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Traumatic spinal cord injury represents a lifelong disease, for which there is no consistent therapy for restoration of lost neurological function. The variability of the limited natural recovery after spinal cord injury is insufficiently explained. A maladaptive systemic immune response (MSIR) occurs early after spinal cord injury and is characterized by at least two hallmarks: i) an emerging immune reaction against components of the central nervous system and ii) an immune deficiency, which is related to central nervous system injury. In this project, we use specimen and data collections from recent and upcoming trials conducted for characterization of the MSIR after spinal cord injury and combine them with experimental methods. We address the questions whether i) autoimmunity against spinal cord and brain tissue is extending over time, ii) the targets of the autoimmunity are relevant for the function of the central nervous system, iii) the autoimmunity can be linked to clinical outcome of the patients, and iv) whether autoimmunity is also present after other injuries to the central nervous system such as traumatic brain injury. An international consortium of experts in different research fields such as the immune system, proteins, neurological injuries and disease mechanisms as well as diagnosis, treatment and rehabilitation of spinal cord injury will investigate distinct patterns of autoimmunity in experimental as well as clinical studies. The results of these studies can be linked to long-term recovery of the patients’ functional abilities such as self-care and walking. Based on data from pilot studies, we will challenge the hypothesis whether patients with poor response to rehabilitative treatment differ from normal rehabilitation responders in terms of distinct autoimmunity patterns. To characterize spinal cord injury patients by the occurrence and severity of the MSIR can be used for the definition of patient subgroups as a basis for the development of new individualized treatment concepts after spinal cord injury.