

*Efecto de la suplementación con concentrado de inmunoglobulinas a partir del suero bovino en la Microbiota y su contribución a la salud intestinal y al sistema nervioso central*



**Dr. Javier Polo**  
Vice President Research & Development



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- **EFFECTOS EN LA SALUD GASTRO INTESTINAL**
- **EFFECTOS EN LA SALUD DEL SISTEMA NERVIOSO CENTRAL**



THE LAURIDSEN GROUP, INC



Vegetal & Animal Health/Nutrition

Human Nutrition

Pharma/Biologicals/Human health

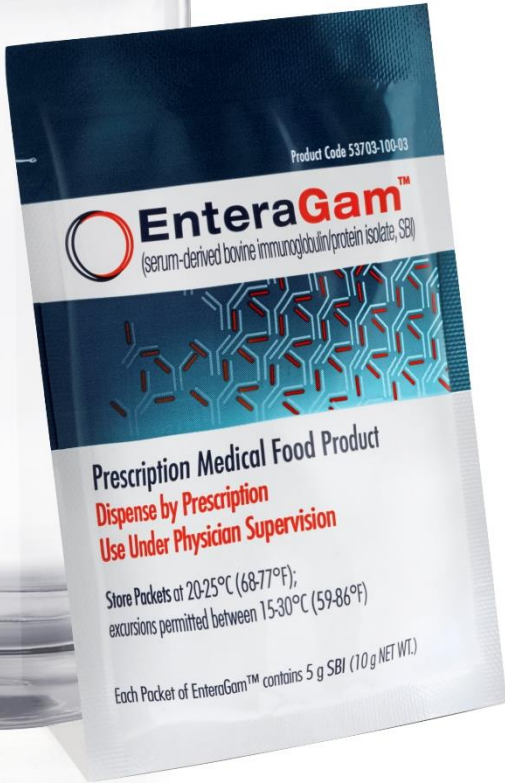
Raw material

Blood, Bones, Feather, Fatty tissues	all by-products	Blood	Dairy	Blood, Skin, Fatty Tissue, Bones	Blood	Blood
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The LGI Group serves industrial, veterinary and human applications with high quality, natural source proteins.



# Medical Food Product



## Specialties Targeted:

### infectious

- HIV Enteropathy
- Norovirus and Cryptosporidium
- C. Difficile

### Cancer Cachexia

- Cancer Associated weight Loss Syndrome
- Gut Barrier Dysfunction and microbial translocation
- Chemotherapy Induced Mucocitis

### Other DI

- Celiac and Gluten Sensitivity
- Antibiotic Induced Diarrhea
- DMARD-Induced Diarrhea
- Chronic Mesenteric Ischemia
- Lymphocytic Colitis
- Chronic Diarrheal Ileorectal Anastomosis
- Fecal Incontinence
- Mastocytic Enterocolitis
- Short Bowel Syndrome

### IBS

- Post-Infectious Diarrhea
- Pediatric IBS-D
- Infant Diarrhea
- Symptom Management
- Small Intestine Bacterial Overgrowth

### IBD

- Chron's Disease
- Ulcerative Colitis
- Pediatric UC
- Pouchitis

GI Anti-inflammatory

Hypercholesterolemia

Microbiome Dysbiosis

Autism

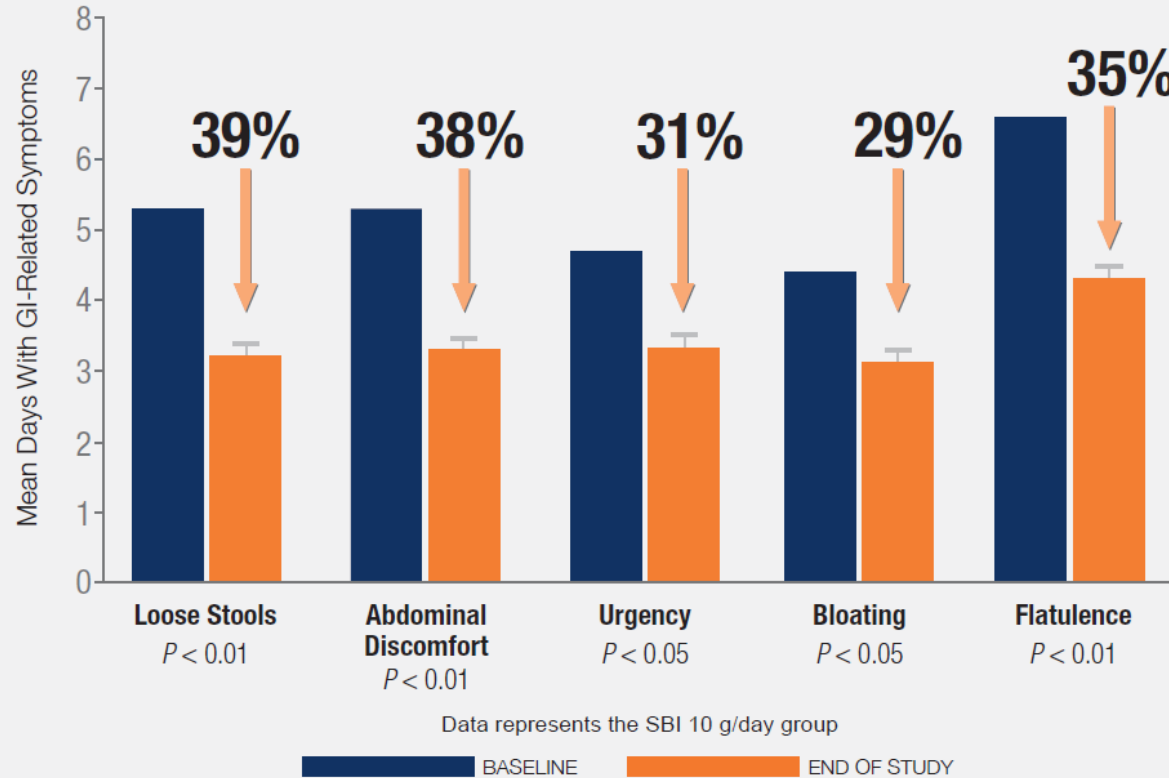
Hepatic

Leaky GUT

Acid Reflux

H. Pylori

## Decrease in Mean Number of Days With Global IBS-D Symptoms\*



# Significantly reduced the days

patients experienced loose stools and other IBS-D related symptoms

Pilot study results suggest that EnteraGam® provides for a distinctive nutritional requirement unique for IBS-D patients which could not be received from soy protein.

### Clinical Medicine Insights: Gastroenterology

*Evaluation of Serum-Derived Bovine Immunoglobulin Protein Isolate in Subjects with Diarrhea-Predominant Irritable Bowel Syndrome*- 2013:6 49-60.

Dale Wilson, Malkanthi Evans, Eric Weaver, Audrey L. Shaw, Gerald L. Klein

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4020402/>

\* Results from a 6-week, randomized, double-blind, placebo-controlled study (N = 66). Subjects received either EnteraGam® 10 g daily, 5 g daily, or placebo. Subjects self-assessed presence and severity of GI symptoms daily using a 4-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). Number of days with symptoms was calculated for each 2-week period per subject. Data represents within-group changes from baseline to end of study among: (1) Subjects taking 10 g dose of EnteraGam® daily (n=15); and (2) subjects within soy protein placebo group (n=22). No statistically significant reduction in the number of days with any GI-related symptoms for placebo group. Study was not powered to demonstrate between-group differences.



# Published Clinical Cases – Irritable Bowel Syndrome w/ Diarrhea (IBS-D)

Research Article <http://www.alliedacademies.org/biology-and-medicine-case-report/>

## Oral serum bovine immunoglobulin improves IBS-D symptoms analyzed from patient medical charts.

Larry Good<sup>1</sup>, Audrey Shaw<sup>2</sup>, David Wei<sup>3</sup>, René E. Vasquez<sup>4</sup>, Raymond Panas<sup>5</sup>, Brooke Jackson<sup>6</sup>, Tim Bradshaw<sup>7</sup>, Bruce P. Burnett<sup>8</sup> for The SBI Retrospective Study Group  
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### Abstract

**Purpose:** To examine clinical practice effectiveness of a medical food containing serum-derived bovine immunoglobulin (SBI) for its effect on symptoms in irritable bowel syndrome with diarrhea (IBS-D) patients.

**Methods:** From 165 IBS-D patient medical charts [mean age=59.6 years (range: 19-98), female (n=109), Caucasian (n=144)], recorded daily stools/consistency, abdominal pain, and patient/physician reported quality of life (QoL) scores were retrospectively collected on those prescribed SBI for a minimum of 8 weeks. A generalized estimating equations model was used to analyze and compare changes for scores of symptoms and QoL.

**Results:** Where data existed in charts, 46% of patients on SBI had a combined mean score reduction in daily stools, improvement in stool consistency (Bristol Stool Scale from >5 to <5) and decrease in abdominal pain (250%). Significant improvements (p<0.001) in individual symptom and QoL scores with a high response were also reported for daily stools (76%), consistency (78%), abdominal pain (69%), as well as patient (79%) and physician QoL (73%). Eleven patients experienced 13 adverse events (AEs) while receiving SBI with nausea (n=6) most prevalent. No serious AEs were reported, but 4 patients discontinued SBI.

**Conclusion:** In this retrospective chart analysis of IBS-D patients who took a medical food containing SBI for 8 weeks, there were statistical improvements in daily stool number, stool consistency, abdominal pain and QoL scores supporting its use in IBS-D.

**Keywords:** Irritable bowel syndrome, Diarrhea, Abdominal

**Abbreviations:** AE: Adverse Events; CFR: Code of Federal Regulation; GI: Gastrointestinal; GEE: Generalized Estimating Equations; IBS-C: Irritable Bowel Syndrome with Constipation; IBS-D: Irritable Bowel Syndrome with Diarrhea; IBS-M: Irritable Bowel Syndrome with Mixed Bowel Syndrome; SAE: Serious Adverse Events; SBI: Serum-Derived Bovine Immunoglobulin

### Introduction

Irritable bowel syndrome (IBS) is a chronic gastroenterology (GI) disorder affecting 10-25% of the general population. Patients with IBS can alternate over time between constipation (IBS-C) or diarrhea (IBS-D) predominant, a so-called IBS-M phenotype [1]. The exact cause of IBS is not clear, however, diverse etiologies such as alterations in motility, hypersensitivity, brain-gut interactions, various sensitivities, malabsorption, intestinal inflammation, gut barrier function, and dysbiosis have all been implicated. While prescription and over-the-counter standard-of-care agents are available to treat this condition, many IBS patients are refractory to these therapies adversely affecting their quality of life (QoL) [4]. IBS-D is defined by Rome cri-

## Case Series of 10 Drug-Refractory IBS Patients Who Respond to Oral Serum-Derived Bovine Immunoglobulin/Protein Isolate (SBI)

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### Abstract

**Aim:** The responses of 10 patients with long-standing, symptomatic, intractable drug-refractory histories of irritable bowel syndrome with diarrhea (IBS-D) and with abdominal pain, gas/bloating and distention, termed IBS undefined (IBS-U), were evaluated when administering a medical food product containing serum-derived bovine immunoglobulin/protein isolate (SBI). **Methods:** Patients in this case series were chosen based on their lack of satisfactory response to a variety of drugs, including antidiarrheal and antispasmodic medications, serotonin 5-HT<sub>3</sub> receptor antagonists, selective serotonin re-uptake inhibitors (SSRIs), proton pump inhibitors (PPIs), antibiotics, and antidepressive drugs. Patients met Rome III criteria and were administered 5 g/day of SBI as standard-of-care nutritional support. A scale of 0% - 25%, 25% - 50%, 50% - 75%, 75% - 100% response to SBI was used for patient-reported improvement in overall IBS symptoms following administration for one month. Exact methods for calculating confidence intervals and p-values were used to assess complete management of symptoms and response to therapy. Adverse events were also monitored for this nutritional product. **Results:** The onset of gastrointestinal (GI) symptom reduction utilizing nutritional management with SBI occurred within an average time of 2-4 weeks with improved or near complete management in all 10 patients who were refractory to previous drug therapies by 4 weeks. When prompted, patients reported significant IBS symptom improvement which averaged between 50% - 100% (p = 0.002) with an average for complete management in all patients of 69%. No side effects were reported after SBI administration even when taken for up to 28 weeks. **Conclusion:** Based on the safety profile and reported outcomes in

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How to cite this paper: Hilal, R., Mitchell, P., Guerra Jr., E. and Burnett, B.P. (2014) Case Series of 10 Drug-Refractory IBS Patients Who Respond to Oral Serum-Derived Bovine Immunoglobulin/Protein Isolate (SBI). *Open Journal of Gastroenterology*, 4, 323-328. <http://dx.doi.org/10.4236/ojgas.2014.41004>

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DOI: 10.3748/wjg.v21.i11.3261  
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CASE REPORT

## New therapeutic option for irritable bowel syndrome: Serum-derived bovine immunoglobulin

Larry Good, Roxanne Rosario, Raymond Panas

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Raymond Panas, Department of Medical Affairs, Entera Health, Inc., Cary, NC 27518, United States  
**Author contributions:** Good L and Rosario R had full access to review and full available data from the medical records. Good L and Panas R consolidated and analyzed the collected data. Good L, Rosario R, and Panas R contributed to the organization and writing of the manuscript.  
**Open Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non-Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

well as other symptoms (i.e., abdominal pain, bloating, and urgency) in patients with irritable bowel syndrome with diarrhea (IBS-D) and human immunodeficiency virus-associated enteropathy. This case series reports the outcomes of 14 IBS patients who received SBI as an addition to standard of care at an individual physician's clinical practice. The patients: 2 IBS with constipation (IBS-C), 7 IBS-D, 2 mixed diarrhea and constipation (IBS-M) and 3 undefined IBS (IBS-U); also described by some physicians as IBS-bloating), ranged in age from 22-87 years. SBI (5 g or 10 g daily dose) was added to the patient's current standard care and followed for several weeks to determine if symptoms were improved with the addition of SBI. Overall, 12 of the 14 patients reported some level of improvement through direct questioning of the patients regarding changes from the prior visit. One IBS-bloating patient had a resolution of

Open Journal of Gastroenterology, 2014, 4, 329-334  
Published Online October 2014 in SciRes. <http://www.scirp.org/journal/ojgas>  
<http://dx.doi.org/10.4236/ojgas.2014.41004>

## Serum-Derived Bovine Immunoglobulin/Protein Isolate Therapy for Patients with Refractory Irritable Bowel Syndrome

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### Abstract

**Background:** A small double-blind study showed benefits of serum-derived bovine immunoglobulin/protein isolate (SBI) for diarrhea-predominant irritable bowel syndrome (IBS-D) [1]. The purpose of this chart review was to assess safety and clinical outcomes of SBI in refractory irritable bowel syndrome (IBS) patients. **Methods:** A retrospective review of 35 IBS patients with diarrhea or mixed bowel constipation patterns (IBS-M) who were administered SBI 5 grams twice daily was performed. Clinical response ("good response" or "no response") and adverse events were determined by follow-up after four weeks of therapy. Patients were included for evaluation if a lactulose breath test (LBT) had been performed prior to SBI. All patients were refractory to common IBS therapies. The response rate to the inclusion of SBI was divided in three separate groups: dividing patients based on their LBT results (positive or negative), including patients by their IBS diagnosis (IBS-D or IBS-M) and grouping all patients together. **Results:** Analysis was carried out on 26 IBS-D/M patients with LBT results. Two patients were lost to follow-up and were excluded from data analysis. The positive LBT group (N = 11) had a 73% (p = 0.117) positive response rate to SBI. The negative LBT group (N = 13) had a significant response rate of 77% (p = 0.049). If patients were divided by IBS diagnosis or grouped together, the response rate to SBI was similarly ranging from 69% - 88%. Adverse events leading to cessation of SBI occurred in 3 of 24 patients. **Conclusion:** SBI appeared to be a safe and effective nutritional moiety in refractory IBS-D and IBS-M patients. Larger, double-blind studies are needed.

### Keywords

Irritable Bowel Syndrome (IBS), Small Intestinal Bacterial Overgrowth (SIBO), Serum-Derived Bovine Immunoglobulin/Protein Isolate (SBI)

How to cite this paper: Weinstein, L.B. and Jasion, V.S. (2014) Serum-Derived Bovine Immunoglobulin/Protein Isolate Therapy for Patients with Refractory Irritable Bowel Syndrome. *Open Journal of Gastroenterology*, 4, 329-334. <http://dx.doi.org/10.4236/ojgas.2014.41004>

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ISSN 2224-9912 (print) ISSN 2224-6809 (online)

CASE REPORT

## Post-Infectious Irritable Bowel Syndrome with Functional Diarrhea Following C. difficile Infections: Case Studies of Responses Using Serum-Derived Bovine Immunoglobulin

Carl Crawford, Raymond Panas

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Published online: April 21, 2015

a 57-year old Caucasian female, experienced ongoing diarrhea with alternating bouts of constipation after clearance of her recurrent CDI. Upon use of SBI 5g BID, she noticed better management within a few days. Therapy was reduced to SBI 5g QD to avoid possible constipation and the reports regulation of her bowel habits. **Discussion:** These cases highlight specific symptoms that result from C. difficile-associated P-IBS, the management that SBI can provide when considered an option for therapy, and the impact disease manifestation can have on quality of life. These cases further suggest the need for additional study of this nutritional agent in post-C. difficile infectious IBS patients.

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### ABSTRACT

**Introduction:** Post-infectious (PI-IBS) may occur in these patients tend to a serum-derived bovine immunoglobulin/protein isolate (SBI) considered for the management of refractory irritable bowel syndrome (IBS). **Case Presentations:** I and eventually cleared. **Conclusion:** SBI as the setting of modest condition led her to BI SBI 5 g QD, her first natural upon discontinuation of complete management on SBI 5g QD and her

Healio > Gastroenterology > Irritable Bowel Syndrome

MEETING NEWS COVERAGE

## Nutritional management with serum-derived bovine immunoglobulin benefits refractory IBS-D patients

September 4, 2015

READ/SUBMIT COMMENTS EMAIL PRINT SAVE

For patients with refractory diarrhea-predominant irritable bowel syndrome, nutritional management with serum-derived bovine immunoglobulin/protein isolate, a prescription medical food, effectively improved their symptoms, according to data presented at the AGA's 2015 James W. Freston Conference in Chicago.

### See Also

8 recent developments in IBS  
Researchers identify potential non-invasive biomarkers for ...  
Herbal tablet reduces hepatic fat in patients with NAFLD

### Featured



Digestive Disease Week

MORE FEATURED:

International Liver Congress  
Advances in IBD  
The Liver Meeting  
Ulcerative Colitis Resource Center

2015, Chicago.

Follow-up in previous studies of serum-derived bovine immunoglobulin (SBI) for IBS-D was limited to 4 to 6 weeks, so researchers performed a single-center, retrospective chart review of 28 refractory IBS-D patients (16 female, mean age, 64 years) who received 5g SBI per day for 16 weeks. Patients rated symptom management by a 4-point Likert scale at least once per month throughout the treatment period.

Mean Likert score at the end of the treatment period was 2.4 (moderate to significant symptom management), and 23 patients reported at least a moderate management compared with five who reported minimal or no management. "This is statistically significant (Chi-squared = 11.571; P = .0007) compared to a null hypothesis in which SBI administration would have no effect or minimal effect on patient response", the researchers wrote.

By weeks 2 to 4, patients reported improved stool frequency, stool consistency, cessation of fecal incontinence, management of abdominal discomfort and bloating, and these changes were maintained through the treatment period.

"SBI afforded an effective option in managing difficult-to-treat IBS-D, allowing significant management as reported by patients," the researchers wrote. "These outcomes support use of SBI as a novel, effective nutritional management option for IBS-D." — by Adam Leitenberger

### Reference:

Shafrafi, et al Presented at: James W. Freston Conference; August 29-30, 2015, Chicago.





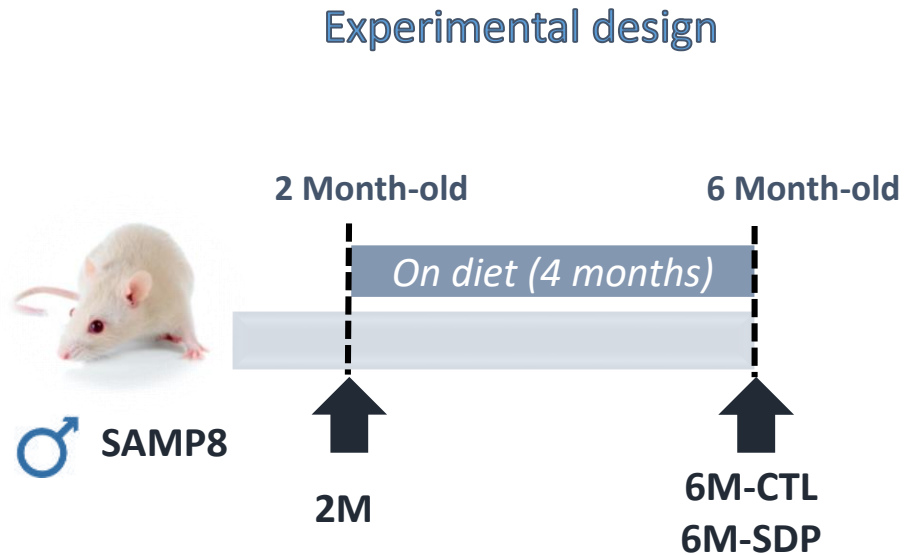
# Mode of Action

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<https://www.youtube.com/watch?v=Zf4C-Plk908>



# Effect of SDP/SBI supplementation in Aging Model



## INTESTINAL EFFECTS

Dietary supplementation with SDP will reduce the magnitude of intestinal dysfunction associated with aging

## SYSTEMIC EFFECTS

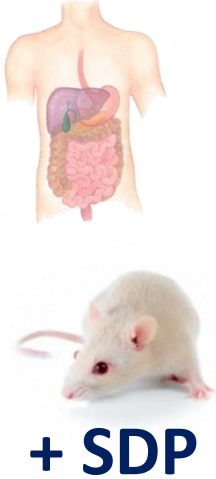
Effects of SDP supplementation on inflammatory markers & plasma amino acid profile

## CENTRAL NERVOUS SYSTEM EFFECTS

SDP supplementation may reduce the inflammatory state of the CNS during aging and prevents the cognitive dysfunctions

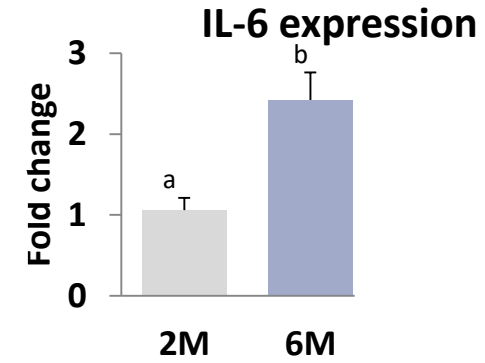
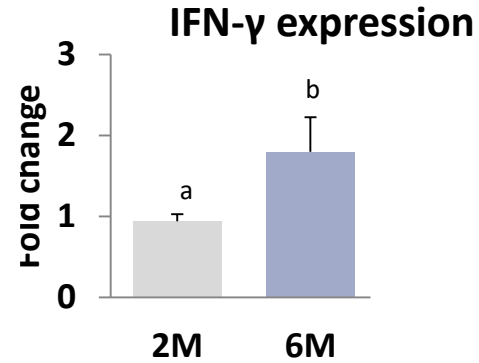
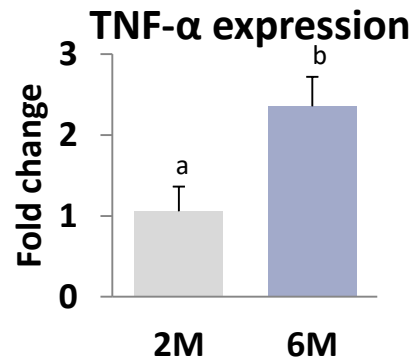
# Intestinal Effect on Senescent Mice

Intestinal effects



## Pro-inflammatory cytokines

Mean  $\pm$  SEM (N = 5-8 mice/group)  
a  $\neq$  b, P<0.05



## Conclusions

Six month-old SAMP8 mice showed a low-grade inflammatory state in the jejunum mucosa. SDP supplementation was able to prevent this effect, confirming observations from other inflammatory models (SEB-Intestine, Colitis or LPS-Lung models)

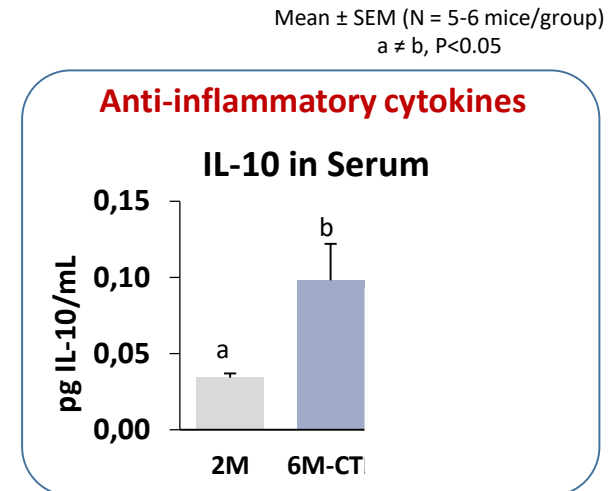
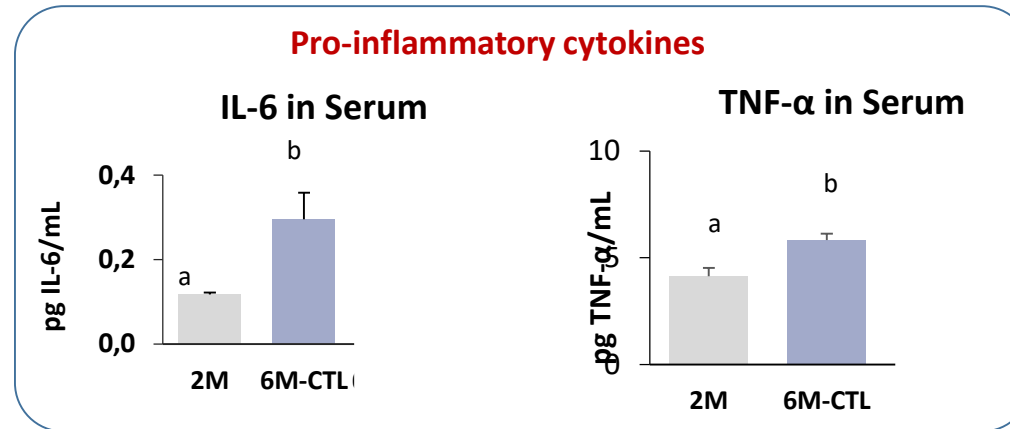
⇒ **Reduces the Inflammatory Effects in the Intestine**

# Systemic Effects on Senescent Mice

Systemic effects



+ SDP

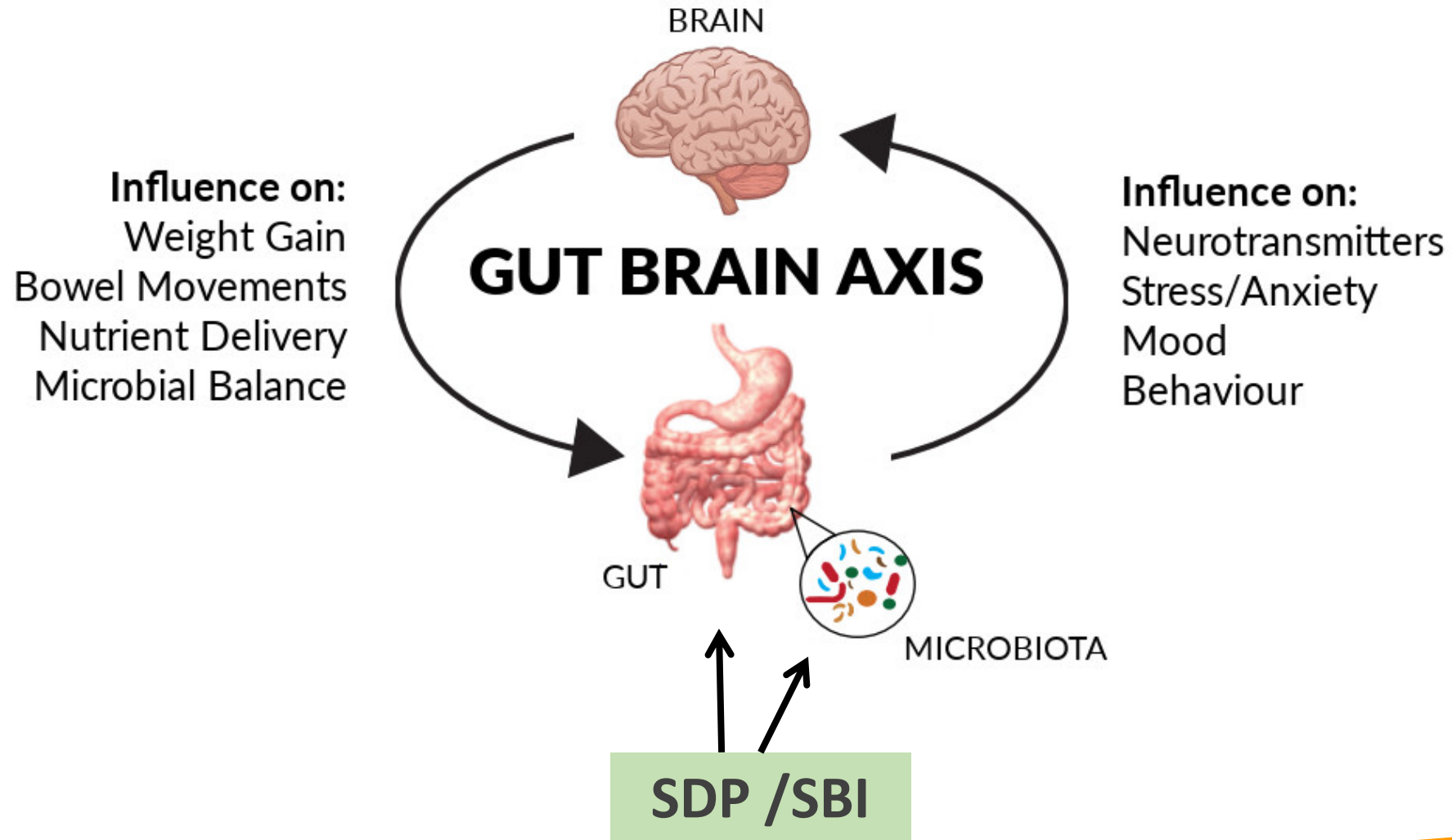


## Conclusions

Six month-old SAMP8 mice showed a systemic low-grade inflammatory state. As previously observed in other inflammatory models (SEB-Intestine, Colitis or LPS-Lung models), SDP supplementation was able to prevent this effect

**$\Rightarrow$  Reduces Systemic Inflammation**

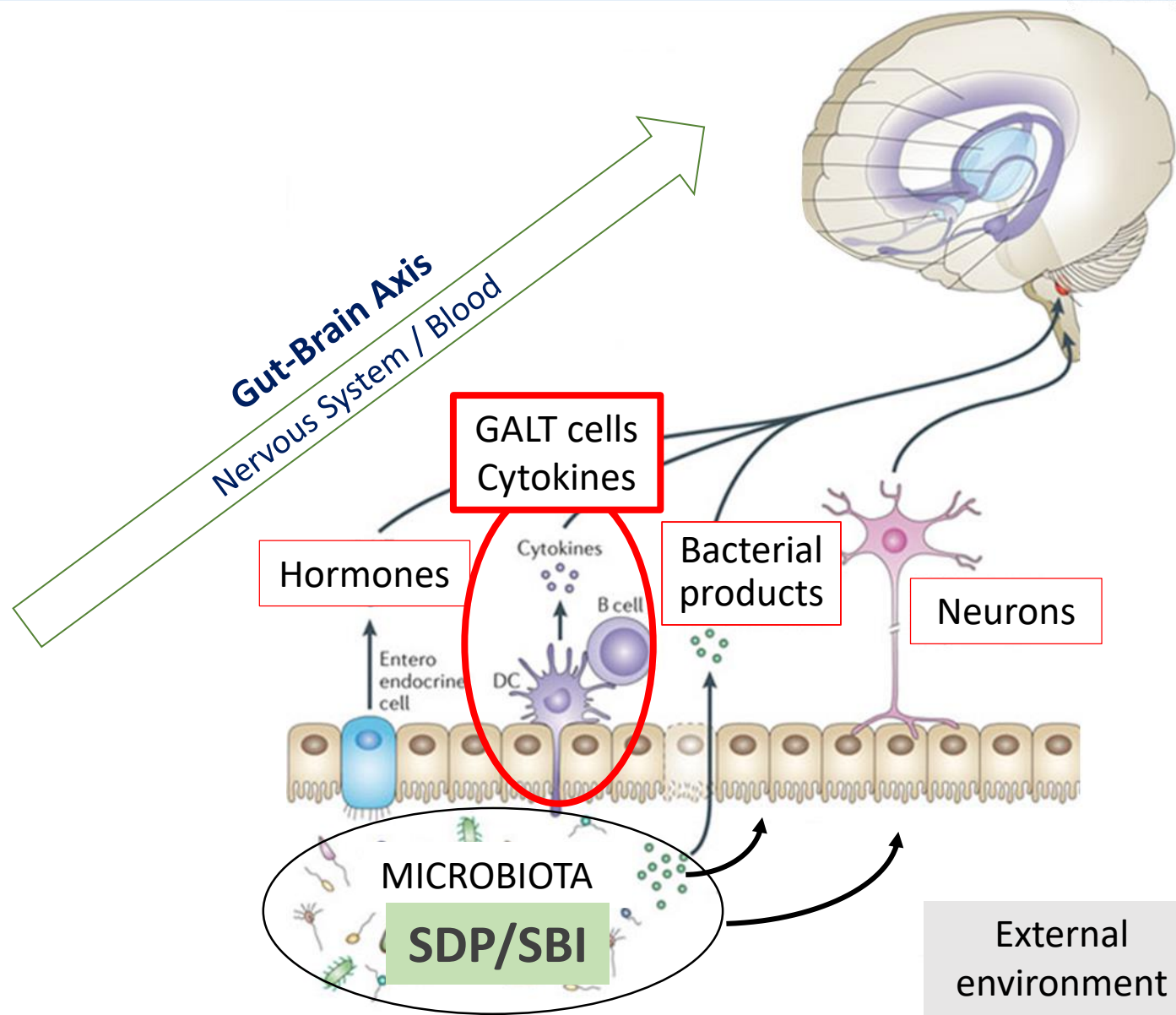
# Effects on the Central Nervous System



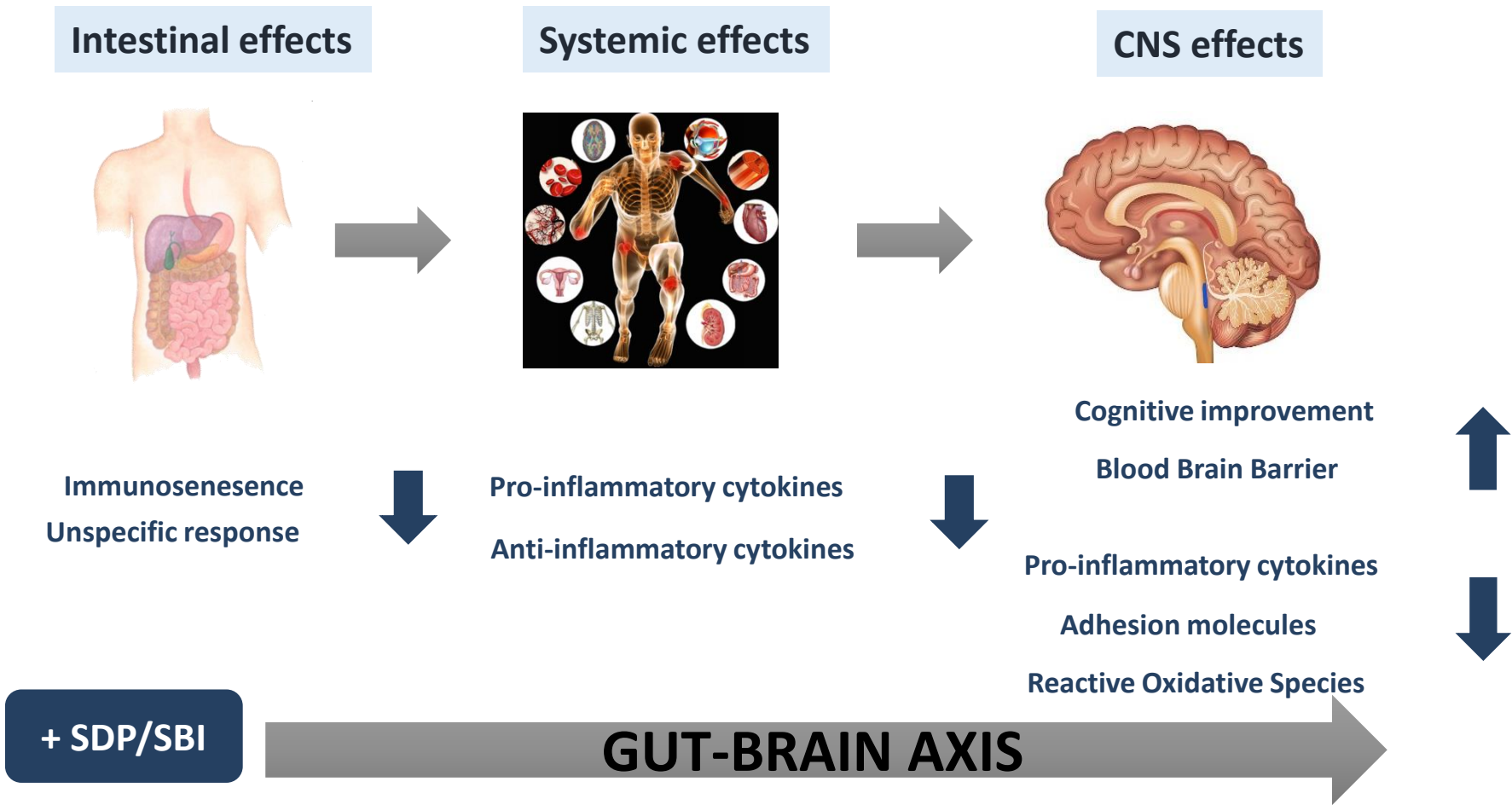


# Effects on the Central Nervous System

Collins MS et al (2012) Nature Rev Microbiol 10, 735-742



# Biological Functionality of Serum fractions, a Summary



## Concluding Comments

- APC and Entera Health's Serum proteins are widely used in humans and other many species, including companion animals
- It is recognized that these functional proteins are a mixture of proteins that mitigate the negative effects of inflammation
- Used appropriately, functional proteins can be a tool to improve humans and animal well being