# Abstract

The T cell receptor (TCR) is characteristic receptor of a T cell that belong to the adaptive arm of an immune system and is known for its specific immune response against the identified antigen. A naïve T cell first sets out in search of its specific antigen, once the TCR makes contact with such antigen, the T cell gets activated, proliferates itself into effector cells and flawlessly neutralizes the antigens.

The TCR is a unique receptor in itself, with a large extracellular domain and a short cytoplasmic tail and it associates with several subunits of CD3 to become a functional TCR complex. The CD3 subunits have long cytoplasmic domains but are non-receptor. The TCR complex set out in their immunological journey to identify antigens and on finding a specific antigen, it directs the cell towards its activation. In order to do so, it recruits Lck, a non-receptor kinase which gets activated and phosphorylates the cytoplasmic tails of CD3 subunits. Lck also phosphorylates and activates the kinase Zap70, which recognizes the phosphorylation in CD3 and lodges itself onto it, thus at the moment completing a receptor tyrosine kinase, and promotes the activation signaling. This process is also described as proximal signaling.

On the journey from naïve to effector cell the T cell encounters several non-pathogenic as well as self-antigens and through this navigation it precisely targets specific harmful pathogens. The source of this virtue lies in the execution of proper activation. Failure of this machinery has been manifested as autoimmune diseases, allergies and immunodeficiencies. Therefore, it becomes essential to understand the T cell receptor activation signaling. As of now, most of the signaling events and participants have been well characterized. Nevertheless, the mechanism through which a TCR communicates the activation signals upon antigen binding, with high accuracy and sensitivity, are largely unknown today. Moreover, several studies have shown that the TCR signaling is extremely fast and completes the proximal signaling in less than 60 seconds.

We investigated this phenomenal mechanism by starting at the activation from 1 second and following it up to 10 minutes using state of the art mass spectrometers for quantitative post-translational modification (PTM) omics with special focus on the kinases and phosphatases involved, hence phosphoproteomics. We characterized the behavior of T cell signaling players along the time course. In addition, we investigated the role of, not very well studied, reversible modified cysteine containing proteins and have indicated their role in T cell activation.