



# PROTEODERM INC

## Secreted Matrix™ and Matrix NC-138™ White Paper by Michael Cohen

### Abstract

Among the many cosmetic actives available, proteins have stimulated substantial interest for several years. The main reason is that one of the properties of proteins is the delivery of a chemical message that up or down regulates particular cell functions. An accepted view of protein activity is that their amino acid constituents have structures which send a specific signal to the specific cells, for example to the fibroblasts to increase collagen production. Particular proteins are therefore ideal cosmetic ingredients that can be used to counteract the formation of wrinkles and loss of skin elasticity. Proteoderm has used its expertise in proteomics and protein technology to develop a unique natural matrix of proteins called **Secreted Matrix™ and Matrix NC-138™** for use in anti-ageing skin products.

### Introduction

The combination of age, environmental factors and genetic component can contribute to changes in the appearance, viscoelastic properties and topography of the skin, particularly of the face, changes which in many cultures are considered undesirable if not pathologic. While such changes are usually superficial and have no physical impact on the function of the body's major organs, manifestations on the face, neck and, to a lesser extent, the hands are enduring targets for the application of myriad agents in an ongoing attempt to effect a dramatic reversal or at least arresting the progression of the ravages of time. Most attempts and agents are superficial, short term and ineffective.

During pregnancy, a woman's body increases the production of specific proteins in response to secretions produced by the embryo. These specific proteins effect specific receptor in both fibroblasts and keratinocytes that increase the production of collagen. Proteoderm has **patented** these secretions and developed **compositions including topical formulations** comprising secreted products obtained from the culture medium of human stem cell derivatives and particular combinations of components thereof are provided for treatment of various dermatological conditions, such as adverse consequences of aging, wrinkling, altered pigmentation, altered viscoelasticity, and altered thickness,

among others. Further, Proteoderm has developed methods for using these compositions and topical formulations for treating adverse or undesirable dermatological conditions are also provided, as well as preventing the appearance of undesirable dermatological conditions. **Unlike injection of collagen that occupies extracellular space Proteoderm methods and product enhance the natural formation of collagen** (Figure 1).

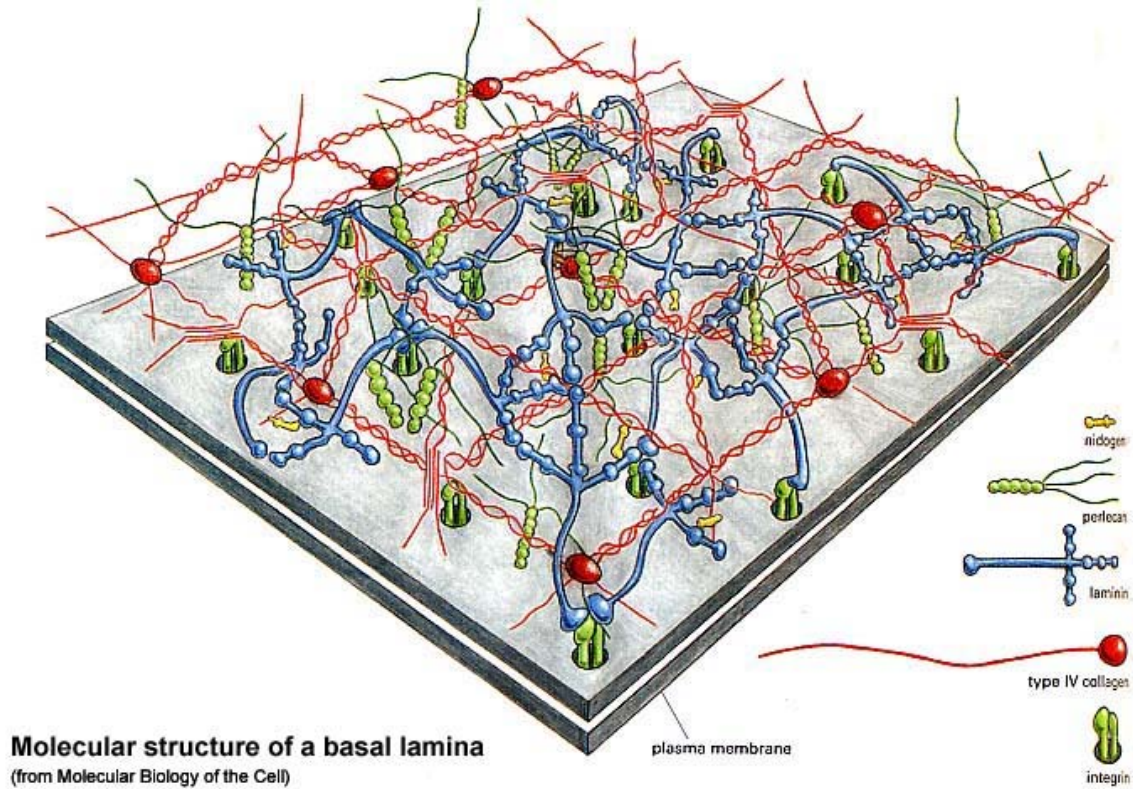


Figure 1

## The Science behind the Activation Mechanism

### Function

Proteins are important signal transducing molecules in cells. In fact, diseases such as diabetes and certain forms of cancer, among other pathologies, are thought to arise due to derangement of protein signaling.

### Types of protein signaling

Protein can refer to two distinct families of proteins. Heterotrimeric proteins sometimes referred to as the large proteins that are activated by specific protein-coupled receptors. There are also small proteins (20-25kDa).

### Heterotrimeric proteins

Heterotrimeric proteins share a common mode of action, i.e., activation in response to a conformation change in the protein-coupled receptor and dissociation in order to activate further proteins in the signal transduction pathway. However, the specific mechanism differs between different types of proteins.

### **Activation**

When a ligand activates the protein-coupled receptor, it induces a conformation change in the receptor (a change in shape) that allows the receptor to function. In the traditional view of heterotrimeric protein activation, it can then activate different signaling cascades (or second messenger pathways) and effector proteins.

### **Termination**

The activated protein receptor will eventually hydrolyze and disassociate from the heterotrimeric activating protein.

### **Matrix NC-138™**

Bioactive proteins have been defined as specific protein that have a positive impact on body functions or conditions and may ultimately influence health. The activity of these biofunctional proteins contained in the isolated Secreted Matrix™ is based on their inherent amino acid composition and sequence. The length of active proteins may vary from two to more than 100 amino acids and are known to have multifunctional properties. Matrix NC-138™ is a further isolation of Secreted Matrix™ for the specific bioactive proteins whose action on skin is to enhance activities through stimulation of collagen production, glandular production or reduction of wrinkles. This is the efficacy of the Proteoderm Matrix NC-138™ product as demonstrated in vitro and in vivo at University Laboratory studies. Our University Laboratory in vivo studies demonstrated high level of efficacy of Matrix NC-138™. These laboratory studies correlate with our on going large scale clinical trials.

### **Efficacy studies and applications of Matrix NC-138™ in cosmetic In vitro studies**

#### **Material and methods**

Fibroblasts and keratinocytes from 63 years old donor were incubated 96 hours with either Matrix NC-138™ or a positive control (transforming growth factor beta-1 = TGF- B1).

Stimulation of collagen production was measured by immuno labelling fluorescence assay.

## Results

Matrix NC-138™ induced very effectively collagen production by more than 300% in aged, senescent fibroblasts.

(Figure 2). With only 1.00% Matrix NC-138™, collagen is induced 2.1 fold over the control. The highest induction levels were observed using 2.00% (3.2 fold) or 3.00% (5.5 fold) Matrix NC-138™.

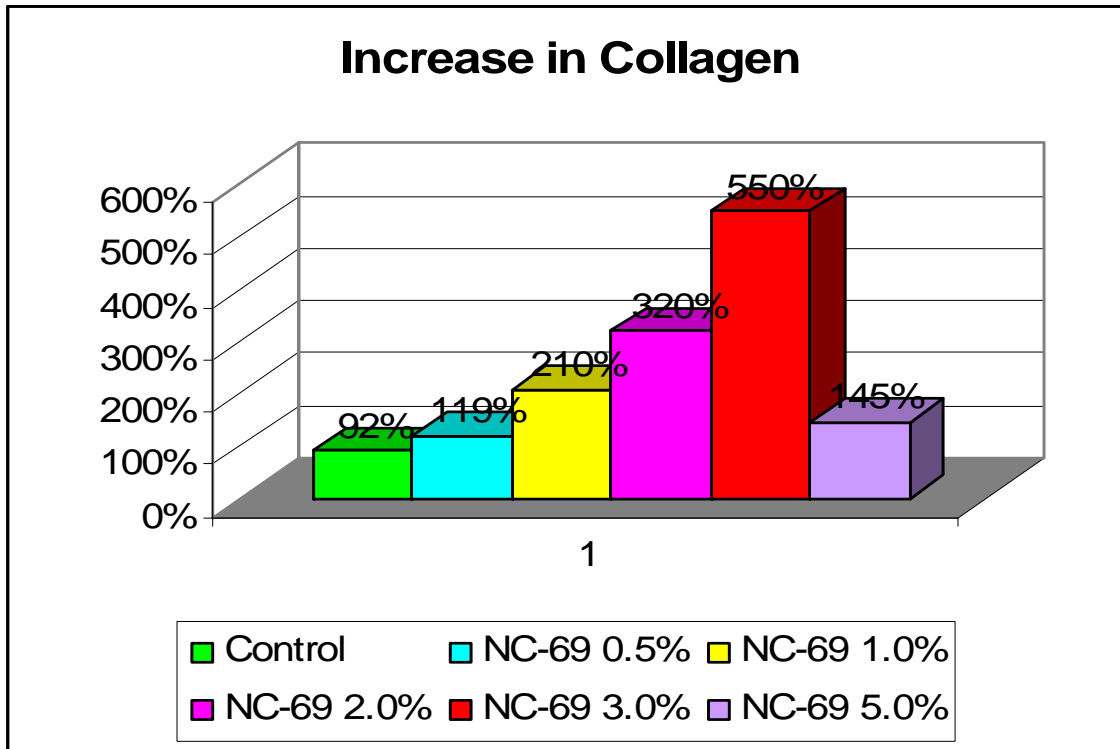


Figure 2

In addition it was demonstrated that Matrix NC-138™ rejuvenates skin cells (keratinocytes and fibroblasts). Keratinocytes represent 90% of the epidermal cell population and, with time, they lose their proliferative capacity and their longevity. This leads to reduced skin renewal and slow healing of minor injuries. Fibroblasts are the main cells of the dermis. They are responsible for the synthesis of many tissue proteins, like collagens which are integral building blocks of the dermal matrix. The dermal collagen network keeps skin elastic, supple and wrinkle-free. The dermal network which contributes to skin firmness, elasticity and smoothness breaks down with age and becomes disorganized, leading to wrinkles. As it is shown on Figure 3, Matrix NC-138™ extended the longevity of keratinocytes and fibroblasts and thereby helps the skin fight against the signs of aging.

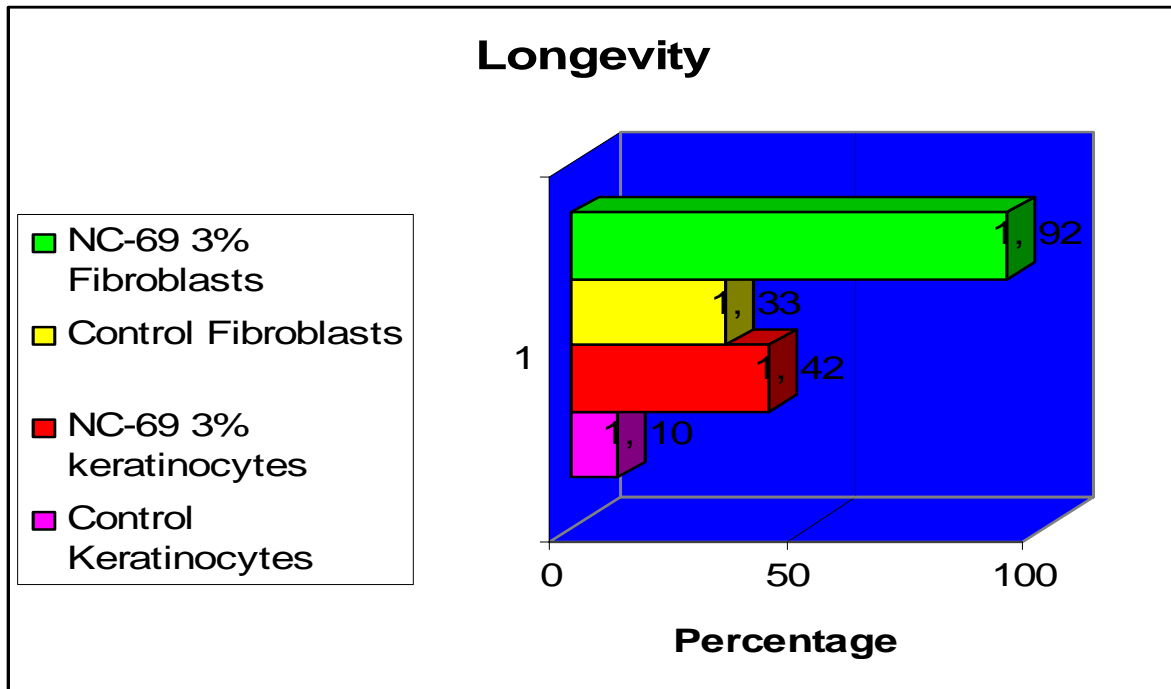


Figure 3

## In Vivo Studies

### Material and methods

An O/W emulsion containing 3.0% Matrix NC-138™ has been tested on 12 volunteers against a placebo in a half-face double blind study. Volunteers were asked to apply the cream twice daily for 6 weeks on the crow feet area. Several parameters were analyzed after this period of time: skin profile (with PRIMOS device), skin hydration with a corneometer and a self assessment on the product given by panelists through a questionnaire.

### Results

Matrix NC-138™ reduces wrinkles. After 6 weeks, this wrinkle reduction is highly significant compared to baseline ( $p < 0.001$ ). Regarding subtle wrinkles, Matrix NC-138™ shows better results than a placebo. After 6 weeks treatment, the decrease of subtle wrinkle depth is significant compared to baseline. For the placebo, there is no effect after 6 weeks. Therefore Matrix NC-138™ leads to a refinement of the skin texture and contributes to a youthful look. Additionally, Matrix NC-138™ increases moisture content of the skin. One of the clinical manifestations of skin aging is xerosis (dry skin). Matrix NC-138™ helps to counteract this decrease of moisture retention and gives suppleness to the skin.

The moisture content was clearly improved compared to placebo control after 4 weeks of application. (Figure 4)

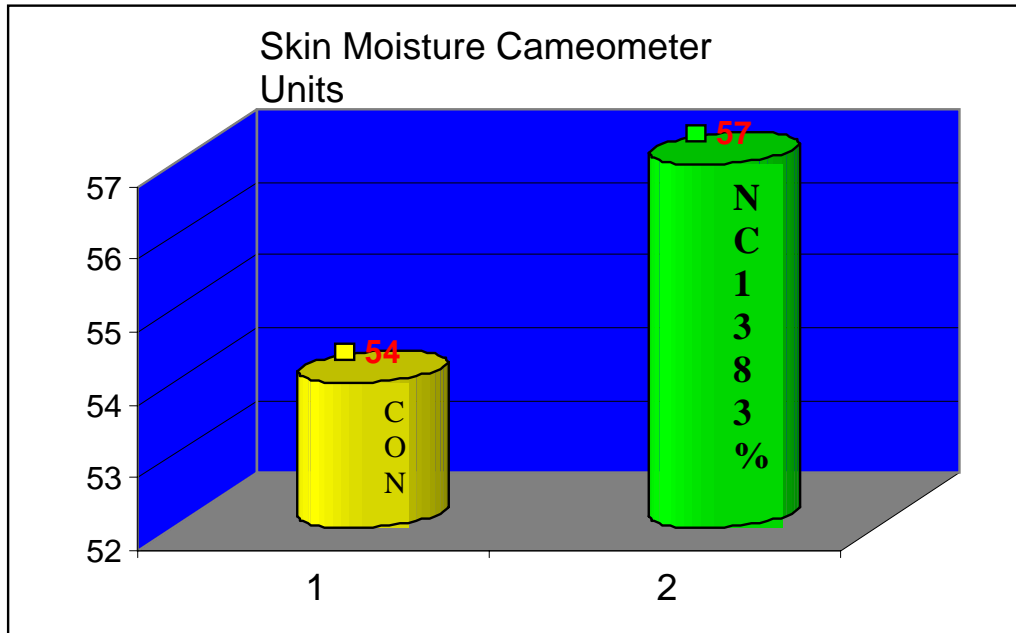


Figure 4

## Conclusion

Using its expertise in biotechnology Proteoderm has developed an innovative protein matrix which is a receptor of specific sequential amino acid grouping. The specific proteins in NC-138 augment the activation of the protein receptor of fibroblasts and keratinocytes and further augment the activation of the signal transduction pathway in these cells to enhance the production of collagen. Proteoderm's products containing Matrix NC-138™ have shown outstanding cosmetic properties. Matrix NC-138™ provides:

- **enhanced skin moisture**
- **radiant and youthful look**
- **smoother and softer appearance of the skin**
- **refined skin structure**
- **reduction in wrinkles**
- **contribution to keratinocytes and fibroblasts longevity**

Matrix NC-138™ is therefore an ideal ingredient for anti-aging products.

## Acknowledgment

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