



# TB-500 Medical Evidence

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## **Abstract**

Thymosin Beta 4, commonly known as TB-500, has demonstrated significant potential in accelerating the wound healing process. It has garnered attention in numerous scientific studies, which explore not only its effectiveness in treating skin-related wounds but also its impact on tissue healing and recovery throughout the body. Additionally, there is growing interest in the peptide's potential anti-aging properties, attributed to its regenerative capabilities. In this white paper, we review the current evidence, focusing on TB-500's role in wound healing and its ability to promote the regeneration of damaged tissue.

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## Introduction

Thymosin beta-4 is a peptide that has been studied for a number of potential benefits. It's known to possess angiogenesis properties and assists the body with wound healing. There is also some evidence that suggests the use of Thymosin beta-4, or TB-500, can have a positive effect on tumor cells.

## Problem Statement

A key question in the medical field is how to reverse the aging process. Anti-aging solutions have long been a topic of interest, with various agents being evaluated for their potential to repair damaged tissue, a fundamental aspect of aging.

Although progress has been made, significant gaps remain in understanding how to accelerate and enhance the body's healing process. This challenge becomes more pronounced when considering how the body's ability to heal declines with age, making it increasingly difficult to restore optimal function over time.

## Literature Review

This white paper focuses on specific scientific evidence that has been previously published, surrounding the use of TB-500 in various settings. K.M. Malinda provided a comprehensive overview of how it works on wound healing, focusing on rat models and comparing the findings to control groups. K. Maar, et al report on a comprehensive list of clinical trials and scientific evidence that have been published on this peptide, with an aim to establish its potential as an anti-aging compound.

C. Stark et al considered the effects of TB-500 on improving ventricular function following a myocardial infarction event. H.P. Ehrlich, et al provide an explanation of how Thymosin Beta-4 improves healing by organizing specific connective tissues, with a focus on collagen fibers. G. Sosne, et al review current evidence that supports the use of Thymosin Beta-4 as a therapeutic peptide in maintaining the health of the cornea, focusing on the anti-inflammatory and wound

healing properties. D. Philp, et al explore the potential of using TB-500 for dermal wound healing in diabetic models.

We also examined a journal entry by J. Zhang, et al on the recovery of neurological functions in mice that have auto encephalomyelitis. A paper by W.S. Yang also goes into detail about the potential of TB-500 for more severe dermal injuries. An update by W. Li, et al describes use-case scenarios where the peptide could also hold the potential to improve the survival of tissue in fat grafting surgeries.

## Methodology

This white paper takes a closer look at evidence related to the use of TB-500 as a wound-healing accelerator. Apart from the focus on wound healing, however, the whitepaper will also consider the potential anti-aging properties that the peptide can offer. These have been the focus points of various clinical studies, and the goal of this paper is to provide an outline and overview of recent findings.

## Results/Findings

### Thymosin Beta-4 Subcutaneous Use Improves Collagen Fibers

A [clinical report by H.P. Ehrlich, et al](#) considers the potential of TB-500 as a peptide to speed up the healing process but goes deeper into the specific pathways. This helps to provide a more comprehensive overview of how exactly the peptide works as a therapeutic agent.

The research paper focused on both the healing potential and considered whether the peptide would be effective at reducing the amount of scarring patients generally have following an injury.

Laboratory rats were used as the subjects for this research. After an incision was made in order to create a wound, a polyvinyl alcohol sponge implant was placed into subcutaneous pockets. The researchers then administered 100 micrograms of Thymosin Beta-4 on days two, three, and four into these sponges.

After 14 days, collagen fiber bundles in the treatment group were thicker and longer. There was a more significant reduction in the width of wounds in the group treated with this peptide. Researchers noted that apart from a faster healing process, there was also less scarring noted in the treatment group.

## Accelerating Wound Healing with Thymosin Beta-4

[K.M. Malinda, et al.](#) conducted a study to determine how Thymosin Beta-4 would affect the wound healing process. Topical and intraperitoneal administration methods were used for the peptide.

The control group used saline solutions to assist with the wound-healing process. Researchers assessed the healing progress on days four and seven. The researchers reported a 42% improved healing status compared to the saline group by day four. At day seven, wound healing was 61% better in the TB-500 group than in the wounds treated with saline.

Apart from these findings, there was an 11% more significant improvement in wound contractions on the seventh day when compared to the control group. Keratinocyte migration was monitored with the Boyden chamber assay. In just five hours, there was an improvement in the stimulation of keratinocyte migration of up to 300% more than the saline group. The researchers found that even in a small concentration of about 10 pg, Thymosin Beta-4 remained a potent option for stimulating wound healing in the laboratory models used for the study.

| Treatment / Days | Day 4   | Day 7  |
|------------------|---|--|
| Thymosin Beta-4  | 42% improvement in reepithelialization over saline group. | 61% improvement in reepithelialization over saline group. 11% better increase in wound contraction compared to saline group. |

## Thymosin Beta-4 Shows Anti-Aging Potential

A [Journal of Cells entry](#), authored by K. Maar, et al, explains the potential that TB-500 possesses as an anti-aging peptide. The researchers focus on the existing evidence surrounding the use of TB-500 in tissue regeneration and the repair of damage in the body.

The research paper explains that Thymosin Beta-4 has the potential to influence several biological elements of the human body that are related to the senescence process. In turn, this may help to promote organ regeneration, with a particular focus on the heart and brain. These two organs are known to possess only minimal capabilities to repair damage, as explained by the researchers behind the paper.

## Thymosin Beta-4 Improves Cardiovascular Healing After Myocardial Infarction

An [investigative report in the Translational Medicine Communications journal](#), by C. Stark, et al outlines the use of Thymosin Beta-4 in heart attack subjects. This investigation was done on laboratory mice. The goal was to determine how the healing and repairing properties of the peptide would affect heart health after myocardial infarction. Researchers reported myocardial damage following the event and then introduced Thymosin Beta-4 as a therapeutic agent afterward.

There were two groups of mice in order to ensure there was a control group for comparison of the effects. Intramyocardial and intraperitoneal injections were used in these groups to administer either a vehicle or the TB-500 peptide.

The first group was used for a short-term study. The second was included in a longer-term experiment.

The researchers then monitored the progress, with a particular focus on doing a follow-up on days two, five, seven, or 28. They also used an echocardiography test on day two and, once again day 28. Apart from the echocardiography tests, the researchers also relied on biochemical analyses.

The researchers found that the use of Thymosin Beta-4 resulted in improvements in left ventricular function. Chitinase 3-like-1 was also upregulated, which plays a critical role in tissue repair and regulating the body's inflammatory responses. The mice treated with TB-500 showed a reduction in inflammation and healing was also significantly faster.

The echocardiography tests were done before the study was initiated and then once again following the study period.

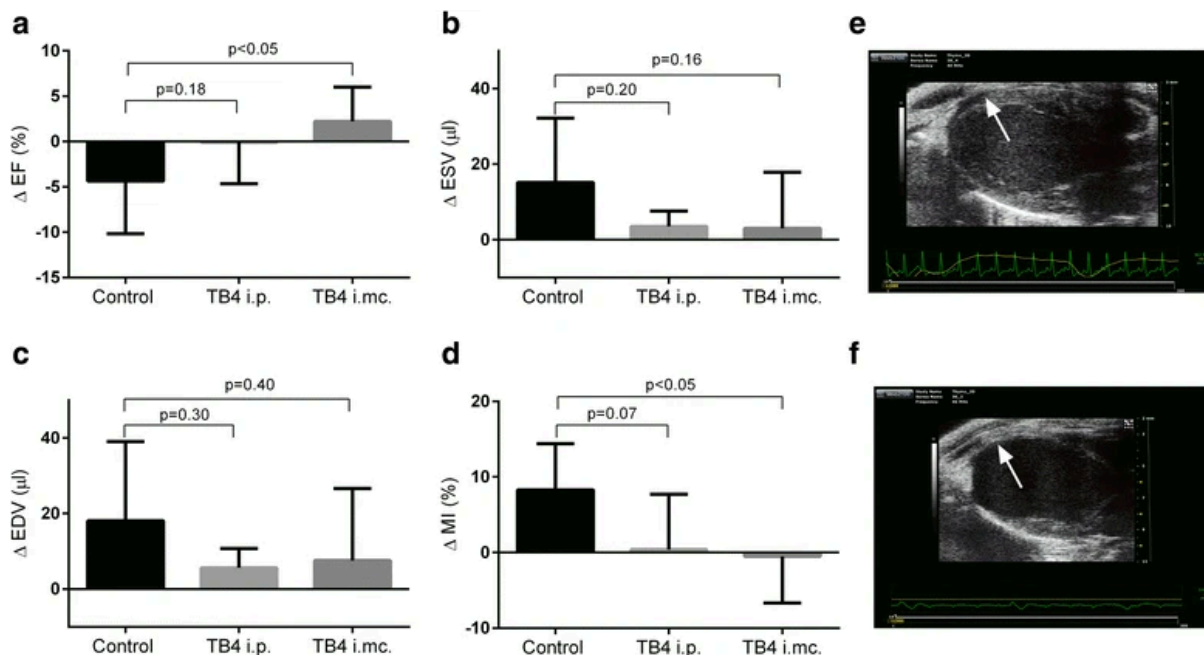


Figure 1 [Comparison between echocardiography tests before and after study period]

The two groups that received treatment with Thymosin Beta 4 experience a significant reduction in the size of the infarct area. This data was compared to the control group.

## Thymosin Beta 4 Improves Corneal Wound Healing

The healing potential of TB-500 has been well-established, but the focus often leans toward the cardiovascular system. A [journal entry by G. Sosne, et al](#) considers the potential that the peptide shows for the cornea. The researchers explain that similar to its impact on other bodily tissues, the healing and anti-inflammatory effects that TB-500 has been shown to possess also play a role in the cornea, an essential part of the eye and human vision.

In this research paper, the authors explain the two major factors that influence the potential of TB-500 for eye health. This includes both its ability to help with cell migration and with cell proliferation. The cell migration process helps to ensure cells move to cover the wound or injured tissue. Proliferation helps new cells develop in the area in order to assist with the overall healing process.

Current evidence shows that TB-500 may not have a significant impact on the proliferation process in the cornea particularly. However, studies have shown improvements in cell migration that are clinically significant. In particular, the migration of specific cells, including keratinocytes, corneal epithelial cells, and tumor cells, has been noted in the cornea treated with this peptide.

These are some of the most important cells that play a role in healing injured tissue in the cornea. Existing research has shown potential in using this type of treatment in a variety of animal models, including those who were exposed to diabetes.

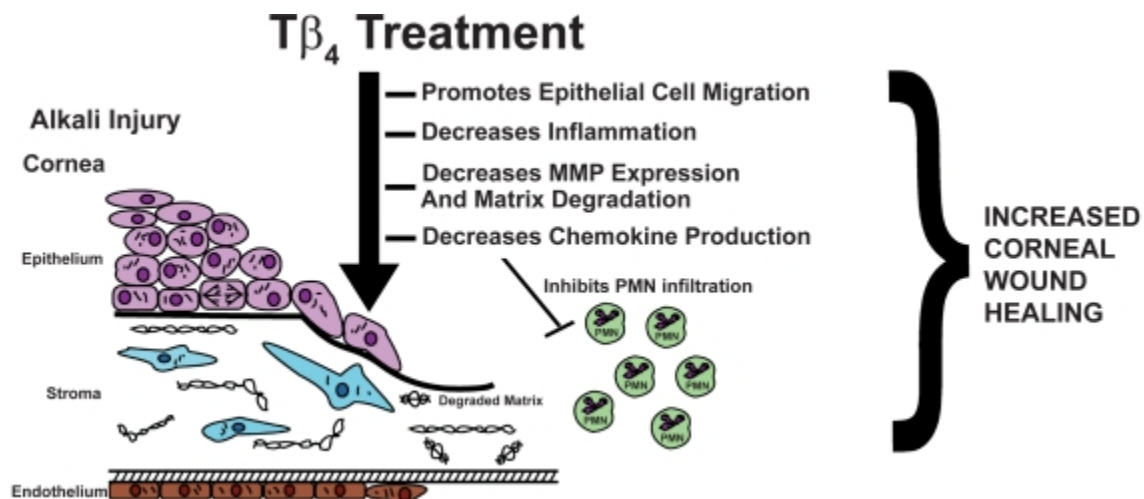


Figure 2 [Results from TB4 treatment shows positive impact on corneal wound healing]

The researchers made a conclusion that TB-500 has the potential to provide improvements in cornea healing due to cell migration, but also because of its ability to help reduce inflammation. It is known that cornea inflammation can cause damage and have an impact on overall vision.

Another study, [authored by J.H.C. Ho, et al](#) also considered the effect of Thymosin Beta-4 on the cornea. This particular study turned to the fact that corneal damage caused apoptosis, which causes cells to die eventually. The researchers used two different toxins, including hydrogen peroxide and Fas ligand.

Multiple groups were used to provide a more details view and to ensure the researchers were able to make a comparison between the results. A pretreatment was used to determine the effect of Thymosin Beta-4 on these two toxins. The cornea of laboratory subjects was then exposed to the toxins.

In the groups pretreated with the peptide, there was a significantly lower level of apoptosis noted by the researchers. HCE-T cell death, which is caused by the exposure to either Fas ligand or hydrogen peroxide, was also less noticeable in the group that had a pretreatment with the TB-500 peptide.

## Thymosin Beta 4 Has a Positive Impact on Diabetic Wound Healing

Wound healing is a serious problem in diabetic patients. Diabetes, especially with uncontrolled blood glucose, can significantly delay the process. This also creates a higher risk of infection and, due to a lower immunity, poses a great threat to the patient's health. [D. Philp, et al](#) investigated the potential of using Thymosin Beta-4 as a peptide therapy in diabetic mice.

While the study had a large focus on diabetic mice in particular, the researchers also considered the effect of this peptide treatment in aged mice. This provides more useful details about its use, as elderly patients also often have trouble with the wound healing process.

Thymosin Beta-4 was used in a hydrogel formula or a phosphate-buffered saline solution. Both of these therapy options showed a significant improvement in the wound healing process. In diabetic mice, wound healing was much faster when compared to other groups that were not treated with the peptide. Similar results were found in aged mice. Keratinocyte migration improved, as well as wound contracture. There was also a notable improvement in collagen formation in the areas where the wounds were made.



## Potential of Thymosin Beta 4 in Autoimmune Diseases

There has been strong interest in understanding the role of Thymosin Beta-4 in autoimmune conditions. This is particularly due to the immune-modulating effects that have been associated with the peptide. In a [study by J. Zhang et al](#), researchers wanted to monitor the impact that the peptide would have on experimental mice models with auto encephalomyelitis, a rare brain condition that sometimes develops after a bacteria or viral infection.

The researchers explained that they had a hypothesis, which led to the creation of this particular study. The hypothesis said that Thymosin Beta-4 could be a possible treatment option for patients who have multiple sclerosis. They then experimented with auto encephalomyelitis on laboratory mice in particular, which could give the scientists behind the study at starting point to move forward from.

Following exposure to this condition, the researchers then initiated treatment with the peptide. Each mice received either Thymosin Beta-4 or a saline solution. A total of five doses were provided to each mice, once every three days.

The dosage of TB-500 was 6mg per 1kg of body weight. A total of 10 mice were treated using this peptide. The researchers considered various measurements, including inflammatory infiltration, mature oligodendrocytes, and oligodendrocyte progenitor cells in the brains of these rats. Neurological function was another marker that the researchers used to determine the efficacy of this treatment.

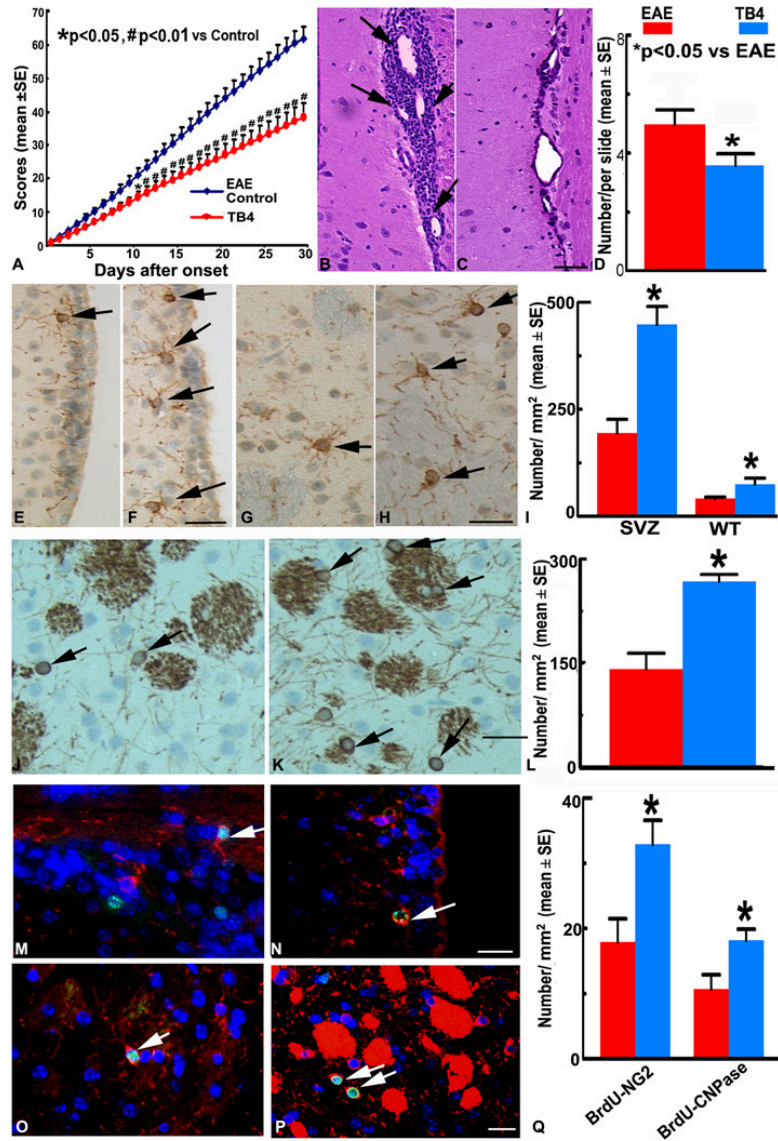


Figure 3 [Neurological response of EAE in control and TB4 treated mice models)

They noted several improvements in the TB-500 group, especially when they compared the results to the mice who were injected with a saline solution. One of the most important findings was the significant reduction in inflammatory cells in the brains of the treated mice. There was also a more noticeable improvement in functionality among these mice, which further shows the potential impact that TB-500 may have on autoimmune conditions.

Inflammatory infiltrates were reduced in TB-500 treatment groups. The peptide was also able to stimulate oligodendrogenesis.

| Measurement | Saline Group | TB-500 Group |
|-------------|--------------|--------------|
|-------------|--------------|--------------|

|   |          |          |
|---|----------|----------|
| Oligodendrocyte progenitor cells in the subventricular zone | 195.2/mm | 447.7/mm |
| Oligodendrocyte progenitor cells in white matter            | 41.7/mm  | 75.1/mm  |

## Thymosin Beta 4 Shows Potential in Speeding Up Recovery of Severe Dermal Injuries

[W.S. Yang, et al](#) provide an overview of this peptide's potential in treating severe injuries to the skin. There's also a focus on treating epidermolysis bullosa using the Thymosin Beta-4 peptide in this study.

The researchers explain that currently, there's a major concern with severe dermal injuries. They lead to itching, scarring, and can develop infection. Some of the wounds in human patients that the researchers noted include stasis ulcers, epidermolysis bullosa lesions, and pressure ulcers. These are some of the most dangerous dermal wounds noted in the general population.

The paper explains that Thymosin Beta-4 is a highly effective choice for speeding up the recovery of these dermal wounds. They also provide an overview of how it can be used in cases of severe blistering and other wounds that can become life-threatening in some cases. The researchers continue to stress on the fact that efficient wound management options are available, as current progress on genetic and stem cell therapies is still limited.

## Thymosin Beta 4 Improves Healing and Reduces Complications Following Fat Grafting

Another area where TB-500 shows potential is in fat grafting. A major concern among surgeons specializing in this kind of process has been fat survival following the grafting procedure. Researchers have previously shown the potential of using Thymosin Beta-4 in these scenarios, but there were limited data on the specific pathways.

An update on current evidence, [authored by W. Li, et al](#), explains the findings of more recent research. They have evaluated the effects of Thymosin Beta-4 on fat tissue after the fat grafting process using adipose-derived stem cells. In the treatment group, there was an improvement in cellular growth. The researchers noted changes in the genetic profile of the tissue, which explains the increase in fat survival in these surgical cases.

Researchers were able to obtain adipose derived stem cells from a total of four patients. All patients were female. These samples were collected following liposuction surgery. Two different research groups were used, with a focus on using TB-500 in one. An exogenous TB4 solution was used. The other sample group did not receive this treatment.

A key focus was to determine the effects of exogenous Thymosin Beta-4 on endothelial cell proliferation.

Researchers used exosomal miRNAs as a focus point to evaluate the efficacy of TB4 in adipose-derived stem cells. There were 2651 exosomal miRNAs that the researchers could recognize in the stem cells derived from the fat samples collected during the liposuction procedure.

A total of 80 exosomal miRNAs were upregulated with TB4, while there was also a down regulation in 99 differentially expressed miRNAs. Cellular growth in the stem cells increased due to the impact of Thymosin Beta-4 on the miRNAs.

## Discussion

The research conducted on TB-500 (Thymosin Beta 4) shows promising potential, with numerous studies exploring its ability to accelerate wound healing. These trials have yielded positive results, but there are notable limitations. Most of the clinical evidence is based on experiments conducted on laboratory rats rather than human subjects, which leaves room for further research on its efficacy in humans.

In addition, we reviewed a study that delves deeper into the internal effects of TB-500, particularly in relation to organ-related damage. This research expands our understanding of the potential benefits of Thymosin Beta-4, highlighting the need for more clinical trials to explore its broader applications.

## Conclusion

Based on the current evidence, TB-500 (Thymosin Beta 4) appears to be effective for topical wound healing. Studies have shown that its topical application accelerates wound healing, enhances wound contraction, and improves overall healing outcomes. Furthermore, TB-500 has demonstrated potential anti-aging properties, particularly through its ability to repair tissue damage at the cellular level.

Additionally, research suggests that TB-500 may restore the body's healing capabilities to a more embryonic-like state, significantly accelerating the healing process. This aspect of the peptide has fueled growing interest in its potential to reverse the effects of aging.

Beyond wound healing, TB-500 shows promise in other areas, such as maintaining corneal health. Studies have highlighted its anti-inflammatory effects on the cornea when pretreated with

Thymosin Beta-4, even in the presence of toxins. Furthermore, evidence suggests that TB-500 may be an effective agent for improving the survival and success rates of fat grafting procedures, underscoring its versatile therapeutic potential.

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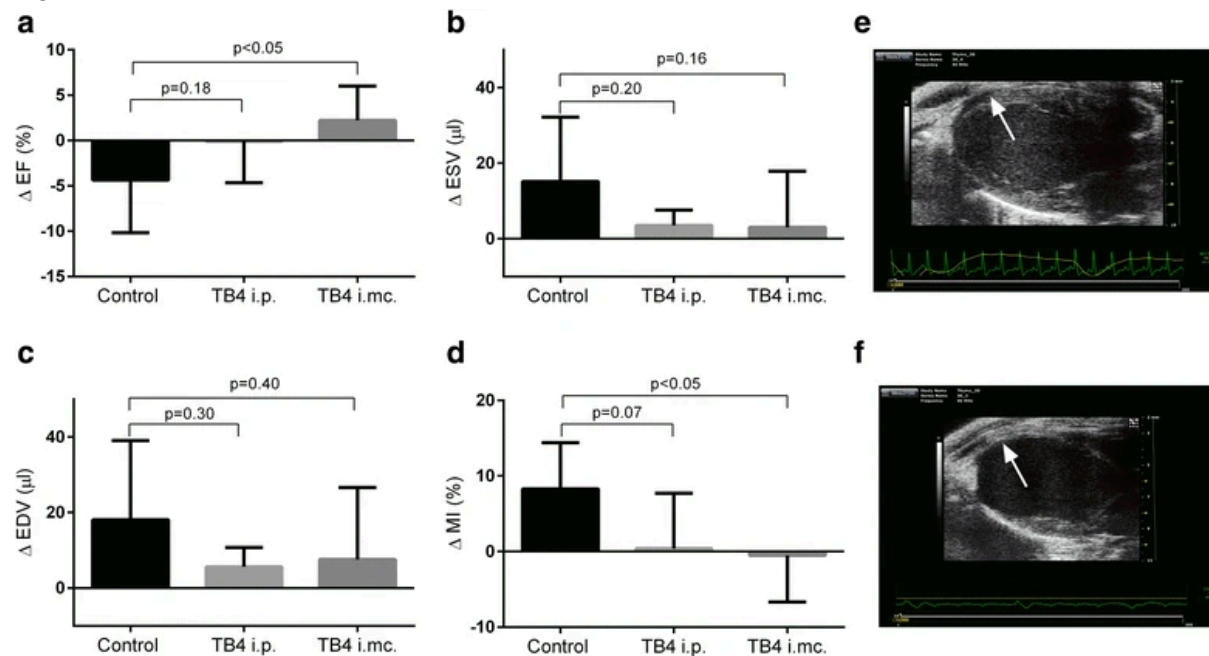
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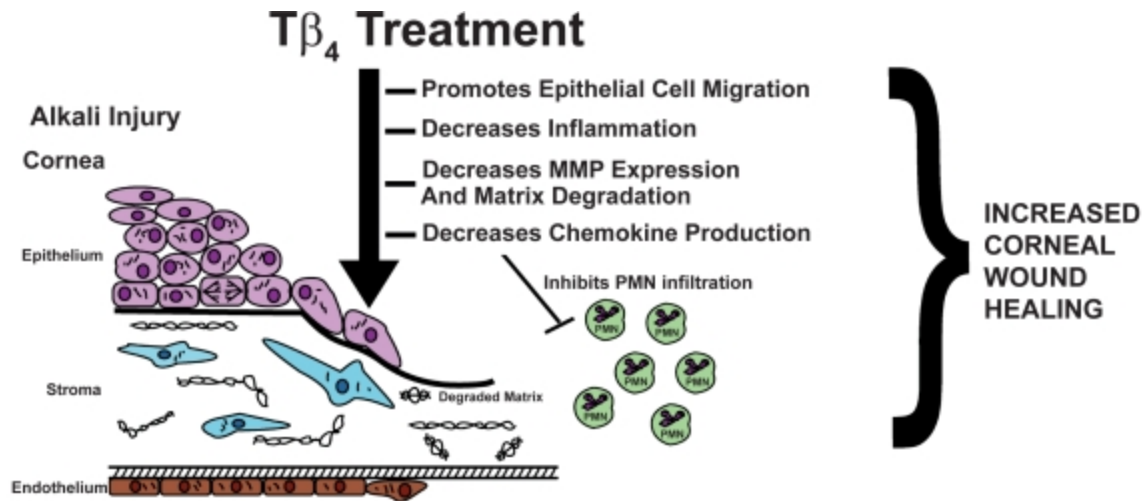
## Appendices

Figure 1



Absolute change in EF (a), ESV (b), EDV (c) and MI size (d) between days 2 and 28 in controls and TB4 treated animals (i.p. and i.m.c.). Representative images of early (e) and late (f) imaging in the same animal. Arrows show the infarct area with LV wall thinning (mean  $\pm$  SD)

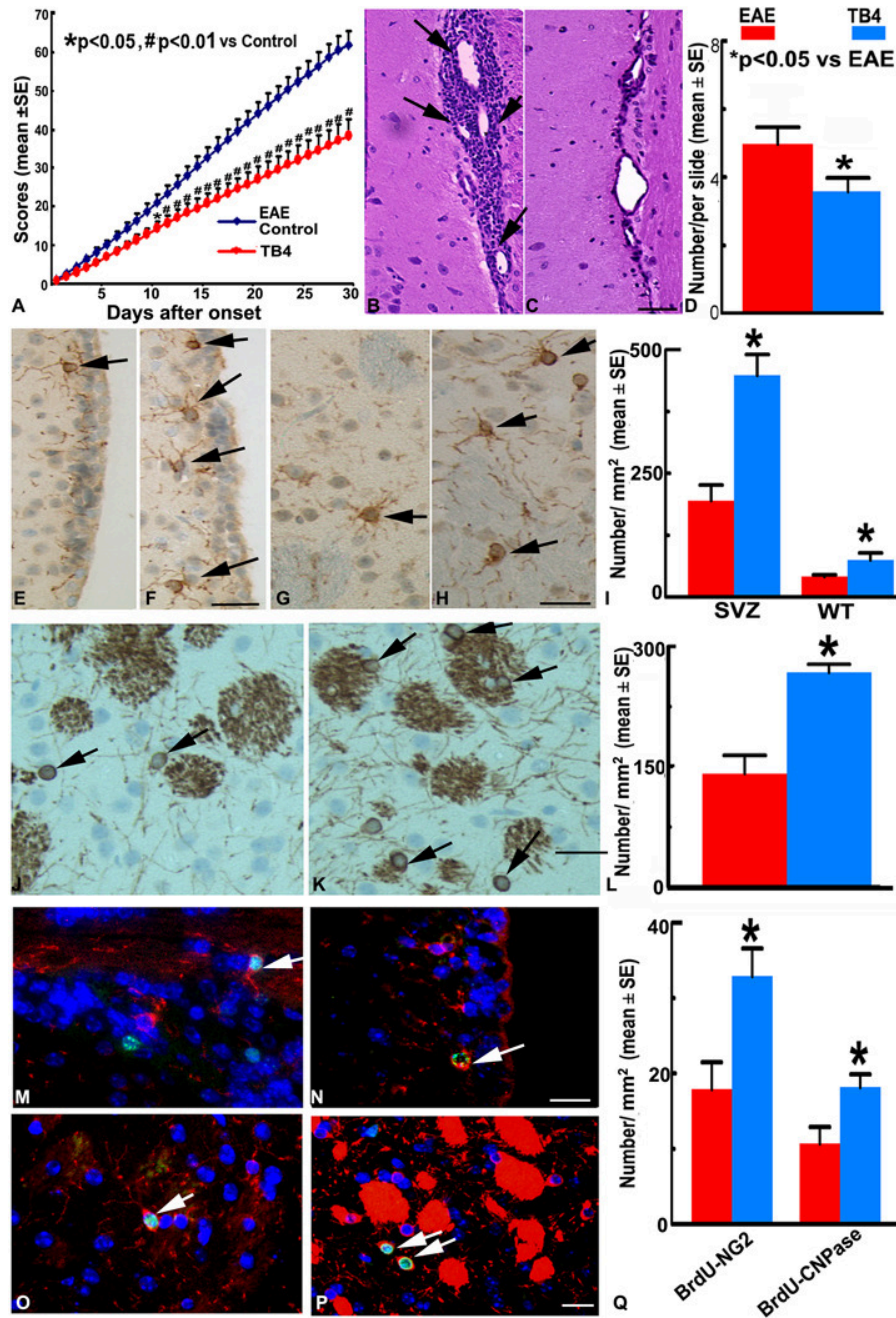
Figure 2



Tβ<sub>4</sub> promotes corneal wound healing. By modulating the corneal inflammatory response and promoting re-epithelialization in response to injury, Tβ<sub>4</sub> may be a new a therapeutic option for ophthalmologists treating corneal inflammatory and wound healing disorders.

Figure 3





The neurological response of EAE mice treated with or without Tbeta4. The significant therapeutic Tbeta4 effects were detected as early as day 11 after EAE onset. Nearly 50% relative functional recovery was observed in the Tbeta4 treated group, compared to the saline controls with  $p < 0.01$  for either the median score or the cumulative score up to 30 days.



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## Conflicts of Interest

There are no conflicts of interested noted for this whitepaper.

## Contact Information

The authors can be contacted directly for any queries regarding the findings of this paper.