One of the most exciting developments in immunology of the last decade has been the commercialization of major histocompatibility (MHC) tetramers, which provide direct measurement of antigen-specific immune responses. MHC tetramers make it possible to measure or monitor a variety of T-cell-associated disease conditions and responses to therapies. Discovered and patented by Stanford University, MHC tetramers have been exclusively licensed to our company since 1999 for diagnostic applications. The two classes of MHC tetramers are: Class I, which measures cytotoxic CD 8+ T-cells, and Class II, which measures CD 4+ “helper” T-cells.

Cytomegalovirus in transplant patients
The study and monitoring of human cytomegalovirus (CMV) is one of the most advanced applications of tetramer technology. CMV is a significant cause of morbidity and mortality in immunocompromised individuals, and infection is particularly prevalent in bone marrow and stem cell transplant recipients. As many as 20% of all transplant patients die from viral infections. Because CMV-specific CD 8+ cytotoxic T-lymphocytes play a critical role in suppressing CMV reactivation, disease can develop when their function is impaired. With iTAg MHC tetramers, it is possible to directly measure frequencies of antigen-specific CD 8+ T-cells in order to assess immune response and identify patients with impaired recovery of CMV-specific immunity. This measurement also identifies patients at higher risk for CMV disease. There is now an MHC tetramer-CMV assay available in five alleles — the first in vitro diagnostic-cleared test using tetramers for clinical applications.

Vaccine and biologic development
The use of MHC tetramers in the development and testing of vaccines also holds promise. A related technology provides a T-cell epitope discovery platform, which identifies and ranks immunologically relevant peptides, from a target protein, that bind to MHC and play a central role in the generation of antigen-specific immune responses. Once the immunogenic peptides are identified, specific tetramers for those peptides can be developed to monitor immune response to the vaccine.

This epitope discovery technology can also be used to optimize patient selection for clinical trials by identifying peptides that are more likely to be immunogenic in specific patient populations based on the population’s human leukocyte antigen, or HLA, types. Research using MHC tetramers to measure patient response in vaccine development has been reported in several academic publications, and an HIV vaccine developed with the help of tetramers has already advanced to Phase II clinical trials.

Autoimmune and infectious diseases
The study and treatment of autoimmune diseases such as type I diabetes, rheumatoid arthritis, systemic lupus erythematosus (SLE or lupus), and multiple sclerosis will also benefit from the use of tetramer technology. One of the key challenges in autoimmune research is identifying the causative antigens. Once identified, the epitope discovery platform is ideal for determining which parts of the causative antigens warrant further study. Tetramer technology is also being used to better understand the pathology of cancer as well as infectious diseases, such as Epstein-Barr virus, hepatitis C, and even dengue fever.

We are just now scratching the surface of tetramer technology as the ability to quantitate antigen-specific T-cells ushers in a whole new era in the development of vaccines and therapies.