



A white paper on an immunoglobulin -rich nutritional extract of bovine colostrum whey



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OVERVIEW

Tegricel™ is a proprietary extract from colostrum whey (bovine). This white paper describes the current state of knowledge, involving specific biological mechanisms of action, proof-of-concept in animal studies, and clinical data in humans, showing support of mucosal defenses and of gut barrier integrity, as well as accelerated recovery after NSAIDs-induced ulceration.

This paper discusses data from research that supports the use of Tegricel™ as a protective nutraceutical, with promise in many situations where food-borne or environmental allergens or pathogens lead to chronic inflammation and ongoing allergic conditions.

COLOSTRUM

Colostrum is the biological fluid produced from the mammary glands of female mammals shortly after giving birth. The fluid has a distinct composition different from the milk produced afterwards. The composition of colostrum provides immediate immune protection to the newborn. In humans, some degree of protective passive immunity is transferred to the fetus during gestation to a higher degree than in a number of other mammalian species, and the human colostrum then further supports the continued development of the newborn's immunity. However, in many other mammals, the newborn baby arrives with no immune protection.

Much research provides evidence for transfer of cytokines, immunoglobulin, growth factors, antimicrobial compounds, and maternal immune cells to the newborn via the feeding of colostrum [1-3].

The supportive properties of bovine colostrum when consumed by other mammalian species, including pigs and humans, are well documented in the literature [4-11]. The immune modulating compounds in colostrum from farm animals have been receiving attention as substitutes for pharmaceutical drugs in a number of clinical applications [12], including sports-induced immune suppression [13-15].

COLOSTRUM COMPOSITION

Colostrum secretions are designed to provide protection critical to neonatal survival during the early days of life as well as sustained growth and development of babies later in their life.

Bovine colostrum is especially rich in immune factors, amino acids, nucleotides and growth factors. Some elements are present in higher quantities in bovine colostrum than in human colostrum.

Bovine colostrum also contains high amounts of immunoglobulins (Ig) which are the molecules that recognize foreign substances that may be potentially harmful.

‘ACTIVE ‘ AND ‘PASSIVE’ IMMUNE PROTECTION

The body constantly defends itself from potential pathogens (bacteria and viruses that can cause disease) and allergens (substances that can trigger allergic reactions). ‘Active’ defenses refer to mechanisms caused by our own immune cells, whereas ‘passive’ defenses

involve transfer of immune protection from another organism.

The immunoglobulin in colostrum is an example of ‘passive’ immune protection, designed to protect the newborn animal against the total sum of environmental pathogens and allergens that the mother was exposed to. It is comparable to the gamma globulin vaccine that some people may chose to receive before traveling to foreign countries; the gamma globulin used for such injections is isolated from human blood.

ANTI-INFLAMMATORY PROPERTIES OF COLOSTRUM

Colostrum provides protection from NSAID-induced intestinal damage [16-18] through several mechanisms of actions:

- Compounds in colostrum inhibit expression of the inflammatory mediator COX-2 in intestinal epithelial cells [19];
- Compounds in colostrum inhibit the inflammatory signaling cascade involving Nuclear Factor kappa B (NFkb) [19];
- The highly stable C-lobe of lactoferrin binds to unabsorbed non-steroid anti-inflammatory drugs (NSAID) rendering them inactive for inducing further gastrointestinal damage [20,21];
- Colostrum reduces the blood levels of toxins from gram-negative bacterial infections [22].

In contrast to these effects, milk did not possess such specific protective properties [23].

COLOSTRUM VERSUS TEGRICEL™

Colostrum whey is the liquid remaining after the removal of casein and fat. Whey protein is a well-known nutritional supplement in the sports arena, including body building and muscle repair.

Tegrice™ is an immunoglobulin-rich extract from Colostrum whey, where compounds responsible for tissue repair and recognition of foreign antigens are fortified.

TEGRICEL™ CHEMICAL COMPOSITION

Tegrice™ was developed to provide a unique blend of key bioactive compounds.

Tegrice™ is enriched in compounds involved in both active and passive immune protection.

These compounds and their known biological properties are listed below in Table 1.

Table 1. Bioactive compounds in TegriceTM.

<i>Actives</i>	<i>Health/Nutrition outcomes</i>
<i>Broad-range specificity Immunoglobulins</i>	Immunoglobulins bind bacteria and other antigens before these enter blood, tissue and organs, and help their elimination
<i>Proline-Rich-Peptide (PRP)</i>	Immune modulation, cognitive enhancement, thymus regulation
<i>Insulin-like Growth Factor-1 (IGF-1)</i>	Sports nutrition, lean body, cell and tissue repair and rejuvenation
<i>Transforming Growth Factor (TGF)-β₂</i>	Cell protection, immune enhancement
<i>Sialic acid</i>	Immune modulation, brain health, prebiotic
<i>Nucleotides</i>	Immune modulation, anti-ageing, stamina

TegriceTM is a blend of the immunoglobulins that support passive immunity and the elimination of potentially harmful bacteria and antigens before they have an opportunity to enter into blood, tissue, and organs, and immune supportive compounds allowing multi-faceted mechanisms of actions to support mucosal immune protection and healthy gut integrity.

MUCOSAL PROTECTION AND INTEGRITY

The gastrointestinal tract is faced with the challenge of allowing nutrient absorption while protecting against entry of disease-causing elements.

In addition, the digestive processes involve acids and enzymes that together are able to break down organic material.

Furthermore, the increasing consumption of NSAIDs, known to be able to induce ulcers and compromise gut mucosal integrity, is a factor in the development of digestive health problems.

The lining of the gastrointestinal tract secretes mucus to limit the damage the digestive processes may do to our own cells and tissue.

Also, a special type of immunoglobulin (called secretory IgA, or sIgA) is produced and secreted to bind to potentially harmful substances before they enter into the gut tissue and the blood stream, to be carried off to various tissue locations.

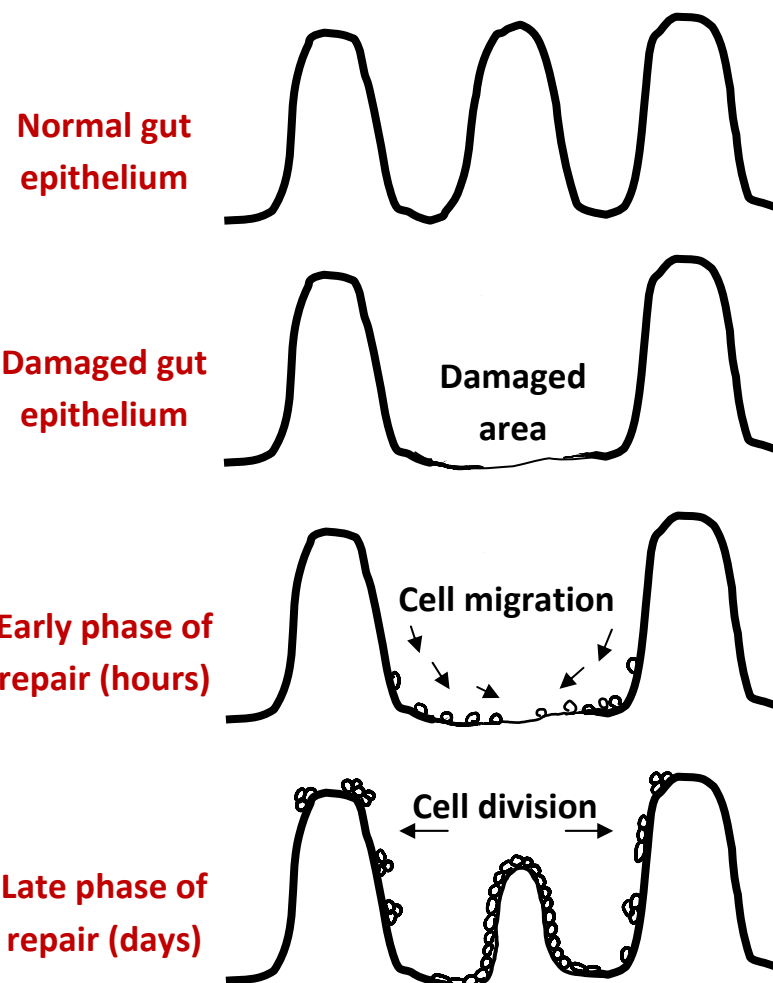
MUCOSAL INJURY AND REPAIR

When mucosal injury happens, the surrounding cells lining the gut wall will attempt to fill the wounded area.

While a damaged area is healing, especially in the earliest phase of repair, the endothelial lining is vulnerable to attack from bacteria in the gut lumen, leading to delayed wound repair and prolonged inflammation.

The recovery of the integral uniform layer depends on two factors:

1. Healthy cells from the surrounding area migrate into the damaged area;
2. Cells divide to produce more cells and help re-occupy and heal the damaged area.

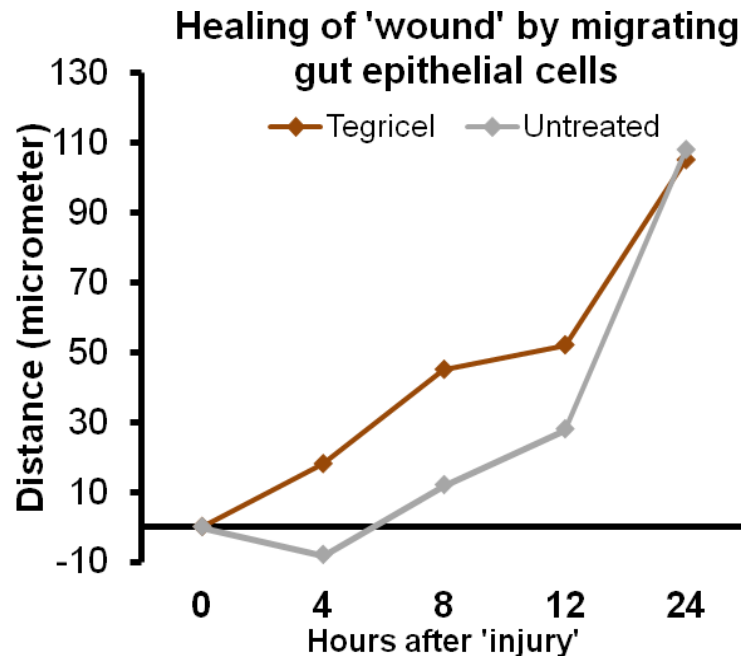


Tegricel™ supports a healthy gut barrier

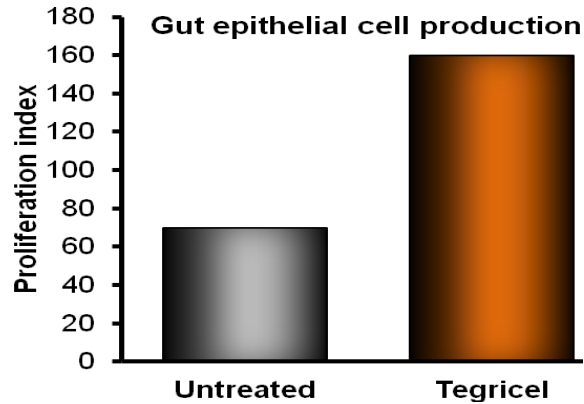
Gut epithelial cells (the HT29 cell line) were cultured in the laboratory until they formed a uniform layer, similar to the gut epithelium separating the gut lumen from underlying tissue.

An artificial ‘wound’ was induced by scratching a line of damage across the layer of cells.

In the presence of Tegricel™ both the migration and production of more cells was supported in the cell cultures.



On the graph above, the migration of gut epithelial cells increased when treated with Tegricel™ (1 mg/mL). This was obvious already 4 hours after injury. The repair happened faster in the presence of Tegricel™.



In addition, Tegriceal™-treated gut epithelial cells divided faster, and produced more cells than the untreated cultures.

ANIMAL DATA

An animal study was conducted on Tegriceal™ to test whether Tegriceal™ consumption helped reduce the size of stomach ulcers induced by NSAIDs.

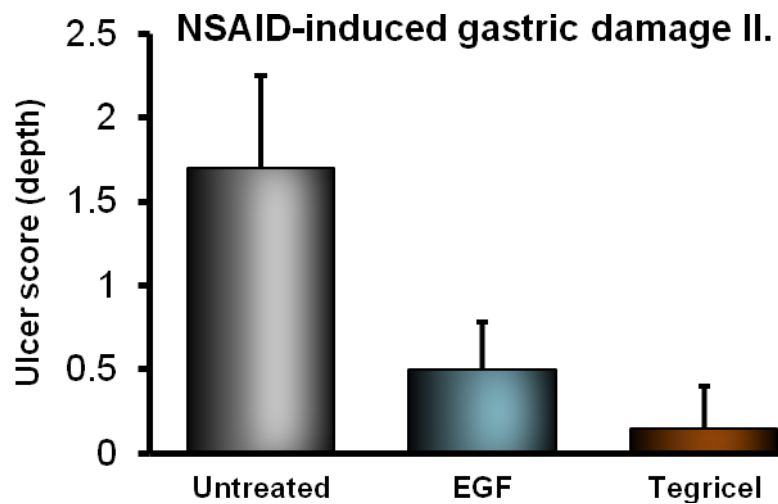
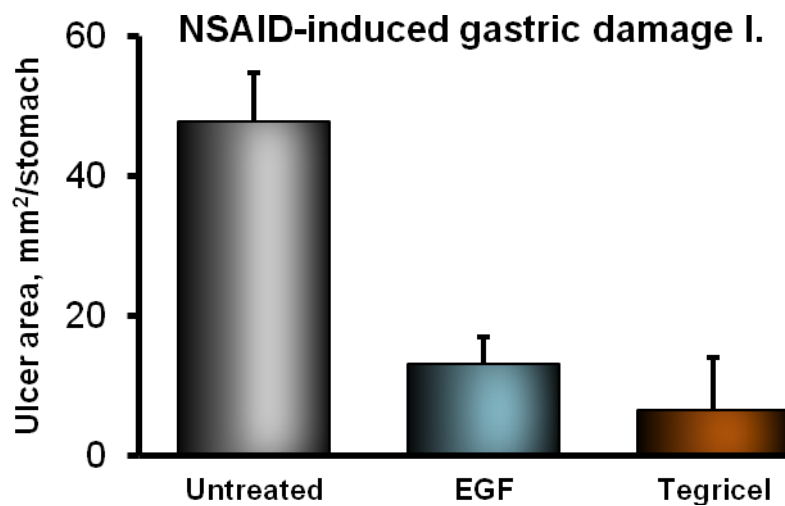
The drug indomethacin was used to induce stomach ulcers in rats, after the rats had been given either saline, epidermal growth factor (EGF), or Tegriceal™ into the stomach.

EGF is recognized as a standard treatment control.

Tegrice[™] reduced the size and severity of NSAID-induced stomach ulcers

The protective effect of Tegrice[™] was dose-dependent for both area and depth of the ulcers.

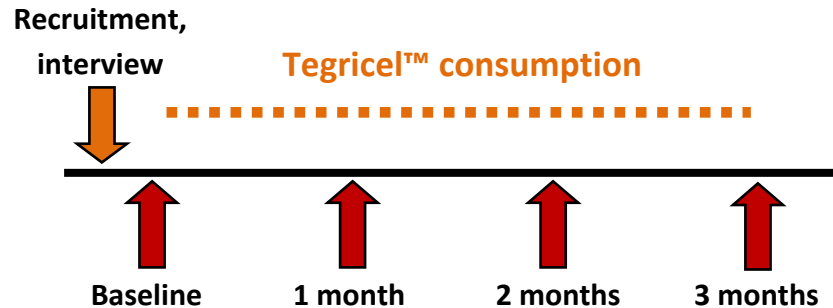
Tegrice[™] performed better than EGF in reducing the damage and accelerating the recovery after NSAIDs-induced ulceration.



HUMAN CLINICAL DATA

Data from a recent human clinical trial further supports that consumption of Tegrice[™] helped reduce allergic symptoms and improved quality of life and ability to perform activities of daily living, in people suffering from various digestive and allergic complaints.

Study design: An open-label study design was used. Twelve healthy human subjects were provided with Tegrice[™] for 3 months, with monthly follow-up visits.



At baseline and at 1, 2, and 3 months of consumption, saliva was collected, blood samples were drawn and questionnaires were used to track gut function, allergies, and other health complaints.

The saliva samples were used for testing of secretory Immunoglobulin A (sIgA), which reflects mucosal immune protection.

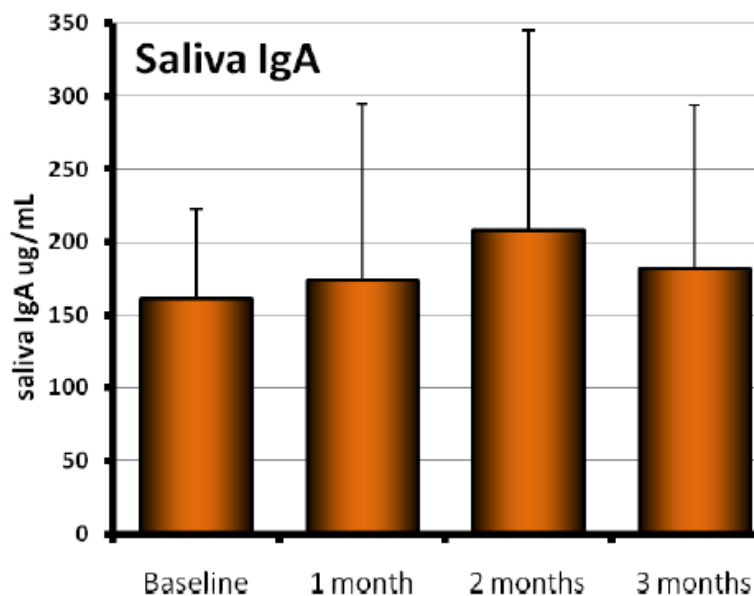
Consumption of TegriceTM results in increased mucosal immune protection in humans

Consumption of TegriceTM resulted in an increase in the salivary sIgA content.

The difference in sIgA levels at study start, compared to the levels after two months TegriceTM consumption, showed a 30% increase.

Even though a slight drop in sIgA was seen between the 2-months and 3 months follow-up visits, the 3-months sIgA levels remained above baseline levels.

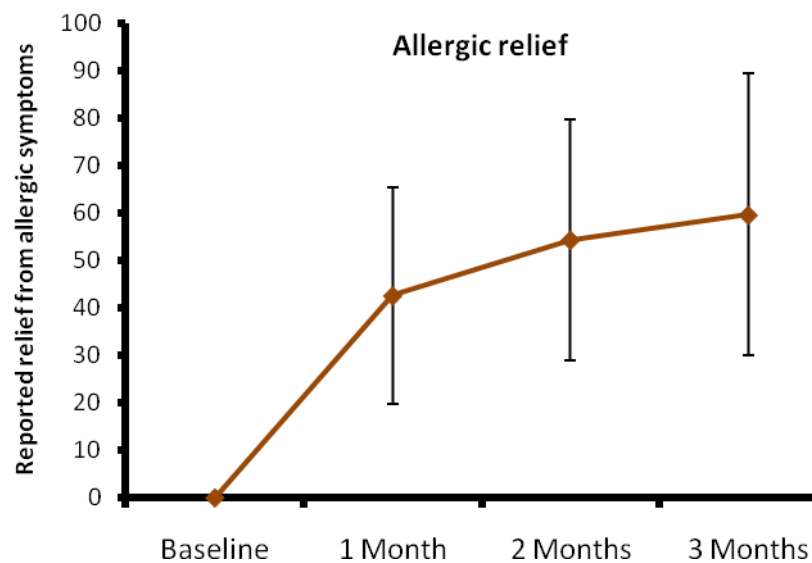
The fluctuations between 2 and 3 months may be due to seasonal effects. The change seen between 1 and 2 months consumption was statistically significant ($p < 0.025$).



Reduction in symptoms associated with allergies after consumption of TegriceTM

Specifically, consumption of TegriceTM reduced the complaints of allergic symptoms.

The reported relief was highly statistically significant after 1 month consumption of TegriceTM ($p < 0.002$), and remained significant throughout the study.



There is a link between immune dysregulation, gut inflammation, and allergies [24], and the immune system is more likely to make inappropriate decisions regarding friendly or foreign antigens under chronic inflammatory conditions.

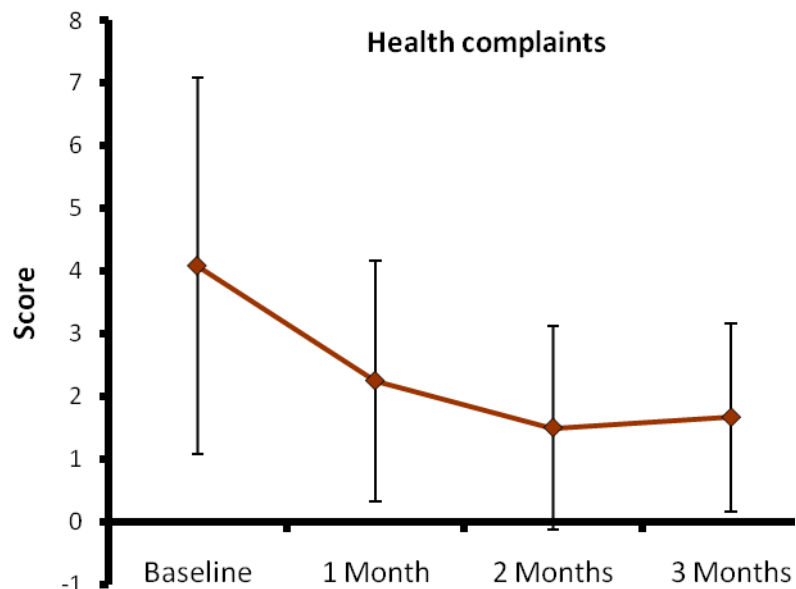
Thus, reducing gut inflammation may be one of several underlying mechanisms for the observed reduction in allergic symptoms.

Reduction of health complaints after consumption of TegriceTM

Minor health complaints were evaluated by asking a series of questions pertaining to issues that are seen in everyday life, including questions related to digestive health. These questions range from constipation, indigestion, heart burn, bloating, unpleasant sweating, frequent infections, nausea, muscle cramping, poor gums, poor circulation, and sleep problems.

The volunteers were asked to rate the level for these specific factors 0 = no effect, 1 = mild effect, 2 = moderate effect, 3 = severe effect. The averages between all volunteers were evaluated before and after 1, 2, and 3 months consumption of TegriceTM.

It was observed that minor health complaints, including those related to gut and digestive function, decreased by 47% and the data was found to be statistically significant ($p < 0.02$).

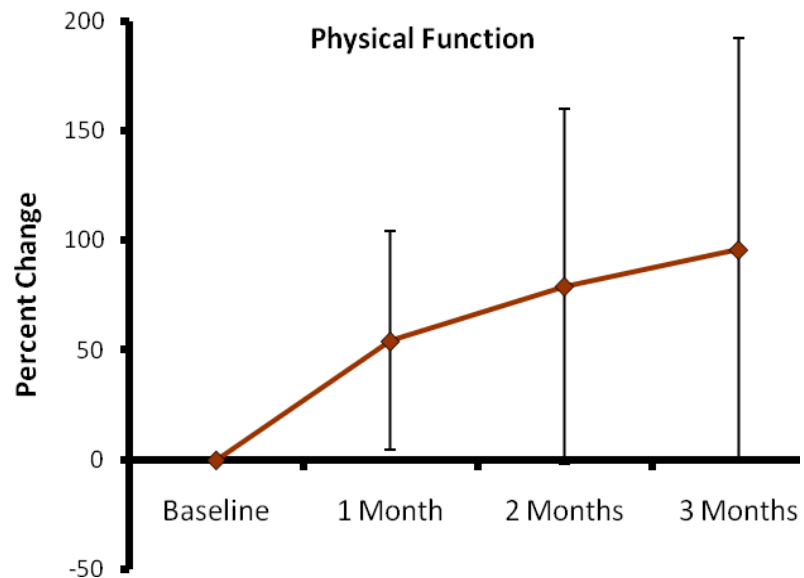


Improved ability to function after consumption of TegriceTM

The ability to perform physical work and feel a sense of accomplishment may be associated with gut health and proper digestive function. Physical function increased in the study population after consumption of TegriceTM. Study participants reported increased ability to focus on work, spend more time on work or other physical activities, and perform activities with greater accuracy.

A steady increase was seen across the 3-months study period. The change was highly statistically significant already after 1 month consumption of TegriceTM ($p < 0.002$), and remained significant throughout the study.

The timing of improvement of physical functioning correlated with the decrease in health complaints.



CONCLUSION

Data from NSAID-induced damage of gut epithelial cells, combined with animal studies and human clinical data suggests that Tegricel™ supports healthy gut function, allowing for improved physical function.

The in vitro and animal studies show that this happens in part through increased protection of the integrity of the gut barrier.

Particularly the human clinical data on sIgA levels suggest that other key aspects of the effects of Tegricel™ happen through improved mucosal immune protection.

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