## 15. Fetomaternal tolerance

**1 unit,** Gabrielle Rizzuto , February 20, 2026

**Contents of the lecture:**

1) The conceptus (placenta and fetus) is not genetically identical to the mother yet generally fails to elicit a traditional "allograft" rejection response. [i.e. "foreign" organ transplants are rejected by the host immune system; the conceptus is not rejected! The field of "Fetomaternal tolerance" investigates this paradox.] Conceptus-derived antigens include placental and fetal derived major and minor histocompatibility complex antigens, oncofetal antigens, and tissue-specific antigens.

2) Tolerance mechanisms are inextricably linked to the anatomy of the placenta and pregnant uterus. Mice have a similar type of placentation (hemochorial) as humans and are thus an ideal model system.

3) Maternal T cells engage placental-derived antigens via the indirect allorecognition pathway (uptake and presentation by maternal antigen presenting cells) in secondary lymphoid organs (maternal spleen and lymph nodes).

4) Maternal T cell priming to placental-derived antigens is attenuated via multiple mechanisms, including antigen-specific regulatory T cells and suppression of antigen-specific B cells.

5) Rejection of the placenta is prevented by redundant tolerance mechanisms operating at priming and effector phases of an anti-placental immune response. Many of these mechanisms remain undiscovered (and are likely shared by tumors).

6) In contrast to placental antigen, maternal immune responses to fetal blood cell-derived antigens underscore rare adverse pregnancy outcomes, including Hemolytic Disease of the Fetus and Newborn (HDFN).

**Reading (only if interested):**
Chapter 41 "Maternal-Fetal Immunology" from 8th Edition of *Fundamental Immunology* textbook. PDF is provided.