• Definition of organ/tissue transplantation

• Donor/recipient combinations

Acceptance or rejection of organ tissues graft
Molecular basis of tissue organ compatibility

• MHC HLA Class I and Class II Haplotypes

Methods to HLA typing
ABO blood group system

• Blood types and molecular basis
• Principle of red cell transfusions ("blood transfusions")
• Blood typing methods
• Blood transfusion matching
Types of rejection

• Acute
  – Mediators
  – Hypersensitivity
  – Mechanisms of antigen presentation
  – Mechanisms of graft destruction

• Hyperacute
  – Mediators
  – Hypersensitivity
  – Mechanisms of graft destruction
Monitoring of rejection

- Laboratory testing
- Invasive versus non-invasive approaches
- Organ/tissue graft physiology
Modulation and prevention of immune rejection

- Systemic Immunosuppression
The Life Journey of T Cells

Yong Fan

yongf@andrew.cmu.edu
Thymus Glands

Common Lymphocyte Progenitors
Commitment

1) Restricted to T cell lineage.
2) Expression of the RAG1 and RAG2 genes to initiate somatic recombination of the TCRβ chain.
3) Expression of pre-TCRα.
4) Proliferation
5) Initiation of TCRα recombination.
Training I: Positive Selection

- To ensure the usefulness of the developing T cells
- Mediated solely by cortical thymic epithelial cells (cTECs)
**Training II: Negative Selection**

To distinct self- from non-self antigens by eliminating T-cells with high affinity to self

1. Thymic dendritic cells (migratory and residential) to present blood borne self-antigens, peripheral acquired antigens and thymic locally expressed self-antigens.

2. Thymic medullary epithelial cells (mTECs) express peripheral tissue restricted antigens (TRAs) at low levels with at least two mechanisms: 1) Autoimmune regulator (Aire) gene modify chromatin status to allow TRA transcription; 2) Fezf2 gene regulate TRA transcription through traditional mechanism.

3. Mechanisms of selection: 1) Direct selection by DCs; 2) Direct selection by mTECs; 3) Passing self-Ags from mTECs to DCs.
Selection a Path

αβ T cells

CD4  
CD8  
CD4+ Treg  
γδ T cells
The work force

Mature DC

Naive CD4\(^+\) T-cell

Signal 3
1
2

IL-12, IFN-γ
IL-4, IL-2, IL-3, TGF-β
IL-6, TGF-β
IL-2

Major cytokines:
Th1: IFNγ, IL-2, TNF
Th2: IL-4, IL-5, IL-6, IL-13
Th17: IL-17A, IL-21, IL-22
Treg: IL-10, TGFβ, IL-35

Other cytokines:
LT, GM-CSF, IL-3
The police to control a mob

Foxp3+ CD4+CD25+ T regulatory cells
Antibody - Antigen Interactions

- haptens
- protein antigen

VH
VL

Hybridomas:
- How they are made
  - fusion B + myeloma
  - Selection media
    - HAT

Application of Antibodies - Cancer treatment
- toxin delivery
- growth factor receptor binding (Herceptin)
- chimeric antibodies
- V-seq murine
- C-seq human
- humanized
  - anti CD3 antigen
  - anti tumor antigen

Solid phase assays

ELISA - Sensitive
- Enzyme catalytic
  - $S \rightarrow P$
  - detecting
- primary or secondary
- Indirect ELISA - detect Ab
  - serum
  - antigen
- Sandwich ELISA (detect antigen)

ELISPOT - proteins produced by cell

Activate Tc
- Don't activate Tc naive

Activator cell

DC
Th
Activated
Dendritic cell
RIA - radioactive antigen
- protein (tyr labeled)

- mixing fix (known amount radioactive) + unknown antigen
  → displacement of radioactive by unlabeled antigen

FACS
- detecting surface proteins
- Fluorescent Ab
  a) measure protein on surface by amount of fl.
  b) sort cells based on fluoro.

SPR - measure mass on the surface

TCR

β = HC (VDJ joining), VJ joining is allowed

N-base addition

CD3

Experimental data of MHC - peptide interactions

MHC - peptide → RIA with modified peptide

MHC - TCR → transgenic mouse → introduced rearranged α chain (peptide)

allel exclusion screening single α chain
3. Detection of Rejection by MRI
   - Advantages: Rapid, non-destructive, and whole organ can be characterized.
   - Methods: Label macrophages (or T-cells) with contrast agent (USPIO) and look for accumulation of macrophages in transplant.

4. Immunosuppressive therapy.
5. Detection of histocompatibility.
   - HLA typing – Should know how it works and that it is limited to only detecting a subset of alleles.
   - Mixed lymphocyte assay – Should know how it works and why it is better than HLA typing.

I. Infectious Diseases:
   - i) Immune response to extra-cellular and intra-cellular bacteria/viruses.
   - ii) Antigenic shift, definitions and examples - e.g. bacteria pilli, pandemic flu
   - iii) Antigenic drift, definitions and examples - e.g. HIV, seasonal flu
   - iv) Pathogen evasion/invasion mechanisms: pilli for attachment, degradation of IgA, complement inactivation, intracellular growth, multiple serotypes, latent viruses, interference with presentation of viral antigens on class I and class II MHC.
   - v) Immunology of Dengue fever, antibody-enhanced infection.

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[Diagram showing immune response and cell interactions]