



Press Release

Exposed Region Is Indispensable

Research team explains important step in the activation of T-cells in the immune system

A team headed by Prof. Dr. **Wolfgang Schamel** from the Institute of Biology III of the University of Freiburg and Prof. Dr. **Balbino Alarcón** from the Center for Molecular Biology Severo Ochoa of the Autonomous University of Madrid, Spain, has succeeded in explaining an important step in the activation of the so-called T-cells in the immune system. In humans and mice, T-cells are responsible for deciding whether a defense reaction should be activated to combat foreign substances. Scientists want to prevent the receptor of the T-cells (TCR) from mistakenly also identifying the body's own tissue as a foreign substance to be fended off, because this can lead to autoimmune diseases such as multiple sclerosis. In order to do so, it is first necessary to elucidate the individual steps of TCR activation. Alarcón and Schamel published their findings on the exposure of the proline-rich region, an amino acid sequence in the TCR, in the current issue of the *Journal of Immunology*. The American Association of Immunologists selected this publication as a highlight of the issue.

As soon as foreign substances like bacteria or viruses engage with the TCR, this binding triggers the process of phosphorylation of the receptor, activating the immune defense. Scientists were previously unable to explain how the information that binding has taken place is transmitted into the inside of the TCR. Some time ago, Alarcón and Schamel already established that the receptor undergoes a change in structure as soon as a foreign substance from the outside binds: The proline-rich region is hidden inside of

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the TCR, and after a binding the lower area of the receptor opens, exposing the region. By studying the proline-rich region, the scientists have now succeeded in demonstrating that this exposure is important for phosphorylation.

The team led by Alarcón changed the receptors in mice by removing the proline-rich region. Dr. **Aldo Borroto** in Madrid and Dr. **Elaine P. Dopfer** in Freiburg determined that the TCR no longer functions correctly without this region, as it is no longer phosphorylated. In a receptor that has not been changed, however, the proline-rich region binds to the adapter protein Nck after the region has been exposed. Dopfer performed an in vitro reconstruction of this interaction, thus providing quantitative evidence for the study. This was done within the EU consortium SYBILLA “Systems biology on T-cell activation”, where Schamel and Alarcón are partners.

Through their joint research, the scientists in Freiburg and Madrid verified that the presence and exposure of the proline-rich region is of fundamental significance for activating the TCR, and consequently the immune defense. This finding will enable scientists to reach a more complete understanding of the process, from the binding of a foreign substance to the response from the immune system. It will now be possible to elucidate the subsequent steps, which have not yet been analyzed.

Schamel is a member of the Freiburg Cluster of Excellence BIOSS Centre for Biological Signalling Studies, the Spemann Graduate School of Biology and Medicine, and the Center for Chronic Immune Deficiency at the Freiburg University Medical Center. He also serves as coordinator of the EU FP7 network SYBILLA.

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