

The aim of the project is to study the effect of adipose tissue-derived stem cells (ADSC) on the inflammatory process in necrotising enterocolitis (NEC).

Necrotizing enterocolitis (NEC) is an inflammatory disease that affects the intestine of the neonate causing necrosis and general inflammation. It can affect as many as 20% of the prematurely born babies. The treatment consists of starving and antibiotic administration, and it is focused mostly on the limitation of symptoms as there are no specific treatment options. In more severe cases a surgical intervention and a bowel resection is necessary. The etiology of NEC is still not well known and it is assumed to be a combination of infectious and proinflammatory components.

There are three possible mechanisms of action of stem cells from which the strongest research supports paracrine effect – secreting anti-inflammatory mediators. The other two are: migration and engraftment – building into the host tissue and heterotopic cell fusion, that is connecting with host cells and transferring genetic information. This results in preservation of the intestinal barrier, limiting of inflammation and promotion of intestinal regeneration.

There is very little research concerning the role of stem cells in necrotising enterocolitis. The types of cells that have been researched so far, are bone marrow-derived mesenchymal stem cells (BMDSC) and amniotic fluid-derived stem cells (AFDSC). Both types significantly reduced the amount and severity of NEC in the animal models. ADSCs share similar surface markers and differentiation potential with BMDSCs.

The hypothesis of the study is that giving the ADSCs before the onset of the disease will result in limiting the inflammatory response and promoting regeneration, thus effecting in lower incidence of NEC. On a molecular level this should result in lowering the levels of proinflammatory cytokines IL-1, IL-6 and TNF α and upregulating regeneration pathways of WNT/betaCatenin and molecule Ki67. We also hypothesise that when administered during the course of the disease, the ADSCs will effect in limiting the damage of the bowel wall.

In preliminary study we have created a neonatal NEC model in a rat that mimics the intensive care unit environment as close as possible. This model is created by exposing newborn rat puppies to hypothermia, hypoxia and formula feeding.

100 rat puppies will be divided into three experimental groups and two control groups to measure the influence of ADSCs administration on the onset and course of the inflammatory changes in NEC, the level of cell engraftment, the inflammatory profile and the regeneration potential. In one group ADSCs will be administered at the beginning of the NEC protocol, and in the second group after 24 hours of the protocol duration. After 72 hours, animals will be sacrificed and small and large intestine will be collected for further analysis.

By demonstrating not only the impact of ADSCs on: the morphology of the NEC affected bowel, the inflammatory profile and the regeneration and proliferation abilities we will confirm the possible mechanisms of action of mesenchymal stem cells for ADSCs. In the future, the inflammatory cascade and regeneration pathways will possibly be the aim for developing targeted treatment strategies for NEC