DKMS Stiftung Leben Spenden

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PROTECTOR (**Pro**tecting **t**he barrier by **E**ngagement of **C**y**to**solic nucleic acid **R**eceptors)

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The aim of this research project is to characterize the intestinal stem cells and Paneth cells in order to protect the patient from the very beginning against the development of Graft-versus-host disease (GvHD).

Our current limited ability to protect the patient against the development of GvHD is at least in part due to a limited understanding of the function of the intestinal stem cells. Paneth cells and intestinal stem cells contribute to the defense provided by the epithelia – a specific cell layer which protects the inner lining of the stomach and gut (gastrointestinal tract). The gastrointestinal tract represents the first line of defense from microbial challenge (e.g. bacteria).

Total body irradiation or chemotherapy can cause loss of intestinal barrier function, which in turn enhances the development of inflammatory diseases after stem cell transplantation, such as GvHD. The white blood cells from the transplant react against the organs of the patient.

In this context, specific types of proteins (Type I Interferons) play an important role. These proteins are produced by Paneth cells in the gut. Type I Interferons stimulate a response of the immune system, especially against viruses and tumor cells. However, the detailed biological context which triggers these reactions during acute tissue damage in the gut and stomach is unclear. It has been shown that the production of Interferons is controlled by a specific pathway: a stimulus outside the cell is recognized, translated and transported into the cell, and an answer or reaction of the cell follows.

More specifically, the aim of this project is then to analyze the signaling in intestine stem cells and Paneth cells which seems to be involved in protecting the epithelial. By characterizing this pathway and understanding the mechanisms, the immune system can improve barrier function to enhance healing after tissue damage in the patient.

Therefore, this project has the potential to develop novel target therapies, in order to (i) promote intestinal barrier integrity (ii) prevent the development of GvHD and (iii) to analyze the regenerative response of other tissues.