

Immunology-Inflammation

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Immunology of Pregnancy

- Medawar recognized the paradox that the fetus is (in genetic terms) a semi-allograft which escapes rejection.
- The presence of immune cells at the implantation site has been considered as a proof of a response by the maternal immune system to the fetus

Immunology of Pregnancy

- The studies in the area of Immunology of Pregnancy have focused on Graft-Host response

Immunology of Pregnancy: Old Paradigms

- Mechanical Barrier
- Suppression of the Maternal Immune System
- Th-2 type Immune Response

Mechanical Barrier: Old

- The placenta prevents the movement of cells and antigens from the fetus to the mother and from the mother to the fetus

Mechanical Barrier: New

- Evidence for traffic in both directions across the maternal-fetal interface includes studies reporting migration of maternal cells into the fetus and the presence of fetal cells in the maternal circulation.

Suppression of the maternal Immune System: Old

- Pregnancy is characterized by a state of immune suppression

Suppression of the Maternal Immune System: New

- Maternal antiviral immunity is not affected by pregnancy
- HIV+ pregnant women do not suffer from AIDS-like disease
- ◆ Systemic Immune Suppression represents a danger to the species

Pregnancy is a TH2 Inflammatory condition: Old

- Pregnancy is a TH2 condition and inflammation is detrimental for pregnancy

Inflammation and Pregnancy: New

- Inflammation is necessary for Implantation and parturition

First Trimester

Second Trimester

Third Trimester

Inflammation
TH1

Growth
TH2

Inflammation
TH1



Inflammation



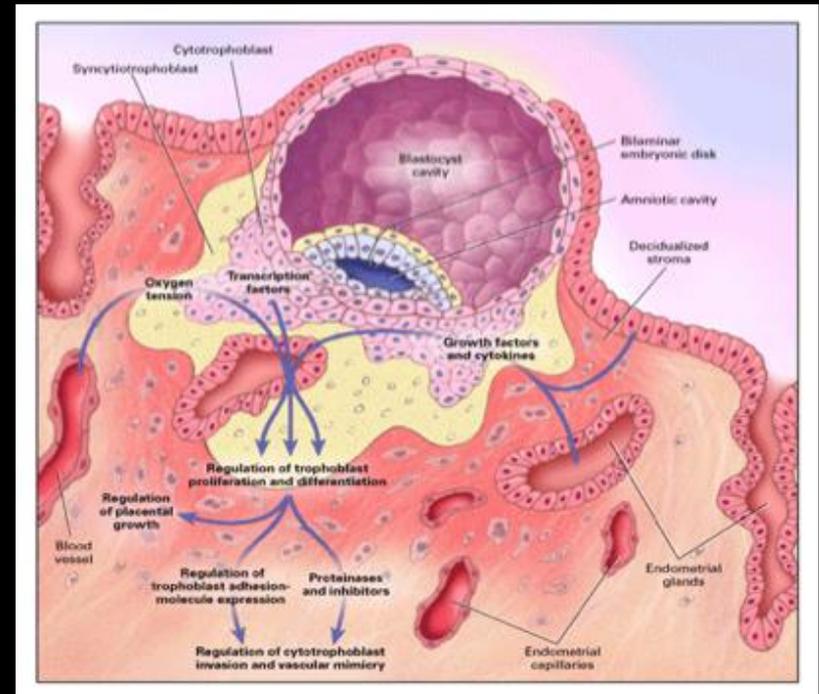
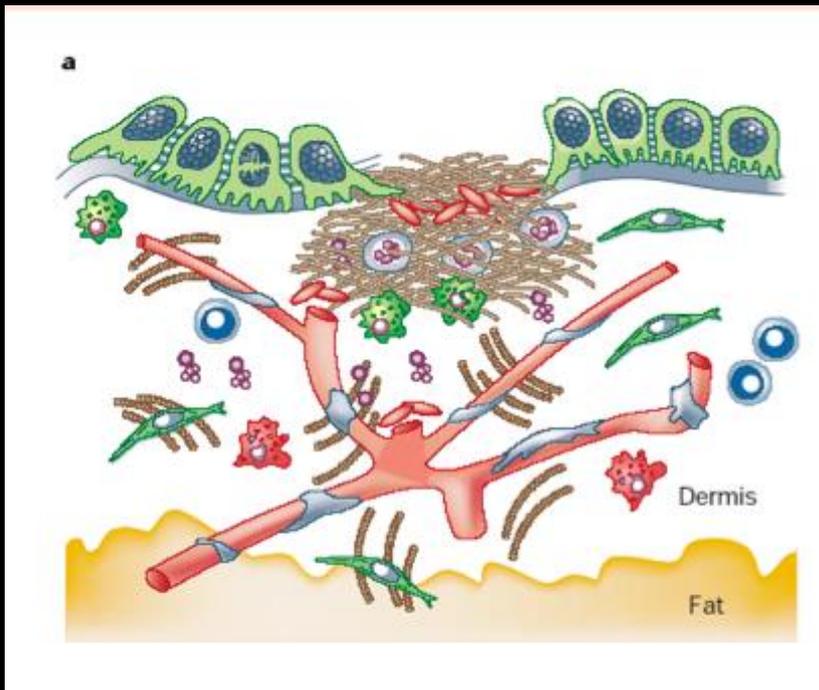
8-12 WEEKS

3-6 MONTHS

7-9 MONTHS

	8-12 WEEKS	3-6 MONTHS	7-9 MONTHS
IMMUNE REACTION	Open-wound stage: embryo elicits mother's immune response (inflammation)	No inflammation: mother and fetus reach symbiosis	Another inflammation leads to labor
SYMPTOMS	Nausea, fever; contributes to "morning sickness"	None (mother feels good)	Fatigue, muscle contractions, possible fever
POSSIBLE COMPLICATIONS	Infection leading to miscarriage; Lack of inflammation, leading to failure of pregnancy	Viral infection (may lead to preterm labor)	Preeclampsia, prolonged pregnancy, intrauterine fetal death

Inflammation and Wound Repair: The implantation wound



New Aspects for Placenta-Maternal Immune Interactions

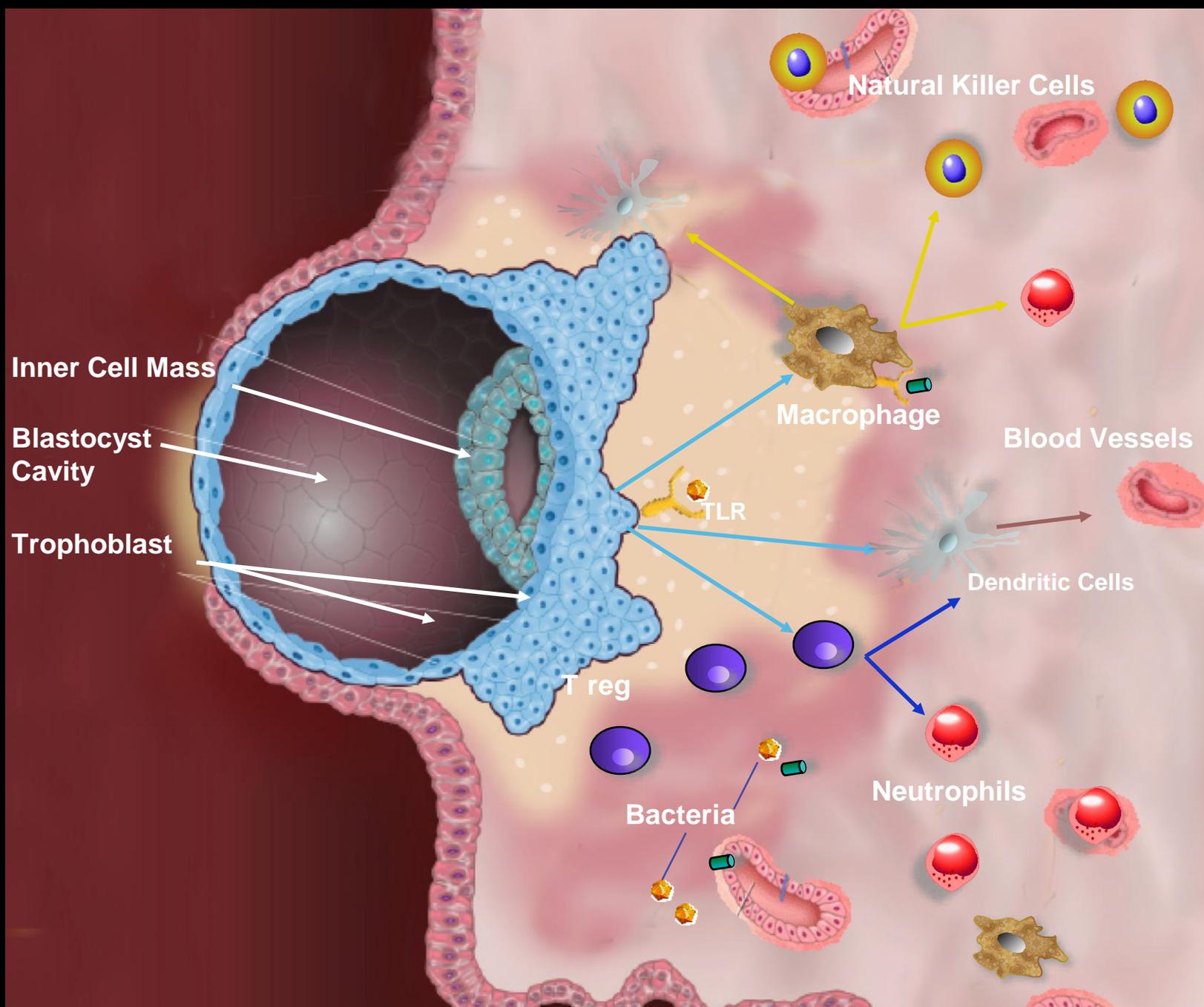
- Role of the maternal immune system during pregnancy
- Role of the placenta as an immune regulator
- Role of the placenta during infection

*The Role of Maternal Immune
Cells During Pregnancy:
Effect of Depletion of Maternal
Immune cells*

Maternal Immune System: Necessary for the Success of Pregnancy

- Natural Killer Cells- transformation of the blood vessels by the trophoblast
- Macrophages- Migration and survival of the trophoblast
- T Regs- Maintenance of tolerance
- Dendritic Cells-Implantation

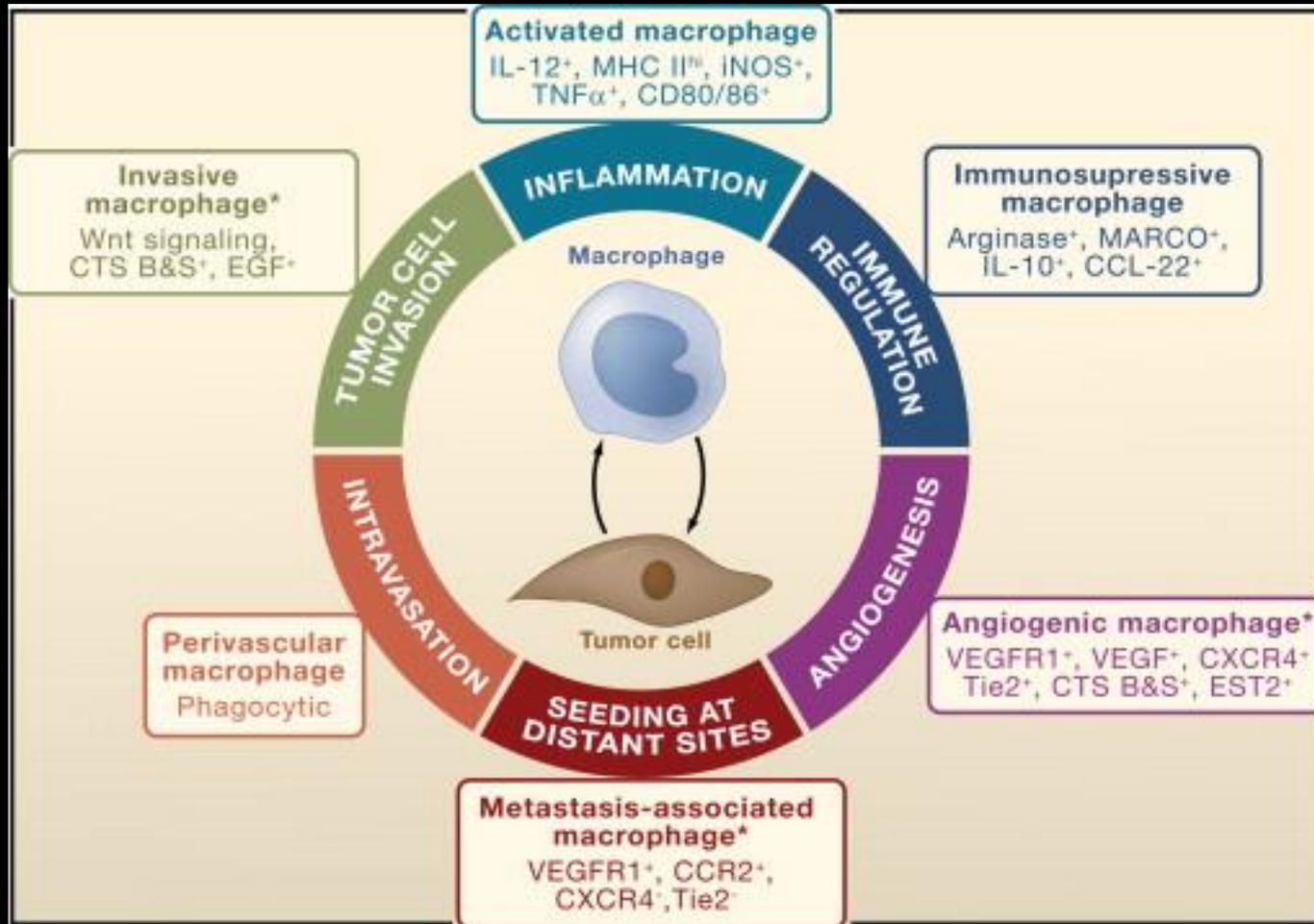
*Redefining the
Immunology of Pregnancy*



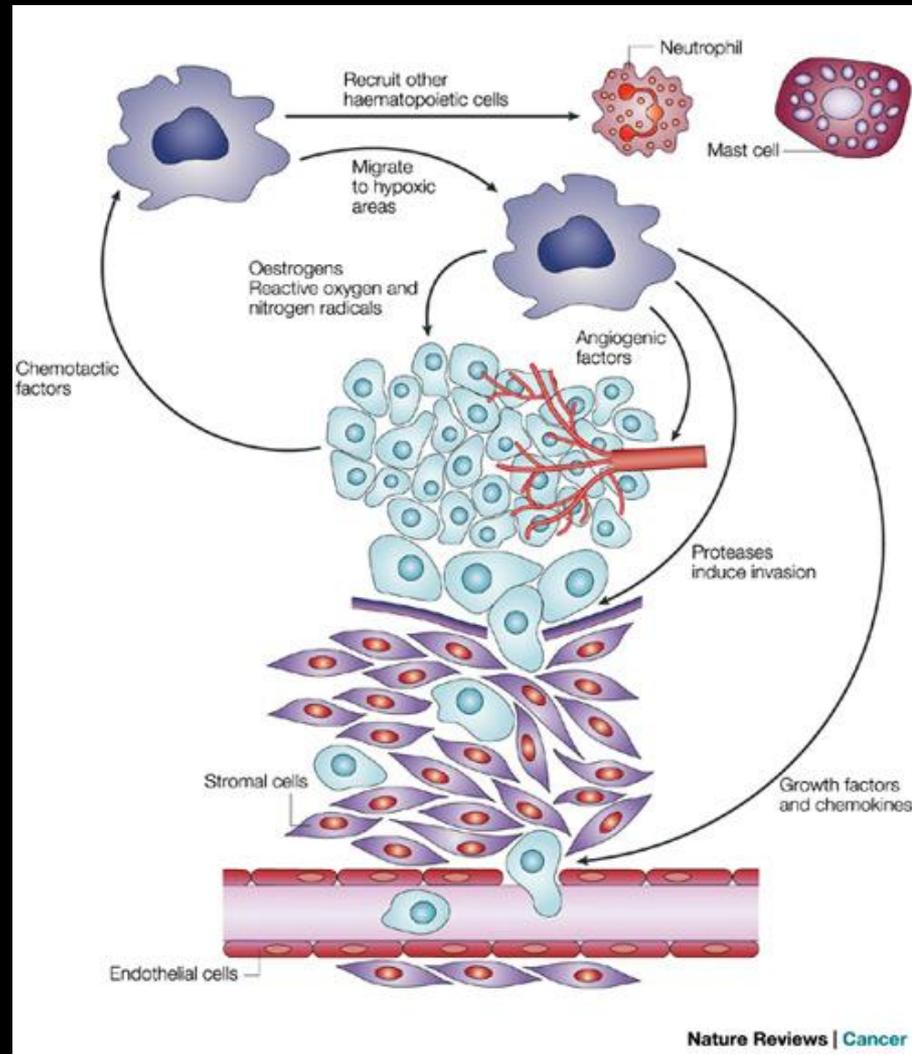
Trophoblast Maternal Immune Interactions

- Graft/Host response vs Tumor/immune interactions

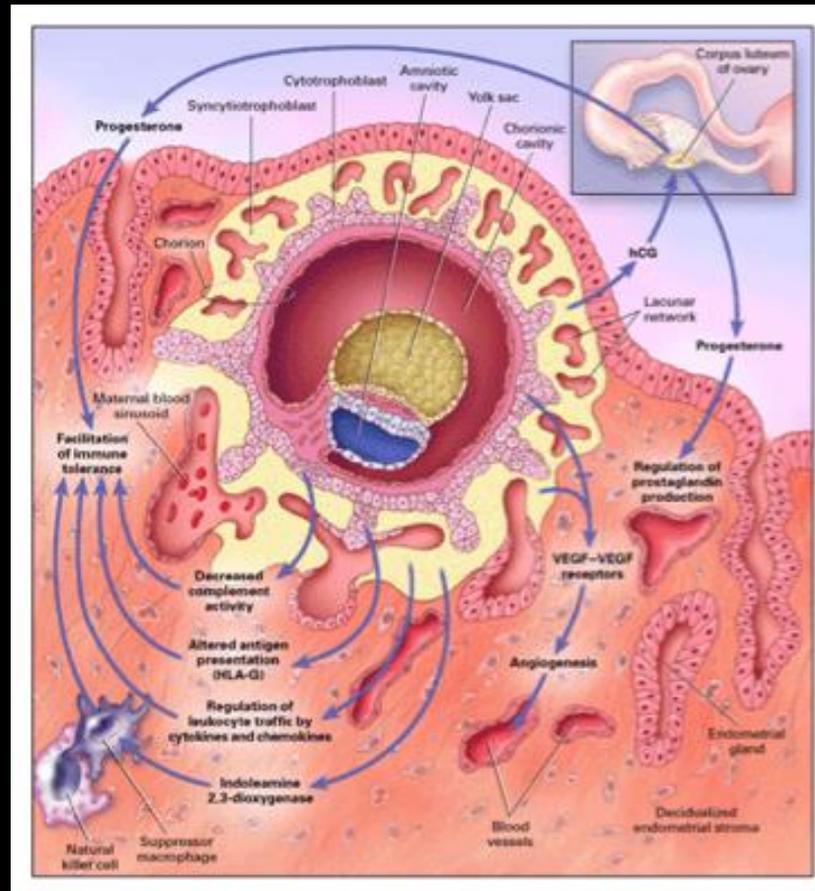
The Placenta as a Natural Tumor



Immune cells Promote Cancer cells migration, invasion and vascularization

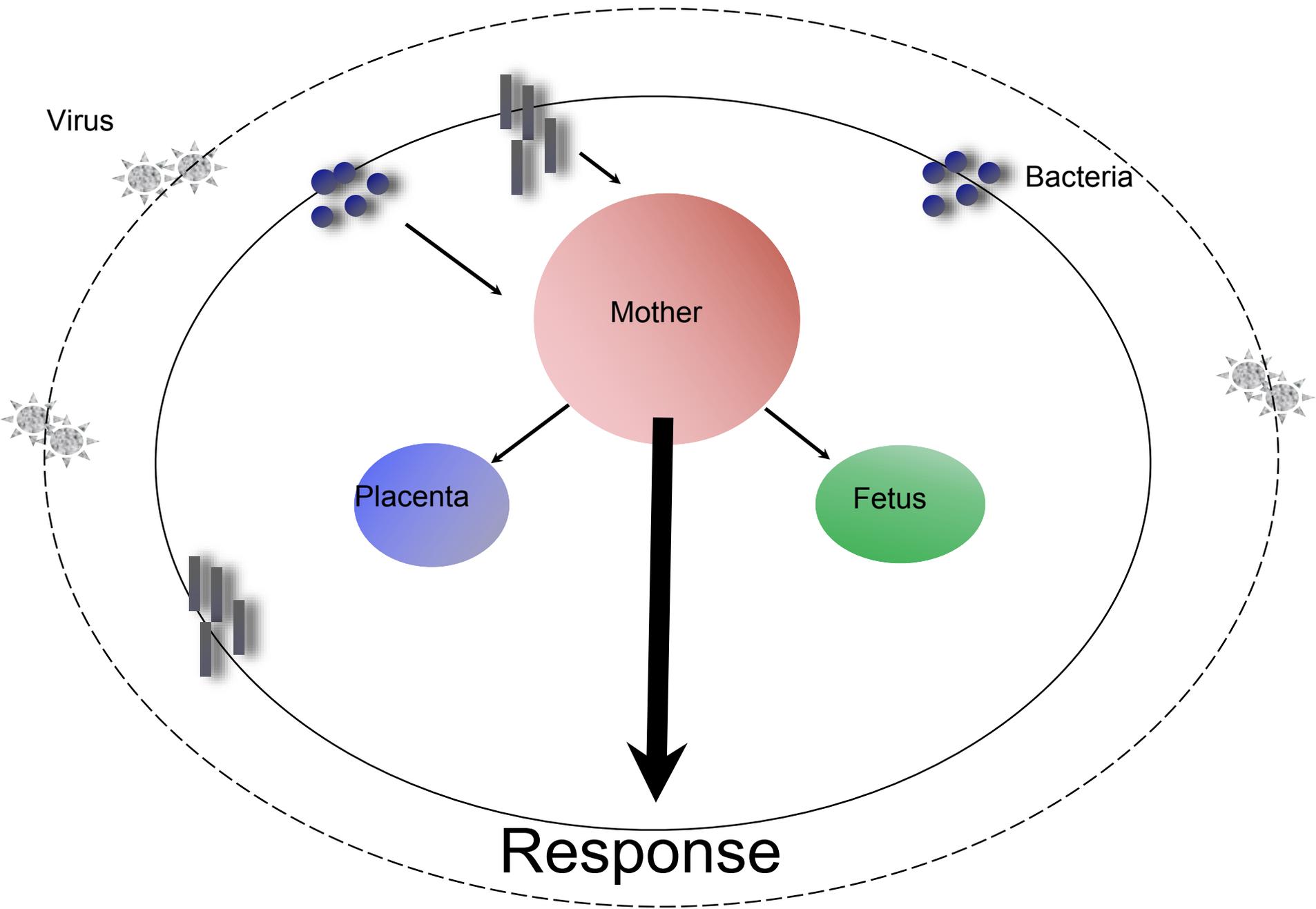


Immune cells Promote Trophoblast cells migration, invasion and vascularization



Infection and Pregnancy: Old Paradigms

- Response to infection during pregnancy has focused on the maternal immune system as the main and only player.
- Maternal immune system is suppressed to prevent responses to paternal antigens.
- Increased mortality during pregnancy due to infection has been attributed to maternal immune suppression.



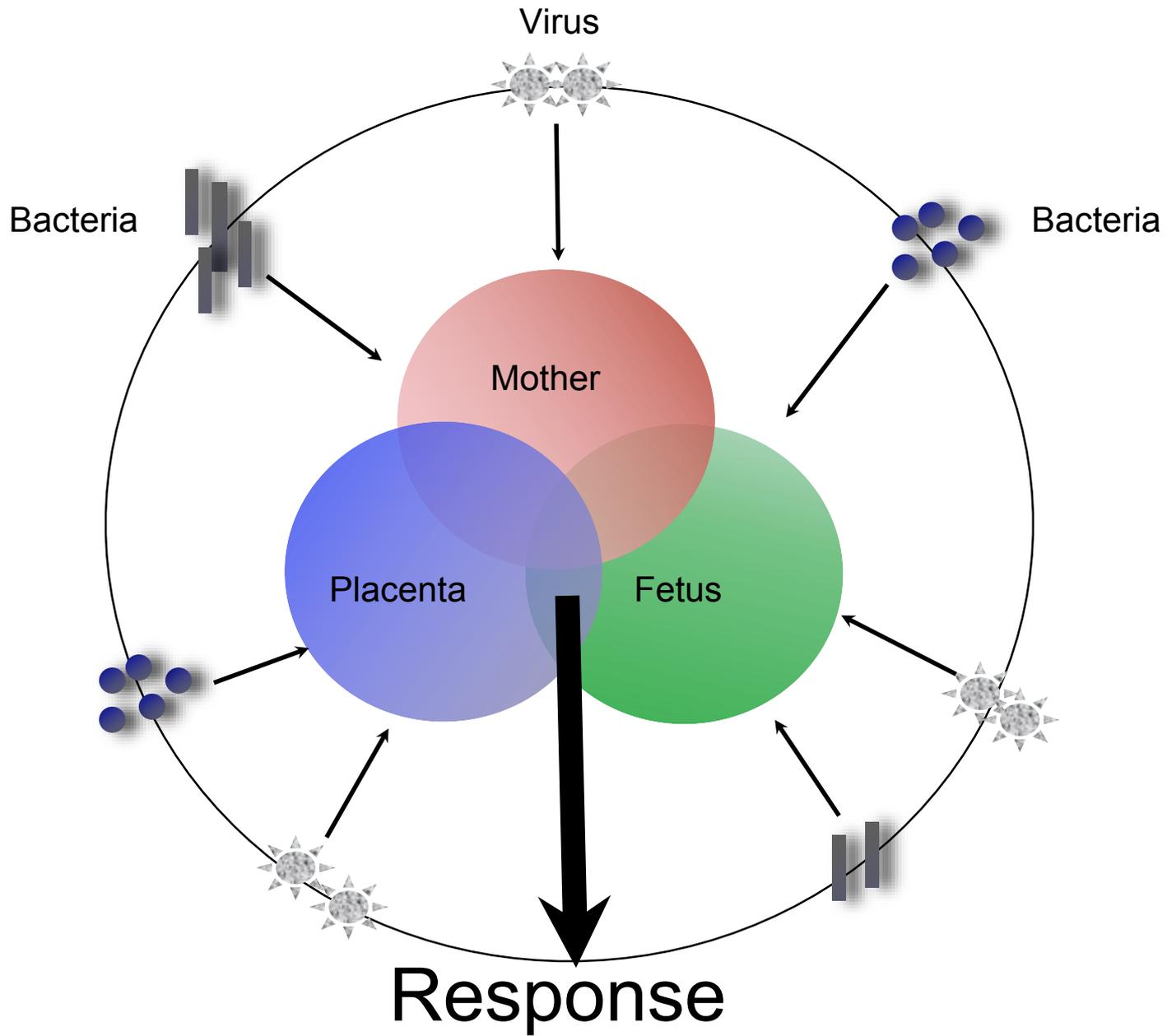
Infection and Pregnancy: New Paradigms.

- The maternal immune system is not suppressed during pregnancy.
- The placenta plays a critical role in the response to infections, affecting not only the fetus but the maternal systemic immune response.

Infection and Pregnancy

□ Therefore:

- There are major limitations to our understanding of the role of infection during pregnancy.
- These limitations have a severe impact on how we:
 - Identify women at risk for preterm birth
 - Treat pregnancy complications due to infections
 - Prevent maternal mortality during pandemics



The inflammatory status of the placenta will influence the development of the fetal immune system as well as the maternal immune responses

