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November 27, 2017

Nandita Singh, Ph.D.
Senior Science Editor
JoVE

Dear Dr. Singh,

Enclosed please find our manuscript entitled “Protocol to Create Chronic Wounds in Diabetic Mice” by J. H. Kim and M. Martins-Green that we wish to submit to the JoVE. This manuscript describes in great detail the steps needed to create chronic wounds in an *in vivo* diabetic mouse model. Chronic wounds are wounds that do not heal despite conventional antibiotic therapy and standard wound care management. The presence of bacterial biofilms significantly hinders physicians’ efforts to heal these already complicated wounds. These wounds affect millions of Americans and cost the US healthcare billions. Diabetics are especially at great risk for developing chronic wounds and even greater risk of lower limb amputation if bioburden cannot be controlled. Our model was designed specifically to understand the pathophysiology of these wounds.

The manuscript instructs the use of 6 month old *db/db*^{-/-} mice, both male and female, that are both diabetic and obese. The 7mm full-thickness skin excision is treated with inhibitors for antioxidant enzymes to increase levels of oxidative stress in the wounds. After treatment, the wound has chronic inflammation, high oxidative stress levels, poor angiogenesis and damaged vasculature, similar characteristics found in human chronic wounds. The bacteria in the skin microbiome also begin to form biofilm as early as day 3 after wounding, causing extra damage to host tissue. These wounds are fully chronic in 20 days and can remain open with continual bioburden past 60 days, reflecting the long duration of open wounds experienced by humans. The manuscript also describes key instructions that make the chronic wound a reliable model for studying the fundamental wound healing processes that when impaired lead to the initiation of chronicity.

In addition to the manuscript and suggested potential reviewers and editors for review purposes, an amendment for video recording the surgery procedure has been approved by our Institutional Animal Care and Use Committee (IACUC).

JoVE is our journal of choice for publication because it is highly regarded, and the videos published provides visual instruction that is more intuitive and helpful in teaching the community how to successfully reproduce the model.

Please do not hesitate to contact me if you need any additional information. I look forward to hearing from you.

Sincerely,

A handwritten signature in cursive script that reads "Manuela Martins - Green".

Manuela Martins-Green
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