

"R" framework of immune functions

In all of our courses, we used the "R" framework to emphasize conceptual understanding of the immune system as one that maintains homeostasis in response to internal and external changes. We provide an example list of broad topics from our upper-level immunology survey course within the "R" framework as a guide for other educators who might adapt this framework into various other immunology courses.

Recognition - How do cells recognize strangers, danger, and death? Detection of intracellular and extracellular perturbations and consequent signaling cascades.

Response - Immediate inflammatory tissue responses, including local mediator release and threat neutralization by tissue resident immune cells and structural tissue cells.

Recruitment - Cytokine and chemokine-based recruitment of neutrophils, macrophages for rapid containment and clearance; alerting T cells and B cells for slower antigen-specific responses. T cell and B cell maturation pathways and repertoire development

Resolution and repair - Continued focus of immune actions at the site of infiltration, damage, or death; antigen-specific mechanisms as means of focusing and amplifying targeted neutralization and initiating tissue repair.

Regulation - Central role of antigen as regulator; once the threat is absent, the immune response is dialed down. What happens when antigens are persistent: chronic infections, self-antigens etc.? Tissue repair and remodeling - restorative and pathological.

Remembering - Circulating and tissue-resident memory immune cells - origin, maintenance, recruitment into active response; implications for vaccines, allergies, and autoimmunity.

Supplementary Table 1: Outline of broad weekly topics within the “R” framework

Week	Broad lecture topics	Portions of the “R” framework emphasised
Week 1	Introductions and course overview; Locating the immune system	Location of the immune system: All cells act as pattern recognition machines in homeostatic systems
Week 2	Multicellular organisms and immune specialization; Hematopoiesis	Immune responses in single-celled, opportunistic multicellular (<i>D. discoideum</i>), and multicellular - plants, invertebrate, and vertebrate/jawed organisms; Hematopoiesis - specialized immune cells and their mostly common origin in hematopoietic stem cells in vertebrates
Week 3	Pattern recognition and an innate sense of “danger”	Recognition and Response
Week 4	V(D)J recombination and B cell development	Recruitment and Response
Week 5	Know thyself: T cell development and selection	Recruitment and Response
Weeks 6-8	The arc of an immune response: Integration of innate and adaptive responses	Recognition, Response, Recruitment and Resolution
Week 9	Harnessing the immune system: Vaccine and immune memory	Remembering
Week 10	Harnessing the immune system: Cancer immunology and immunotherapy	Entire R framework applies
Week 11	Allergies and responses to parasites	Entire R framework applies
Weeks 12-13	Autoimmunity and autoinflammation	Entire R framework applies
Week 14	The other in the self: Transplantation and pregnancy; Immunodeficiencies	Entire R framework applies
Week 15	Wrap up, final projects and presentation, and final exam	