# TRANSFORMATION™ CLINICAL TRIAL

## The Effect of TPP Protease™ on Inflammation*

### BACKGROUND

Is all inflammation bad? Not necessarily. Inflammation is your body's natural defense system to cellular damage. In a healthy individual, it tells you that something is going on with your body that you should pay attention to and correct. Inflammation can be caused by many things – stress, infections, physical injury, autoimmune disorders, and even free radicals. The latest research has also found that some of the foods we eat as well as chemicals in our environment can also cause inflammation.

Regardless of the cause, the body responds with an increase in movement of plasma and immune cells from the blood into the injured tissues. This is known as the inflammatory response and involves your vascular and immune system. The immediate response and repair known as acute inflammation is necessary and very beneficial to your health. But sometimes we do not feel inflammation and it can persist unchecked. When the inflammation response is chronic or uncontrolled, inflammation becomes a problem. We call this "silent" inflammation.

Chronic inflammation also accelerates the aging process. A chronic inflammatory condition overwhelms the system and undermines the body's healing process. Keep in mind, inflammation is not always accompanied by pain, redness, or swelling. Furthermore, because there are no normal sensory signals, oftentimes this "silent" inflammation goes untreated. This inflammation is at the cellular level and research has shown it can be linked to the onset of many degenerative diseases. In fact, inflammation (aka cellular damage) is a common denominator in all disease.

### RATIONALE

Transformation Enzyme Corporation (TEC) understands the importance of helping your patients manage both acute and chronic inflammation. In 2009, TEC partnered with Baylor University on a double-blind, placebo-controlled study to assess the effects of Transformation's Professional Protocol (TPP™) Protease™ on acute inflammation (Buford et al). In this study the participants were subjected to a strenuous exercise bout to induce acute inflammation. The "protease" group showed positive results with more controlled levels of pro-inflammatory cytokines (TNFα, IL1β, IL6, and IL12) and a decrease in COX2 activity as well as improved muscle strength.

In May of 2012, Dr. Milton Bastidas began a 12-week clinical trial at the TEC clinic in Houston, TX. The goal was to assess the benefits of TPP Protease™ in healthy individuals with varying levels of "silent" inflammation. The inflammatory markers C-reactive protein (CRP), Homocysteine,

Fibrinogen, and erythrocyte sedimentation rate (ESR) were chosen as a representative group of blood markers for assessing changes in the level of inflammation in the participants. The optimal ranges for each marker are based on what is seen in healthy individuals rather than pathological ranges seen in disease states.

CRP is an acute phase reactant which increases sharply in response to inflammation. It binds to phosphocholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system. It is synthesized by the liver in response to cytokines such as IL1β, IL6, IL12, and TNFα released by macrophages and fat cells. Healthy CRP levels are less than 0.55 mg/L.

Homocysteine is a non-protein amino acid which can be recycled into methionine or converted into cysteine with the aid of B12, B6, Betaine, or Folic acid. It accumulates in circulation when there is a deficiency of aforementioned methyl donors. When there is too much Homocysteine in the blood it sets the stage for formation of atherosclerotic plaques. It does this by stopping the production of nitric oxide (vasodilator), increasing blood viscosity, and facilitating oxidation of LDL cholesterol. Homocysteine values should be less than 7.2 umol/L.

Fibrinogen is an acute phase reactant which increases sharply in states of inflammation and the presence of IL6. It is a key factor in blood viscosity and promotes the formation of blood clots inside coronary arteries. The optimal fibrinogen range is 200-300 mg/dL.

ESR shows the rate of settlement of whole blood against gravity in a one hour period. It is a rough measure of abnormal concentration of acute phase proteins. This marker is a non-specific indicator of tissue damage and inflammation. It is mainly influenced by fibrinogen and less by globulins. Healthy ESR levels are below 10 mm/h.

## METHODS

The participants were recruited through the local Chamber of Commerce and by word of mouth. Qualified participants were male or female between the ages of 30 and 65 with no known health concerns. Those on statins, NSAIDS, or chemotherapy were not accepted for this trial. A total of 22 participants began the trial with 18 completing the trial.

Baseline evaluations (week 1) performed in-house included metabolic and body type questionnaires, body composition analysis (RJL), lipid profile, and dark field microscopy. The in-house parameters were monitored for educational and control purposes. Blood was also drawn through Quest Diagnostics® labs and analyzed for CRP, Homocysteine, Fibrinogen, and ESR. All tests were performed at weeks 1, 6, and 12.

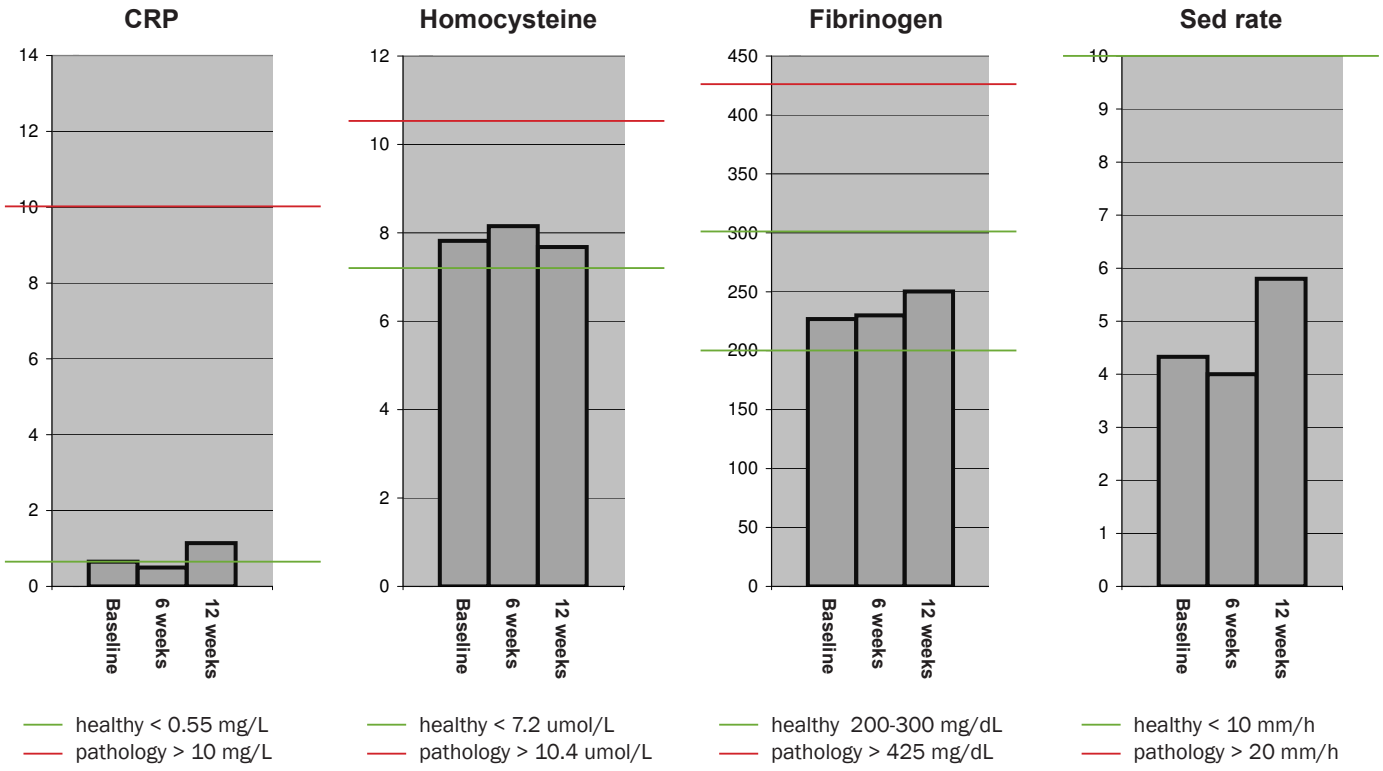
The participants were divided into 4 groups and given the following protocols. They were instructed not to change their diet or exercise patterns during the 12 week trial.

1. low dose = 1 cap TPP Protease™ 2 x day between meals
2. medium dose = 2 caps TPP Protease™ 3 x day between meals

3. high dose = 3 caps TPP Protease™ 4 x day between meals
4. placebo = 1 cap 2 x day between meals

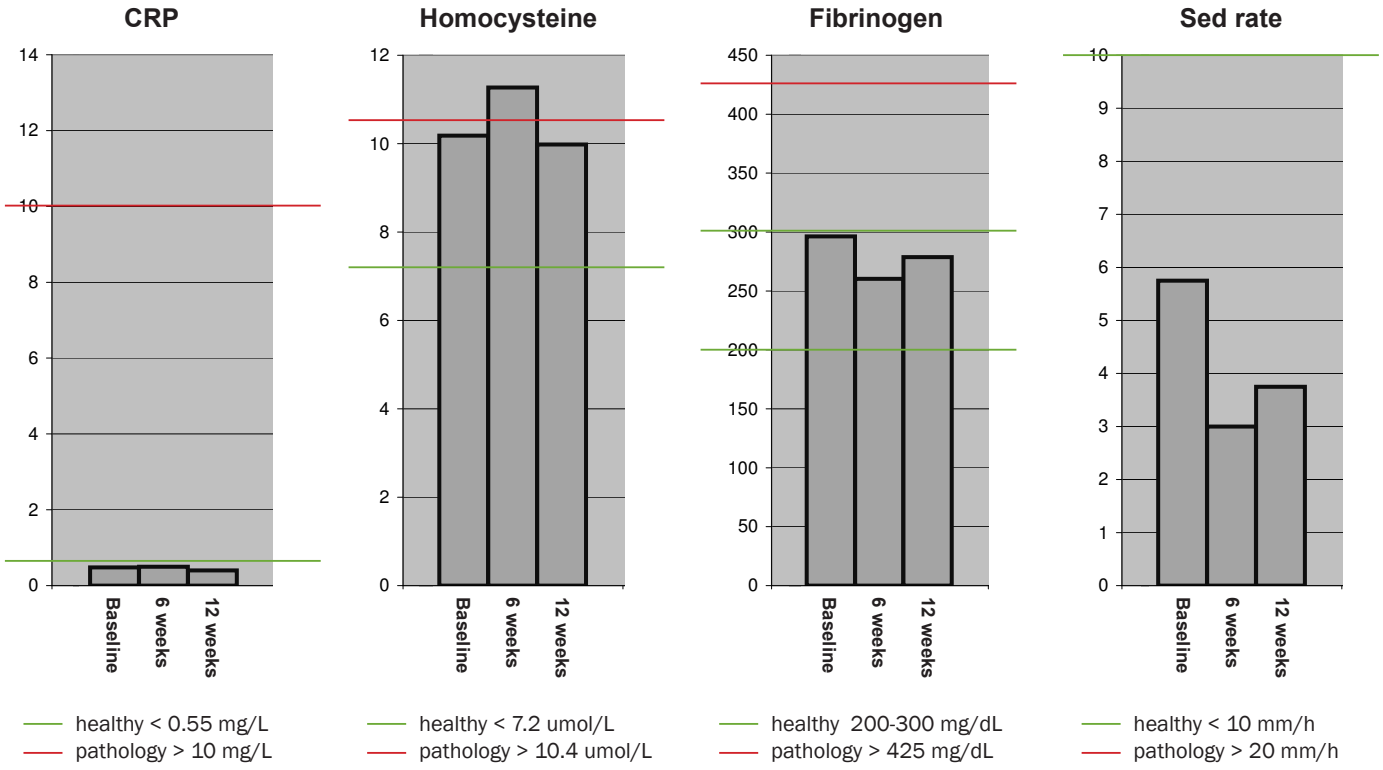
## RESULTS

Group 1 – Low Dose (1 cap TPP Protease™ 2 x day)



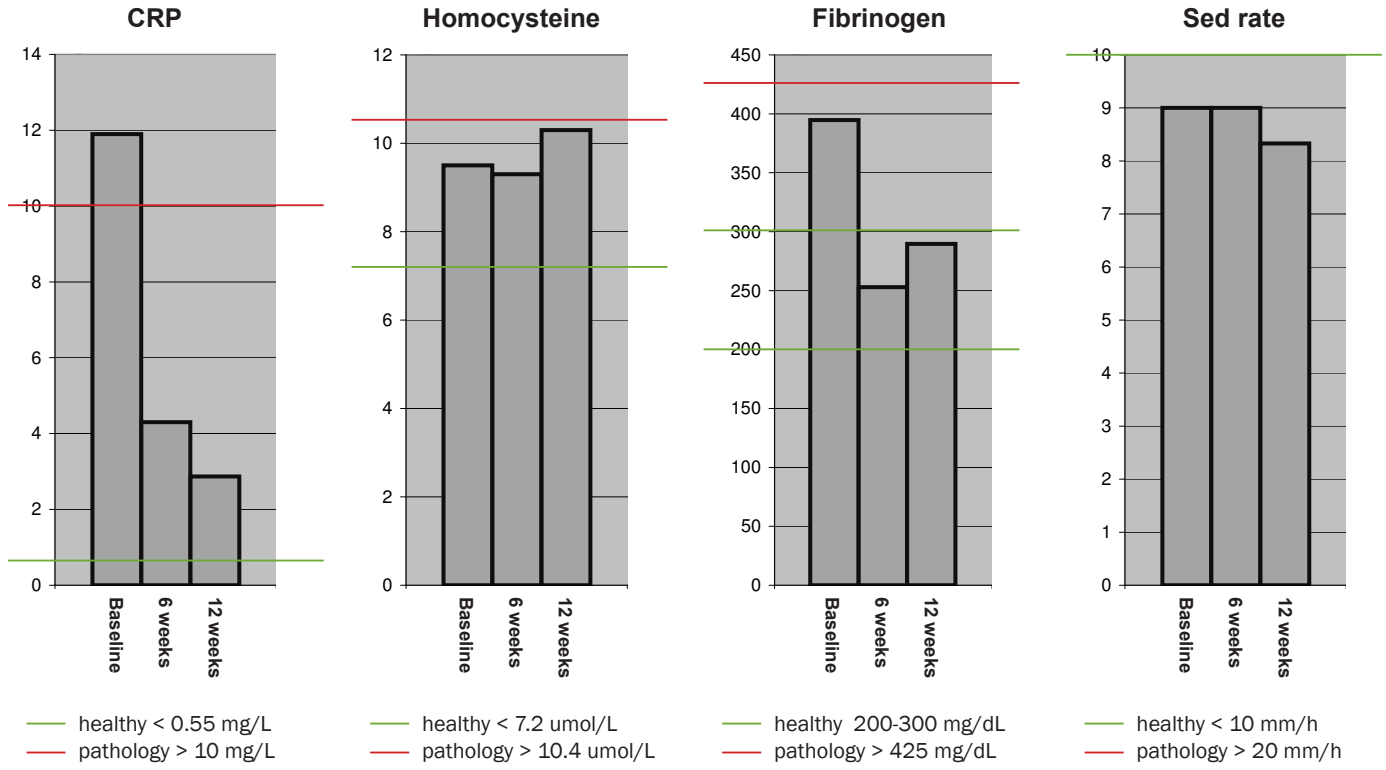

- This group showed low levels of inflammation at baseline.
- Group 1 averages (6 pts.) showed no significant changes from baseline values.
- 3 pts. had mild decrease in CRP, 4 showed slight drop in homocysteine, and 4 had moderate drops in Fibrinogen.
- In addition, 3 out of the 6 pts. in this group did not comply with all three blood draws which did not allow us to see a trend in results.

Group 2 – Medium Dose (2 caps TPP Protease™ 3 x day)



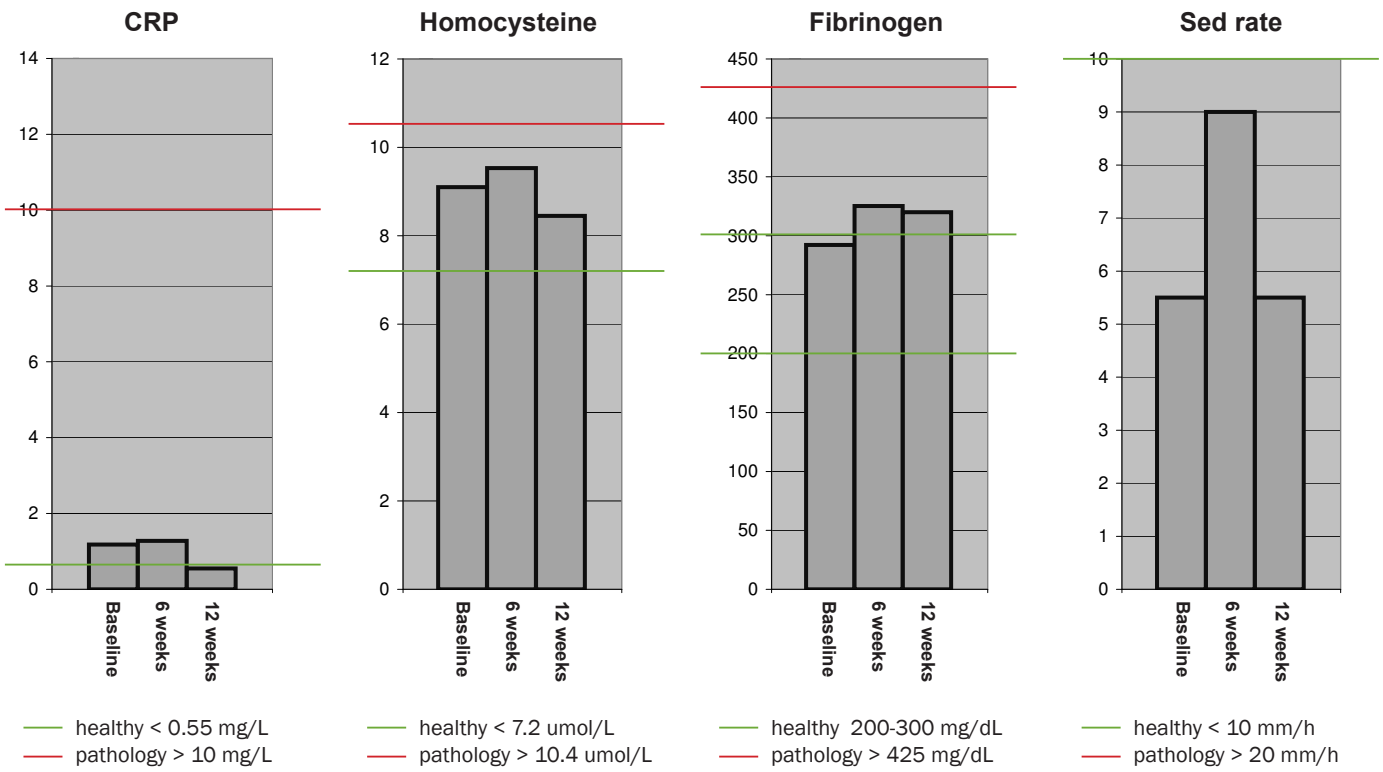

- This group had moderately elevated levels of inflammation at baseline.
- Group 2 averages (4 pts.) showed a 16.7% reduction in CRP, 2% reduction in Homocysteine, 6% reduction in Fibrinogen, and a 35% reduction in SED Rate.

Group 3 – High Dose (3 caps TPP Protease™ 4 x day)




- This group had elevated levels of inflammation at baseline.
- Group 3 averages (3 pts.) showed a 75% reduction in CRP, 8% increase in Homocysteine, 26% reduction in Fibrinogen, and a 7% reduction in Sed Rate.
- This group outperformed the rest in terms of reducing inflammation with significant decreases in CRP and Fibrinogen.

Group 4 – Placebo




- Group averages (4 pts.) did not show significant changes in inflammatory markers from baseline values.
- We were not able to obtain exact figures due to the fact that 2 of the 4 pts. in this group did not perform their last blood draw which did not allow us to see a trend in results.

## CONCLUSION

Elevated levels of CRP and Fibrinogen have been correlated with a significant increased risk of future heart attacks although they have not been proven to be a causal risk factor of Coronary Heart Disease. Both are acute phase reactants which rise sharply in states of inflammation or tissue damage including low grade inflammation in healthy individuals.

Of the 4 markers observed in all 4 groups there was ***a significant decrease in CRP and Fibrinogen*** in the high-dosed group compared to the other 3 groups. This finding is consistent with the study performed at Baylor University where Protease™ proved its strength against inflammatory cytokines such as IL1β, IL6, TNFα, and IL12.

In reviewing the medical literature, IL6R Genetics Consortium and Emerging Risk Factors Collaboration has shown that a genetic variant (Asp358Ala) in the IL6R gene can dampen the inflammatory effect of IL6 receptor, reduce CRP and Fibrinogen, and decrease Coronary Heart

Disease. This finding demonstrates a cause and effect relationship between a specific inflammatory protein and the development of Coronary Heart Disease. If we were able to dampen inflammation like the genetic variant then we can also possibly affect cardiovascular consequences.

Of the 4 markers observed, homocysteine is a non protein amino acid and although it is considered a marker of inflammation we did not expect an improvement due to the fact that it is highly dependent on methylation rather than proteolytic activity.

Inflammation is a common denominator in almost all chronic conditions that come into our office, from cardiovascular disease to auto-immune conditions. Transformation's Protease™ blend has again demonstrated its strength in impacting markers of inflammation and gives us a healthy and effective alternative in supporting diet and lifestyle changes when dealing with these chronic conditions that we see on a day to day basis.*

## REFERENCES


Buford TW, Cooke MB, Redd LL, Hudson GM, Shelmadine BD, Willoughby DS. "Protease supplementation improves muscle function after eccentric exercise." Med Sci Sports Exerc. 2009 Oct;41(10):1908.

The Emerging Risk Factors Collaboration. "C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis." Lancet. 2010 Jan 9;375(9709):132-140.

IL6R Genetics Consortium Emerging Risk Factors Collaboration. "Interleukin-6 receptor pathways in coronary heart disease: a collaborative meta-analysis of 82 studies." Lancet. 2012 Mar 31;379(9822):1205-13.


**About Dr. Milton Bastidas:**

Dr. Bastidas was born in Cali, Colombia, and raised in Houston, Texas. He received a bachelor degree in Biology and is a graduate of the Texas Chiropractic College. He has been in practice since 1998 and treats musculo-skeletal conditions, sports injuries, and systemic disorders. He has obtained a certificate of achievement from Functional Medicine University which allows him to provide a functional and natural approach to well being. Dr. Bastidas believes in investigating the underlying causes of disease by way of special laboratory analysis instead of guessing what product is the best for a presenting symptom. This allows for a specific treatment protocol depending on the biochemical individuality of the patient instead of a cookie cutter approach to care. Every patient gets a treatment protocol specific to their condition and their biochemical makeup.