Case Report

Stem Cell & Regenerative Medicine

# Decrease in CD10 (NEP) Expression in Non-Alzheimer's Dementia Patients after SB Cells® Treatment

**Monica Lui[1*], Jonathan Tang[1], Wen Ying Lee[1], Xiao Chen[1], Lee Chen[1], Tina Zhang[1], Puning Cheng[1], Jessica Ding[1], Tom Flashman[2] and James Wang[1*]**

[1]*StemBios Technologies, Inc., 2530 Corporate Pl, SuiteA112, Monterey Park, California, 91754, USA.*

[2]*Tom Flashman, MD, 8920 Wilshire Blvd, Suite 301, Beverly Hills, California, 90211, USA.*

**[*]Correspondence:**
James Wang & Monica Lui, 2530 Corporate Place, A112, Monterey Park, CA 91754, USA, E-mail: jwang@stembios.com, monicamhlui@stembios.com.

**Received:** 26 September 2017; **Accepted:** 15 October 2017

**Citation:** Monica Lui, Jonathan Tang, Wen Ying Lee, et al. Decrease in CD10 (NEP) Expression in Non-Alzheimer's Dementia Patients after SB Cells® Treatment. Stem Cells Regen Med. 2017; 1(3) 001: 1-3.

## ABSTRACT

***Aims:*** *Dementia is characterized by cognitive decline and memory loss, as well as impairment in short-term memory, long-term memory, and judgement. The cognitive deficits associated with dementia can interfere significantly with their social relationships and activities, as well as their occupational functioning. We believe that our SB cell® therapy may be the next step in treating non-Alzheimer's dementia.*

***Presentation of Case:*** *We describe four patients who have been diagnosed with non-Alzheimer's dementia and have experienced significant improvements in their memory, mood, cognitive functioning, and ability to do daily tasks after receiving our SB cells® treatment.*

***Discussion:*** *Patients receiving our stem cell therapy showed a significant decrease in CD10 expression, a marker for NEP. It suggested that there may be a beneficial effect of pharmaceutical inhibition of cerebral NEP on learning and memory due to the accumulation of peptides other than Aβ degradable by NEP.*

***Conclusion:*** *Our study may validate the existence of peptides targeted by NEP that may improve learning and provide a promising avenue to the treatment of non-Alzheimer's dementia. We hoped to continue investigating new patient cases to determine the potential CD10 has as a genetic marker of dementia.*

## Keywords

Dementia, Small Stem Cell, CD10.

## Abbreviations

SB cells®: StemBios Stem Cells, Aβ: Extensive β-amyloid, NEP: Neutral endopeptidase, CD10: Cluster of differentiation 10, hBM: human bone marrow, hPB: human peripheral blood, CD349: Frizzled-9, LGR5: Leucine-rich repeat-containing G-protein coupled receptor 5, CD45: Protein tyrosine phosphatase, receptor type C, CD66e: Carcinoembryonic antigen-related cell adhesion molecule 5, VSEL: Very Small Embryonic Like Stem Cells, HSC: Hematopoietic stem cells, BLSC: Blastomere-Like Stem Cell, SCID: Severe combined immunodeficiency, MME: Membrane metallo-endopeptidase.

## Introduction

From our previous publication, StemBios cells, SB cells®, are adult pluripotent stem cells found in human Bone Marrow (hBM) and human Peripheral Blood (hPB) [1]. They are between 3 to 6 μm in diameter and CD349+ and Lgr5+ [1]. SB cells® are capable of differentiating into all three germ layers as shown in our previous publication [1]. SB cells® do not form teratoma which makes it a great candidate for use in stem cell therapy. SB cells® are CD133-, CD34-, and CD66e-; therefore we concluded that SB cells® are different from VSEL, HSC, and BLSC [1].

Dementia, also known as senility, is a broad category of brain diseases that cause a long term and often gradual decrease in the ability to think and remember. It is defined as a decline in memory

with impairment of at least one other cognitive function that can affect a person's daily activity, such as skilled movement (limb apraxia), language (aphasia), or executive function (e.g., planning, attention, and abstract reasoning) [2]. Other common symptoms include depression and a decrease in motivation, thus, interfering significantly with their social relationships and activities [3].

The most common type of dementia is Alzheimer's disease, which makes up 60% to 80% of dementia cases [4]. Globally, dementia affects 36 million people worldwide [4]. About 10% of people develop the disorder at some point in their lives; about 3% of people between the ages of 65 and 74 have dementia, 19% between 75 and 84, and nearly half of those over 85 years of age [4]. In 2013 alone, dementia was the cause of over 1.7 million deaths, and has more than doubled from the 0.8 million deaths in 1990 [4].

Now more than ever before, there is an urgent need for the discovery of new dementia treatments. The estimated global cost of dementia is estimated to be around $604 billion dollars a year [4]. There is currently no cure for dementia, and cholinesterase inhibitors, such as donepezil, are often used in mild to moderate cases. However, the overall benefit of the drug may be minor, for both the patient and those who care for them.

Through an in vivo cell tracking assay, SB cells® injections were performed on severe combined immunodeficiency (SCID) mice, which demonstrated that human SB cells® that resided in the mouse brain had differentiated into functional neurons within the host [1].

Neprilysin, also known as membrane metalloendopeptidase (MME), neutral endopeptidase (NEP), and cluster of differentiation 10 (CD10), is an enzyme that is encoded by the MME gene in humans [5]. Neprilysin is a zinc dependent metalloprotease that cleaves peptides at the amino side of hydrophobic residues and inactivates several peptide hormones, including enkephalins, substance P, neurotensin, oxytocin, and bradykinin [5]. One study found that aged mice deficient in amyloid beta (Aβ)-degrading neutral endopeptidase led to improved learning and memory. It suggests that there may be a beneficial effect of pharmaceutical inhibition of cerebral NEP on learning and memory due to the accumulation of peptides other than Aβ degradable by NEP [6].

In this case study, we described four patients with non-Alzheimer's dementia who have shown significant improvements in memory and psychological symptoms, along with a significant decrease in CD10 (NEP) expression after receiving our SB cells® treatment.

## Methods

SB cells® were collected from patients using SB cells® purification protocol from our previous publication - Identification of a distinct small cell population from human bone marrow reveals its multipotency in vivo and in vitro [1]. SB cells® were then injected back to patients following the guidelines described in our procedural IRB: SB-IN-4222.

Patients and their care takers reported any changes in patients' memory after SB cells® treatment.

Blood samples were collected both before and after SB cells® treatment. SB Cells® were purified using SB cells® purification protocol and stained with CD10 for flow cytometry test; refer to protocol from our previous publication [1].

## Results

Patient 80 was an 86-year-old Caucasian female who had been diagnosed with dementia and hypertension. She was not taking any medication at the time of her SB® cell treatment, and within 24 hours after the treatment, she displayed improvements in her memory, mood, cognitive abilities, and general recall. When Patient 80 returned for her second SB cells® treatment, she reported significant improvements to her memory at both our 24-hour and 1-week time points.

Patient 131 was an 82-year-old female who had been diagnosed with dementia. At both the 24-hour and 1-week time points, we noted significant improvements in her cognitive function, such as a reduced tendency to repeat herself.

Patient 187 was an 87-year-old female who had been diagnosed with dementia. Within 24 hours of her SB cells® treatment, she reported having an increase in energy levels, less fatigue, and a greater ability to do perform daily tasks. After 1 week, we also found significant improvements in her memory and recall for specific personal events.

Patient 165 was a 61-year-old Hispanic female who had been diagnosed with dementia. After her first SB cells® treatment, her family reported that her old personality was coming back to her, along with an increased awareness and clarity of thought. When Patient 165 received her second SB cells® treatment, we noticed a tremendous increased in her energy level and she reported feeling better all-around. During her third round of treatments, she reported continued improvements in her memory, and was aware of the fact that she had forgotten something, which was something she would have ignored before treatment. For her fourth round of SB cells® treatments, she reported improvements in her long-term memory, factual recall, and ease of executing daily cognitive tasks.

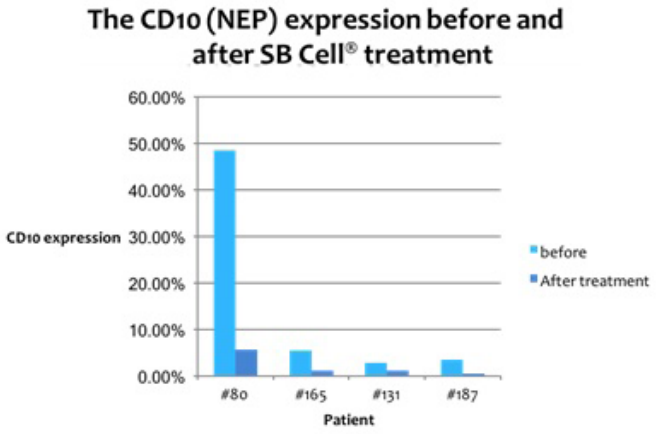

**Figure 1:** Flow cytometry data for all four non-Alzheimer's dementia patients. CD10 populations difference was compare for both before and after treatment.

In all four non-Alzheimer's dementia patients, we observed a significant decrease in overall CD10 (NEP) expression levels after our SB cells® treatment, along with marked improvements in memory, mood, cognitive functions, and many psychological syndromes (Figure 1).

## Discussion

All four patients showed improvement after receiving SB cells® treatment. The increased CD10 expression from post SB cells® treatment reflects patients' self-report. As mentioned in our previous publication, SB Cells® were CD133-, CD45-, and CD66e-, so these positive effects were not contributed from VSEL, HSC, and BLSC [1]. Our previous publication also showed the ability for SB® Cells to regenerate both in vitro and in vivo (in mouse) [1]. Here we showed that the SB® cells are able to differentiate in vivo in human.

One of the biggest advantages of our SB cells® therapy is that there are currently no known side effects that accompany the treatment. None of our patients report any side effects post treatment. In addition, because of the analogous nature of our IV injection, there is little to no chance of the patient having an immune rejection to the stem cell treatment.

## Conclusion

While finding a treatment for dementia and other neurodegenerative diseases has proven elusive for science and modern medicine, there has been evidence that stem cell therapy may be the next step. The improvements seen in these non-Alzheimer's dementia patients after our SB cells® treatment raise hope for the development of stem cell therapies and their potential role in treating human neurodegenerative disorders. In addition, the existence of peptides targeted by NEP that improve learning and memory in older individuals may represent a promising avenue for the treatment of non-Alzheimer's dementia.

To further validate our findings and investigate the potential CD10 has as a genetic marker of dementia, we will be starting a new treatment proposal targeting 100 unique patients with non-Alzheimer's dementia. They will be split into three arms and a control round. The first arm consists of one round of IV treatment with SB cells® on 25 patients. The second arm consists of two consecutive rounds of IV treatment with SB cells® performed weekly on 25 patients. The third arm consists of three consecutive rounds of IV treatment with SB cells® performed weekly on 25 patients. Lastly, 25 patients will undergo a control round of saline. We will measure the change in neprilysin levels for each patient at time points of 0, 7, 14, 30, and 90 days after each SB cells® treatment. We will also be recording changes in behavior and memory for each patient at time points of 0, 7, 14, 30, and 90 days after each SB cells® treatment.


## Acknowledgment

TriMax LLC provides funding for this paper.


## Consent

The risks, benefits, side effects, and alternatives have been discussed with the patient. The patient understands all post-procedure instructions and follow-ups. All questions were answered to satisfaction.

## References


1. Wang J, Guo X, Lui M, et al. Identification of a distinct small cell population from human bone marrow reveals its multipotency in vivo and in vitro. PLoS ONE. 2014; 9: e85112.
2. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-V-TR). Arlington, VA: American Psychiatric Association. 2016; 624-841.
3. Scott KR and Barrett AM. Dementia syndromes: evaluation and treatment. Expert Rev Neurother. 2007; 7: 407-422.
4. Alzheimer's Association. 2016 Alzheimer's Disease Facts and Figures. Alzheimer's & Dementia. 2016; 12.
5. El-Amouri SS, Zhu H, Yu J, et al. Neprilysin: an enzyme candidate to slow the progression of Alzheimer's disease. Am J Pathol.2008; 172: 1342–1354.
6. Walther T, Albrecht D, Becker M, et al. Improved learning and memory in aged mice deficient in amyloid beta-degrading neutral endopeptidase. PLoS ONE. 2009; 4: e4590.