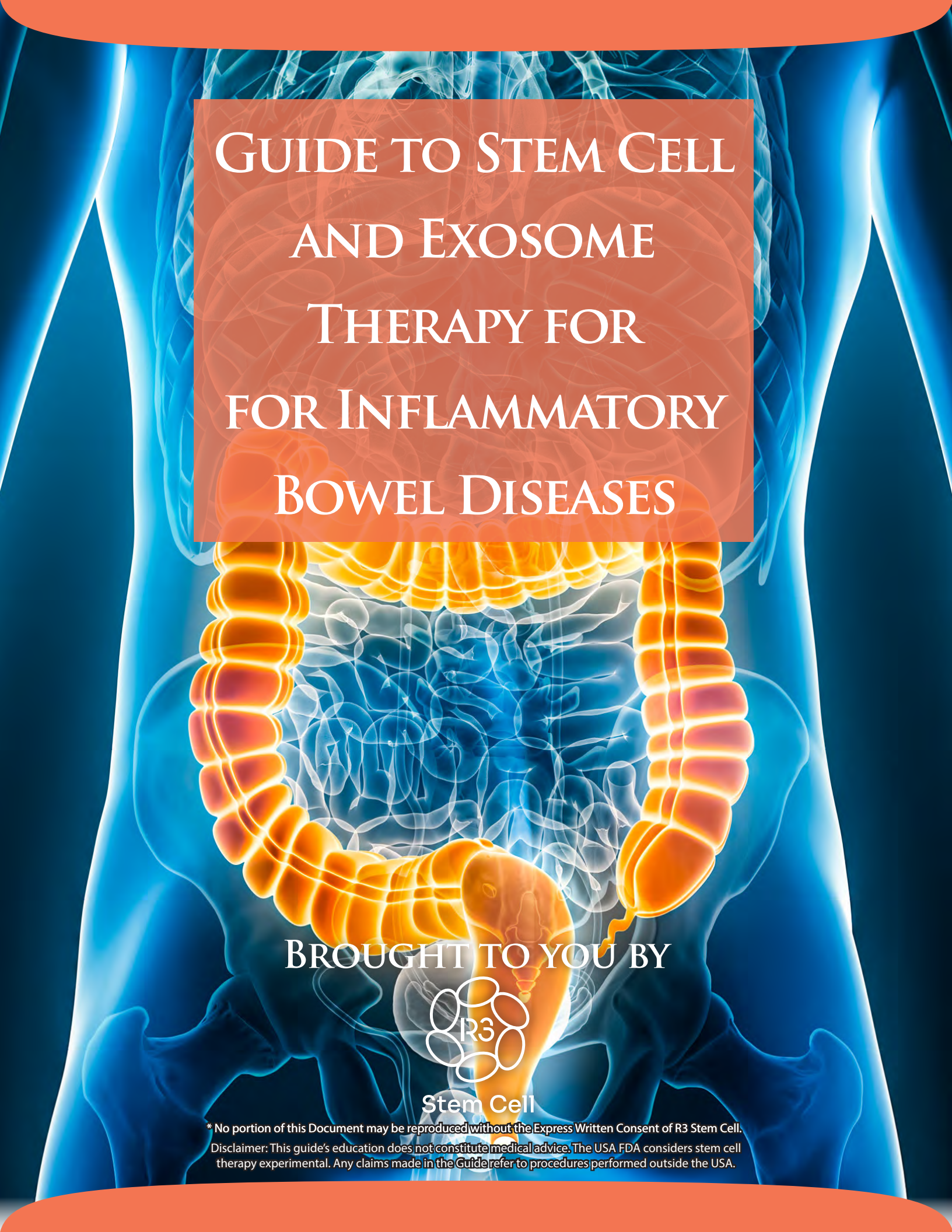
Guide to Stem Cell and Exosome Therapy for for Inflammatory Bowel Diseases



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R3 Stem Cell

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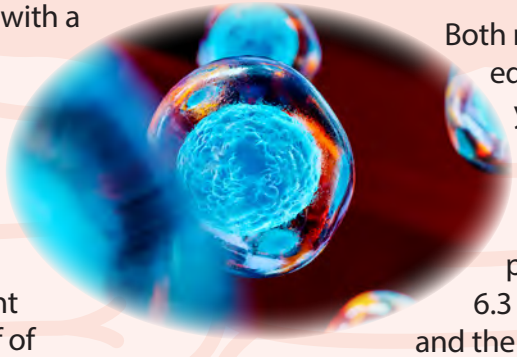
Guide to Stem Cell and Exosome Therapy for Inflammatory Bowel Diseases

Every day, R3 Stem Cell receives inquiries worldwide from individuals asking if stem cell therapy can help for inflammatory bowel diseases, such as Ulcerative Colitis and Crohn's Disease. Spoiler alert: It can help a lot! In this guide, we'll go through the basics of how stem cells and exosomes work for IBD relief, the latest research, and what to expect with a regenerative procedure.



Conventional treatments for Inflammatory Bowel Diseases (IBD) have improved dramatically over the past decade. Despite the efforts being made to optimize use of the existing drugs, the current situation is far from ideal. Up to half of all IBD patients stop responding to conventional medications, and continue to suffer complications that may end up with surgery, fistulas and hospitalizations.

Stem cell therapy for IBD is turning out to be an excellent opportunity for individuals to potentially achieve remission, improve function and to avoid the need for potentially risky surgery. Let's dig in!

A Significant Global Issue

Inflammatory bowel diseases (IBDs) represent a group of chronic inflammatory disorders of the gastrointestinal (GI) tract including ulcerative colitis (UC), Crohn's disease (CD), and unclassified IBDs.

According to epidemiology, the prevalence of IBDs in Western countries is significantly higher than that in Eastern countries, but it is also rapidly increasing in Asian countries.

Both male and female are affected equally, specially adults aged 30–40 years. The incidence of Ulcerative Colitis (UC) has been increasing around the world. The highest annual incidence reported was 24.3 per 100,000 person-years in Europe, 6.3 per 100,000 person-years in Asia and the Middle East, and 19.2 per 100,000 person-years in North America.

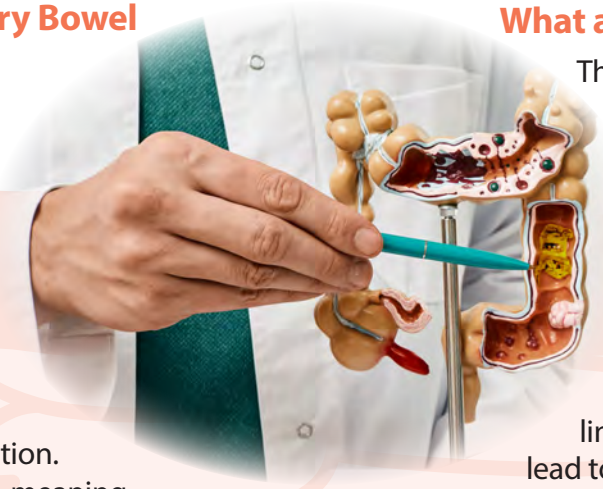
Furthermore, in the last few decades there has been an increase in the disease in low-incidence zones as South Korea, China, India, Iran, Lebanon, Thailand, the French West Indies, North Africa and Japan. IBD poses an important health problem, since its worldwide incidence is increasing.

The condition affects young people and persists for life - exerting a strong impact upon quality of life, in the professional setting, and in patients' personal relations. Furthermore, IBD is associated with considerable healthcare costs

TABLE 1 The difference between Crohn's and Ulcerative colitis.

Items/ Type	Crohn's (CD)	Ulcerative colitis (UC)
Causes	Inappropriate response of the immune system	Immune reaction, genetics
Risk factors	Smoking, environmental factors	Age, ethnicity
Lesion site	Anywhere between the mouth and anus	Rectum, colon
Symptoms	Abdominal cramping, diarrhoea, bloody stool, mucous stool, loss of appetite, weight loss, tiredness and mouth ulcers.	Diarrhoea, abdominal, anal pain, weight loss, tiredness, fatigue, rectal ulcers, bleeding, fevers, chills, anorexia and nausea
Complications	Nutritional deficiencies, fistulas, toxic, megacolon, narrowing of the intestines	Bleeding, toxic colitis, blood clotting, bowel cancer
Characteristics	Discontinuous lesions	Continuous lesions
Treatment	Lifestyle changes, medication and surgery	Self-care, medications and surgery
Medication	5-aminosalicylic acids, corticosteroids, immune system modulators, tumor necrosis factor-alpha antagonists, antibiotics, antidiarrhoeal medications	aminosalicylic acids, corticosteroids, biological therapies, antibiotics, probiotics and iron supplements
Surgery	It is used for fistulas, strictures (narrowing of the gut), large abscesses or other therapies have failed.	Medications is ineffective, precancerous or cancerous changes in the bowels, severe symptoms
Canceration	Low	High
Prognosis	Some people can be symptom-free for decades, while others may experience symptoms every few months.	There is a greater risk than normal of developing bowel cancer, usually after 7-10 years with ulcerative colitis.

What causes Inflammatory Bowel Diseases?



At present, IBD is regarded as the result of an abnormal host immune response to intraluminal antigens occurring in a genetically predisposed individual, with the production of chronic inflammation of the gastrointestinal tract, accompanied by tissue destruction. IBD is an autoimmune disorder, meaning the body's immune system attacks healthy tissues. It is not yet known what triggers these attacks and why IBD develops in some people and not in others.

The cause of IBDs is very complicated and has not yet been completely understood. IBD is the consequence of complex interaction among genetic, environmental and microbial factors, producing sustained inflammation at intestinal level, favored by alteration of the mucosal barrier and immune system defects. Among the environmental factors, smoking, drug use, diet habits, mental stress, and many other external factors are related to the occurrence of IBDs.

In particular, smoking increases the risk of CD and is related with an increase in the recurrence rate. Air pollution can also increase the risk of CD and UC disease. At the same time, Bitton et al. also proposed that people with less stress would have less chance of developing IBDs.

In addition, IBDs has a strong genetic tendency, especially in the first-degree relatives of patients who are at higher risk for IBDs. Compared with fraternal twins, identical twins have a higher prevalence rate of IBDs. Genetic studies have reached a consistent conclusion: genetic factors play an important but non-decisive role in the occurrence of IBDs.

What are the symptoms of IBD?

The clinical signs and symptoms of the IBDs mainly include enteritis, diarrhea, recurrent hemorrhage, abdominal pain, reduced appetite, and weight loss. Currently, there is still no cure for IBDs.

People may experience ulcers and inflammation of the inner lining of the colon , that may also lead to rectal bleeding.

Common IBD symptoms include:

- Abdominal pain (pain in the stomach area)
- Diarrhea, sometimes with blood
- Urgency to have a bowel movement and fecal incontinence
- Rectal bleeding
- Weight loss
- Fever
- Anemia
- Malnutrition and delayed growth in people who develop IBD as children
- Anxiety and depression

If inflammation is not controlled, over time IBD can damage the intestines, causing

- **Abscesses:** pockets of infection that can result in tearing of the intestinal wall.
- **Strictures:** areas of narrowing in the bowel.
- **Fistulas:** abnormal passageways between two organs or vessels that normally do not connect. Fistulas happen when inflammation and pressure inside the bowel break down tissue, and can cause bowel contents to leak into the bladder, urethra or vagina.
- **Long-term inflammation in the colon increases the risk of colon cancer.**

In some people with IBD, the inflammation can affect areas of the body outside the intestines:

- **Eyes:** redness and inflammation due to episcleritis (inflammation between the inner eyelids and the white of the eye) or uveitis (inflammation inside the eye). Experts estimate that 10% to 43% of people with IBD develop eye problems, and regular visits to the eye doctor are important.
- **Mouth:** inflammation (stomatitis), mouth sores and ulcers
- **Liver:** fat in the liver (steatosis)
- **Biliary tract:** gallstones and inflammation of the bile duct system (sclerosing cholangitis)
- **Kidneys:** kidney stones, hydronephrosis (swollen kidneys caused by a backup of urine), fistulas and urinary tract infections
- **Skin:** erythema nodosum (tender, red bumps on the shins), pyoderma gangrenosum, a rare condition that causes severe skin ulcers on the legs.
- **Joints and spine:** spondylolysis (stress fracture of the vertebrae), sacroiliitis(inflammation of the joints connecting the lower spine with the pelvis) and IBD in the limbs
- **Blood circulation:** including phlebitis (inflammation of blood vessels)

Traditional Treatments

Medications are key to treating IBD. The goal is easing symptoms, halting inflammation and reducing flare-ups.

Conventional medication options include

- Immunosuppressants for IBD
- Topical anti-inflammatory medications
- Pain medications
- Antibiotics
- Steroids

If medications do not calm the inflammation, over time the intestines can become damaged, making symptoms worse and increasing the need for surgery. About half of people with IBD may need surgery at some point in their lives to:

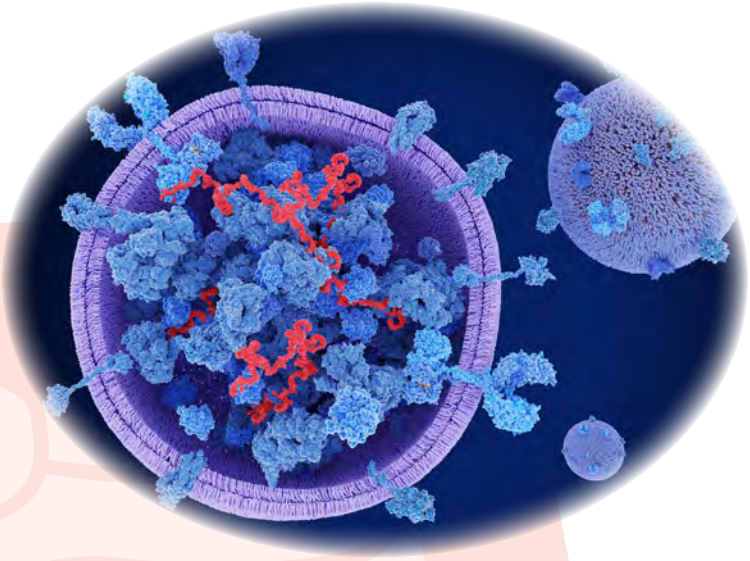
- Remove areas of the intestine
- Repair blockages, strictures, abscesses or fistulas.

The majority of ulcerative colitis (UC) patients would be subject to medications including anti-inflammatory agents such as 5-aminosalicylic acids (5-ASA), systemic corticosteroids, and topical corticosteroids, as well as immunomodulators like azathioprine, 6-mercaptopurine (6-MP), cyclosporine, and methotrexate.

Unfortunately, 74% of UC patients experience at least one relapse during 5-year observation in a prospective population-based cohort study. A meta-analysis conducted by Ford et al. has shown that 887 (60.3%) of 1470 UC patients fell short of achieving remission in randomized to receive 5-ASA, indicating that more than half of UC patients may not be able to have a positive response to traditional medications.

What is more, taking these drugs could lead to the occurrence of various adverse effects. The use of corticosteroids is confirmed to be associated with cutaneous effects, weight gain, hyperglycemia, osteoporosis, adrenal insufficiency, and cataracts. Moreover, corticosteroid therapy is capable of increasing risk of opportunistic infections, especially when administered in combination with other immunosuppressive drugs. The intolerance or potential occurrence of myelotoxicity and hepatotoxicity generated by immunomodulators could make nearly one fourth of patients discontinue the treatments.

Among the recently available therapies, anti-tumor necrosis factor α (anti-TNFα) agents are the most notable predecessors (infliximab, adalimumab, etc.), resulting in improved health outcomes and decreased need for surgical intervention. However, treatment failure is observed in many patients treated with anti-TNFα agents, including primary and secondary nonresponders. Additionally, anti-TNF-α agents are associated with rare but serious adverse effects, including serious infection, paradoxical autoimmune reactions, and a small but increased risk of malignancy.



Stem Cell Therapy for IBD

The effects of systemic administration of autologous or allogeneic MSCs have been evaluated in clinical trials., indicating that the systemic administration of mesenchymal stem cells significantly improved the clinical outcome and prognosis for IBDs.

Stem Cells have been found to inhibit intestinal inflammation, promote long-term intestinal mucosal healing, and significantly improve patient quality of life, making them a valuable alternative IBD treatment.

Table 1 Two types of stem cell therapy are currently used for the treatment of inflammatory bowel disease

Type of therapy	Mechanisms of action
Hematopoietic stem cells	Autologous transplant: Elimination of reactive T lymphocytes (lymphoablation, new reconstitution of the immune system of the patient with more tolerogenic naïve lymphocytes). The genetic predisposition of the patient is not modified Allogenic transplant: Replacement of the immune system with the donor immune system, correcting patient genetic predisposition. Not accepted due to high morbidity-mortality
Mesenchymal stem cells (autologous or allogenic)	Systemic and local administration: Immunemodulating and trophic action

R3 Stem Cell does not use Hematopoietic Stem Cell Therapy (HSCT). This treatment actually has an unfortunate name, because hematopoietic stem cells are a component of umbilical cord blood. R3 uses cord blood internationally in some locations for treatments, but not HSCT. Let me explain.

HSCT is a treatment where a patient receives a myeloablation. This involves administering a chemotherapy regimen to knock out a person's immune system, and then applying a person's own bone marrow for replenishing the immune system. It's basically a cancer style treatment with an autologous bone marrow transplant.

While there are some very good published results, there are significant risks associated with HSCT. One may experience opportunistic infection, anemia, and death in rare circumstances. So R3 Stem Cell does not perform HSCT, rather, mesenchymal stem cell therapies are performed that do not involve knocking out a person's immune system.

Wang et al published a meta-analysis in 2021 where they evaluated 18 human studies on IBD, including 360 patients. In the studies that looked at remission rates with mesenchymal stem cells, rates at 1, 3, 5, 12, 24, and 36 months after stem cell therapy were 43%, 68%, 73%, 54%, 52%, and 46%, respectively, thus both high and stable.

In 2006, Onken et al published an abstract on mesenchymal stem cells used to treat 10 patients with active Crohn's Disease (CDAI >220, C-reactive protein ≥ 5 mg/L) refractory to treatment with corticosteroids, immune modulators and infliximab.

The patients were randomized to two groups, both of which received two intravenous doses of MSCs, spaced one week apart. One group received high-

dose MSCs (8 million MSCs/kg), while the other group received low dose MSCs (2 million MSCs/kg). The primary endpoint was percentage clinical response, defined as a reduction in the CDAI score of ≥ 100 points.

All subjects presented a mean reduction in CDAI score of 105 points on day 28. The CDAI scores decreased to a greater extent in the high-dose group.

In 2014, Forbes et al published a study looking at donor mesenchymal stem cells in patients with luminal Crohn's Disease who were nonresponders to traditional therapies. Sixteen patients were given intravenous infusions of allogeneic MSCs (2 million stem cells/kg body weight) weekly for 4 weeks.

Among the 15 patients who completed the study, the mean CDAI score was reduced from 370 to 203 at day 42 ($P < .0001$). That's a decrease of 46%!

The mean CDAI scores decreased after each MSC infusion (370 before administration, 269 on day 7, 240 on day 14, 209 on day 21, 182 on day 28, and 203 on day 42). Twelve patients had a clinical response, 8 had clinical remission.

In 2018, Zhang et al published the BEST study to date on umbilical cord MSC's for Crohn's Disease. The study sought to investigate the efficacy and safety of UC-MSCs for the treatment of Crohn's Disease.

Eighty-two patients who had been diagnosed with CD and had received steroid maintenance therapy for more than 6 months were included in this study. Forty-one patients were randomly selected to receive a total of four peripheral intravenous infusions of 1 million umbilical cord stem cells/kg, with one infusion per week. Patients were followed up for 12 months.

The Crohn's disease activity index (CDAI), Harvey-Bradshaw index (HBI), and corticosteroid dosage were assessed. Twelve months after treatment, the CDAI, HBI, and corticosteroid dosage had decreased by 62.5, 3.4, and 4.2 mg/day, respectively, in the UC-MSC group

In the control group, the CDAI, HBI, and corticosteroid dosage had decreased by 23.6, 1.2 and 1.2mg/day, respectively.

The superiority of umbilical cord mesenchymal stem cells was statistically significant, and patients were able to avoid the side effects of chronic steroid use! No serious adverse events were observed. The conclusion was that umbilical cord mesenchymal stem cells were effective in the treatment of Crohn's Disease and produced mild side effects.

Below you will see before and after endoscopic results of two patients in the study who received the mesenchymal stem cells. Complete colon healing!

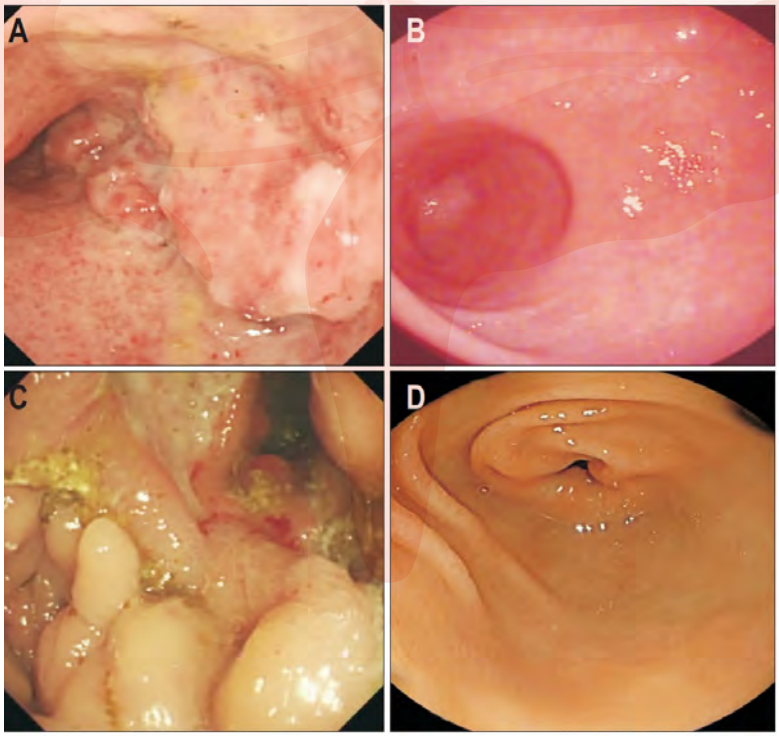


Fig. 3. Colonoscopy showed remarkable mucosal recovery at 12 months compared with baseline findings. (A, B) Panels depict images for patient 14 and (C, D) depict images for patient 23.

Below is a table of several clinical trials showing the dose of stem cells used, number of patients, follow up duration and the outcome. The results are extremely impressive!

Table 2 Clinical findings of the MSCs therapy in IBD patients

MSC type		IBD type	Administration schedule	Number ofpatients	Follow-up duration	Clinical phase	Outcome	References
BM-MSCs	Autologous	Luminal CD	Two doses of 1–2 × 10^6 cells/kg, IV injection, 7 days apart	9	6 weeks	Phase I	The decrease in CDAI score in 3 patients after 6 weeks	[26]
		CD	A single dose of 2 × 10^7, 5 × 10^7, or 10 × 10^7 cells/kg, IV injection	12	2 weeks	Phase I	Safe and feasible at the doses of up to 10 million cells/kg	[27]
	Allogeneic	Perianal fistulizing CD	A single dose of 1 × 10^7, 3 × 10^7, or 9 × 10^7, local injection	24	24 weeks	Phase II	No severe adverse events 3 × 10^7 MSCs induced healing of perianal fistulas	[24]
		UC/CD	A single dose of (1.5–2) × 10^8, IV injection	21	6, 12, and 24 weeks	Phase II	The decrease in the clinical and morphological indices of inflammatory activity in 34 (72%) patients	[28]
		Luminal CD	A single dose of 2 × 10^6 cells/kg weekly for 4 weeks, IV injection	16	6 weeks	Phase II	The decrease in CDAI score in 15 patients after 6 weeks	[25]
AD-MSCs	Autologous	Perianal fistulizing CD	2 × 10^7 cells/kg, local injection	12	24 weeks	Phase I	Complete clinical healing in 9 patients after 12 weeks Complete clinical healing in 10 patients after 24 weeks	[33]
		Perianal fistulizing CD	1 × 10^7, 2 × 10^7, or 4 × 10^7 cells/ml in three groups	9	8 weeks	Phase I	2 patients treated with 2 × 10^7 cells/ml showed complete healing and 3 patients treated with 4 × 10^7 cells/ml showed complete healing at week 8	[34]
		Perianal fistulizing CD	3 × 107 cells per centimeter length of the fistula	43	8 weeks	Phase II	Complete fistula healing in 27/33 (82%) patients after 8 weeks Complete closure of fistula in 23/26 (88%) patients after 1 year	[32]
	Allogeneic	Perianal fistulizing CD	A single dose of 1.2 × 10^8, Intralesional injection	212	24 weeks	Phase III	Combined remission in 50% of patients	[30]
		Perianal fistulizing CD	A single dose intralesionally If 2 × 10^7 failed, 4 × 10^7 subsequently	24	24 weeks	Phase II	The decrease in the number of draining fistulas in 69.2% of patients Complete fistula closure treated in 56.3% of patients Complete closure of all existing fistula tracts in 30% of patients	[35]
hUC-MSCs	Allogeneic	UC/CD	1 × 10^6 cells/kg, IV injection	7	6 months	Phase I	The decrease in clinical activity index scores in all patients The decrease in fistula size and drainage in one patient The decrease in rough mucosa, polypoid lesions, and ulcers in three patients The decrease in the extent of the inflamed area and the dense lymphocytic infiltration in the mucosa propria A relapse in two patients at 6 and 7 months after treatment At the 3-month visit, five patients achieved remission and maintenance of remission lasted for more than 24 months in two patients	[36]

How do Stem Cells Work in the Body?

They act through:

1. **Angiogenesis** – provokes formation of new blood vessels.
2. **Reduce inflammation** – IBD is associated with significant inflammation, and the regenerative biologics reduce it nicely.
3. **Immune system modulation** – the stem cells and exosomes modulate the immune system very differently than steroids. Instead of blanketly suppressing the immune system, the regenerative biologics tamp down the harmful processes while amping up the beneficial ones. This includes ramping up production of several helpful growth factors and cytokines, while tamping down harmful ones.
4. **Cellular signaling** – the biologics are able to perform "cell to cell" communication. This promotes recipient cells to proliferate their growth factor production, protein production and regenerate tissues that are damaged.
5. **Prevent cell death** – most cells have a timed death, where they are only allowed to live a certain length of time. This is called apoptosis. The regenerative biologics allow normally functioning cells (i.e. chondrocytes) to live longer, and spare them from the pre-programmed death. This can reduce the rate of cartilage loss in a joint!
6. **Preventing scar tissue** –Once that scar tissue forms, it becomes nonfunctional. Stem Cells and exosomes are great at preventing scar **tissue (anti-fibrosis).**

Table 1. Proteins involved in the therapeutic mechanism of MSCs.

Therapeutic Benefits	Proteins	Mechanisms
Attenuate inflammation through immunomodulation	IL-1, IFN-γ, TNF-α, MCP-1	Decreased pro-inflammatory cytokines to attenuate inflammation [17,18]
	IL-4, IL-10, TNF-β	Increased anti-inflammatory cytokines to attenuate inflammation [17,18]
	PGE2	Mediated the expression of TNF-α and IFN-γ [19]
	HMGB1	Late pro-inflammatory cytokine [20,21]
Release trophic factors to promote therapeutic effects	BDNF	Promoted neurological recovery [22] and directed differentiation of MSCs [7]
	GDNF	Reduced infarct volume [23]
	NGF	Prevented neuron apoptosis and increased neuron proliferation [24]
	VEGF	Induced angiogenesis [25]
	PDGF	Promoted the migration of cells, promoted the growth of primary cortical neurons, inhibited neuroinflammation, and promoted angiogenesis and axon growth [26–28]
Induce angiogenesis	Ang1 and tyrosine protein kinase receptor Tie-2 VEGF and VEGF receptor 2 (Flk1)	Increased these proteins to increase blood vessel density at the site of vascular injury [29]
Proliferate neuroblasts	Axonal growth-associated proteins and axonal growth-inhibiting proteins	Increased axonal growth-associated proteins and decreased axonal growth-inhibiting proteins to promote axonal growth [30]
	Collagen IV and tight junction protein ZO-1	Increased these proteins to decrease BBB disruption and neuronal loss [31,32]
	p53 protein	Reduced the activity of p53 protein to decrease neuron apoptosis [33]
Replace damaged cells	MAP2 and NeuN	Differentiated into new neurons to replace damaged neurons [9]
	GFAP and CNPase	Differentiated into new glial cells to replace damaged glial cells [9]

Stem Cells can also release a huge variety of molecules into the extracellular environment. These molecules, which include extracellular vesicles (exosomes), lipids, free nucleic acids, and soluble proteins, exert crucial roles in repairing damaged tissue. Along with offering stem cells for treatment of IBD, R3 Stem Cell includes stem cell exosomes, which are a type of extracellular vesicle participating in extensive cell to cell communication for cartilage tissue repair and regeneration.

The stem cells administered by R3 are not the ones that become a patient's new mucosal cell. The administered mesenchymal stem cells are not specifically designed to replace damaged and lost cells in the intestines, but rather coordinate and enhance this repair response by one's own mechanisms.

Where do the stem cells and exosomes come from?

R3 Stem Cell's regenerative biologics originate from umbilical cord tissue that has been donated after a scheduled c-section. No baby (or mother) is harmed during the c-section procedure. The umbilical cord tissue is normally discarded, but if the mother passes screening test then the umbilical cord is immediately sent to the lab.

The lab carefully processes the umbilical cord to generate large amounts of stem cells and exosomes that are of the highest quality possible. The lab team consists of multiple PhD's working in ISO Certified, cGMP compliant clean rooms to ensure quality assurance that exceeds USA FDA standards. The proprietary production process combines the highest potency, safety and affordability for providers to confidently offer exosome procedures.

Millions of dollars have been invested into the pharmaceutical grade production of the biologics including first rate clean rooms, bioreactors, nano-particle tracking analyzers, cytometers, PCR, tangential flow machines and real time environmental monitoring. The quality assurance testing complies with screening and testing stan¬dards consistent with the American Association of Tissue Banks, cGMP standards, FDA regulations and the highest level of any regulatory agency globally.

Stem Cell Derived Exosomes

R3 Stem Cell's Centers of Excellence globally include umbilical cord stem cell derived exosomes with umbilical cord stem cells to provide enhanced results. Exosomes are lipid bound vesicles (acellular) produced by cells which contain a plethora of growth factors, cytokines, mRNA and other proteins.

They are exceptionally helpful in cell to cell communication, and very effective for reducing inflammation when they become ingested by their recipient cell. They act as shuttles to send nucleic acids, cytokines, growth factors and proteins to the recipient cells, in this way, allowing cell-to-cell communication and transporting molecules among both close and distant cells.

As IBD involves significant intestinal inflammation, the exosomes will travel there and be ingested by cells. Then they will release their "payload" and facilitate mucosal repair.

Exosomes are most likely the mediators of most stem cell-associated therapeutic activities. Therefore, adding them along with the mesenchymal stem cells during the therapy acts as a "1-2 punch" for patient outcomes

Is stem cell therapy safe?

After a decade of performing over 24,000 stem cell procedures worldwide, R3 knows that the regenerative procedures are safe at our clinics. The quality control employed during the stem cell production is second to none, and the side effects R3 sees are usually mild to moderate and temporary.

They may include itching, dizziness, lightheadedness, low grade fever, chills, headache, nausea. These are typically temporary. If a patient has an allergic reaction to the multivitamin or a preservative, all of R3's Centers have the medications to resolve it quickly.

One of the questions we get asked a lot is, "Will the stem cells get rejected?" The answer is NO.

MSCs do not express major histocompatibility complex (MHC) antigens of the class II subtype and contain low levels of MHC molecules of the class I subtype. MSCs also lack the co-stimulatory molecules essential for immune detection, including CD40, CD80, and CD86.

Therefore, MSCs generally have low immunogenicity and can avoid immune rejection by the recipient, which serves as the foundation for their successful application without needing to match the donor to the recipient. Scientists call this being "immunologically privileged".

Another question often asked is "Is there a chance of a tumor forming?" Once again the answer is NO. The mesenchymal stem cells and exosomes used during treatment have never been shown to have tumor forming potentials. In fact, they have been shown to be anti-tumor forming.

Treatment Protocol

For the past decade, R3 has been successfully treating IBD patients with stem cell and exosome infusion therapy. The cells and exosomes are attracted to inflammation, which is a large component of inflammatory bowel diseases.

R3's providers use between one to three million stem cells per kilogram (depends on severity of IBD). R3 Stem Cell's IBD treatment protocol includes intravenous mesenchymal stem cells and exosomes along with a multivitamin. Safety is paramount with the biologics products being rigorously tested prior to use, and expert providers managing each treatment as if you are a family member!

Why does R3 Stem Cell use donor tissue for its stem cells?

Although autologous (your own) stem cells provide significant advantages, allogeneic (donor) stem cells have more advantages. First of all, autologous MSCs need a long time to culture and expand, which limits its application in treatment, while allogeneic stem cells can be obtained and expanded more quickly, thus avoiding the delay of time window.

Second, age is a factor that affects the physiological characteristics of MSCs. Studies have shown that stem cells from elderly donors have decreased proliferation and differentiation ability. This means they are less in number and less effective!

What are the Outcomes?

Similar to the research mentioned above, R3 Stem Cell's outcomes for IBD patients have been exceptional! The patient satisfaction rate is 85% year over year. Patients typically see exceptional pain relief, less bleeding, less urgency and long term complications (e.g. fistulas).

It may take six to twelve weeks for the results to kick in, although we have had patients symptomatically feel much better within the first couple of weeks. It should be noted, again, that stem cell therapy does not eliminate IBD, and may need to be repeated every one to two years.

Affordability

Because stem cell therapy for IBD is not a "one and done" cure, it's important to make it affordable. Repeat therapies every few years can help people achieve continued pain relief and functional improvements. So a lot of IBD patients seek additional treatments at R3 Stem Cell every one to two years.

Unfortunately, stem cell clinics in Colombia, China and Panama charge over $20,000 USD for IBD treatment. Because the one treatment cost so much, how are individuals supposed to budget for that every few years?? R3 Stem Cell's fees are less than half that for full treatment, which also includes free exosomes and a multivitamin infusion!

R3's Experience

For the past decade, R3 Stem Cell's Centers globally have performed over 24,000 regenerative procedures in six countries. Over a thousand have been for IBD. Patient satisfaction across all conditions treated is 85%!

R3 combines safety, effectiveness and affordability for the therapies. Internationally, the Intellicell is used, which is culturing the most active mesenchymal stem cells to create the "smartest" stem cell in the world!

R3 Stem Cell offers free consultations for individuals to discuss whether regenerative therapy is indicated for your IBD pain relief. Simply call +1 (844) GET-STEM to schedule yours!

References:

1. Che Z, Ye Z, Zhang X, Lin B, Yang W, Liang Y and Zeng J (2022) Mesenchymal stem/stromal cells in the pathogenesis and regenerative therapy of inflammatory bowel diseases. Front. Immunol. 13:952071. doi: 10.3389/fimmu.2022.952071.
2. Wang et al. Stem cell therapy for Crohn's disease: systematic review and meta-analysis of preclinical and clinical studies, Stem Cell Res Ther (2021) 12:463https://doi.org/10.1186/s13287-021-02533-0.
3. Bernardi et al, TRANSPLANTATION OF ADIPOSE-DERIVED MESENCHYMAL STEM CELLS IN REFRACTORY CROHN'S DISEASE: SYSTEMATIC REVIEW, ABCD Arq Bras Cir Dig 2019;32(4):e1465 DOI: /10.1590/0102-672020190001e1465.
4. Shi et al. Stem Cell Research & Therapy (2019) 10:266, https://doi.org/10.1186/s13287-019-1336-4Mesenchymal stem cells for the treatment of ulcerative colitis: a systematic review and meta-analysis of experimental and clinical studies
5. Martinez-Montiel et al, Therapy with stem cells in inflammatory bowel disease, World J Gastroenterol 2014 February 7; 20(5): 1211-1227
6. Mao et al, Mesenchymal stem cells and their therapeutic applications in inflammatory bowel disease, Oncotarget, 2017, Vol. 8, (No. 23), pp: 38008-38021
7. Eiro, N.; Fraile, M.; González-Jubete, A.; González, L.O.; Vizoso, F.J. Mesenchymal (Stem) Stromal Cells Based as New Therapeutic Alternative in Inflammatory Bowel Disease: Basic Mechanisms, Experimental and Clinical Evidence, and Challenges. Int. J. Mol. Sci. 2022, 23, 8905. https://doi.org/10.3390/ijms23168905
8. Kim Y, Can Umbilical Cord Mesenchymal Stem Cells Treatment Be a Hope for Patients with Refractory Crohn's Disease?, Gut and Liver, Vol. 12, No. 1, January 2018, pp. 5-6.
9. Wang Y, Huang B, Jin T,Ocansey DKW, Jiang J and Mao F(2022) Intestinal Fibrosis in Inflammatory Bowel Disease and the Prospects of Mesenchymal Stem Cell Therapy. Front. Immunol. 13:835005.doi: 10.3389/fimmu.2022.835005
10. Zhang et al, Umbilical Cord Mesenchymal Stem Cell Treatment for Crohn's Disease: A Randomized Controlled Clinical Trial, Gut and Liver, Vol. 12, No. 1, January 2018, pp. 73-78

About R3 Stem Cell

David Greene, MD, PhD, MBA, Founder/CEO

R3 Stem Cell offers treatments that bring patients hope and options. Hope that surgery can be avoided, and tissue injury can be repaired with patients being able to get back to desired activities.

Founder and CEO David Greene, MD, PhD, MBA writes extensively on regenerative medicine and gives many seminars worldwide on a regular basis. With over forty Centers of Excellence globally, R3 is at the forefront of regenerative therapies.

R3's Centers have successfully performed over 24,000 regenerative procedures to date. Call today for your free consultation **(844) GET-STEM!**

Disclaimer: This guide's education does not constitute medical advice. The USA FDA considers stem cell therapy experimental. Any claims made in the Guide refer to procedures performed outside the USA.