Dr. Ashwell received his M.D. from Columbia University College of Physicians and Surgeons. He trained in internal medicine at Presbyterian Hospital in New York City. Following a postdoctoral fellowship in immunology in the laboratory of Dr. Ronald Schwartz (National Institute of Allergy and Infectious Diseases/NIH), Dr. Ashwell joined the NCI as a principal investigator. He was named Chief of the Laboratory of Immune Cell Biology in 1992.

Dr. Ashwell's laboratory focuses on areas in immunology and cell biology that fall broadly in the category of signal transduction. These include protein modifications and interactions downstream of the T cell antigen receptor (TCR), TNFR superfamily members, and Toll-like receptors, and the role of endogenous glucocorticoids in regulating thymocyte development and innate immune responses.

Dr. Ashwell's laboratory established that T cells possess a unique mechanism for TCR-mediated activation of p38. This alternative pathway is required for normal proinflammatory cytokine production, and is activated in tumor-infiltrating T cells in certain inflammatory neoplasms. Efforts are being made to characterize and target this pathway for therapeutic benefit.