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# StemCellBiologyonAutoimmuneDisease-Crohn'sDisease,ComplexPathogenesisCurethroughRegenerativeDisease

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# Abstract

The attack on immune system in the gut which leads to bowel obstruction, severe diarrhoea, rectal bleeding are major symptoms in individual's intestinal tissue. This disease is Crohn's disease. The inflammation in the intestine is caused due to mucosal immune reactivity to antigen found in the lumen. The cost of cure is significantly higher in terms of health care. Now there is a chance for exploration of stem cell cure for Crohn's disease. Although surgical restructure is required, the disease seems to appear even after surgery. It rejects restructuring unit. Hence surgery is often a failure. After careful experiments on CD patients, Mesenchymal Stem Cells and Hemopoietic Stem Cells are the best available options to cure CD. This case study shows how stem cells works and its results. The results have restructured the way stem cells have been to put to best use in patients that suffer the most with CD. At certain point, the results have high effects in its clinical emission with no medication <sup>1</sup>Director, Principal Scientist-Poichyadical Stem Cell Centre for Research and Development(POSCERD), Chicago, USA, CEO-La'zer Healthcare, Chicago, USA

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required. CD patients had adverse effects while in medication and no serious effects with no medication. The definition of stem cells has been smeared all over this Crohn Disease patients and the results have been amazing.

**Keywords:** Autoimmune disease; Crohn's Disease (CD); Mesenchymal Stem Cells (MSC); Hematopoietic Stem Cells (HSC); Fistulation; Inflammation; Gastrointestinal barrier.

# Introduction

Crohn's Disease (CD) inflammatory bowel disease (IBD) is a chronic systemic condition highlighted by gastrointestinal inflammation (shown in the Figure below) and deregulation of mucous associated immune system. The pathogenesis is complex that features reduced gastrointestinal barrier protection and innate immune system [1]. Environmental factors, infections trigger the disease, also biological factors such as corticosteroids, anti TNF alpha antibodies suppresses the immune system. Few years now stem cell biology and regenerative medicine has shown significant development in curing autoimmune disease [2].



Figure 1: Crohn's disease shown thickening of wall [2].

Crohn disease is a disease that ruptures, Figure 1 shows area where linen of colon is present in normal intestine and Crohn disease with patchy inflammation. Crohn disease shows thickening of colon wall along with cobblestone appearance of surface. This autoimmune disease is deadly with inflammation of wall [3].

Both Mesenchymal Stem Cells (MSc) and Hematopoietic Stem Cells (HSc) have shown significant progress in treating. Stem cells have shown the potential to counter the rheumatoid arthritis, hepatitis and systematic sclerosis [3]. MSc have low immunogenicity and immunoderegulation when injected they show improved CD related perineal fisulation. HSc show restored immunization and relieved CD.

Stem cells basically exhibited long term intestinal mucous healing and intestinal inflammation. The quality of life has improved significantly in many patients. Several studies have shown significant improvement in intestinal wall inflammation [4].



**Figure 2:** Stem cell-MSc and HSc therapy on Crohn's disease, the figure shows how stem cells work on Crohn disease. Placenta from umbilical cord is lab processed, suppressor of cells is removed and inserted in inflammation area [4].

# Influencing the immune system using MSc

Stem cells through mesenchymal cells have the potential to reduce inflammation throughout the digestive tract, regulate the immune system and repair the injured tissue within gastrointestinal tract [5]. It has the potential to modulate the immune response.

How it actually works? T-cells activation within the tract helps conduct the immune response leading to chronic inflammation causing pain [6]. MSc targets the inflammation within the body and repair damaged tissue. Hence stem cells become an effective tool for treatment of Crohn's disease.

MSc can suppress the pro inflammatory response in the gut and promote antiinflammatory cytokines to improve healing of the gut tissue [7]. T-helper 17 cells activity is reduced with MSc aiding in development of chronic inflammation. They also differentiate different types of cells in the gut and help in repair and regenerate damaged tissue.

Intravenous stem cell therapy is cost effective in long term and long lasting for individuals. Since there is improvement in bowel disease and cure is in sight, MSc plays major role in safe delivery mechanism to improve fistula tract.

MSc have shown immunosuppressive effect in condition of polarising anti-inflammatory  $M_2$  macrophages [8]. It further reduces dendritic cells and neutrophils through prostaglandin  $E_2(PGE_2)$  and IL-10 at wound site. MSc activity is modulating differentiation and proliferation of T and B lymphocytes activity. Several clinical phase studies had been conducted for both autologous and allogenic MSc [9].

# Test results

Personalise anti TNF therapy in 1600 patients for Crohn's disease were experimented, response at week 14 were at 23.8%, nonresponse at 66.2%.

Second line of therapy with gut selective interim inhibitor for antibody pf34 (approved by NIH) were shown in patients with CD refractory to or tolerant at conventional immunomodulators [10]. However, in phase 3 the experiment for therapy showed significant progress with remission of patients rising up to 67% from 23.8%.

Therefore, patients with CD face persistent symptoms related to less disease activity in addition to morbidity associated with chronic illness. Patients with refractory CD, had and MSc has been a success with permissible to patients rising up to 85%. Hence stem cell is an exceptional option for patients with CD [11].

Mesenchymal stem cells or stromal stem cells has shown efficacy in treating CD. This is the therapeutic new modality that has regenerative demonstrated effective to mechanism exert clinical effects throughout the injected site in perineal fistulas [12].

Mesenchymal stem cells are new therapeutic modality that has sent the cost lower over the period of time. MScs injected locally into perineal fistulas can lead to healing with meta-analysis of healing rates at 85% [13].



**Figure 3:** Crohn disease analysis and cure, epithelial cells get activated to dendritic cells with tf aloha factors to enable microbes and perpetuates the inflammation to form leukocytes with help of t-cells [14].

# First case of injection

Crohn's disease first case has been successful. 28year old women diagnosed with Crohn's disease with history of orthostatic syndrome, adrenal thyroid and anaemia issues. The patient's condition worsened prompting medical intervention with frequent bowel movement, diarrhoea, abdominal pain and cramps [15]. The patient was prescribed with TNF alpha blockade for inflammation. Pre lab treatment was done and inflammation markers showed abnormal inflammatory responses. After TNF alpha blockades of 8.3, inflammatory marker improvement is seen. Three months after treatment, patient showed reversal of bowel movement indicating 95% improvement in inflammation and no discomfort in bowel and blood per rectum, also 80% improvement in energy level [16].

Comparative study in clinical trial. Below Figure 4 shows, combined repose, clinical remission and clinical response after using stem cells [17].



Figure 4: The graph shows reduction in inflammation at controlled arm after stem cell administration [17].

The incidence of CD increasing in young adults is worrisome. Patients with refractory CD have decreased quality of life and disease. Refractory CD has direct impact on health care cost and livelihood. Quality of life is decreased increasing financial burden on patients. Repeated trials show improved signs in patients (Figure 5) [18].



#### Key Secondary Endpoints: Clinical Remission & Response (Twenty-Four Weeks)

**Figure 5:** Result of repeated clinical trials and improved lifestyle with low cost, the graph shows paroxysm index of its use of MSc at three phases or at time interval of every six months. The MSc shows improvement in inflammation cure [19].

In many experiments, high dose cyclophosphamide is used to mobilise according to the condition of the infection. Many research highlighted the importance of supportive care in reducing incident of inflammation. The tradition end point therapy suggested, appears to restore the anti

TNF within patients who are in refraction. Further upon use of therapy, the inflammation showed consistent reduction in mobility and condition regiments that have been associated have shown lower morbidity in malignant auto immune disease [20].



Figure 6: Results and comparison of TNF and surgical treatment, patients have good recovery with medical treatment. The pie chart shows medical treatment effective [21].

Upon further study with patients' Figure 7 shows the time point of assessment with

different drug and stem cell therapy treatment on CD patients [22].

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Figure 7: Different drug and stem cell therapy treatment assessment on CD patients [22].

# New modality in the study

Considering the complications in the inflammation that includes dehydration, stoma related complications and wound care, the dehydration is 15% (lower range frequency, upper range frequency 20%) stoma related complications such as hernia retraction, relapse, prolapse and obstruction occurred at 26.5% (lower range 17%, upper range 40%) skin breakdown and wound occurred at 31% (lower range 20%, upper range 30%) [23]. Only probable treatment is MSc and HSc. The use of stem cells was

approved by GMP cells adversely used in clinical trials. Effectiveness in clinical trial and response showed in improvements in systemic review and meta-analysis. The closure in trials showed 60% remission of fistulas openings and 66% of healing in inflammation.

Figure 8 shows the healing rates of patients, out of five patients, experiments for MSc done in 4 patients has high set healing rate within 9 days. It is good due to treatment effectiveness [24].

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Figure 8: Healing rates of patients.

# Discussion

CD is a distressing condition and with treatment options are not a feasible one, patients have poor quality of life. HSc and MSc aims to show beneficial effects in clinical efficacy and gives long term mobilization of cells followed by lower intensity in conditioning of CD therapy [25].

# Ethics

There has been a favourable opinion from ethics committee on use of cells in clinical trial, all protocol approved through the third committee and regulatory authority before being notified by trial regulators [26].

# Conclusion

The study concluded proves stem cell-based therapy is promising new treatment options for refractory CD making MSc a promising treatment option for patients in inflammation within digestive tract. In all forms the findings and experiments show cure for CD through regeneration of cells thus preventing threats.

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