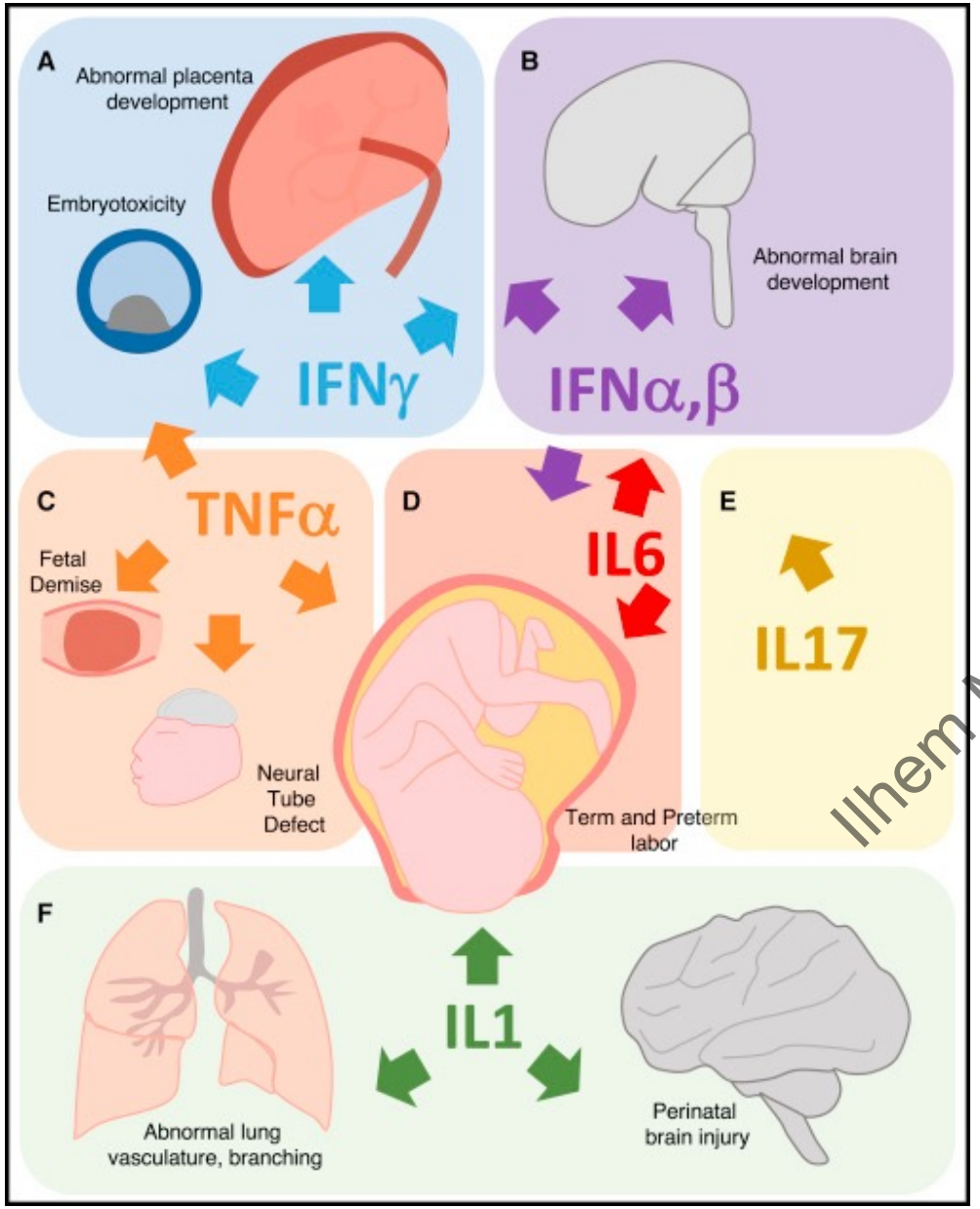


Waldorf K.M.A., and McAdams R.M.
https://doi.org/10.1530/REP-13-0232



Maternal immune activation is sufficient to remodel immune development in the offspring

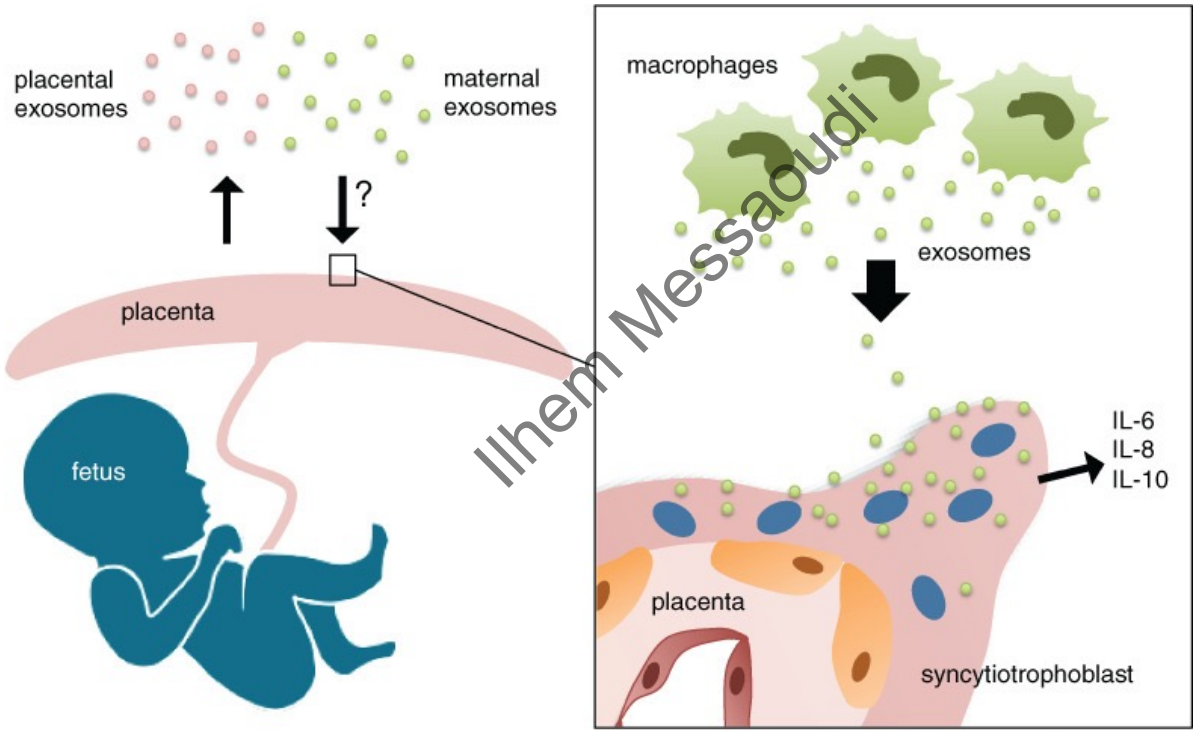
Singh R.
HIV infection in Children and Adolescents 2020



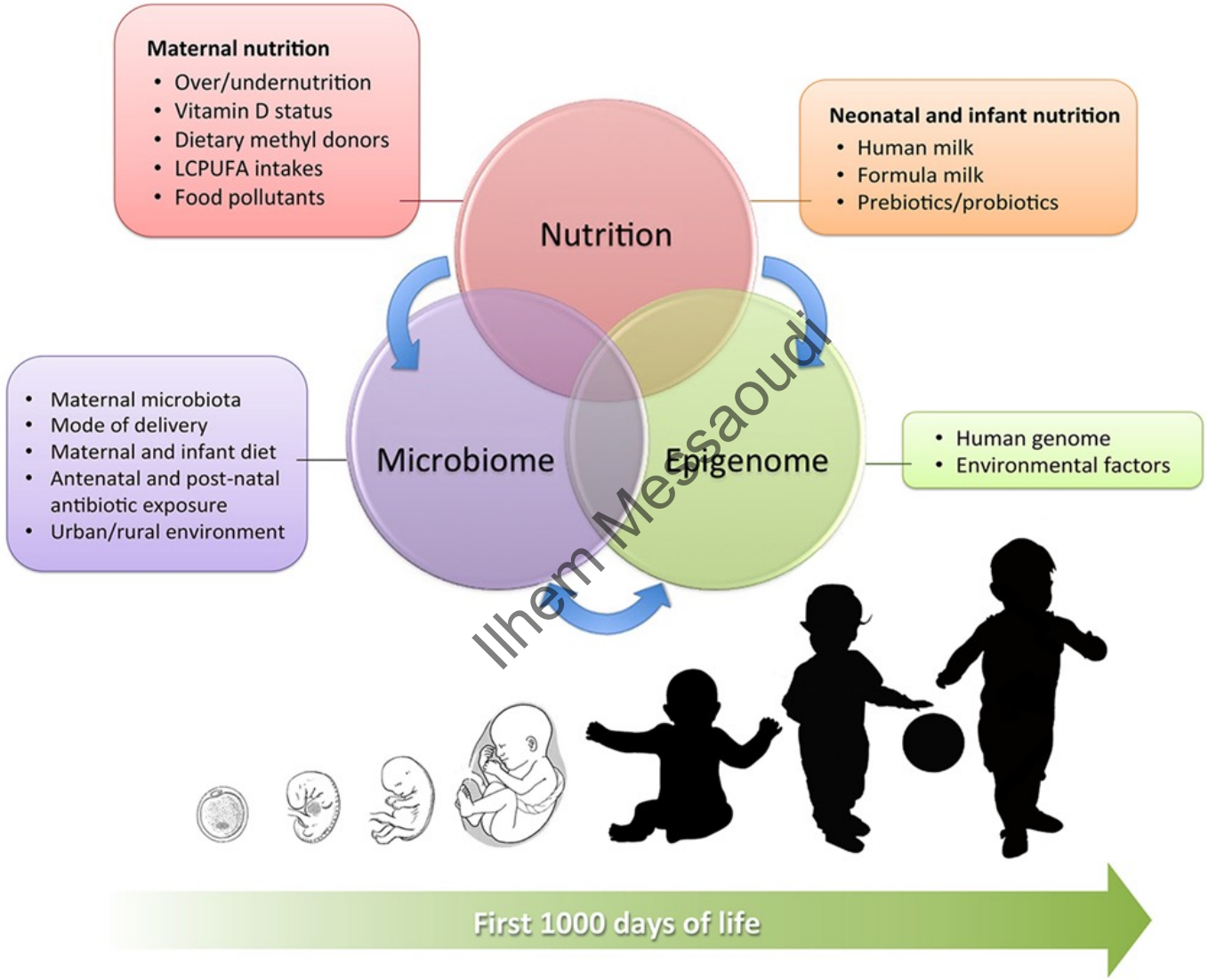
Maternal inflammation critically impacts fetal health and development

https://doi.org/10.1016/j.immuni.2018.07.017

Other modes of communication between maternal circulation and developing fetus



Holder et al. Traffic 2016; 17(2) 168–178



https://www.frontiersin.org/articles/10.3389/fped.2017.00178/full

Summary and future directions

Successful pregnancy requires carefully-coordinated communication between mother and fetus

Immune development occurs in highly regulated cascade of events starting with the yolk sac, then transitioning to fetal liver and finally bone marrow

Maternal health impact immune system development and maturation during these critical windows

Exposure to environmental pollutants, microbes and nutritional stressors can all modulate fetal health with long-lasting ramifications

Most dramatic effects have been reported for fetal nervous system, but impact on fetal immune system is beginning to emerge

Next areas of research

What are the factors that can modulate fetal immune development?

Do they cross the placenta?

How do they modulate fetal immune system development?

Are these epigenetic changes reversible? If yes, is there a specific window for intervention?

What are the consequences of alterations in offspring immune development on the response to infection/vaccination/development of chronic diseases