OUTLINE

- Development of Immune Competence
- Maternal/fetal relationships, exchange of cells and proteins
  - IgG transport
  - Prenatal diagnosis
  - PEP
  - Mating choice

Antigen-independent differentiation. Takes place during fetal development, also continues throughout life.

Immunological Maturity at Birth

**Mouse:**
- No T-cells (empty diffuse cortex)
- Some B-cells
- No serum Ig
- Little immune responsiveness

**Human:**
- Both T- and B-cells present
- Normal lymphoid architecture (but only 1st follicles, no G.C.’s yet)
- Normal serum IgG levels (??)
- Functional immune responsiveness, both humoral and cell-mediated (although not at adult levels)
A developing embryo is a histoincompatible graft; why is it not rejected?

- Isolation provided by placenta
- Decreased HLA expression on trophoblast
- Production by placenta of inhibitory cytokines (local) and hormones (systemic)
- Presence of maternal anti-HLA Abs ("enhancing antibodies")??
- Maternal leukocytes colonize fetus, promote generation of Treg cells & tolerance

Neonatal FcR in the Rat

- Transport of IgG across gut wall into blood during first ten days after birth
- Limited to specific region of ileum
- Mediated by FcRn ("neonatal Fc Receptor")
- Cousin of MHC Class I, has α-like chain and β2m, but lacks ability to bind any peptide
- IgG taken up by pinocytosis on luminal side, bound by NNFcR in lysosomal vacuoles (low pH), released on abluminal side (high pH)
- Is there a human homolog of NNFcR?
  - Yes - expressed in placenta, responsible for transport of maternal IgG to fetal circulation
  - Also in vasculature, "FcRn" regulates IgG turnover

Prenatal Diagnosis of Fetal RhD status

- Used PCR to identify RhD DNA sequences in the blood of Rh– mothers
- 45/45 concordance in third trimester
- 10/12 concordance in first trimester (missed 2 RhD+)

Lo et al., NEJM 339:1734, 1998

Specificity and sensitivity are now close to 100%, may eventually replace amniocentesis for genetic testing...
**Fetal DNA in skin biopsies of Polymorphic Eruptions of Pregnancy (PEP)**

- Pruritic Urticarial Papules and Plaques of Pregnancy, “PUPPP”
- Cutaneous disorder (~0.7%)
- Use PCR to detect SRY (male-specific gene) in skin biopsies
- 6/10 positive in women with PEP carrying male fetuses
- 26/26 negative in women with no PEP (13 male, 13 female fetuses)
- What fetal cells are involved??
- Reaction of fetal cells vs. mother, or vice versa??


**Olfactory Influence on Mating Choice**

- People “prefer” the smell of others who have a very different HLA type
- Married couples (in at least some populations) are significantly more disparate at HLA than expected
- Couples with similar HLA types show reduced fertility

**Significance of HLA**

- Ag presentation (Class II), targeting of cytotoxicity (Class I)
- Polymorphism: Inheritance, genetics of graft rejection and GvH
- Maternal-fetal interactions: immunoreaction, immunoprotection, immunosuppression
- Olfactory influence on mating choice
  - Genetic control of responsiveness...later

**TUESDAY**

Tolerance, Chapter 18
Autoimmunity, Chapter 19

**WEDNESDAY**

Genetic Control of Immune Responses
POPS 2- Transplantation, 1:00 PM

**THURSDAY**

Clinical Correlate: Autoimmunity-Rheumatoid Arthritis (Dr. Pamela Prete)