Statistical Analysis of Graft vs. Host Disease and Immune Reconstitution in Humanized Mice

Swartz, Avi

To overcome ethical and technical concerns, humanized mouse models are often used to study the human immune system. Specifically, immunodeficient mice are engrafted with human fetal tissue and hematopoietic stem cells, which then reconstitute a human immune system in mice. On the one hand, the new immune system has to be strong enough to be studied. On the other hand, the reconstituted human immune system often starts attacking the mouse organs, resulting in graft-versus-host disease (GVHD) and deleterious symptoms or death. In this project, I statistically analyzed data accumulated from 8 years of humanization experiments in a humanized mouse facility to determine factors that affect reconstitution and GVHD (no mouse/human experimentation was performed in my project). I found that better overall reconstitution was linked to a higher risk of GVHD, but residual mouse immune cells as well as reconstituted B cells lowered the risk of GVHD. Different sources of mice are linked with different reconstitution levels. Older donor embryo age is linked to higher reconstitution. There was a correlation between the year of mouse engraftment surgery and reconstitution level, suggesting a possible increase in mouse or surgical quality over the years. Finally, it takes 6-8 weeks for increased immune cell counts to be manifested as increases in GVHD severity. These results provide hypotheses on the mechanisms of GVHD and immune reconstitution as well as possible therapeutic options for GVHD which can be further tested.