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Ideas to Impact




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A treatment to promote skin wound healing

Inventor: William Gause & Rick Maizels
NJMS, Rutgers Health
& School of Infection-Immunity, Univ of Glasgow

Rutgers docket number/s: S11-119

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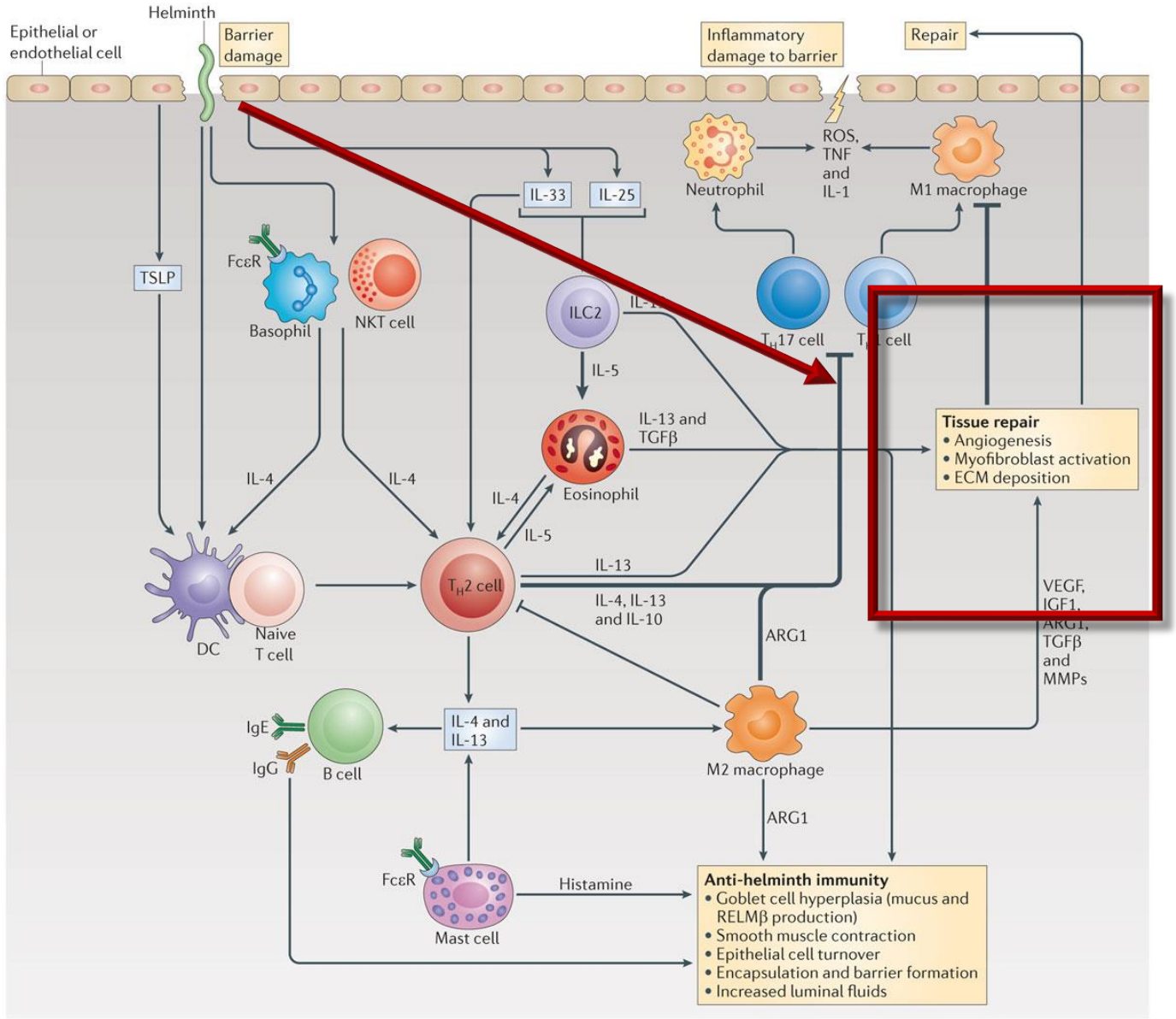
marketingbd@research.rutgers.edu
innovate@research.rutgers.edu

Cells in the helminth-induced type 2 response play a role in the tissue repair response.



Gause et al, Nature Reviews Immunology, 2013, 13(8)608-614

Nature Reviews | Immunology

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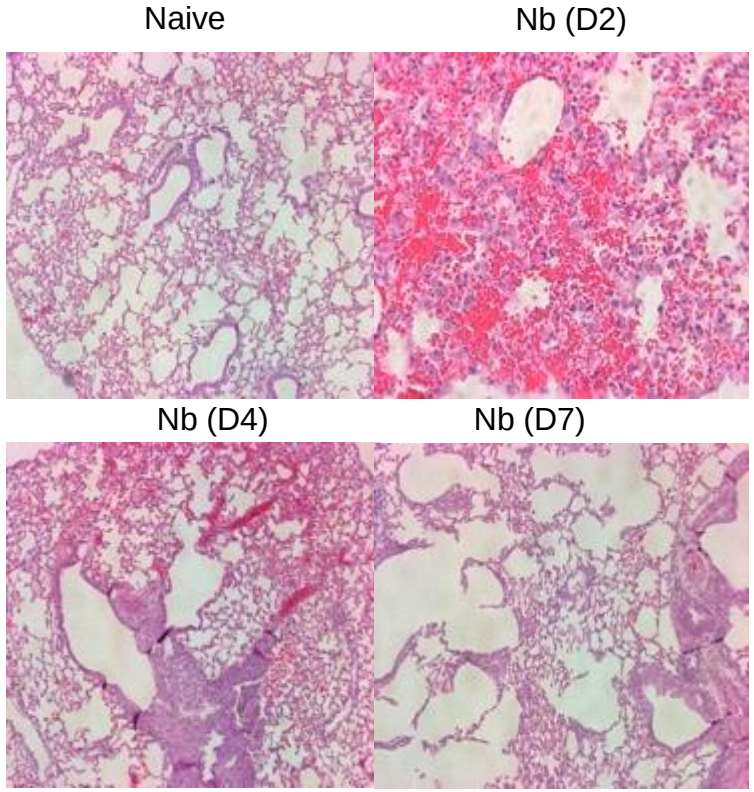
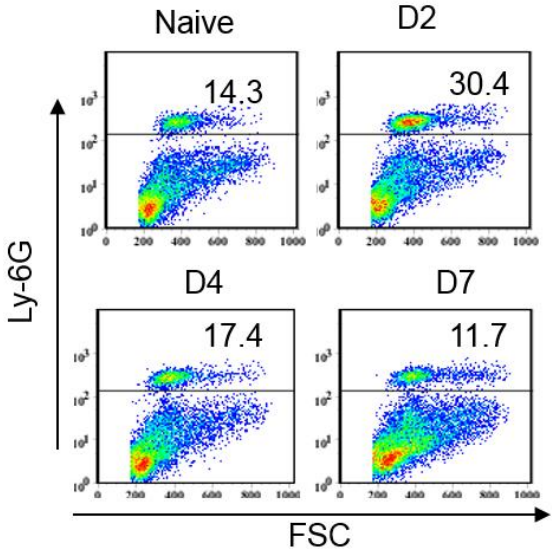
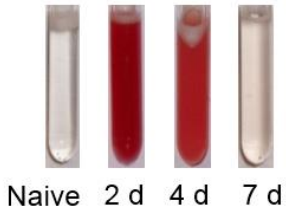
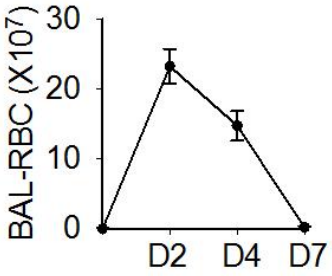
Migrating Nb larvae induces lung injury and airway neutrophilia, which are quickly resolved starting 4 days after inoculation

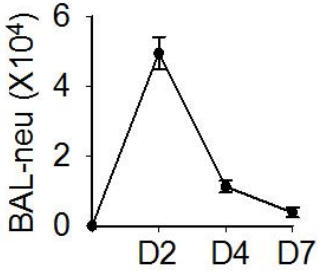






BAL fluid





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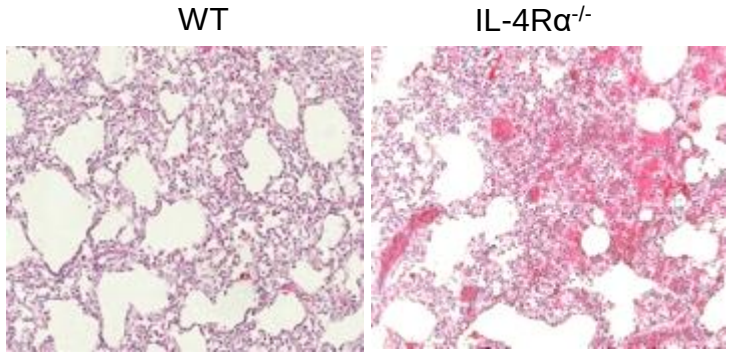
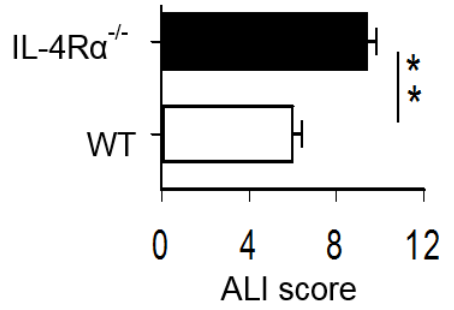
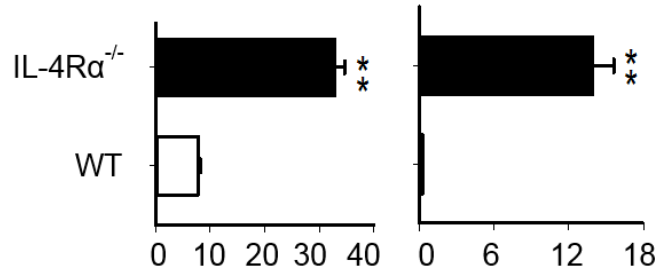
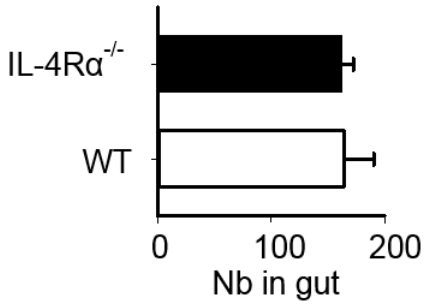
Chen et al., Nature Medicine, 2012

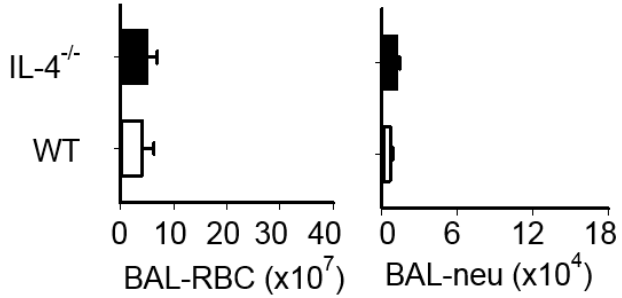
IL-4 or IL-13-mediated signaling controls acute hemorrhaging and inflammation after *N. brasiliensis* lung migration at day 4

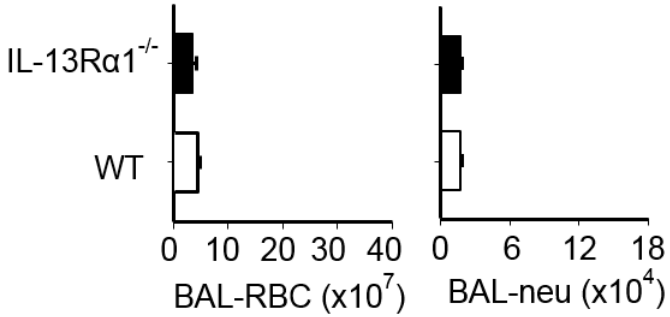












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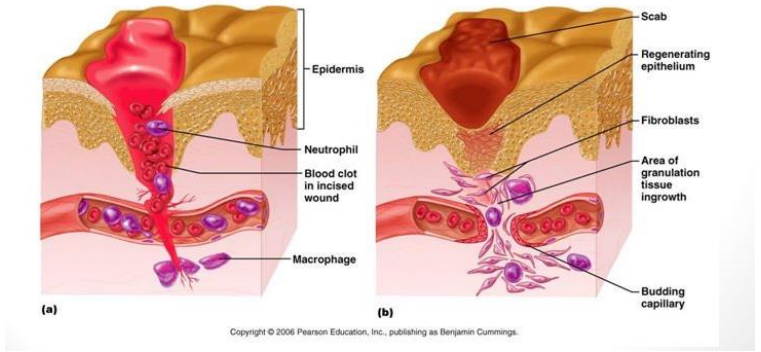
ES products including synthesized small molecule analogues are now being tested in experimental models and clinical trials

ES products:
Drug discovery

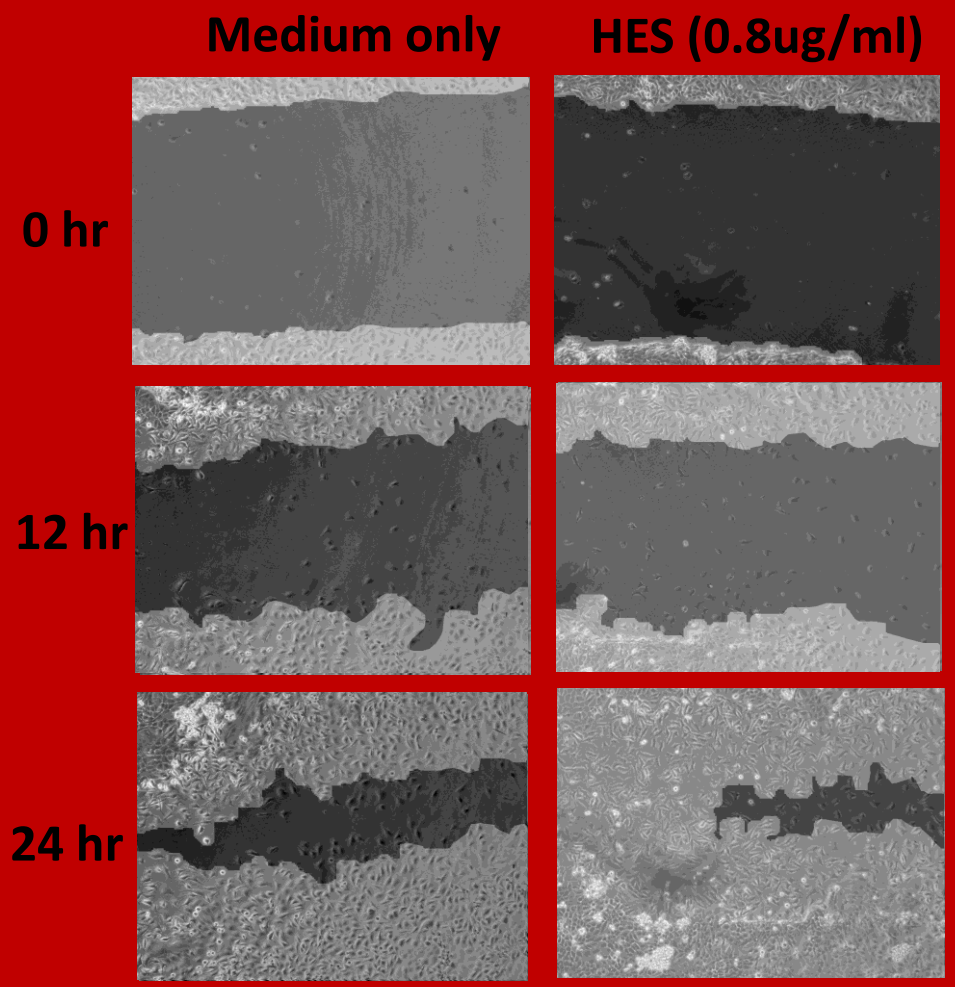
Downregulate harmful inflammation that contributes to tissue damage

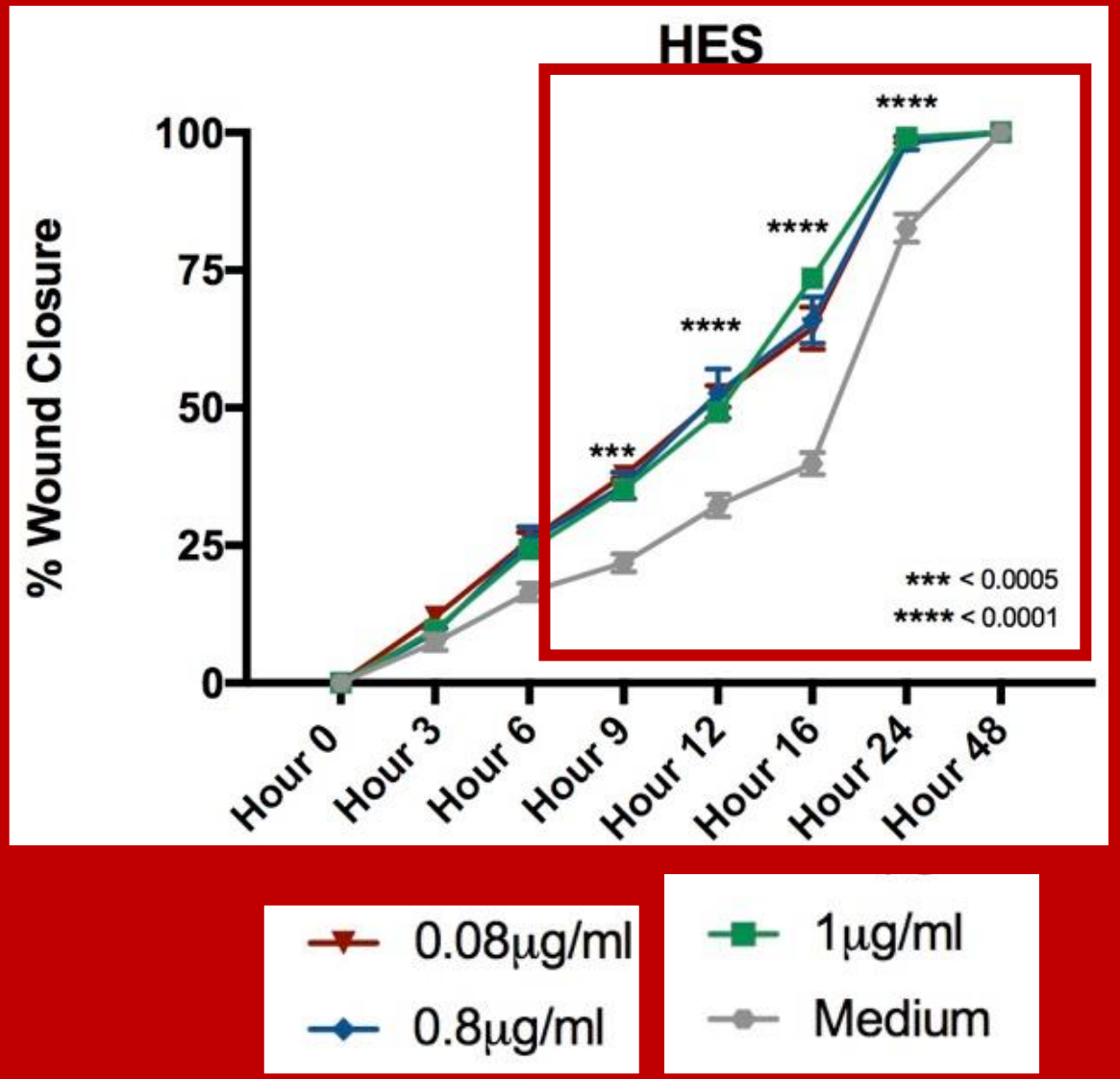
Direct stimulation of tissue repair

ES products may promote wound healing



HES accelerates wound closure in a 2-D *in vitro* scratch test.





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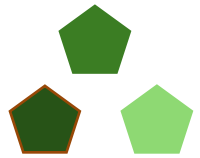
ES products include proteins and associated moieties

Characterization of ES products is at early stage



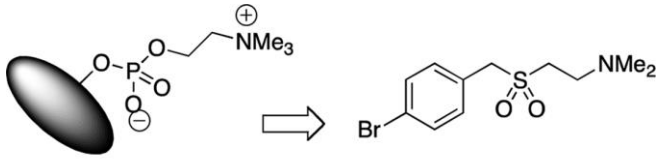
Peptides

TGFbeta Mimic

IL-33 antagonist

Nonpeptides

Phosphorylcholine derivatives

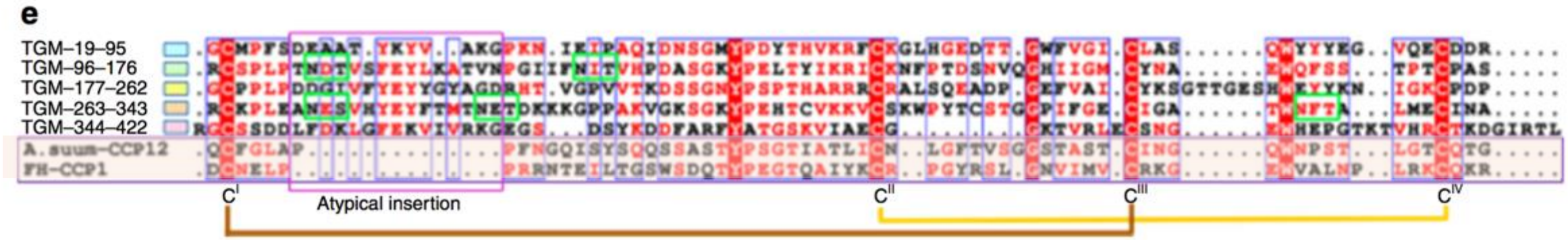


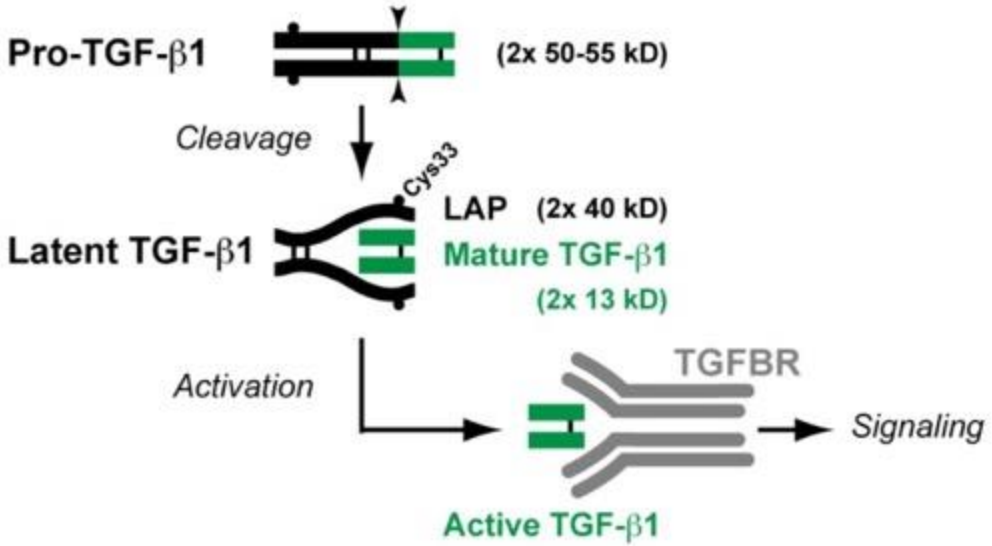
ES-62 Immunomodulatory Protein with PC

Anti-inflammatory small molecule. Prototype drug.

J. Med. Chem. 2013, 56, 9982−10002

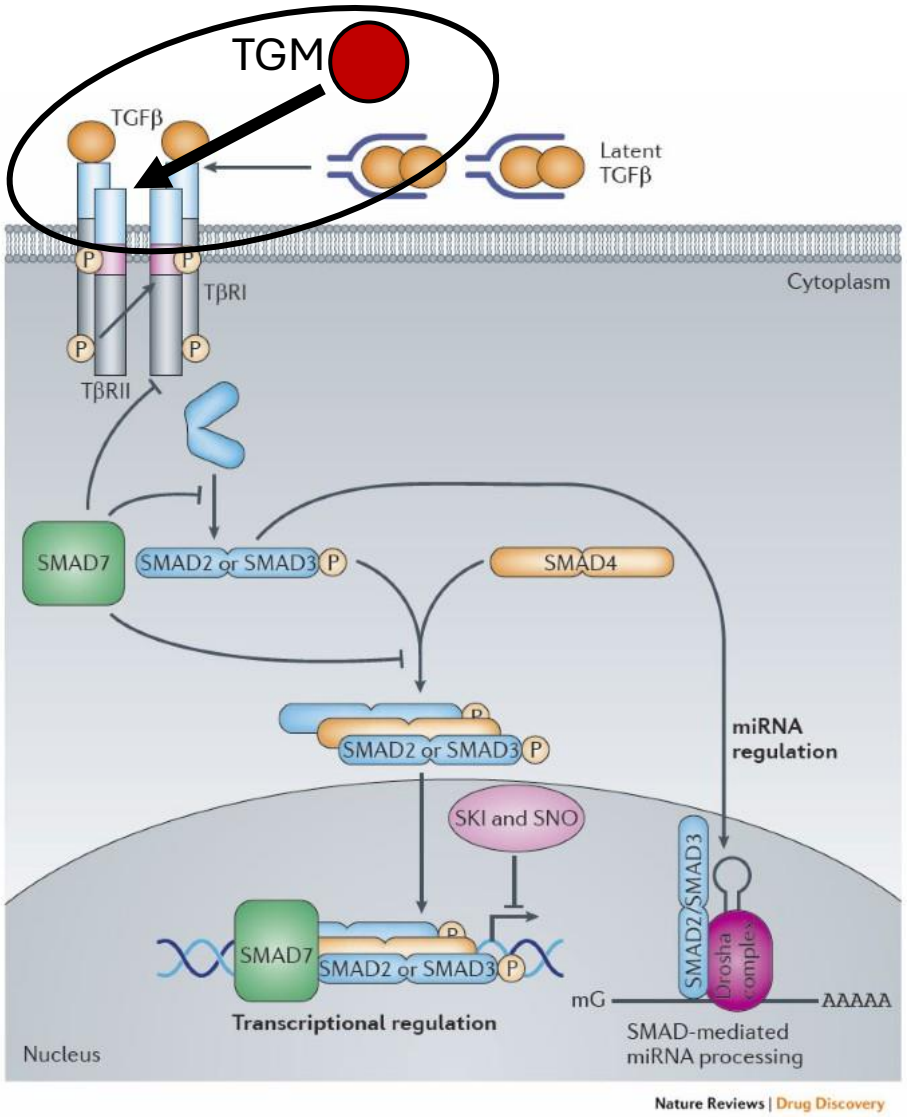
TGF-β Mimic (TGM)





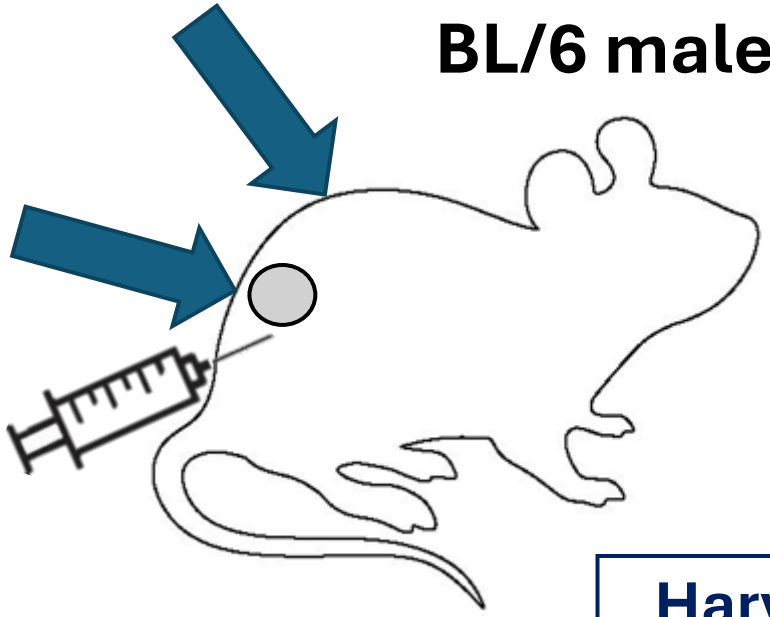
- A member of the CCP (Complement Control Protein) superfamily
- Structurally distinct from TGF-β
- Shares no sequence homology with TGF-β
- Twice the size (404aa) of TGF-β homodimer
- Is constitutively active compared to TGF-β which has to be processed

Johnston et al, Nature Communication, 2017



Adapted from Akhurst et al, Nature Reviews Drug Discovery, 2012, 11:790-811

in vivo wound biopsy study design



Shave + Depilatory cream

5 mm Wound

s.c. TGM or Control

Harvest

Day -3 0 1 2 3 4 5 6 7

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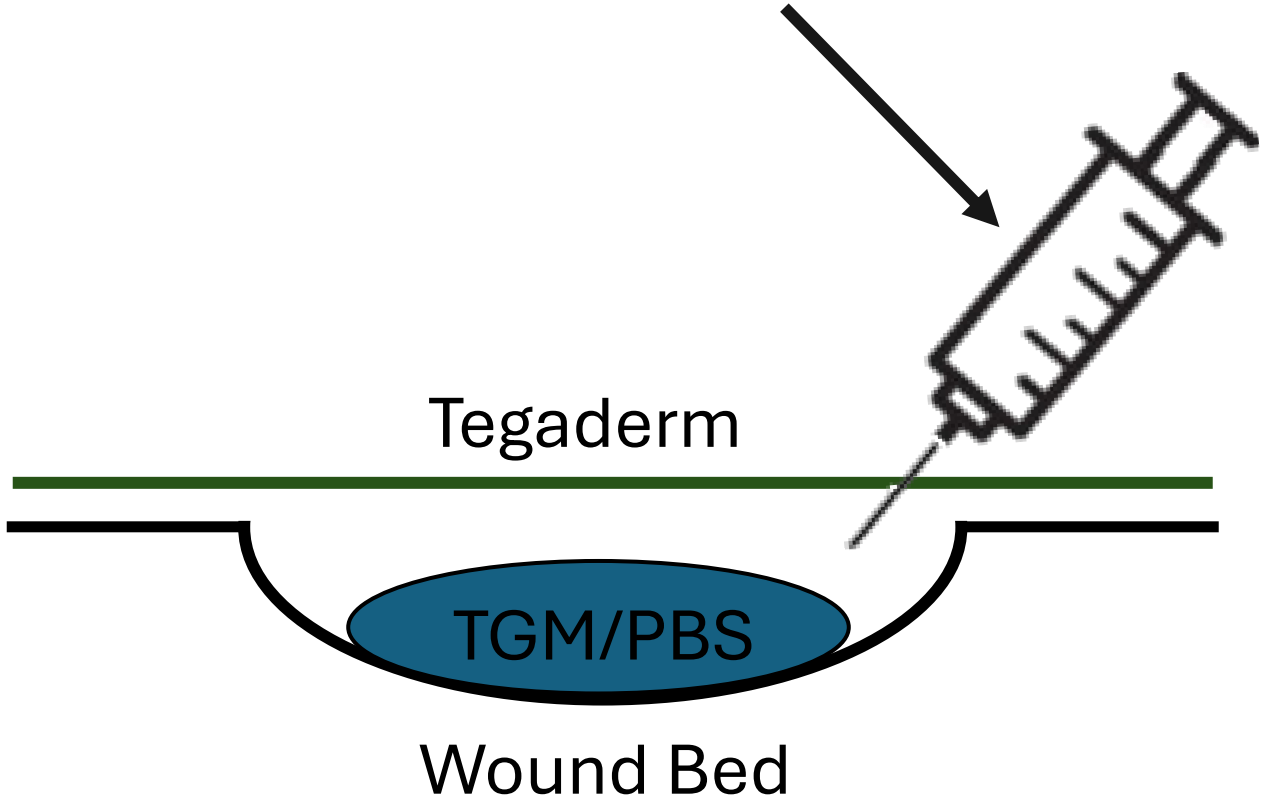
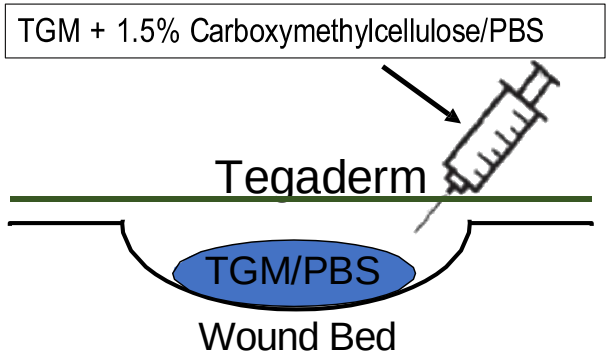
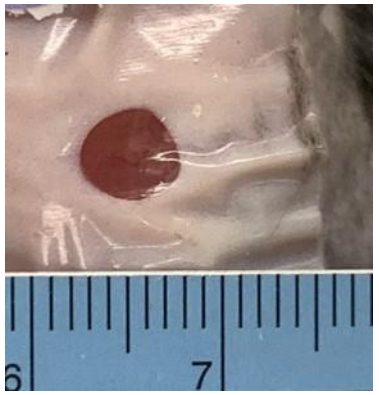
Tegaderm

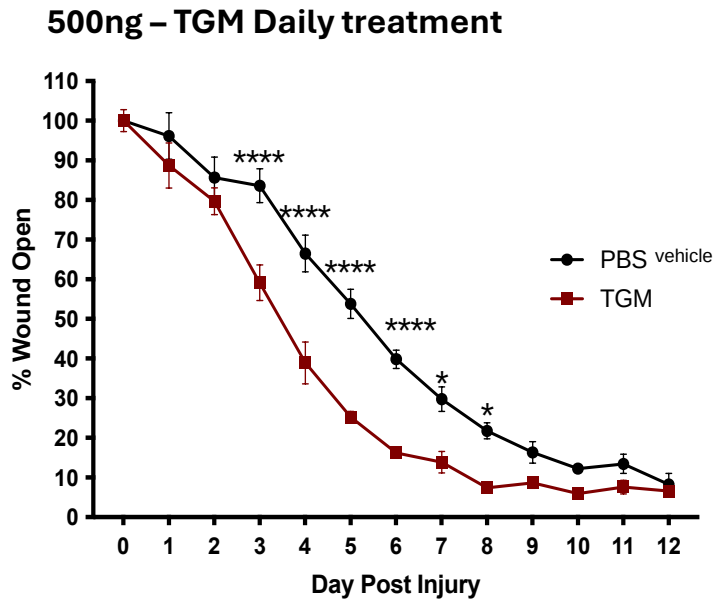
TGM + 1.5% Carboxymethylcellulose/PBS

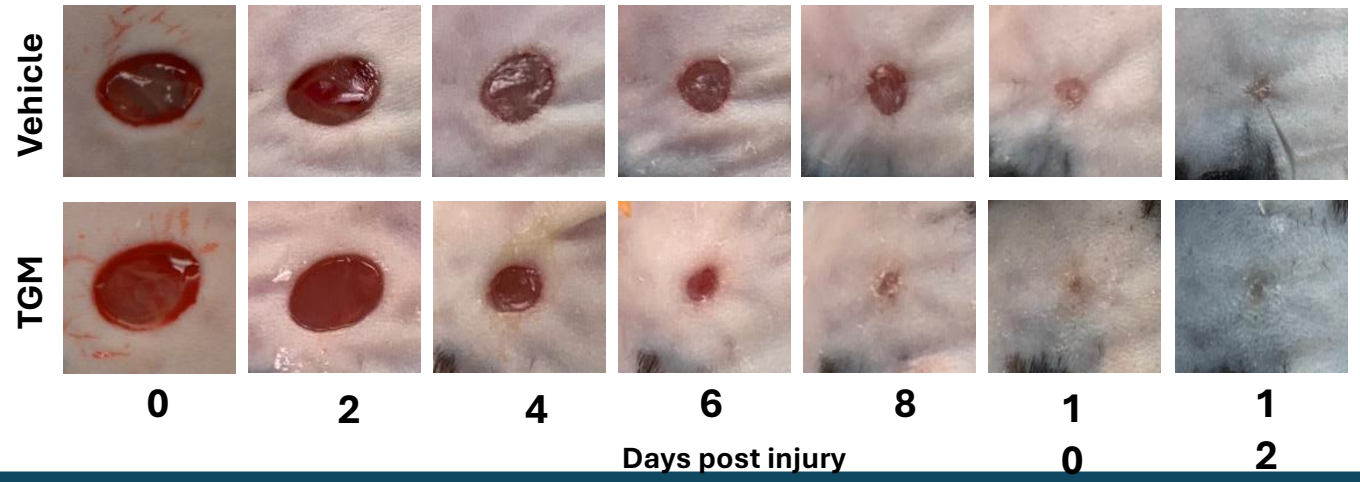


TGM significantly enhances the rate of wound closure with increases in serous volume and concentrations of factors associated with augmented wound healing.









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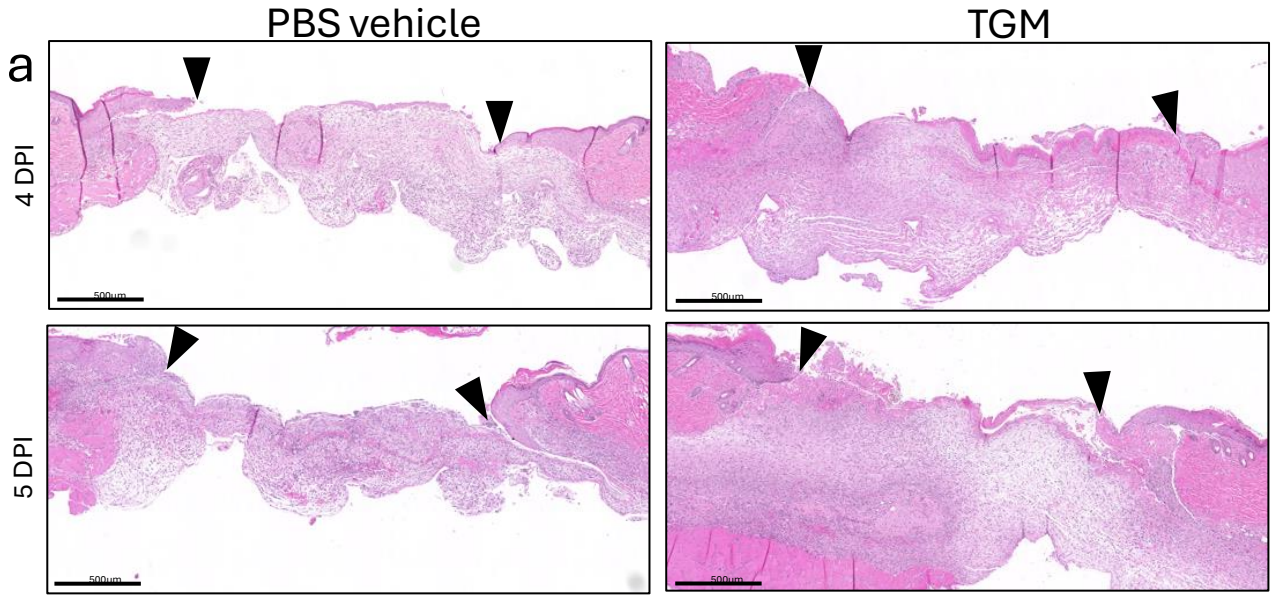
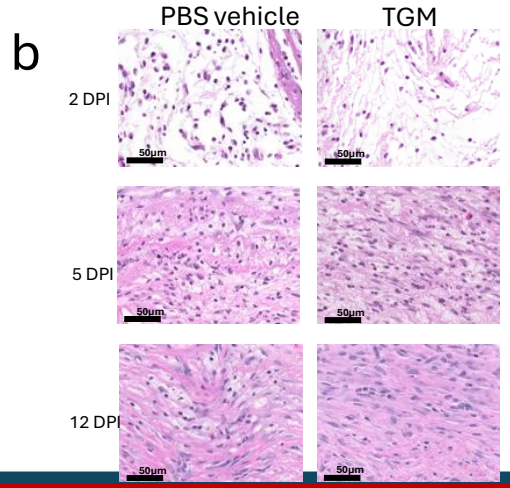
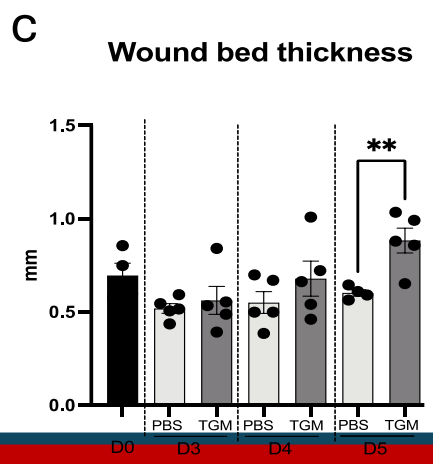
Enhanced tissue thickness suggests that TGM is amplifying the formation and increasing the strength of the developing tissue as it heals and matures.







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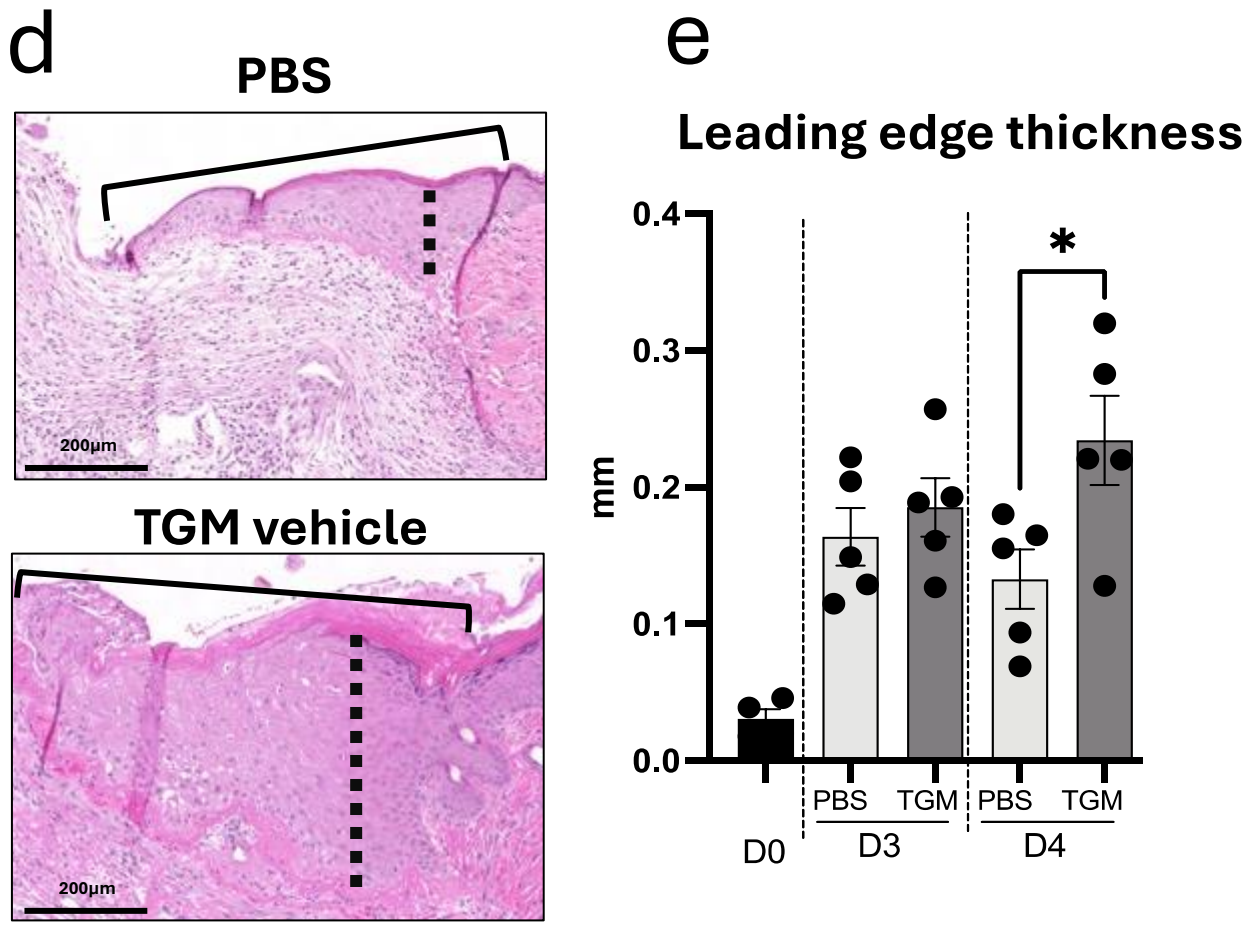
With TGM treatment, there was a significant increase in wound leading-edge thickness by day 4, which correlates with the enhanced wound closure that was first observed at this early time point.



On day 12, TGM-treated wounds showed enhanced skin tissue regeneration with reduced scarring.

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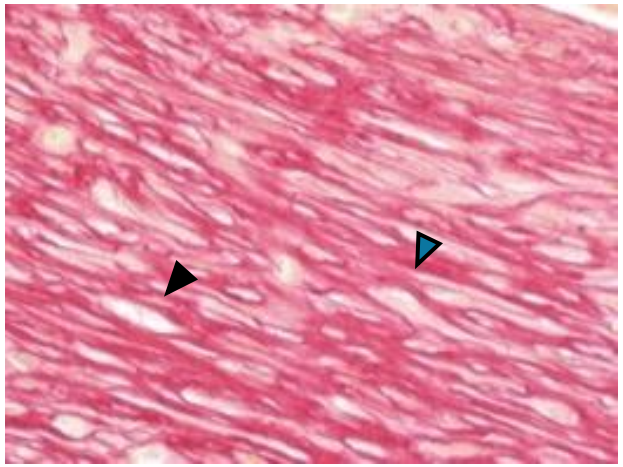
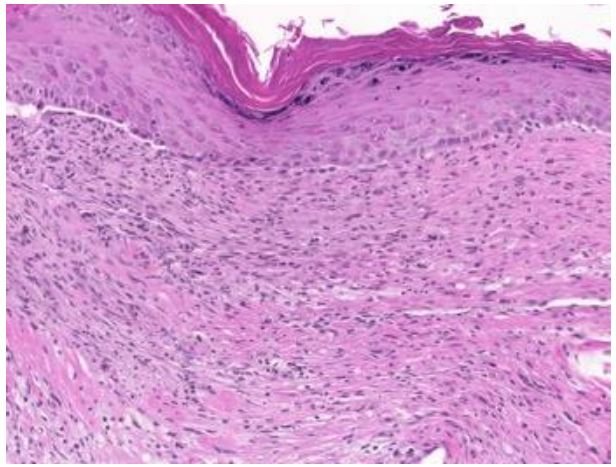
Enhanced basketweave collagen morphology and formation of hair follicles with complete sebaceous glands were observed

Day 12

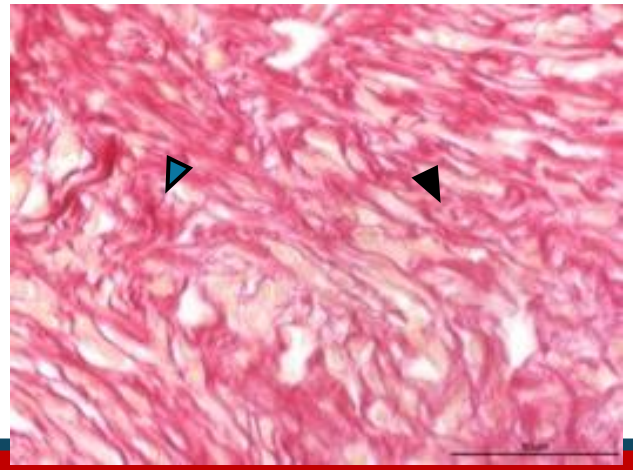
Day 12

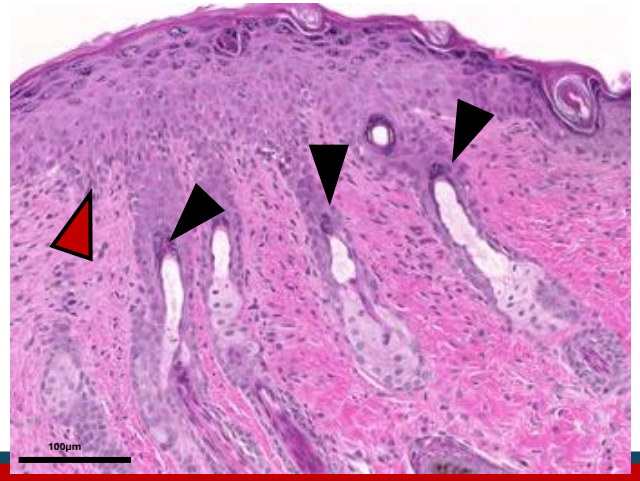
PBS vehicle

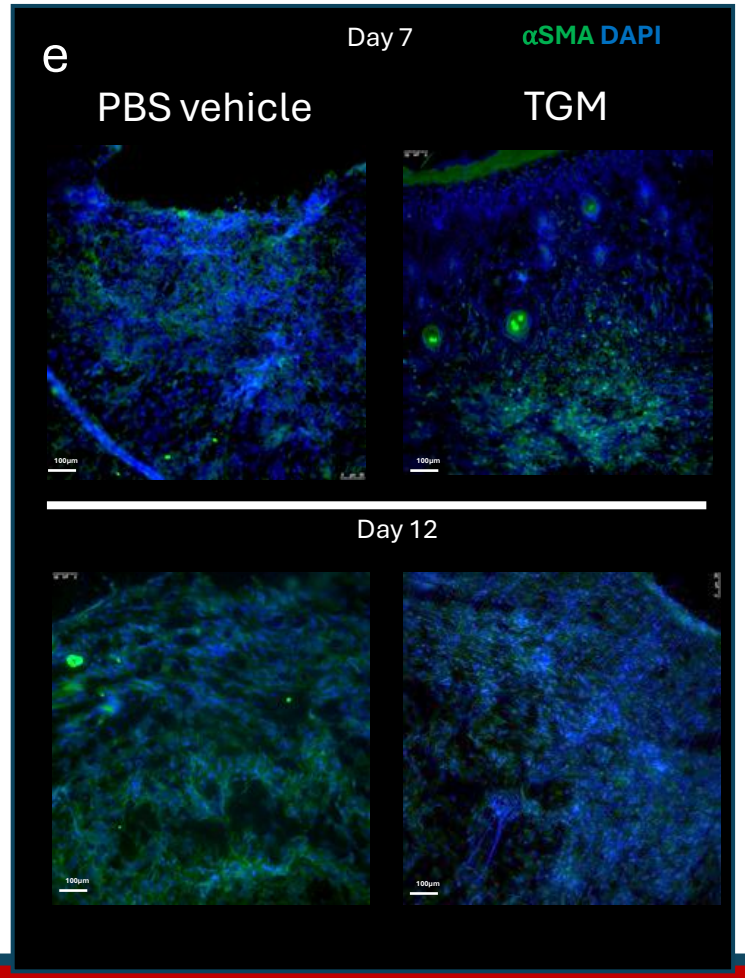


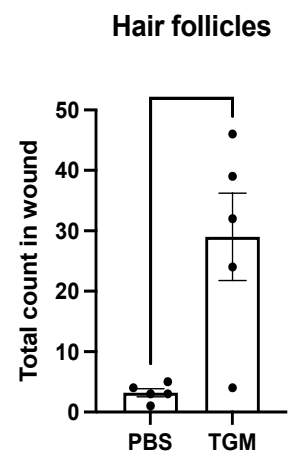


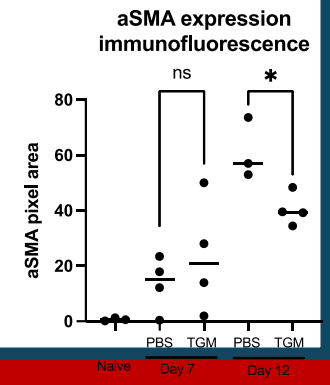
TGM



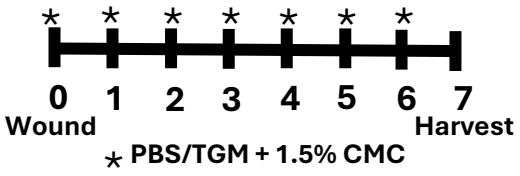








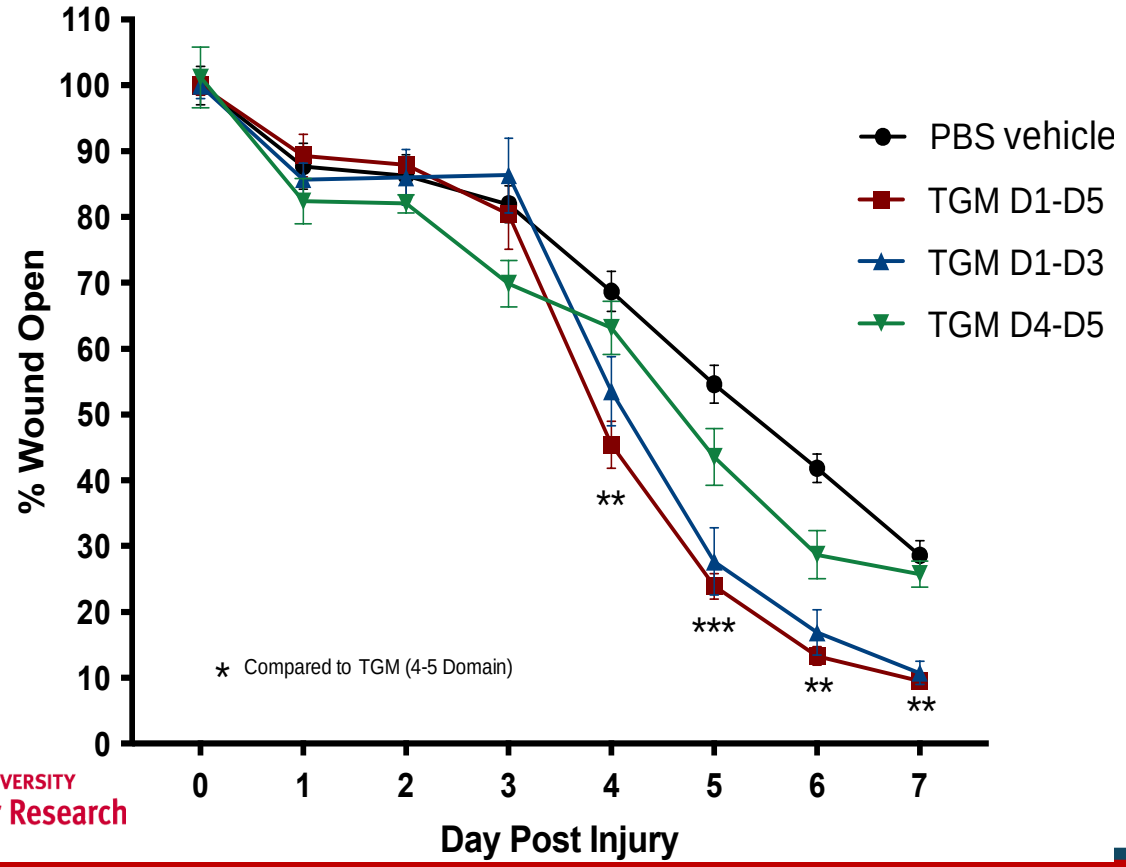
TGM mediates enhanced wound healing through TGF- βR domain activity.



Domains required for activity

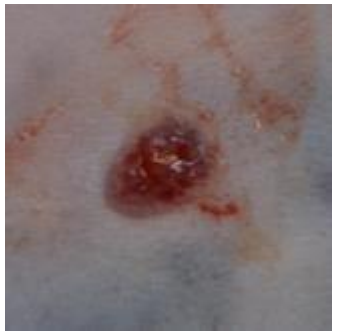
	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5
TGM-1	100	100	100	100	100

Modified from Smyth *et al*, Int J Parasitol , 2018, 48(5):379-385

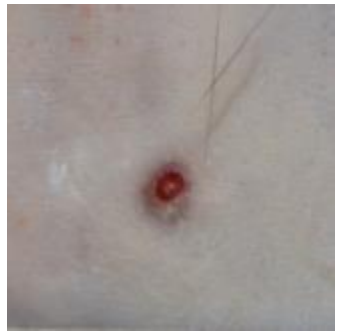


Day 7

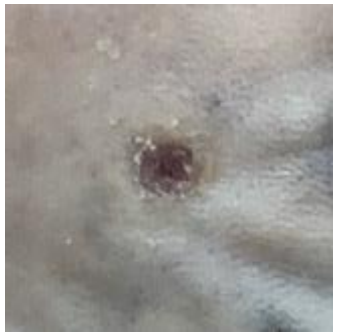
PBS



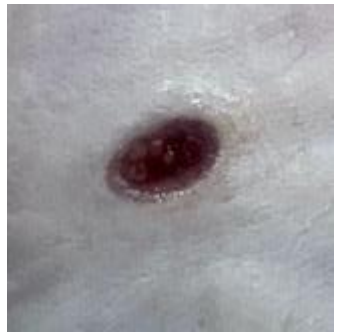
TGM Whole



TGM Domains 1-3 (TGF-ßR activity)



TGM Domains 4-5 (no TGF-ßR activity)



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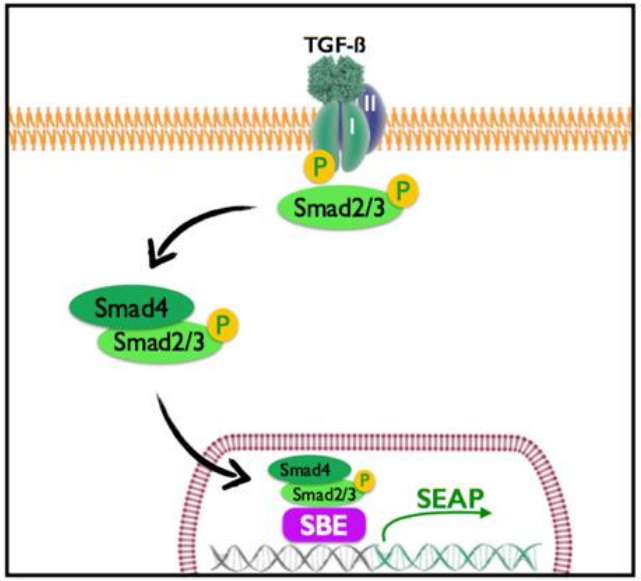
Summary

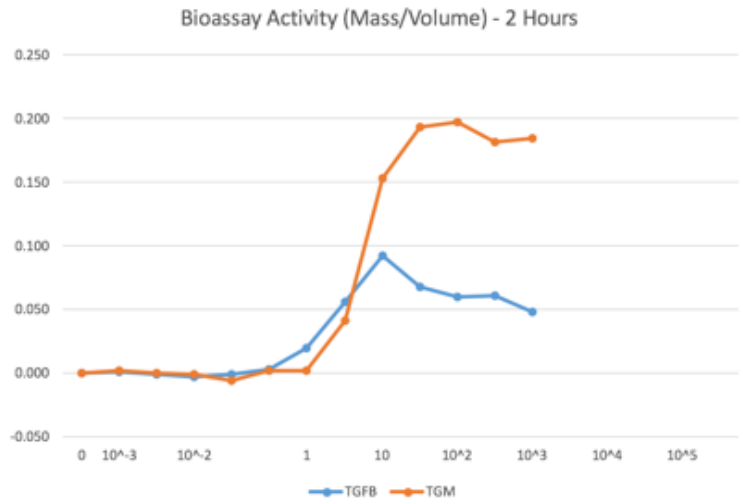
- Daily TGM application significantly enhances the rate of cutaneous wound closure at 5 days following injury.
- TGM demonstrated overall better wound reorganization at later phases as observed through collagen orientation and hair follicles.
- TGM's activity leads to increased inflammation into the wound bed including accumulation of migratory Ly6C+ myeloid cells.
- TGM treatment reprograms macrophages favoring expansion of a CD206- subset expressing markers associated with wound healing.
- TGM's wound healing activity and macrophage modulation is predominantly mediated through TGF-ßR signaling.

https://techfinder.rutgers.edu/tech/A_treatment_to_promote_skin_wound_healing

TGM demonstrates greater therapeutic potential compared to TGF-β

- Is constitutively active compared to TGF-β which had to be processed
- Binds independently to both TβRI and TβRII
  - TGM binds directly to TβRI with high affinity
- TGM proved to be more active at a lower dose
- Easier to produce
- Low immunogenicity
- Very stable during storage





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USDA

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Dr. Alexander Lemenze

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Tammy Galenkamp

Cellular Imaging and Histology Core

Luke Fritzky
Joel Pierre

The Center for Advanced Proteomics Research

Dr. Hong Li
Dr. Tong Liu

Comparative Medicine Resources (CMR)

Marleata Anderson

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