Projektzusammenfassung

„The Role of mesothelial stem cells of the peritoneum in peritoneal adhesions after gynecological surgery".

Peritoneal adhesions (PA) are connective tissue bands between two normally separate anatomical structures within the abdominal or pelvic cavity and are the most common complication after surgery involving the peritoneal cavity, leading to both clinically and economically significant consequences. They produce substantial patient morbidity, often making additional surgery necessary. Recent studies looking at the cellular mechanisms of fibrin deposition and the constitution of peritoneal adhesions showed evidence for multipotency in mesothelial cells. Additionally, multiple germ layer differentiation and a populational celltype shift contributing to the genesis of peritoneal adhesions point towards a central role of multipotent progenitor cells. Therefore, a mesothelial multipotent cell population has been postulated but as of yet could not be characterized. Additionally, PA have a very similar time - dependent emergence to scarring skin wounds. In skin wounds, Prof. Bader was able to identify a mesothelial precursor cell population, which could be influenced to produce scar- free skin healing in 2b burn wounds of the skin. This was possible through topical treatment of burn wounds of the skin with Erythropoietin (EPO), as the CD90 - positive cells expressed the beta-er subunit.

Considering this information, we developed three hypotheses: Firstly, we hypothesize the existence of a mesothelial stem cell population in the peritoneum, expressing the CD90 surface glycoprotein. Secondly, we hypothesize, that these CD90 positive stem cells are similar to CD90 mesothelial stem cells in the skin, therefore expressing the beta - er subunit as well. Our third and last hypothesis is, that these cells are responsible for the formation of peritoneal adhesion after injury to the peritoneum. In order to disprove / prove our first hypothesis, we want to take mesothelial and submesothelial samples from patients undergoing elective surgery at the Pius - hospital in Oldenburg to characterize the postulated cell population. The CD90 marker will be used for identification and double stainings with stem cell markers will be used to show multipotency, as CD90 alone can also be expressed in neurons. To disprove / prove our second hypothesis, we will analyze the expression of beta-er receptors in the acquired cell samples by cell sorting. Our third hypothesis will then be disproven / proven in a mouse - adhesion study. We want to examine the effect of the EPO - containing hydrogel on adhesion formation by inducing adhesions in mice with and without the application of the EPO - containing hydrogel, and the respective control groups.

In a pilot study conducted by us with regard to our first hypothesis, we were able to see promising results: typical CD90 stainings could be seen in all usable peritoneal samples. We will continue to double stain our samples with multipotency markers. We expect our current pilot study to run for an additional 12 months, consisting of 9 months for the analysis of our samples, including 4 months for additional sample recruitment, as it is unclear, whether we will be able to use our current samples for cell sorting. 3 months for the writing and publication of the corresponding paper. The following disproving / proving of our third hypothesis is expected to take about 17 months, consisting of 7 months for the writing of the proposal and acceptance of the ethics committee, 5 months to execute the mouse - adhesion experiment, including 3 months to test the protocol for adhesion induction in mice, 1 months to analyze the data and 3 months to write and publish the associated paper. 6 months will be used to write the thesis of Mr. Leichers Doctorate and its defense.