Open Access

Informed Consent Guidelines for Optimizing the Use of Telomerase-Positive Stem Cells

Henry E Young^{1-3*}, Mark O Speight⁴⁻⁶

¹Dragonfly Foundation for Research & Development, Macon, GA 31210, USA

²Henry E Young PhD Regeneration Technologies LLC, USA

³Mercer University School of Medicine, Macon, GA 31207, USA

⁴Research Designs, Charlotte, NC 28105, USA

⁵The Charlotte Foundation for Molecular Medicine, Charlotte, NC 28105, USA

⁶Center for Wellness, Charlotte, NC 28105, USA

***Corresponding Author:** Henry E Young PhD, Chief Science Officer, Dragonfly Foundation for Research & Development, 101 Preston Ct, Suite 101, (Corporate Office), Macon, GA 31210 USA; Tel: +478-3191983;
Email: young.hey1@yahoo.com

Received Date: 24-06-2020; **Accepted Date:** 15-07-2020; **Published Date:** 22-07-2020

Copyright© 2020 by Young HE, et al. All rights reserved. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Abstract

The objectives of the work, based on previous characterization studies, pre-clinical animal models of induced diseases, e.g., Parkinson disease, cardiovascular disease, pulmonary disease, and type-I diabetes mellitus, and early clinical human studies of Parkinson disease, cardiovascular disease, and pulmonary diseases, were to establish a set of criteria that needed to be followed for using telomerase-positive stem cells in future human clinical trials. From this set of criteria, informed consent guidelines were established to optimize the safety and efficacy of using endogenous adult-derived telomerase-positive stem cells to restore organ function by either repair and/or regeneration of cells and tissues resulting from tissue damage and/or loss. Inclusion criteria were any male or female, 18 to 120 years of age, with preferably no serious comorbidities. Exclusion criteria were use of alcohol, tobacco products, vaping, recreational drugs, lidocaine, and/or chemotherapeutic drugs. We also cautioned use of caffeine and corticosteroids, as well as limiting moderate to strenuous physical activity within a two-

Young HE | Volume 1; Issue 1 (2020) | JRMBR-1(1)-003 | Clinical Trial Report

Citation: Young HE, et al. Informed Consent Guidelines for Optimizing the Use of Telomerase-Positive Stem Cells. J Reg Med Biol Res. 2020;1(1):1-20.

DOI: <http://dx.doi.org/10.46889/JRMBR.2020.1103>

week window before and after stem cell treatment. Following these inclusion and exclusion criteria, endogenous adult-derived autologous and/or allogeneic telomerase-positive stem cells have proven to be both safe and effective at restoring (up to 50% above pre-treatment values in compliant individuals) organ function for diseases and/or disorders caused by trauma or chronic diseases. Conditions treated thus far, within IRB-approved human study protocols, include neurodegenerative, cardiovascular, pulmonary, autoimmune, renal, and orthopedic disorders.

Keywords

Adult; Stem Cell; Telomerase; Informed Consent; Human; Regenerative Medicine

Introduction

Research Designs and The Foundation for Molecular Medicine in conjunction with Dragonfly Foundation for Research and Development and Henry E Young PhD Regeneration Technologies, is inviting you to participate in a clinical trial involving multiple case studies of those who have one of the following disorders: Traumatic Tissue Injury or Chronic Organ Dysfunction to include but not limited to Neurodegenerative, Cardiovascular, Pulmonary, Autoimmune, Renal, Musculoskeletal disorders.

Telomerase-positive stem cells are a type of stem cell that has been identified in the tissues and blood of animals and humans [1]. Early laboratory research has shown that animals and humans, after birth, have these primitive cells that live in their tissues and organs [2]. These cells also circulate in the blood stream and have been found to be similar to the stem cells found in embryos and those induced from adult cells [3,4]. We utilize three types of telomerase-positive stem cells, e.g., totipotent stem cells that will form all cell types of the body, including germ cells (sperm and ova) and nucleus pulposus of intervertebral disc (the only adult derivative of the notochord); pluripotent stem cells that will form all tissues of the body, except germ cells (sperm and ova) and nucleus pulposus of intervertebral disc; and mesodermal stem cells which will form muscle, fat, cartilage, bone, tendons, ligaments, connective tissues, organ capsules, organ trabeculae, blood cells, blood vessels, lymphatic vessels, all cell types of the immune system, lymph nodes, free lymph nodules, tonsils, Peyer's Patches, GALT (Gut-Associated Lymphatic Tissue), appendix, spleen, kidney, ureter, urinary bladder, upper 2/3's of urethra, testicle (without sperm), and ovary (without ova). These types of stem cells have been found to be able to differentiate (transform) into the all types of cells needed for repairing an injury in the body [1]. Additional research has shown that large numbers of these telomerase-positive stem cells are released into the peripheral circulation following trauma [5]. It is theorized that the introduction of the telomerase-positive stem cells to your body will aid in the repair of acute and chronic organ dysfunction and traumatic tissue injuries, and thereby increase function.

Purpose, Selection and Voluntary Participation

Young HE | Volume 1; Issue 1 (2020) | JRMBR-1(1)-003 | Clinical Trial Report

Citation: Young HE, et al. Informed Consent Guidelines for Optimizing the Use of Telomerase-Positive Stem Cells. J Reg Med Biol Res. 2020;1(1):1-20.

DOI: <http://dx.doi.org/10.46889/JRMBR.2020.1103>

The purpose of this Phase-I study is three-fold:

1. To assess the safety and the body's response to your own (autologous) telomerase-positive stem cells.
2. To assess the safety and the body's response to donor (allogeneic) telomerase-positive stem cells.
3. To assess the body's ability to have improved function or lessening of disease symptoms when these stem cells have been isolated, activated and after they are reintroduced into the body.

All subjects will receive telomerase-positive stem cells through one or more of the following routes: intra-nasal for neurogenic issues, slow and regular intravenous infusions for cardiovascular issues, nebulized (placed in a vapor to be inhaled) for pulmonary issues, regular intravenous infusion for autoimmune, systemic and renal issues, and/or direct tissue injection for musculoskeletal or organ issues.

You have been selected to consider participation as a case study subject based on the requirements (inclusion and exclusion criteria of this study) related to a diagnosis that falls in the category of either: traumatic tissue injury (crush injury, brain trauma, spinal cord trauma, etc.), autoimmune disease (disease where the body attacks its own tissues), acute or chronic organ dysfunction related to or independent of trauma, e.g., nervous system, cardiovascular system, respiratory system, and/or systemic organ systems. Your participation is completely voluntary and you have the right to withdraw from the study at any time. If you choose to participate in this case study trial, your current or future medical care in this clinic will not be affected.

Interventions and Procedures

In the case of your disease/disorder affecting the entire body, the research intervention will be up to six visits in which a blood collection of approximately 1-1 3/4 cups (8 to 14 ounces or 300 to 400-cc's) of blood at each visit is taken over the course of a consecutive period of time; typically 12 to 18 months. Additional monthly assessments may be required based on your disease/disorder that is under study. You will be notified in writing of any changes to the protocol. In the case of localized trauma resulting in osteoarthritis to the knees or blunt injury to the joints, you will be treated one time with your own cells directly injected into the area of concern. At the discretion of the treating physician you may be treated every 2 months for up to five additional treatments.

In the case of diseases affecting the entire body known as systemic diseases, up to six stem cell treatments will be given over a 6-18-month time period with one blood draw and telomerase-

positive stem cell treatment approximately every other month. The initial visit is a screening visit, at which time after you have read, asked questions, initialed, and signed this informed consent document to participate in the study, the principal investigator or an associate will review your medical records and provide a physical assessment. At the discretion of the principle investigator and with your agreement, a second type of procedure known as cytophoresis may be offered if you fail to improve with the initial telomerase-positive stem cell isolation and treatment technique.

Cytophoresis involves the use of a machine that will withdraw your blood through two venous lines and separate the telomerase-positive stem cells and other cells from the red blood cells. Cytophoresis may allow for a higher yield of telomerase-positive stem cells, while returning your red blood cells back to your body rather than having to discard them as in the first procedure, described above and below. Cytophoresis requires Intravenous (IV) access in two large veins and requires that you be seated for approximately two to four hours. If the principle investigator determines you are a candidate for this procedure and wish to undergo this procedure a separate consent will be offered and must be initiated and signed.

If cytophoresis is not chosen, at the discretion of the principle investigator and with your agreement, a third type of procedure known as allogeneic donor telomerase-positive stem cell transplant may be offered if you fail to improve with the initial isolation and treatment technique. This procedure utilizes telomerase-positive stem cells isolated from a gender-matched, ABO-blood group-match or O-negative donor that has been screened for infectious diseases and harmful genetic mutations. If this procedure is chosen you will also need to be screened for infectious diseases. We need to make sure that either the donor is free of any infectious disease or that the donor shares the same infectious disease as you do. In either case, the donor telomerase-positive TSCs and PSCs will be used for your treatment.

We do not use donor MesoSCs for treatments because MesoSCs express self-recognition molecules on their cell surface. An intact immune system can distinguish these cell surface molecules and mount a “search and destroy” mission to eradicate any non-self-entities. Also, since MesoSCs can form cells of the immune system, a donor immune system could be created in your body, where that immune system recognizes you as “non-self” and tries to eradicate you. The above description is called a Graft Versus Host Disease (GvHD) response, in which either the donor cells are destroyed or the recipient is destroyed. To prevent that from happening, donor MesoSCs are not utilized for your transplant, rather, they are returned to the donor.

If the use of donor telomerase-positive stem cells is not chosen, at the discretion of the principle investigator and with your agreement, a fourth type of procedure known as “Combinatorial Nutraceutical-SP (CN-SP)” may be offered. This would occur if you either fail to improve with the initial isolation and treatment technique and do not to accept to receive someone else’s stem cells or you cannot afford to acutely lose 300-400cc’s of blood, which will be discarded after processing, due to underlying health condition(s). This procedure entails ingestion of CN-SP

daily. This option is less effective than activated stem cell transplant at restoring diseased and/or damaged tissue and function.

A fifth potential option for your treatment, once the others have been exhausted, involves the use of universal donor (O-negative) totipotent stem cells matched for gender and screened for infectious diseases and deleterious genetic mutations. The universal donor TSCs are propagated outside the body in a closed containment Biospherix system following FDA-mandated GMP protocols. This allows for the use of trillions of TSCs for treatment on a weekly basis. However, due to potential side effects with respect to compatible personality, behavior, memory replacement, hair color, and hair pattern transfer from the donor, it is not recommended for treating any type of neurogenic issues.

The initial visit will also involve taking a history of your blood relatives, e.g., brother(s), sister(s), mother, mother's parents and grandparents, your first and second cousins on your mother's side of the family, father, father's parents and grandparents, your first and second cousins on your father's side of the family, to determine if you have the potential for any genetically-inherited diseases.

The initial visit will also entail some laboratory tests as well as other testing procedures specific to your illness. These tests are performed in part to confirm your eligibility and to provide an overview of your health status prior to any treatments. These tests may include one or more of the following:

1. Urine and blood tests
2. A timed observation of the gait up to 20 feet
3. Pulmonary function tests (breathing test)
4. Echocardiogram (ultrasound of the heart)
5. Neurocognitive testing including, but not limited to EEG and/or a battery of cognitive tests (Mental Exercises)
6. Allergen panel testing
7. Grip strength test
8. Video-taping for visual documentation
9. One or more questionnaires

Following these assessment exams, you will meet with the primary investigator or an associate to discuss your initial evaluation and potential treatment options.

There will be treatment visits and assessment visits. The visits 1, 3, 5, 7, 9, 11 are treatment visits which will be preceded or followed by an assessment visit. In treatment visits

approximately 1-1 3/4 cups (8 to 14 ounces or 300 to 400cc's) of blood will be taken from your arm.

The procedure to collect telomerase-positive stem cells will begin with an intravenous catheter being placed in one of your veins. You will be given 250-cc of normal saline through this access. The purpose of this is to better hydrate you and dilate the blood vessels, allowing the blood to flow more freely for the harvest.

Immediately after hydration, the collection of 1-1 3/4 cups (300 to 400cc's) of blood will be obtained. Although you will not have a running infusion (drip) the entire time of the visit, the catheter will remain in your arm for the duration of the visit. If timing allows, your harvested cells may be isolated, activated and given back to you at the same visit, however you may be asked to return to receive your infusion within the next 24 hours, in which case the option of leaving in the catheter or removing and later replacing it will be given. You agree to allow replacement of the intravenous catheter as needed to return your cells to you.

Telomerase-positive stem cell treatments will be administered by intravenous infusion and other additional routes as deemed necessary to address your disorder. These routes include: intranasal infusion, slow intravenous infusion, inhaled delivery, direct tissue or joint injection, and/or regular intravenous infusion. These treatment visits may take 4 to 6 hours.

After you are approved to enter the study, a series of steps are required to improve your ability to proliferate your telomerase-positive stem cells throughout your body and release the stem cells into your circulation. You will be instructed to take a Nutritional Supplement known as "Combinatorial Nutraceuticals (CN)" or "Combinatorial Nutraceutical-SP (CN-SP)" capsules, based on your body weight. You will take one capsule (for every 50 pounds you weigh) every day for a year. After taking CN or CN-SP capsules for at least one month you may begin your first stem cell treatment. You need to schedule your six stem cell treatments so that they occur every two months. You are requested to be on site for 4-5 days for each treatment.

Figure 1: Each of ten adult equines, with an average weight of 545 Kg, were fed Combinatorial Nutraceuticals (CN), based on body weight, daily for 30 days. Horses ingested 6 grams of mobilization agent (Glacial Caps, GC) at time zero (0-hr). Prior to ingestion of GC and at 1-hr, 3-hr, 6-hr, 12-hr, 18-hr and 24-hr post ingestion 5cc's of blood were withdrawn from each horse by venipuncture, and processed for telomerase-positive stem cells, e.g., Totipotent Stem Cells (TSCs), Pluripotent Stem Cells (PSCs) and Mesodermal Stem Cells (MesoSCs). One hundred microliters of cell suspension from each sample were mixed with 100 microliters of 0.4% Trypan blue and counted on a hemocytometer. Counts were repeated in triplicate for each sample for each horse. Values were expressed as a percentage of each respective horse's 0-hr control value and then the respective values averaged. As noted, 18 hours post-ingestion demonstrated the highest percentage of telomerase-positive TSCs + PSCs + MesoSCs in the peripheral vasculature.

Every Stem Cell Harvest/Treatment Consists of the Following:

Failure to follow these guidelines will result in a decrease in the efficacy of the procedure (Table 1)

S. No.	Description	Your Initials
1	You ingest the contents of CN or CN-SP capsules (based on your body weight in pounds, with one capsule for every 50 pounds of body weight) daily for at least 30 days prior to your first harvest/treatment and then every day thereafter throughout your stem cell harvest/treatments.	Initial: _____

2	You abstain from any alcohol throughout your harvest(s)/treatment(s), because alcohol KILLS telomerase-positive stem cells.	Initial: _____
3	You abstain from any tobacco products throughout your harvest(s)/treatments, because tobacco products KILL telomerase-positive stem cells.	Initial: _____
4	You abstain from any vaping products throughout your harvest(s)/treatment(s), because vaping products KILL telomerase-positive stem cells.	Initial: _____
5	You abstain from any recreational drugs throughout your harvest(s)/treatment(s), because recreational drugs KILL telomerase-positive stem cells.	Initial: _____
6	You abstain from the use of the local anesthetic lidocaine throughout your harvest(s)/treatment(s), because lidocaine KILLS telomerase-positive stem cells.	Initial: _____
7	You abstain from the use of chemotherapeutic agents throughout your harvest(s)/treatment(s), because chemotherapeutic agents KILL telomerase-positive stem cells.	Initial: _____
8	You abstain from the use of corticosteroids (e.g., prednisone, dexamethasone), because corticosteroids prematurely induce telomerase-positive totipotent stem cells, pluripotent stem cells, and mesodermal stem cells to form all cells types of the musculoskeletal system, e.g., muscle, fat, cartilage, bone, connective tissue, and endothelial cells, simultaneously.	Initial: _____
9	You abstain from caffeine two weeks before to two weeks after a stem cell harvest/treatment, because caffeine prevents differentiation of telomeres-positive stem cells, in a dose dependent manner.	Initial: _____
10	However, you may have caffeine outside that time frame, but must limit your caffeine intake to 95 milligrams of caffeine (equivalent to 1 cup of coffee) per day throughout your harvest(s)/treatment(s).	Initial: _____
11	You abstain from any moderate to excessive physical activity 7 days prior to 7 days after your stem cell harvest(s)/treatment(s). Your body will use the newly generated telomerase-positive stem cells to repair any damage done to your tissues resulting from the moderate to excessive exercising.	Initial: _____
12	24 hours before to 24 hours after your telomerase-positive stem cell harvest(s)/treatment(s) is a period of rest.	Initial: _____
13	Six days before to 6 days after your telomerase-positive stem cell harvest(s)/treatment(s) is light exercise ONLY.	Initial: _____
14	Eight to 14 days before to eight to 14 days after your telomerase-positive stem cell harvest(s)/treatment(s) is moderate exercise.	Initial: _____

15	From three weeks (21 days) after your telomerase-positive stem cell harvest/treatment to two weeks (14 days) before your next telomerase-positive stem cell harvest/treatment you may resume normal activity levels.	Initial: _____
16	You need to be well hydrated (water) for two weeks before transplant.	Initial: _____
17	The first day of stem cell harvest/treatment or the day immediately after, will be your day for assessment re-examinations.	Initial: _____
18	If you are traveling from a distance more than a day's travel time, day two is a day of rest for 24 hours prior to telomerase-positive stem cell harvest/treatment.	Initial: _____
19	Eighteen hours before your scheduled harvest time you will take another supplement known as Glacial Caps. The glacial capsules mobilize the connective tissue-resident telomerase-positive stem cells into your blood stream.	Initial: _____
20	Day two or three (depending on your length of travel) is blood harvest day. An intravenous catheter will be placed in your arm. You will be given 250cc's of sterile normal saline through this access line. The purpose of the saline is to better hydrate you to dilate your blood vessels, allowing the blood to flow more freely. Immediately after hydration, 1 to 1 and 3/4 cups (8-12 oz, or 300-400cc's of blood will be collected through the intravenous catheter.	Initial: _____
21	Your blood is given to the isolator, where the telomerase-positive stem cells are separated from the Red Blood Cells (RBCs), White Blood Cells (WBCs) and platelets.	Initial: _____
22	The telomerase-positive stem cells are segregated into three populations, e.g., Totipotent Stem Cells (TSCs), Pluripotent Stem Cells (PSCs), and Mesodermal Stem Cells (MesoSCs), based on unique characteristics of each stem cell type.	Initial: _____
23	Isolation of the TSCs, PSCs, and MesoSCs will occur using FDA-mandated minimal manipulative procedures, e.g., zeta potential, gravity, differential centrifugation with serum gradients, sterile normal saline gradients, and sterile distilled water gradients, following GMP (General Manufacturing Procedure) guidelines.	Initial: _____
24	Each stem cell population is then activated prior to further processing.	Initial: _____

25	<p>“Rule of thumb” to keep in mind:</p> <p>a) if you have a condition that your body views as life-threatening, the activated TSCs, PSCs, and MesoSCs will be re-directed by the body to that location to repair the damage no matter where the stem cells are placed in your body</p> <p>b) The last tissue damaged is the next tissue to be repaired</p> <p>c) Tissue repair occurs in reverse chronological order, unless the body is placated with a supply of activated stem cells for its own use.</p>	Initial: _____
26	TSCs, PSCs, and MesoSCs are then prepared for treatment, e.g., neurological, see #s 27-37; cardiovascular, see #s 38-47; pulmonary, see #s 48-56; autoimmune, systemic, and renal, see #s 57-65; and direct injection, see #s 66-74. Then go to # 75 to continue with procedure.	Initial: _____
27	Neurological treatments: The smallest stem cells (TSCs) will be in one group and the intermediate (PSCs), and larger (MesoSCs) stem cells will be pooled.	Initial: _____
28	The TSCs are concentrated into 0.5cc’s of sterile normal saline and then divided into two equal aliquots of 0.25cc’s each.	Initial: _____
29	The mucus secretions (snot) in the patient’s nostrils are cleaned out using 0.65% sterile saline.	Initial: _____
30	The patient is placed into the reverse Trendelenburg position, i.e., head down and open nostrils pointing upwards.	Initial: _____
31	The TSCs are given by intra-nasal infusion, i.e., one aliquot of TSCs is placed in each nostril in a dropwise fashion. After the application of the second aliquot of TSCs into the patient’s other nostril, the patient remains in the reverse Trendelenburg position for an additional 5 minutes to allow the TSCs to complete their travel to the brain and spinal cord.	Initial: _____
32	Because the TSCs are so small (0.1 to 2 microns in size, compared to RBCs which are normally 7 microns in size) they can migrate between the nasal epithelial cells; “crawl” along the outside of the olfactory nerve rootlets; “crawl” through the cribriform plate in the skull to by-pass the blood-brain barrier; “crawl” to the olfactory bulbs; “crawl” along the outside of the olfactory nerves past the optic nerves to cisterns around and within the brain and spinal cord. From there the TSCs migrate to areas of damage within the brain and spinal cord and restore function by either regeneration and/or repair. It takes from one to four weeks before a noticeable effect is seen.	Initial: _____
33	For those individuals where the reverse Trendelenburg position is NOT an option, the TSCs are resuspended in 250cc’s of normal sterile heparin/saline and given by quick intravenous infusion (flow rate of 250cc’s in 15 minutes).	Initial: _____

34	As long as there is no pre-existing damage to either the heart or the lungs, the TSCs are so small (0.1 to 2 microns) that they can easily flow through the heart and lungs without getting “stuck” and flow out the ascending aorta, where 60% the blood goes to the brain and spinal cord and 40% goes to the rest of the body.	Initial: _____
35	Because the TSCs are so small (0.1 to 2 microns) as they flow through the arterial/venous system in the brain and spinal cord, they can leave the capillaries, pass around and through the blood-brain barrier, and migrate into the brain and spinal cord. However, the efficacy of this procedure is less than the intra-nasal route of delivery for the activated TSCs.	Initial: _____
36	The pooled pluripotent stem cells and mesodermal stem cells are resuspended in 250cc’s of normal sterile heparin/saline and will be given by regular intravenous infusion (flow rate of 250cc’s in 45 minutes). The body has a tendency to “steal” activated stem cells during the second and subsequent treatments and place activated stem cells in areas where it thinks the need is greater than the patient or Principal Investigator would like. Therefore, we give the regular intravenous infusion of pluripotent stem cells and mesodermal stem cells so the body has sufficient numbers of activated telomerase-positive stem cells for its own use.	Initial: _____
37	Cardiovascular treatments: The smallest cells (TSCs) will be in one group and the intermediate (PSCs) and larger (MesoSCs) stem cells will be pooled.	Initial: _____
38	There are two vascular systems in the heart, the coronary arterial/venous system along the outside of the heart and sending tributary branches into the heart muscle and the Thebesian veins that run through the wall of the heart. The Thebesian veins are small vascular channels that are smaller in diameter (5 microns) than red blood cells (7 microns) or white blood cells (10-12 microns).	Initial: _____
39	The Thebesian veins run from inside the chambers of the heart, e.g., both atria and both ventricles, through the heart muscle (myocardium), to just inside the outer covering of the heart (epicardium, e.g., visceral pericardium).	Initial: _____
40	During systole (contraction) only the fluid portion of the blood enters the Thebesian veins and runs through the heart muscle. During diastole (relaxation) the fluid portion of the blood returns to the chambers of the heart through the Thebesian veins.	Initial: _____

41	The TSCs are resuspended in 250cc's of normal sterile heparin/saline and given by slow intravenous infusion (flow rate of 250cc's in 120 minutes). Because TSCs are so small (0.1 to 2 microns), they can flow back and forth in the Thebesian veins through the heart muscle during systole and diastole and migrate to areas of tissue damage, e.g., heart muscle, blood vessels, and the connective tissue cardiac skeleton, to repair the damage.	Initial: _____
42	The pooled pluripotent stem cells and mesodermal stem cells are resuspended in 250cc's of sterile normal heparin/saline and are given after the TSCs infusion is completed by regular intravenous infusion (flow rate of 250cc's in 45 minutes).	Initial: _____
43	During systole, as the pressure inside the heart exceeds the aortic pressure, the aortic valve opens and the whole blood, containing the activated PSCs and MesoSCs, leaves the left ventricle into the ascending aorta.	Initial: _____
44	As the heart muscle relaxes during diastole, and the pressure in the aorta exceeds the pressure in the heart, the aortic valve closes revealing the openings to the left and right coronary arteries which were previously covered by the open aortic valve leaflets.	Initial: _____
45	Due to the elastic recoil in the ascending aorta (a large elastic artery), blood is forced into the openings of the coronary arteries to vascularize the heart muscle. From their position within the coronary vessels, tributaries, and branches, PSCs and MesoSCs can migrate to areas of damage within the heart to repair the damage.	Initial: _____
46	If there are no life-threatening co-morbidities, the MesoSCs restore the vasculature to the damaged tissues and the PSCs restore innervation to the damaged tissues. In contrast, the body has a tendency to "steal" activated telomerase-positive stem cells and place the activated stem cells in areas where it thinks the need is greater than either the patient or the Principal Investigator would like. Therefore, we give PSCs and MesoSCs by regular intravenous infusion so the body has sufficient numbers of activated telomerase-positive stem cells for its own use.	Initial: _____
47	Pulmonary treatments: the smallest stem cells (totipotent stem cells, TSCs) and the intermediate stem cells (pluripotent stem cells, PSCs) will be pooled into one group and the larger stem cells (mesodermal stem cells, MesoSCs) will be in a separate group.	Initial: _____
48	Pooled TSCs and PSCs will be resuspended in 2 to 3cc's of sterile normal saline and inhaled as a vapor (nebulized).	Initial: _____
49	Both TSCs and PSCs have the capability to form the lining cells of the lungs that were originally derived from endoderm, e.g., type-I and type-II pneumocytes, and lining epithelial cells of the bronchioles and bronchi; as well as nervous tissue to innervate the tissues of the lungs.	Initial: _____

50	The TSCs and PSCs migrate to areas of tissue damage and either repair the damage or regenerate new cells and tissues lining the inside of the respiratory portion of the lungs to replace the damaged tissues.	Initial: _____
51	The MesoSCs are re-suspended in 250cc's of sterile normal heparin/saline and given by regular intravenous infusion (250cc's in 45 minutes).	Initial: _____
52	The MesoSCs have the capability to form the vasculature and structural framework for the lungs that was originally derived from mesoderm, e.g., bronchial rings of cartilage, lung stroma, and the two vascular systems within the lungs: bronchial vasculature (for vascularizing the lung itself), and pulmonary vasculature for gas exchange.	Initial: _____
53	MesoSCs will migrate to areas of the lung that are damaged and containing the TSCs and PSCs as they transform into the missing tissues.	Initial: _____
54	The MesoSCs will form supporting blood vessels to complete the regeneration of gas / blood - oxygen / carbon dioxide exchange units (e.g., alveolar sacs and alveolar ducts), as well as form any damaged lung supportive tissues.	Initial: _____
55	If there are no life-threatening co-morbidities, the MesoSCs will restore the vasculature to the damaged tissues and the connective tissue skeleton (stroma) of the lung. In contrast, the body has a tendency to "steal" activated telomerase-positive stem cells and place the activated stem cells in areas where it thinks the need is greater than either the patient or the Principal Investigator would like. Therefore, we give MesoSCs by regular intravenous infusion so the body has sufficient numbers of activated telomerase-positive stem cells for its own use.	Initial: _____
56	Autoimmune and systemic, including renal treatments: the smallest stem cells (totipotent stem cells, TSCs) will be in one group and the intermediate (pluripotent stem cells, PSCs) and larger stem cells (mesodermal stem cells, MesoSCs) will be pooled.	Initial: _____
57	The TSCs are resuspended in 250cc's of normal sterile heparin/saline and given by quick intravenous infusion (flow rate of 250cc's in 15 minutes).	Initial: _____
58	As long as there is no pre-existing damage to either the heart or the lungs, the TSCs are so small (0.1 to 2 microns) that they can easily flow through the heart and lungs quickly without getting "stuck". 60% of blood leaving the heart goes to the brain and spinal cord. The remaining 40% vascularizes the remaining organs and tissues of the body.	Initial: _____

59	Because TSCs have the capability to form ANY cell type of the body, including the gametes (sperm, ovum), and nucleus pulposus of the intervertebral disc (the only derivative of the notochord in a person after birth), they will migrate to areas of tissue damage and begin repairing existing damage or regenerate new cells and tissues to replace the lost ones.	Initial: _____
60	The PSCs and MesoSCs are resuspended in 250cc's of sterile normal heparin/ saline and given by regular intravenous infusion (250cc's in 45 minutes).	Initial: _____
61	The PSCs have the capability to form any tissue of the body, EXCEPT the gametes (sperm and ovum) and nucleus pulposus of the intervertebral disc. PSCs will migrate to the same area as the TSCs and aid in the restoration of the damaged or lost tissues.	Initial: _____
62	The MesoSCs have the capability to form any tissue of the body that forms from mesoderm, e.g., muscle, fat, cartilage, bone, connective tissues, tendons, ligaments, organ capsules, organ trabeculae, blood vessels, lymphatic vessels, blood cells, platelets, cells of the immune system, spleen, tonsils, appendix, kidney, ureter, urinary bladder, testicle (without sperm), ovary (without ova) and upper 2/3's of urethra.	Initial: _____
63	The MesoSCs will migrate to the area of tissue damage, restore a vascular supply to that area, and then assist TSCs and PSCs in the formation of any tissue of mesodermal origin that is required for restoring function to the organ.	Initial: _____
64	If there are no life-threatening co-morbidities, the MesoSCs restore the vasculature to the damaged tissues and the PSCs restore innervation to the damaged tissues. In contrast, the body has a tendency to "steal" activated telomerase-positive stem cells and place the activated stem cells in areas where it thinks the need is greater than either the patient or the Principal Investigator would like. Therefore, we give PSCs and MesoSCs by regular intravenous infusion so the body has sufficient numbers of activated telomerase-positive stem cells for its own use.	Initial: _____
65	Direct injection treatments: The smallest stem cells (totipotent stem cells, TSCs) are divided into two aliquots of equal numbers, the intermediate (pluripotent stem cells, PSCs) are divided into two aliquots of equal numbers, and the larger (mesodermal stem cells, MesoSCs) are divided into two aliquots of equal numbers.	Initial: _____
66	Each ½ volume of TSCs, PSCs, and MesoSCs are pooled, for two aliquots with each containing ½ of TSCs, PSCS, and MesoSCs.	Initial: _____

67	One aliquot, containing ½ of the TSCs, PSCs, and MesoSCs, is re-suspended in 1-5cc's (dependent on structure to be injected) of sterile normal saline for single to multiple direct injection(s) into joint(s), tissue (e.g., skeletal muscle), or organ(s).	Initial: _____
68	Because TSCs have the capability to form ANY cell type of the body, derived ectoderm, mesoderm, endoderm, gametes (sperm, ovum), and nucleus pulposus of the intervertebral disc (the only derivative of the notochord in a person after birth), TSCs will migrate to areas of tissue damage and begin repairing existing damage or regenerate new cells and tissues to replace the lost one.	Initial: _____
69	The PSCs have the capability to form any tissue of the body, derived ectoderm, mesoderm, endoderm, except the gametes (sperm, ovum) and nucleus pulposus of the intervertebral disc. PSCs will migrate to the same area as the TSCs and aid in the restoration of the damaged or lost tissues.	Initial: _____
70	The MesoSCs have the capability to form any tissue of the body that forms from mesoderm, e.g., muscle, fat, cartilage, bone, connective tissues, tendons, ligaments, organ capsules, organ trabeculae, blood vessels, lymphatic vessels, blood cells, platelets, cells of the immune system, spleen, tonsils, gut-associated lymphatic tissues, Peyer's patches, free-lymphatic nodules, appendix, kidney, ureter, urinary bladder, testicle (without sperm), ovary (without ova), and upper 2/3's of urethra.	Initial: _____
71	The MesoSCs will migrate to the area of tissue damage, restore a vascular supply to that area, and assist TSCs and PSCs in the formation of any tissue of mesodermal origin necessary to restore function.	Initial: _____
72	The other aliquot, containing ½ of the TSCs, PSCs and MesoSCs, is re-suspended in 250cc's of sterile normal heparin/saline and given by regular intravenous infusion (250cc's in 45 minutes).	Initial: _____
73	If there are no life-threatening co-morbidities, the MesoSCs restore the vasculature to the damaged tissues, the PSCs restore innervation to the damaged tissues, and the TSCs restore any damaged tissues to increase function. In contrast, the body has a tendency to "steal" activated telomerase-positive stem cells and place the activated stem cells in areas where it thinks the need is greater than either the patient or the Principal Investigator would like. Therefore, we give PSCs and MesoSCs by regular intravenous infusion so the body has sufficient numbers of activated telomerase-positive stem cells for its own use.	Initial: _____
74	When your treatment is completed you can go back to where you are staying near the treatment site, but you are requested to minimize activity to REST level for the next 24 hours.	Initial: _____

75	After the 24-hour rest period, you may return home, but only with light physical activity for the next 7 days.	Initial: _____
76	Week two after transplant you may resume moderate activity levels.	Initial: _____
77	Week three to week seven you may resume normal activity.	Initial: _____
78	Throughout the entire time period (daily), from 30 days before first treatment and throughout your treatments you are ingesting CN or CN-SP capsules (one capsule for every 50 pounds of body weight).	Initial: _____
79	If swallowing capsule(s) with cold or room temperature liquids is too difficult, the CN or CN-SP capsule can be opened and contents put into cold or room temperature liquids, soft foods, etc., just nothing HOT (i.e., nothing above normal body temperature, e.g., above 98.6°F or 37°C).	Initial: _____
80	Temperatures above 98.6°F or 37°C can destroy active ingredients within the CN or CN-SP capsules.	Initial: _____
81	Combinatorial nutraceutical-SP (CN-SP) treatment: Is given to individuals where an acute loss of 300-400cc's of blood is NOT an option. In this case, the individual will ingest CN-SP capsules daily, based on body weight, one capsule for every 50 pounds of body weight (1-50 pounds = 1 capsule; 51-100 pounds = 2 capsules; 101-150 pounds = 3 capsules; 151-200 pounds = 4 capsules; 201-250 pounds = 5 capsules, etc.).	Initial: _____
82	Ingestion of CN-SP causes your connective tissue-resident telomerase-positive stem cells, e.g., Totipotent Stem Cells (TSCs), Pluripotent Stem Cells (PSCs), and Mesodermal Stem Cells (MesoSCs) to proliferate, thus making you your own bioreactor for increasing the numbers of telomerase-positive stem cells inside your body.	Initial: _____
83	Ingestion of CN-SP causes your telomerase-positive stem cells to migrate into your blood stream in a bell-shaped curve fashion with the peak of migration at 18 hours after ingestion of the capsules.	Initial: _____
84	Components within the CN-SP supports immune system function.	Initial: _____
85	To maximize your body's ability to heal itself, you need to optimize the number of telomerase-positive stem cells circulating through your blood stream at any given time.	Initial: _____
86	To determine when you should be ingesting your CN-SP capsules, what time do you routinely go to bed?	Initial: _____
87	Add two hours, then what time is it ?	Initial: _____
88	Subtract 18 hours from the time in #87? This is the time that you need to take your first CN-SP capsule.	Initial: _____

89	If you only ingest two CN-SP capsules daily, you need to add six hours from the time in #88? This is the time you need to take your second CN-SP capsule.	Initial: _____
90	If you ingest three CN-SP capsules daily, you need to add six hours from the time in #89? This is the time you need to take your third CN-SP capsule.	Initial: _____
91	If you ingest four CN-SP capsules daily, you need to add six hours from the time in #90? This is the time you need to take your fourth CN-SP capsule.	Initial: _____
92	If you ingest five CN-SP capsules daily, you need to add six hours from the time in #92? This is the time you need to take your fifth CN-SP capsule.	Initial: _____
93	Due to the bell-shaped release curve of telomerase-positive stem cells, following the above protocol, #s 81-92, you will be flooding your body with TSCs, PSCs, and MesoSCs continuously, 24 hours per day (Fig. 1).	Initial: _____
94	Once your body recognizes the telomerase-positive stem cells for what they are and their capabilities, your body will be repairing its damaged tissues on a continual basis, 24 hours per day, seven days per week, 52 weeks per year, as long as you ingest the CN-SP capsules.	Initial: _____
95	“Rule of thumb” to keep in mind: If you have a condition that your body views as life-threatening, the activated circulating stem cells will be directed by the body to that location to a) Repair the damage and restore function b) Otherwise, the last tissue damaged is the next tissue to be repaired c) Tissue repair occurs in reverse chronological order	Initial: _____
96	Therefore, it is imperative that you try not to injure yourself while taking the CN-SP. Unless it is a life-threatening injury, the mobilized telomerase-positive stem cells will treat the most recent injury first (#95b).	Initial: _____
97	Telomerase-positive stem cells, induced to proliferate and mobilize into the blood stream by CN-SP are not inherently activated.	Initial: _____
98	The body requires approximately two weeks to activate these newly CN-SF-mobilized telomerase-positive stem cells as they traverse through the circulation.	Initial: _____
99	Telomerase-positive stem cells isolated from blood can be activated outside the body in about two hours.	Initial: _____
100	TSCs, PSCs, and MesoSCs that have been activated outside the body will begin to show an increase in function from one to four weeks after implantation in compliant individuals (those that follow these guidelines).	Initial: _____
101	TSCs, PSCs, and MesoSCs that were induced to proliferate and mobilize into the circulation with CN-SP, without external activation, will start to show an increase in function from three to six weeks after mobilization into the vasculature in compliant individuals (those that follow these guidelines).	Initial: _____

102	Therefore, the CN-SP proliferation and mobilization procedure is currently less efficacious than the CN proliferation, isolation, segregation, and external activation procedure for increasing function in diseased and/or damaged tissues.	Initial: _____
103	We request that you see your physician or the principal investigator every six months to update your function tests and keep us informed of your progress.	Initial: _____
104	If you stop taking the CN-SP capsules, the unused telomerase-positive stem cells will stop proliferating, will re-sequester themselves into your connective tissue matrices and revert back to their natural quiescent undifferentiated state.	Initial: _____
105	Graft versus Host Disease (GvHD) Response: If your treatment requires the use of allogeneic donor cells to increase stem cell numbers, only TSCs and PSCs from the donor will be utilized.	Initial: _____
106	Self-recognition molecules MHC Class-I and HLA-DR on the surface of cells allows an intact immune system to recognize donor cells as foreign and mount an immune response “seek and destroy mission” to neutralize and destroy the non-self-entities.	Initial: _____
107	TSCs and PSCs do NOT express either MHC Class-I or HLA-DR self-recognition molecules on their cell surfaces in the undifferentiated state.	Initial: _____
108	Therefore, donor allogeneic TSCs and PSCs can be utilized as long as they are implanted in a naïve undifferentiated state.	Initial: _____
109	Neither TSCs nor PSCs will form teratomas (cancerous cells) when implanted in a naïve undifferentiated state.	Initial: _____
110	As the TSCs and PSCs begin to differentiate they begin to express MHC Class-I and HLA-DR molecules on their cell surfaces, indicative of the person the TSCs and PSCs were derived.	Initial: _____
111	However, the time frame necessary for the self-recognition molecules to appear on the surface of differentiating TSCs and PSCs is sufficiently long enough for the recipient’s immune system to accept the differentiated donor TSCs and PSCs as self, and not reject the differentiated cells/tissues.	Initial: _____
112	The MesoSCs contain cell-surface MHC Class-I self-recognition cell surface molecules that an intact immune system can recognize as non-self and mount an immune response to destroy them.	Initial: _____
113	Because MesoSCs can form all cells and tissues of the immune system, you may be regenerating the donor’s immune system in your body.	Initial: _____
114	A functioning immune system can distinguish self from non-self and mount an immune response “seek and destroy mission” against the foreign entity in an effort to eradicate the foreign entity.	Initial: _____

115	This response can lead to a graft versus host disease (GvHD) response, whereby your immune system rejects the donor MesoSCs, or the newly created donor immune system rejects you.	Initial: _____
116	Therefore, to prevent any harm to come to you, the recipient, NO donor MesoSCs are utilized for telomerase-positive allogeneic stem cell treatments.	Initial: _____

Table 1: Guidelines to achieve the best results.

Discussion

Characterization studies, pre-clinical animal models of induced diseases, e.g., Parkinson disease, cardiovascular disease, pulmonary disease, type-I diabetes mellitus, and early clinical human studies of Parkinson disease, cardiovascular disease and pulmonary diseases, established a minimal framework that needed to be followed for using telomerase-positive stem cells [1,6-12]. From this minimum framework, informed consent guidelines were established to optimize the safety and efficacy of using telomerase-positive TSCs, PSCs and MesoSCs, to restore organ function by either repair and/or regeneration of cells and tissues resulting from tissue damage and/or loss. Following these procedural guidelines, endogenous adult-derived autologous and/or allogeneic telomerase-positive stem cells have proven to be both safe and effective at restoring organ function (up to 50% above pre-treatment values in compliant individuals) for diseases and/or disorders caused by trauma or chronic diseases. Disorders treated thus far, using IRB-approved human study protocols, include Alzheimer's disease, amyotrophic lateral sclerosis, blindness, chronic inflammatory demyelinating polyneuropathy, dementia, macular degeneration, multiple sclerosis, neuropathies, Parkinson disease, sciatica, stroke, traumatic brain injury, traumatic spinal cord injury, myocardial infarction, idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, celiac disease, systemic lupus erythematosus, chronic kidney disease, osteoarthritic knee joints, and as a replacement strategy for bilateral total knee replacements and bilateral total ankle replacements [13-21].

Conclusion

Informed consent guidelines were established to optimize the safety and efficacy of using endogenous adult-derived telomerase-positive stem cells to restore organ function by either repair and/or regeneration of cells and tissues resulting from tissue damage and/or loss. Following these procedural guidelines, endogenous adult-derived autologous and/or allogeneic telomerase-positive stem cells have proven to be both safe and effective at restoring (up to 50% above pre-treatment values in compliant individuals) organ function for diseases and/or disorders caused by trauma or chronic diseases.

References

1. Young HE, Speight MO, Williams SE, Black AC Jr. Characterization of endogenous telomerase-positive stem cells for regenerative medicine: a review. *Stem Cell Regen Med.* 2020;4(2):1-14.
2. Young HE, Steele TA, Bray RA, Hudson J, Floyd JA, Hawkins K, et al. Human reserve pluripotent mesenchymal stem cells are present in the connective tissues of skeletal muscle and dermis derived from fetal, adult, and geriatric donors. *Anat Rec.* 2001;264(1):51-62.
3. Young HE, Lochner F, Lochner D. Primitive stem cells in adult human peripheral blood. *J Stem Cell Res.* 2017;1(2):1-8.
4. Young HE, Black AC. Pluripotent stem cells, endogenous versus reprogrammed, a review. *MOJ Orthop Rheumatol.* 2014;1(4): 00019.
5. Stout CL, Ashley DW, Morgan III JH, Long GF. Primitive stem cells reside in adult swine skeletal muscle and are mobilized into the peripheral blood following trauma. *American Surg.* 2007;73(11):1106-10.
6. Young HE, Duplaa C, Katz R, Thompson T, Hawkins KC, Boev AN, et al. Adult-derived stem cells and their potential for tissue repair and molecular medicine. *J Cell Molec Med.* 2005;9(3):753-69.
7. Young HE, Duplaa C, Romero-Ramos M, Chesselet MF, Vourc'h P, Yost MJ, et al. Adult reserve stem cells and their potential for tissue engineering. *Cell Biochem Biophys.* 2004;40(1):1-80.
8. Young HE, Black GF, Coleman JA. Pulmonary diseases and adult healing cells: from bench top to bedside. *J Stem Cell Res.* 2017; 1(2):1-9.
9. Young HE, Limnios JJ, Lochner F, McCommon G, Cope LA, Black Jr AC. Pancreatic islet composites secrete insulin in response to a glucose challenge. *J Stem Cell Res.* 2017;1(1):1-12.
10. Young HE, Hyer L, Black AC Jr. Adult stem cells: from bench-top to bedside. In: *Tissue Regeneration: Where Nanostructure Meets Biology*, 3DBiotech, North Brunswick, NJ. 2013;1-60.
11. Young HE, Hyer L, Black AC Jr. Treating Parkinson disease with adult stem cells. *J Neurol Dis.* 2013;1(2):1-8.
12. Young HE, Limnios JJ, Lochner F. Adult healing cells and cardiovascular disease: From bench top to bedside. *J Stem Cell Res.* 2017;1(3):1-8.
13. Young HE, Speight MO, Williams SE. Telomerase-positive stem cells as a potential treatment for idiopathic pulmonary fibrosis. *Stem Cells Regen Med.* 2020.
14. Young HE, Speight MO, Williams SE. Allogeneic telomerase-positive stem cells as a treatment for celiac disease. *Stem Cells Regen Med.* 2020.
15. Young HE, Speight MO, Williams SE. Allogeneic and autologous telomerase-positive stem cells as a potential treatment for systemic lupus erythematosus. *Stem Cells Regen Med.* 2020.
16. Young HE, Speight MO, Williams SE. Telomerase-positive stem cells as a potential treatment for chronic obstructive pulmonary disease. *Stem Cells Regen Med.* 2020.
17. Young HE, Speight MO, Williams SE, Black AC Jr. Cardiovascular disease treated with telomerase-positive stem cells. *Stem Cells Regen Med.* 2020.
18. Young HE, Speight MO, Williams SE, Black AC Jr. Donor selection is a critical component in allogeneic telomerase-positive stem cell treatments. *Regen Med Biol Therap.* 2020.
19. Young HE, Speight MO, Williams SE, Black AC Jr. Traumatic spinal cord injury treated with autologous telomerase-positive stem cells. *Regen Med Biol Therap.* 2020.
20. Young HE, Speight MO, Williams SE, Black AC Jr. Local anesthetic use with telomerase-positive stem cells. *Regen Med Biol Therap.* 2020.
21. Young HE, Speight MO, Williams SE, Black AC Jr. Alzheimer's dementia treated with autologous and allogeneic telomerase-positive stem cells. *Stem Cells Regen Med.* 2020.