Modified maggots could help human wound healing

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Genetically modified green bottle flies produce and secrete a human growth factor that helps wound healing. Credit: Max Scott

In a proof-of-concept study, NC State University researchers show that genetically engineered green bottle fly (*Lucilia sericata*) larvae can produce and secrete a human growth factor - a molecule that helps

promote cell growth and wound healing.

Sterile, lab-raised green bottle fly larvae are used for maggot debridement therapy (MDT), in which maggots are applied to non-healing wounds, especially diabetic foot ulcers, to promote healing. Maggots clean the wound, remove dead tissue and secrete anti-microbial factors. The treatment is cost-effective and approved by the Food and Drug Administration. However, there is no evidence from randomized clinical trials that MDT shortens wound healing times.

With the goal of making a strain of maggots with enhanced wound-healing activity, NC State researchers genetically engineered maggots to produce and then secrete human platelet derived growth factor-BB (PDGF-BB), which is known to aid the healing process by stimulating cell growth and survival.

Max Scott, an NC State professor of entomology, and colleagues from NC State and Massey University in New Zealand used two different techniques to elicit PDGF-BB from green bottle fly larvae.

One technique utilized heat to trigger the production of PDGF-BB in transgenic green bottle flies. The technique worked - to a point. The human growth factor was detectable in certain structures within the larvae after the larvae were shocked with high heat - a level of 37 degrees Celsius - but PDGF-BB was not detectable in maggot excretions or secretions, making it unworthy of clinical use.

"It is helpful to know that a heat-inducible system can work for certain proteins in the green bottle fly, but the fact that maggots did not secrete the human growth factor makes this technique a non-starter for clinical applications like MDT," Scott said.

The second technique was more successful. Scott and colleagues

engineered the flies such that they only made PDGF-BB if raised on a diet that lacked the antibiotic tetracycline. PDGF-BB was made at high levels in the larvae and was found in the excretions and secretions of maggots, making the technique a potential candidate for clinical use.

"A vast majority of people with diabetes live in low- or middle-income countries, with less access to expensive treatment options," Scott said. "We see this as a proof-of-principle study for the future development of engineered *L. sericata* strains that express a variety of growth factors and anti-microbial peptides with the long-term aim of developing a cost-effective means for wound treatment that could save people from amputation and other harmful effects of diabetes."

The study was published online in the journal *BMC Biotechnology*.

More information: Rebecca J. Linger et al. Towards next generation maggot debridement therapy: transgenic Lucilia sericata larvae that produce and secrete a human growth factor, *BMC Biotechnology* (2016). DOI: 10.1186/s12896-016-0263-z

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