Insufficient physical activity, alcohol, cigarettes, stress or environmental pollution - all these factors can lead to the development of diseases known as diseases of affluence. One of them is type 2 diabetes. Hundreds of millions of people around the world suffer from this chronic disease, and unfortunately it is predicted that in the next two decades this number may increase by up to 50%. Diabetes can lead to a number of dangerous complications, such as ischemic stroke and sudden cardiac death. In addition, these individuals often suffer from impaired wound healing. This is caused by pathological changes both at the systemic level (impaired blood circulation) and at the cellular level (misfunction of crucial signaling pathways, e.g. PI3K/AKT/mTOR). Dressings used to treat these types of wounds are often ineffective and the results are poor. This is why, researchers around the world are faced with the challenge of inventing new therapies. As a solution, my research team proposes a dressing based on an insoluble fraction of keratin, which will be further enriched with macrophage colony-stimulating factor (M-CSF). Keratin is a protein found mainly in the epidermis and epidermal products such as hair, wool and fur. The efficacy of keratin in wound healing has been demonstrated in a few studies, but most of the examined dressings were based on the soluble fraction of this protein. In my team, we use a novel approach of obtaining dressings from the insoluble fraction of keratin. By doing so, not only have we abandoned the use of toxic organic substances that are used in the production of dressings by most researchers, but we have also obtained a unique dressing architecture that allows us to modify it with additional substances that are later secreted into the wound bed over several days in a predictable and reproducible manner. M-CSF (CSF-1) is a macrophage colony-stimulating factor that supports the proliferation and consequently the differentiation and function of monocytes. Many studies show that the role of macrophages in wound healing is invaluable, especially in the final stages of regeneration and reducing the occurring inflammation. Our previous studies have shown that a keratin dressing impacts the number and variety of cells present in the wound bed, promoting the healing process. The goal of this project will be to produce a dressing composed of an insoluble fraction of keratin enriched with M-CSF, a substance with potentially powerful regenerative and inflammation-regulating properties.

Hypotheses and key objectives of the proposed project:

1. Produced experimental dressing based on insoluble fraction of keratin supplemented with M-CSF, will be biocompatible, bioactive and biodegradable. The release of M-CSF into the wound bed will be reproducible and predictable.

2. The proposed dressing will accelerate wound healing in a rat with iatrogenically induced type 2 diabetes.

3. The applied dressing will have a beneficial effect on the structure of the skin and epidermis, which will be confirmed in histopathological, immunofluorescence and molecular studies.

4. The experimental dressing will have an impact on the cells infiltrating into the wound bed and will increase the activity of certain signaling pathways (especially the PI3K/AKT/mTOR pathway), which proper functioning is essential for a successful wound healing process.

The research planned within the project will advance the knowledge of the underlying processes of the impaired wound healing. In addition, they will provide valuable information on the proposed model of type 2 diabetes in the rat, its potential advantages and disadvantages. Ultimately, they may lead to the production of a wound dressing with proven efficacy in rats with induced diabetes. This is a necessary first step before performing further preclinical studies and, eventually, clinical trials.