The immune system is the body's main defense against foreign materials and biologic agents such as bacteria, viruses, chemicals, and foreign cells and tissues. The immune response includes specific action of lymphocytes (one type of white blood cell) and is facilitated by other white blood cells, including neutrophils, monocytes, macrophages, eosinophils, and basophils. The immune system can be viewed as a system controlled by negative feedback, meaning that normally it must reduce the effects of disturbance or invaders through self-regulation.

Immunotoxicity is a measure of a chemical substance's impact on the immune system – suppressing it, prompting allergic reactions, causing an autoimmune condition or other effects. The t-cell dependent antibody response (TDAR) is a measure of immune function that is dependent upon the effectiveness of multiple immune processes including foreign material (a.k.a antigen) uptake and presentation, T cell help, B cell activation, and antibody production.

The TDAR assay is an excellent choice for in vivo assessment of immunotoxicity. It is routinely employed to evaluate investigational drug efficacy in animal pharmacology studies, provide evidence of biological impact in clinical trials, and evaluate immune function in patients with primary or secondary immunodeficiency diseases. TDAR is considered to be the gold standard for assessing the impact of a drug on immune-competence at the preclinical stage of drug discovery.

TDAR testing is versatile and can be inserted into a variety of study designs, using several antigen types and various analytical methods to measure antibody response. Moreover, TDAR analysis can be done with antigens in frozen serum, providing flexibility in analysis by increasing sample stability. It is important to understand that the immune response to a ‘known’ and ‘novel’ or ‘new’ antigen is different. The properly functioning adaptive immune system is naïve to an antigen only once; once the immune system has been exposed to an antigen, it is “recognized” and a ‘memory’ response, both faster and more specific to the antigen occurs. Both naïve and memory responses are monitored by the TDAR assay and can provide vital clues as to the status of immune function.

Keyhole limpet hemocyanin (KLH) is the most popular antigen chosen to drive the TDAR assay. Tetanus Toxoid has been used, and to trigger a new immune response and enable serial testing over time, Covance employs an additional antigen for TDAR assays – hepatitis B (HepB). HepB is particularly relevant in DART studies, as is it considered safe for use in infants.
TDAR can evaluate the influence of a drug on multiple aspects of the immune system. The major implication of having two agents for TDAR is that you can test the same animal at different points in its life for a naïve antigen recognition. For instance, if a study included an early in-life or infant TDAR, you could use Hep B for this TDAR, then later in life ensure that there aren’t long term effects on immune system function by using KLH as a novel antigen and again be able to assess the full naïve and memory response later in life.

Having a more diverse menu of antigen candidates produces a more robust and informative dataset about drug candidates, which in turn enhances the data analysis and interpretation our scientists perform.