The **PHA-Cure** research project aims to create advanced wound dressings made from polyhydroxyalkanoates (PHA) to promote the healing of chronic wounds, particularly diabetic foot ulcers (Fig. 1). These wounds often heal slowly and need amputation due to persistent inflammation and a shortage of healing-supporting cells. The underlying reason is the persistence of immune cells that promote inflammation, the so-called M1 macrophages, and the insufficient presence of pro-regenerative M2 macrophages, which aid the healing process (Fig. 2). The study investigates new strategies to modify the surface of PHA biomaterial by employing distinct physicochemical techniques.

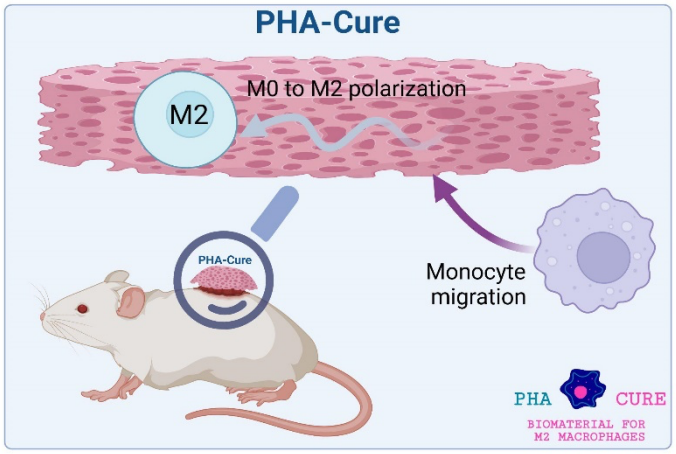

*Fig. 1. **PHA-Cure** biomaterial supports monocyte migration to the injury site and their differentiation into anti-inflammatory and pro-regenerative M2 phenotype, promoting the healing of chronic wounds*

This study will develop and test three different PHA models: one with a chitosan coating, one functionalized with peptide fibrils, and one with a specialized peptide integration technique known as the SpyTag-SpyCatcher technology. Each model utilizes different methods for incorporating and releasing bioactive substances that foster a healing environment by the sequential release of proteins, first to attract monocyte cells from the blood, specifically to the wound location, and then to trigger their M2 polarization.

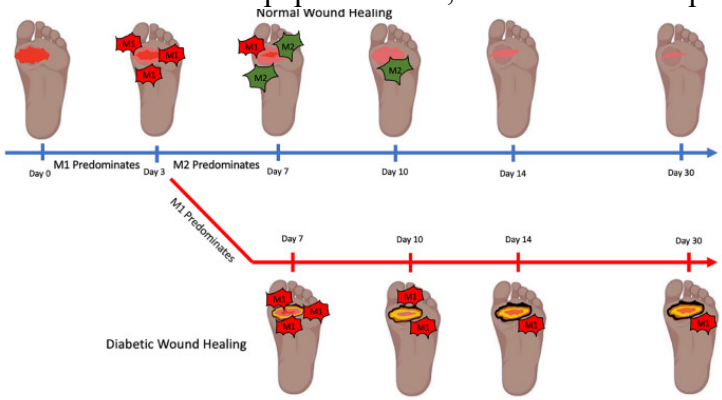

Fig. 2. illustrates macrophage polarization in normal versus diabetic wounds. Day 0 indicates initial wound formation. Days 1-3 show predominantly M1 macrophages in both wound types. After day 3, normal wounds transition to M2 macrophages, while M1 macrophages decrease. By day 10, most macrophages are gone. In diabetic wounds, M1 macrophages persist, with few or no M2 macrophages, resulting in chronic inflammation and impaired healing.

These PHA materials are specifically designed in terms of pore size, water affinity, and mechanical strength to maximize their positive influence on monocyte adhesion and differentiation into different macrophage types. By employing advanced techniques to incorporate active peptides and proteins, the project aims to establish more effective wound-healing strategies. This initiative presents an innovative approach to addressing the challenges of treating chronic wounds by integrating advanced materials with biological therapeutic factors. The collaboration between Polish and Swiss research teams aims to develop improved healthcare solutions for difficult-to-heal wounds, ultimately enhancing patients' quality of life.

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