Fulminant liver failure is defined as severe acute liver failure characterized by serious impairment of liver detoxication and metabolic function in terms of protein synthesis like clotting factors. Accumulation of toxins and protein deficiency leads to hepatic encephalopathy and other life-threatening complications. Without adequate and fast treatment, that disease results in death. In FLF, the availability of matched donors for liver transplants is a key factor limiting patient's survivability. In this condition, antigenic homology criteria are loosed, which allows faster matching between donor and host. Despite this, a significant part of patients in the qualified list died during waiting for a transplant. Therefore, there is a need for a new effective bridging therapy development which would be able to reduce mortality rate, elongate time for donor seeking, and improve prognosis.

Human amniotic epithelial cells therapy which possesses immunomodulatory properties can be a promising alternative for currently used FLF treatment methods. Due to their unique properties, hAECs could be potential material in the therapy of autoimmunological disease or where inflammation plays a crucial role. In recent years, cell-free-based therapies has been extensively investigated. Those therapies are based on administration of factors secreted by the cells and exosomes – small vesicles containing genetic material.

We propose to verify the effectiveness of therapy with the use of immunomodulatory human amniotic epithelial cells (hAECs) and conditioned media enriched with exosomes. Human amniotic epithelial cells have several advantages over others stem cells. hAECs are not rejected by the host and did not cause an inflammatory reaction in the allo- and xeno- implantation model. Moreover, hAECs possess better immunomodulatory properties than other stem cells lines which result in administration efficiency in acute inflammatory conditions where therapeutic effect results from secreted immunomodulatory and anti-inflammatory factors rather than cell mass replacement.

In vitro cell modification before implantation is a modern approach intended to improve therapeutic effects. The aim of this study is a comparative assessment of the effectiveness of 4 experimental therapies in the mice model of FLF:

- Instrasplenic administration of native hAECs
- Instrasplenic administration of activated hAECs
- Intraperitoneal administration of CM produced by native hAECs
- Intraperitoneal administration of CM produced by activated hAECs

Fulminant liver failure in mice will be induced by intraperitoneal injection of hepatospecyfic toxin – D-Galactosamine. After cell or conditioned medium administration mice will be observed in terms of general condition and survival time. From mice spleen and liver will be collected for histopathological examination and blood to perform liver panel and to determine concentration of proinflammatory cytokines.

Experimental confirmation of the effectiveness of planned therapy would allow to plan further experiments aimed at understanding of hAECs mechanism of action in the inflamed organs and make it possible to perform a clinical experiment in the future.