Personalized Diabetic Wound Healing: A CRISPR Based Synthetic Biology Approach Using Engineered Probiotics

Emani, Priya (School: Interlake High School)

Diabetic wounds pose a significant health challenge from the resilience of biofilms and the inflammation of the wound environment. Current antibiotics often lack targeted and adaptive responses. This project introduces a 'living medicine' of a smart bacteria with a novel genetic circuit designed to sense key wound microenvironment signals (low pH, high glucose) to respond with localized delivery of anti-biofilm (DNase I) and anti-inflammatory (IL-10) agents, in a dual manner. The genetic circuit was designed using Benchling, with pH-inducible DNase I expression and glucose-sensitive IL-10 expression units regulated by CRISPRa, based on a PTS/Crp system. The design was tested with PhysiCell that simulated a multicellular system of a virtual wound, validating the engineered bacteria's sensing and secretion logic against the Staph aureus biofilm. The temperature sensitive kill switch (temp >37°C trigger) was modeled for reliability using NetLogo simulations. The engineered bacteria released DNase I predominantly under low pH and IL-10 mainly under high glucose conditions. The quantitative predictions through PhysiCell showed biofilm mass reduction of a potential 50-70%, based on personalization of Hba1c levels. Compared to the 30% Vancomycin biofilm reduction, the genetic circuit outperformed Vancomycin in the different ranges of HbA1c levels. Additionally, the kill switch safety feature demonstrated high predicted reliability in NetLogo models with >97% effectiveness. The in silico simulations validated the design, highlighting specific responses and predicted efficacy that met the engineering goals. The computational results provided promising next steps for in vitro validation and highlighted the potential of personalized synthetic biology for treating diabetic wounds.

Awards Won: