



COMPARATIVE BIOSCIENCES, INC.  
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH



## Technical Bulletin: DERMAL BURN MODELING



Our Purpose:  
To revise and systematize  
scientific knowledge of  
the experimental  
model for cutaneous  
burns in rodents.

### ANIMAL MODELS IN BURN RESEARCH

Whether it is a small nick, a large surgical incision, or a burn, healing is dependent upon the body's ability to heal itself. A vital role is played by our own natural biomolecules in the healing process, including their contribution to the growth of new cells and the development of new blood vessels that provide nutrients to those cells.

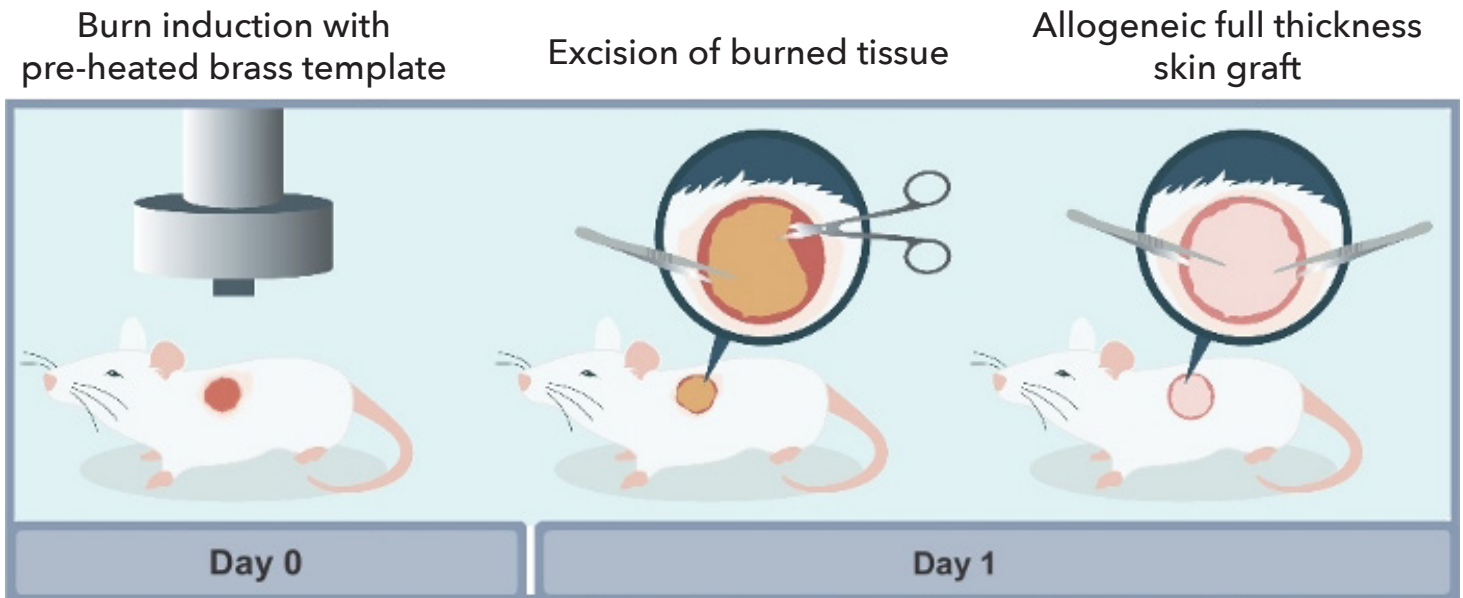
**Here at Comparative Biosciences, Inc.** we are developing the models to test the therapeutics that could accelerate the burn healing process.

#### There are 3 major types of dermal thermal burns:

- First Degree or Superficial: Superficial epidermis with hyperemia and no blistering
- Second or Partial Thickness: Affects epidermis and dermis-superficial (epidermis and papillary dermis) or deep (reticular dermis)
- Third or Full thickness: Affects epidermis and dermis and extends to the subcutaneous tissue

Comparative Biosciences, Inc and GD3 have joined together to providing expert scientific resources and high quality contract research services to all sectors within the biomedical and pharmaceutical community.

## A Murine Model of a Burn Wound Reconstructed with an Allogeneic Skin Graft



Schematic illustration of the different steps required to reproduce the experimental model described in this article. There are three main steps to the procedure: (1) induction of the burn wound using a preheated brass template; (2) surgical excision of the non-viable necrotic tissue at 24 hours after the burn injury; (3) surgical wound reconstruction using a full thickness allogeneic skin graft.

### SUMMARY:

The aim of this study was to develop a murine model of burn wound healing. A thermal burn was induced on the dorsal skin of mice using a preheated brass template. Burned tissue was debrided and overlaid with a skin graft harvested from the tail of a genetically similar donor mouse.

### INTRODUCTION:

**Comparative Biosciences, Inc.** provides a range of sophisticated and customized dermal burn models. The most significant limitation of using mice to mimic human wound closure is the difference between the skin anatomy and physiology. Mouse wounds heal mostly via contraction, whereas human wounds heal through granulation tissue formation and re-epithelialization. To account for this discrepancy, the current model may be modified and used in combination with a splinting ring tightly adhered around the wound to prevent skin contraction. Given some advantages and disadvantages of this *in vivo* protocol, this model could serve as a tool to study certain processes involved in wound healing that are impossible to study *in vitro*.



Second degree burn at time of induction

Gottingen Pig post-surgical bandage

## How is Dermal Burn Modeling used in preclinical research?

### STATE-OF-THE-ART PRE AND POST-SURGICAL CARE

Animal models have been developed to study the complex cellular and biochemical processes of burn and wound repair and to evaluate the efficacy and safety of potential therapeutic agents. Several factors can influence wound healing. These include aging, infection, medications, nutrition, obesity, diabetes, venous insufficiency, and peripheral arterial disease. Lack of optimal preclinical models that are capable of properly recapitulating human wounds remains a significant translational challenge. Animal models should strive for reproducibility, quantitative interpretation, clinical relevance, and successful translation into clinical use. In this Technical Bulletin we discuss animal models used in wound experiments including mouse, rat, rabbit, Göttingen minipigs, with a special emphasis on impaired burn and wound healing models.

### WHY WE LIKE GÖTTINGEN PIGS AT CBI

As we optimized this model, we worked with several strains of pigs and settled on the Marshall Farms Göttingen Minipig. The pigs are physically uniform, free of disease, gentle, have good appetites and easy to handle and carry. Further, they handle multiple anesthetics, multiple sedations and restraint well. Subclinical conditions, particularly respiratory infections, can lead to poor surgical and anesthesia outcomes in swine, but the Göttingens are free of pulmonary pathogens. Another important feature of these pigs is their uniformity in size and shape and their growth curves. This is important in following wound progression and healing over time. We can also conduct modeling in disease states such as hypertension, diabetes and immune suppression in burn- and wound-healing studies to mimic human disorders.

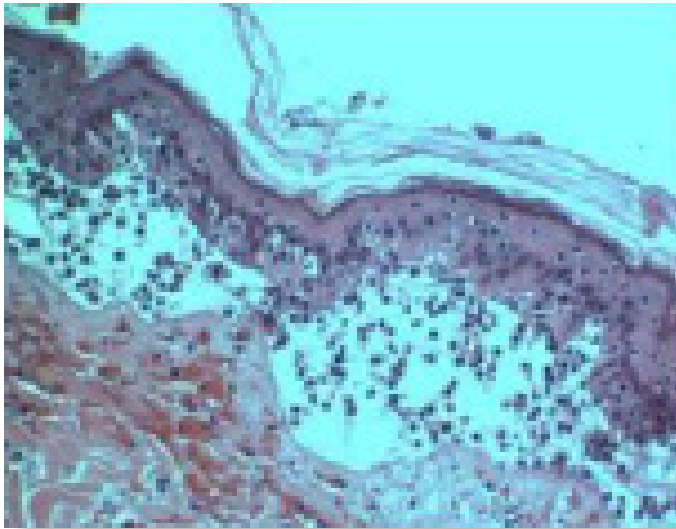
For our burn studies, we design our studies to optimize the success of the study. This means that we have well designed studies with adequate numbers of animals and study endpoints to assure relevance of the data. Initially, preconditioning, acclimation and environmental enrichment are key parts of the study design.

### BURN TREATMENT MODALITIES

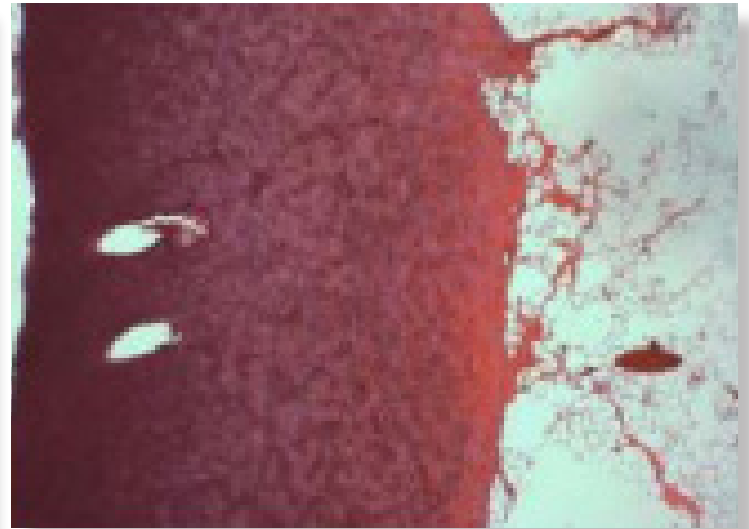
**There is a variety of treatment modalities that are of current interest including:**

- Topical or systemic administration
- Escharotomy and debridement
- Stem cell therapies
- Autologous cells and stem cells
- Small molecules
- Biologics and immunomodulatory agents
- Bandaging or wound dressings
- Sealants
- Minced preps, split and full thickness grafting

Each modality may require variations on the model. Each study protocol is custom tailored to the needs of the client.



Full thickness burn, 2 days. There is a blister with separation of the epidermis from the underlying dermis. There are large, fluid fill blisters containing large numbers of neutrophils. The underlying dermis is exposed with inflammation, edema, hemorrhage and congestion.



Histology Day 3: Full thickness acute thermal damage to the epidermis post -surgically. Note that thermal damage extends through the dermis into the deep adipose tissue. HE 40x

## Histology, full thickness, with loss of epithelium-2 days

### RESEARCH HISTOPATHOLOGY STUDIES

- Surgical biopsies during course of study as well as necropsy
- Tissue stained with HE, trichrome, other stains upon request
- IHC for various markers upon request
- Digital image analysis for wound size, cellular infiltrates, inflammatory markers or other markers
- Photomicroscopy



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### THE FDA AND ANIMAL MODELS:

The FDA relies on data generated from animal models to assess efficacy and safety of new drug entities. The FDA Animal Rule states the FDA can rely on the evidence from animal studies to provide substantial evidence of the effectiveness of a drug only when all of the following four criteria are met:

- There is a reasonably well-understood pathophysiological mechanism of the toxicity of the substance and its prevention or substantial reduction by the product.

The effect is demonstrated in more than one animal species expected to react with a response predictive for humans, unless the effect is demonstrated in a single animal species that represents a sufficiently well-characterized animal model for predicting the response in humans.

The animal study endpoint is clearly related to the desired benefit in humans, generally the enhancement of survival or prevention of major morbidity. The data or information on the kinetics and pharmacodynamics of the product or other relevant data or information, in animals and humans, allows selection of an effective dose in humans.