ImmunoTools *special* Award 2013

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Analysis of the tonsillar T cell function in humans as a surrogate marker of the immune status in patients with sepsis as systemic inflammation versus chronic tonsillitis as local inflammation

Sepsis is a fatal condition that often literally overruns the patients´ natural defence systems. The pathophysiology of sepsis remains inadequately understood precluding the development of more effective and comprehensive therapies. According to the characteristic chronological development of sepsis, an uncontrolled sepsis-induced pro-inflammatory immune response (SIRS) is followed by a massive anti-inflammatory immune reaction in the post-acute phase which often progresses to protracted immune paralysis. In this post-acute period the patient enters a state of immunosuppression and an increasing body of evidence suggests that this can dramatically affect patient survival. This disturbed immune homeostasis concerns nearly all immune functions and is characterized by diverse alterations.

To date a sufficient and potent therapy that decreases mortality after sepsis is still missing. As a matter of fact, despite research and obvious progress in our understanding of sepsis and its characteristics, the precise changes in the immune system and the molecular mechanisms underlying the loss of immune function remain largely obscure.

In this pilot project we intend to study the functional characteristics of T cells in tonsils from patients 1) with sepsis, 2) chronic tonsillitis and 3) tonsil hyperplasia to identify differences of the immune reaction to antigen stimulation in lymphoid cells between 1) systemic versus 2) local inflammation as well as 3) control T lymphocytes. We expect that the investigation of T cell functional perturbations in these 3 settings will

reveal useful parameters and features to discriminate and identify immune aberrancies stemming from systemic (sepsis) vs. local inflammatory processes. Moreover, we intend to explore the fundamental feasibility of using tonsils (as the only readily accessible secondary lymphoid organ) for the analysis and diagnosis of the patient´s immunological status.

For T cell isolation out of tonsils, the tissue will be shredded. T lymphocytes will be isolated magnetically. By using ImmunoTools antibodies we could verify the purity of lymphocyte populations by using leukocyte markers (CD45), lymphocyte markers (CD3) and the distribution of different T cell subsets (CD4, CD8) via flow cytometrical analysis (FACS). In addition we can detect effector memory T cells (CD44), naive T cells (CD62L, CD45RA) and regulatory T cells (CD4, CD25, (FoxP3)) and their alterations in different inflammatory processes. Furthermore it is very important for us to characterize the activation status of T cells after stimulating the cells with a panel of different stimuli. The expression pattern of activation marker like CD25, CD69, CD11a and others will be helpful, especially for the characterization of different stages of activation. Apoptosis is also an important process that can be detected with Annexin V.

Conclusion

In summary, this project represents a pilot study aimed at exploring the usefulness of tonsils as sources for investigating T cell functions in sepsis patients. In particular, we will place a focus in identifying hallmarks of T cell function that enable one to discriminate the systemic inflammation (as found in sepsis) from a local infection as present in tonsillitis.