17. Transplantation

LEARNING OBJECTIVES:

1. Successful allogeneic transplantation exploits the plasticity and regenerative capacity of the immune system
2. ABO and Rh matching and screening for preformed antibodies prevent hyperacute rejection
3. HLA matching reduces acute rejection, but immunosuppression is required to prevent (or treat) acute rejection
4. Chronic rejection is poorly understood, but indirect allo-recognition and alloantibodies play roles
5. Donor organs carry donor dendritic cells that migrate to different tissues and create mixed allogeneic chimerism
6. Immunosuppression increases the risk of infection
7. Cyclosporin and Tacrolimas bind different targets (Cyclophilin and FKBP, respectively), but these complexes both inhibit calcineurin
8. Rapamycin binds FKBP but this complex inhibits mTOR (not calcineurin)
9. Effective drugs were used to interrogate the biology of lymphocyte cell signaling
10. Anti-T cell antibodies (monoclonal and polyclonal) are used to treat acute rejection
11. Host SC may repopulate grafts, but their significance is unknown
12. Pre-treatment with donor stem cells that establishes hematologic chimerism may allow solid organ transplants without immunosuppression
13. Allogeneic stem cell transplantation (aSCT) is a therapy for bone marrow disorders and certain malignancies but has high morbidity
14. Mature T cells in SC grafts mediate both Graft v. Host and Graft v. Tumor effects

SUMMARY:

1. Solid organ transplant is successfully employed to treat organ failure and replace certain tissues

2. Hyperacute rejection is prevented by matching and screening

3. Acute rejection is successfully treated by existing pharmaceuticals

4. Chronic rejection needs new ideas and new therapies

5. Managing episodes of acute rejection involves increasing immunosuppression

6. Allogeneic Stem Cell Transplantation (aSCT) invokes both rejection and Graft v. Host (GvH) responses

7. aSCT to treat malignant disease involves tradeoffs between Graft v. Host (GvH) and Graft v. Tumor responses