A novel quaternary polyethyleneimine (QPEI) accelerates wound closure by promoting re-epithelialization, ECM deposition, angiogenesis, and macrophage polarization

Bithi Chatterjee[1], Markus Rothmaier[1], Leah Cooksey[2], Michelle Rudden[2], Holly Wilkinson[2], Andrea Bell[3], Jeff Hart[3], Matthew Hardman[2], Ran Frenkel[1]

[1]Polaroid Therapeutics AG, Zurich, Switzerland, [2]Hull University, United Kingdom, [3]Cica Biomedical, United Kingdom

Who We Are

Polaroid Therapeutics AG is a Swiss biotech company revolutionizing wound care by developing novel antimicrobial compounds to treat infected wounds.

Partnering

We seek strategic partnerships to advance our clinical pipeline.

We would like to collaborate with clinical and scientific KOLs in this field.

Innovation & Pipeline

We are actively exploring the use of QPEIs in medical devices within the wound care space.

Various innovative and disruptive solutions may be achievable depending on the choice of QPEI and how it is incorporated into the medical device.

Introduction

Globally, 1-2% of the population suffers from chronic wounds each year.

The prevalence of chronic and complex wounds is a significant public health issue requiring novel approaches to improving patient outcomes. We evaluated the potential of the C24J QPEI compound to promote wound healing in a full-thickness wound healing model.

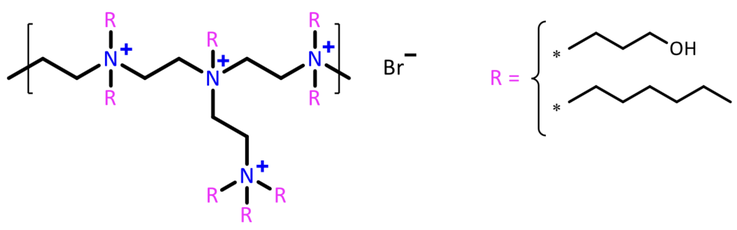


Figure 1. Quaternary ammonium polyethyleneimines (QPEIs) are a family of alkyl-derivatives of a branched polyethyleneimine (a synthetic polymer) with broad spectrum anti-microbial activity.

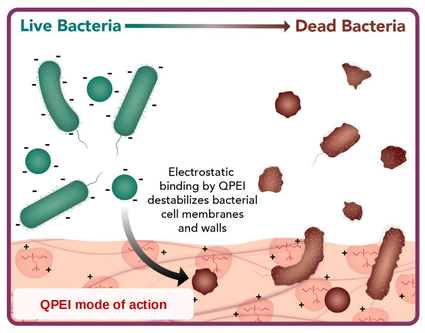


Figure 2. QPEI acts via electrostatic interactions with negatively charged bacterial cell components. While evaluating the safety of QPEI* in an uninfected in vivo mouse wound model, we discovered **improved wound healing**.

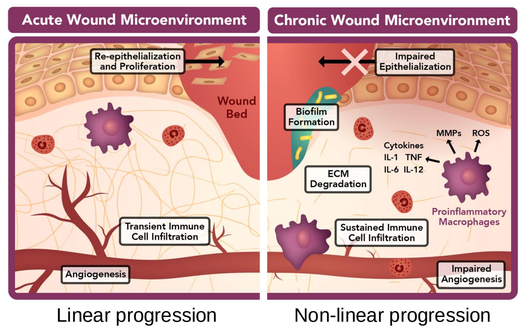
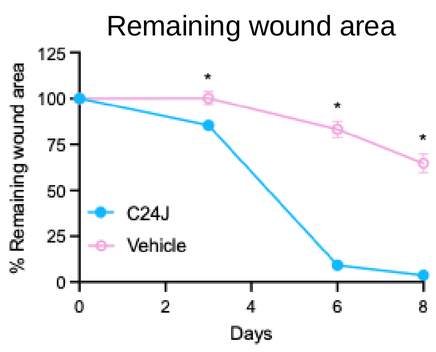


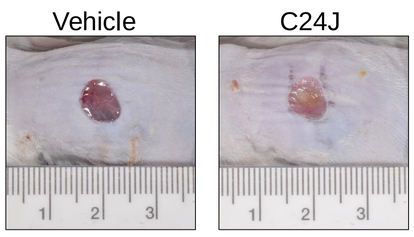
Figure 3. Wound healing is stalled in chronic wounds and treatment with QPEI C24J could remove or modulate the pathways which are blocked.

*data generated using **QPEI polymer C24J** as an aqueous emulsion

Results

C24J accelerates wound closure

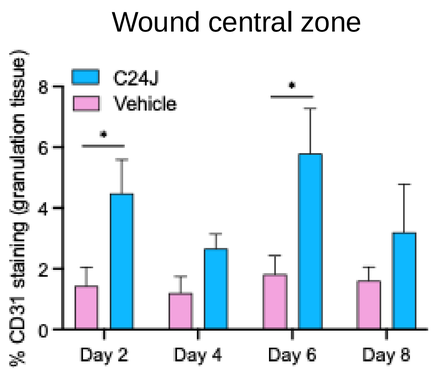




Representative wound images
Day 6

Figure 4. Wound healing study in Balb/c mice with full-thickness wounds with single application of C24J at day 0.
* p ≤ 0.05 compared to vehicle
Wounds were examined visually, and closure was determined using the image analysis software Image Pro. Closure is defined as the presence of an epithelial layer on the wound.

Increased angiogenesis is observed in response to C24J



C24J promotes collagen 3 deposition

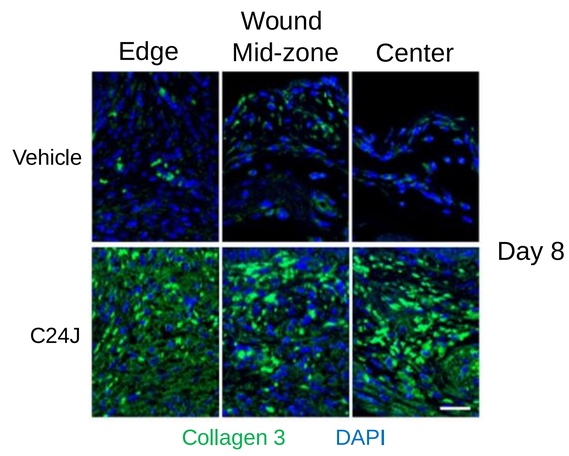
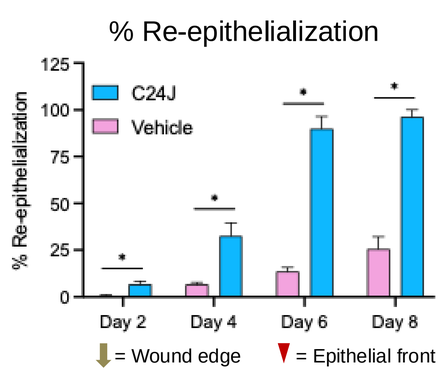


Figure 7. (Left) Upon C24J treatment, increased angiogenesis (CD31+ staining) takes place in granulation tissue compared to vehicle. * p ≤ 0.05 compared to vehicle. (Right) Collagen 3 deposition with C24J treatment indicates improved extracellular matrix features. DAPI marks the nuclei of the cells.

Re-epithelialization is significantly improved with C24J treatment



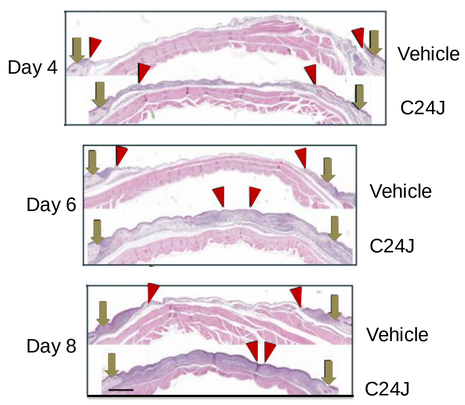


Figure 5. The epithelial front (red arrowheads) comes together rapidly with C24J treatment as compared to vehicle control. This is quantified in the graph over time. * p ≤ 0.05 compared to vehicle.

Differential enhancement of pro- and anti-inflammatory macrophages after C24J treatment

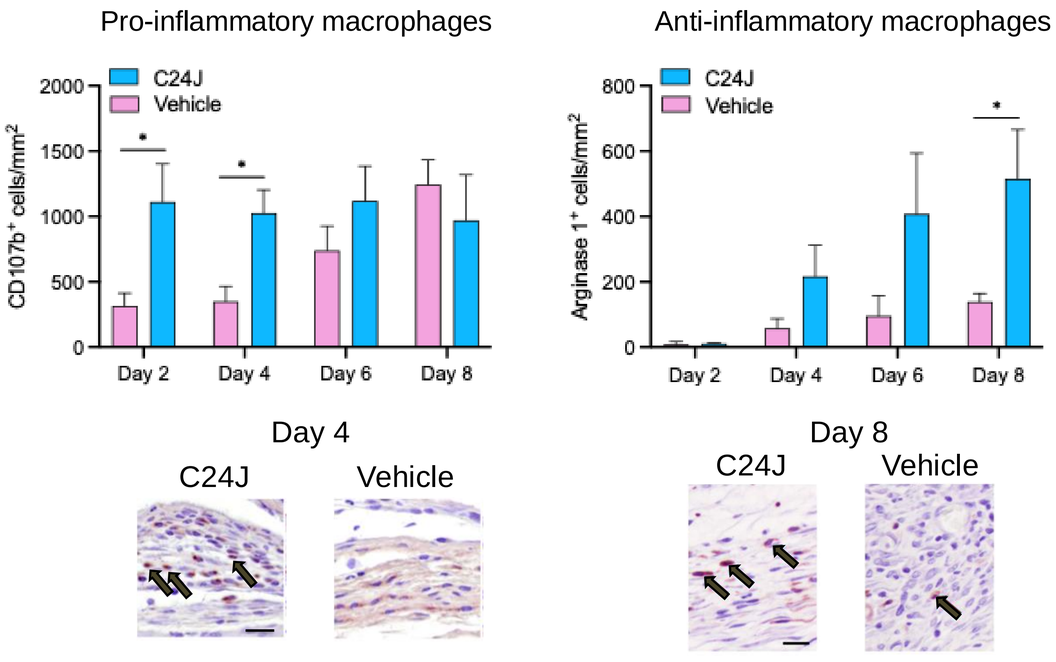
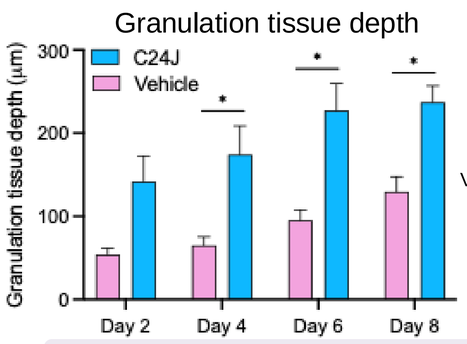


Figure 8. Because proinflammatory macrophages are enhanced in the chronic wound microenvironment, the observed differences in the macrophage populations upon C24J treatment could be responsible for improved wound healing outcomes. * p ≤ 0.05 compared to vehicle.

C24J significantly enhances granulation tissue formation



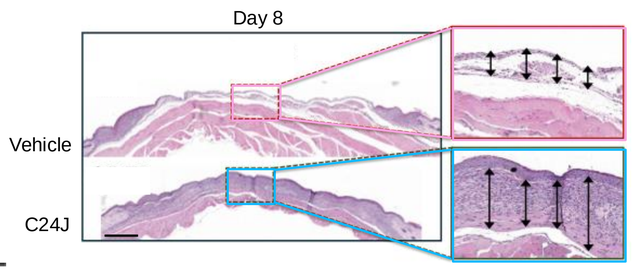


Figure 6. Upon C24J treatment, granulation tissue thickness is increased compared to vehicle, potentially providing more ideal conditions to promote wound healing. This is quantified in the graph over time. * p ≤ 0.05 compared to vehicle.

Methods

Animal Model & Treatment

Male Balb/c mice (n= 9-10 per group) received a single 6 mm full-thickness punch biopsy wound on the dorsal flank. 20 µL of C24J QPEI (2 mg/mL in 0.5% DMSO-H_2O) or vehicle was applied topically at Day 0. Wounds were covered by Tegaderm™ (replaced on Days 3 and 6).

Wound Monitoring

Photographs were taken on Days 0, 3, 6, and 8 to monitor wound closure over time.

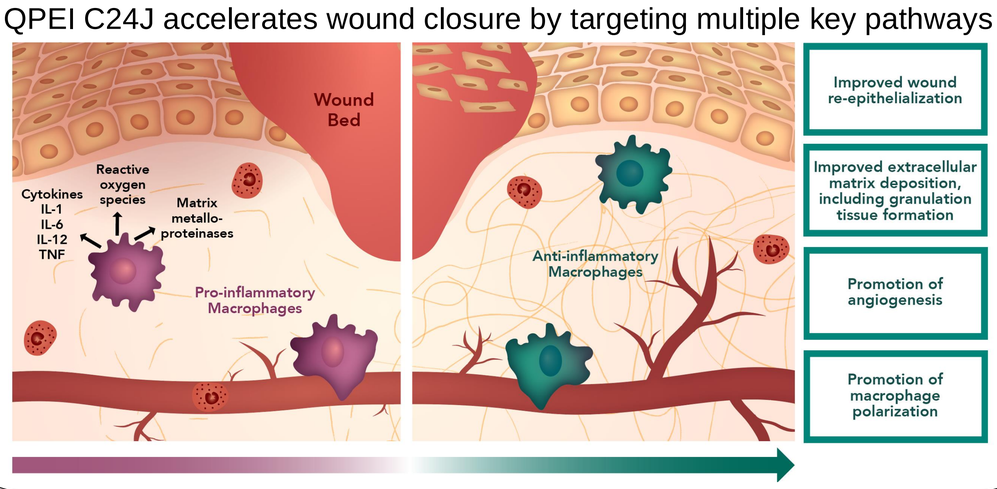
Tissue Collection & Histology

Animals were sacrificed at the indicated time points, and tissues were collected for analysis using immunohistochemistry or immunofluorescence.

We thank our colleagues at Cica Biomedical Ltd. UK and the University of Hull, UK, for their valuable support.

Conclusions

QPEI C24J accelerates wound closure by targeting multiple key pathways



Bithi Chatterjee, PhD | Senior Project Manager | E: bithi.chatterjee@polaroidtx.com | polaroidtherapeutics.com
Polaroid Therapeutics AG | Brandstrasse 24, 8952 Schlieren, Switzerland