CMMRF

CRYPTIC MASONS MEDICAL RESEARCH FOUNDATION

CMMRF Fact Sheet for Grand Council

Purpose: The following information is provided to all York Rite Council Companions concerning the mission of the Cryptic Masons Medical Research Foundation (CMMRF) and the type of medical research that they are currently working on. The objective of this fact sheet is to inform and educate all Companions on the research that is currently underway and supported by CMMRF and the progress that has been achieved in each area. Further, to provide everyone with an idea as to where the research will ultimately lead to, as well as impacts that it will have on those afflicted with the conditions under research.

Currently, the CMMRF is supporting medical research into eight critical areas through the Indiana University School of Medicine. Each of these eight areas are described below. Also, each of the eight research fields are medical conditions that afflict millions of people on an annual basis. Each of you will undoubtedly have multiple relatives and friends; if not yourselves, that are afflicted by these conditions.

The CMMRF program is designed to generate a steady revenue stream that allows for the continued research into each of the designated medical conditions. Although CMMRF is not the only revenue stream for the research being conducted by the Indiana University School of Medicine, it is a main contributor that has allowed for continued research, as well as the purchase of critical research equipment that is now cutting-edge medical technology.

Again, this paper is intended to educate and inform all Council Companions on the charitable outreach program that they have adopted and supported throughout the years.

History: Before delving into the medical research projects that are on-going with the CMMRF, it is important to understand some of the history of how cryptic masonry came to partner with the Indiana University School of Medicine. Having a sense of history allows for us to more readily identify with the goals and objectives of the CMMRF program.

The Cryptic Masons Medical Research Foundation, (CMMRF), was incorporated in the state of Oklahoma, March 6, 1986. The driving force behind this new corporation was interest shown by Most Puissant General Grand Master Ben Mandlebaum, of the General Grand Council, Cryptic Masons International. MPGGM Mandelbaum and two other individuals found the need to develop a foundation that could provide direct support to the Indiana University School of Medicine based upon the critical research that they were performing into areas of medical science that commonly afflict the majority of Americans

in everyday life. These men then created and legally incorporated that foundation to serve as an outreach project that could be supported by cryptic masons everywhere.

CMMRF funds research at Indiana University School of Medicine in Indianapolis, Indiana. Initial research focused on the cause(s) and eventually a cure for atherosclerosis and its complications. In later years, the research has implemented adult stem cell therapies to address a variety of mature health issues but not necessarily restricted to the adult population. This research was previously funded by an Indiana corporation, which ceased to do business upon the death of Dr. Owen L. Shanteau, October 17, 1985. While CMMRF is not a part of that preceding organization and the General Grand Council was not its governing body, CMMRF is continuing the good work that it started.

Sometime in 2001-2002 the CMMRF sponsored laboratory became the Indiana Center for Vascular Biology and Medicine, (ICVBM). After a 3-year search for the best person to fill this newly created position, Chairman Dr. Keith March was selected. The creation of an endowed chair and this new Center attracted more than $2,000,000.00 from non-Masonic sources. Dr. March served in this position until his resignation September 30, 2017. After an in-depth search, Dr. Jay Hess, Dean of the Indiana University School of Medicine, announced on July 17, 2018, that Dr. Michael P. Murphy had been selected as the next holder of the Cryptic Masons Medical Research Foundation Chair.

Since that time, Dr. Murphy has been working in conjunction with the various CMMRF programs throughout the country, to raise funding and awareness of the program.

RESEARCH PROJECTS – The following information is provided on the eight distinct areas of medical research that are supported by the CMMRF program. Each area is distinct and has application to the most common medical conditions that are found in everyday life.

1. Condition Under Study – ABDOMINAL AORTIC ANEURYSM (AAA)

Description - (AAA) is an enlarging of the aorta which is the main blood vessel from the heart to the rest of the body. The enlargement (or dilation) of the aorta many times leads to rupture and death if untreated.

AAA is the 13th leading cause of death in the U.S. but its incidence is probably much higher as it has no symptoms until it ruptures. Of those patients who do rupture, half will die before reaching the hospital. Of the ones who do reach a hospital, half will die after emergency surgery. In total, 70% or more diagnosed with AAA will succumb to the condition, with only 30% or less surviving.

Approximately 200,000 new AAA's are diagnosed each year and surgical repair is not initiated until the AAA grows to a diameter of 5.5 cm. Thus many patients with smaller

AAA's must wait for years before repair and describe it as if having a ticking time bomb in their abdomen.

Current Research: At present are no current medical strategies to prevent or suppress AAA expansion and rupture to avoid surgery. However, the Indiana University School of Medicine (supported through CMMRF funding) is near completion of a Phase I clinical trial in which they are treating patients with small AAA with intra-venous infusions of "mesenchymal" stem cells obtained from young healthy donors.

Note - Mesenchymal stem cells are adult stem cells that have two features: the ability to differentiate along different lineages and the ability of self-renewal. This means that the stem cells introduced into the patients body, will adapt and reinforce the aorta and they will renew themselves as the patient continues in life making surgical repairs unnecessary and a thing of the past.

Patients enrolled into this study are randomized to placebo, low dose MSCs, and high dose MSCs. Since this is a phase one study, there are currently 31 of 36 patients being treated. Preliminary results have shown a significant reduction of inflammatory cells that are related to AAA development and a significant increase in regulatory T cells that suppress inflammation, reaching the primary endpoint. T-cells are part of the immune system and develop from stem cells in the bone marrow. They help protect the body from infection and may help fight cancer

More importantly, using positron emission tomography, the study has shown that MSCs decrease inflammation in the aorta in a dose-dependent fashion and prevent AAA from enlarging. Without the enlargement, the aorta will not rupture.

On-Going and Future Developments - Based on these results; the Indiana School of Medicine is designing a larger Phase II multi-center clinical trial. Research seems to demonstrate that aortic aneurysms are a result of an auto-immune response to proteins in the aorta, specifically to a protein called "elastin". Working with collaborators at Northwestern University they are using state of the art nano-particle technology that will prevent patients from developing this immune response and prevent aneurysms from even starting.

Further, a skin test has been invented that may identify patients at risk for AAA before the aneurysm actually develops. This will allow treatment to suppress aortic inflammation and prevent the AAA from starting.

A recent NIH grant was received and that grant will be utilized to focus on muscle wasting and heart disease in patients with abdominal aortic aneurysms. They previously discovered that 50% of patients who had evidence of muscle wasting prior to surgical repair for their aneurysm died at 3 years. In mouse models of aortic aneurysm, they have developed through Cryptic Masons funds; they are testing their hypothesis that the chronic inflammation associated with aneurysm formation leads to heart failure.

2. Condition Under Study – PERIPHERAL ARTERIAL DISEASE (PAD)

Description – PAD is a greater health care burden than is coronary artery disease. Approximately 8 million Americans are afflicted with it. Critical Limb Threatening Ischemia, (CLTI), is the most severe form of PAD and is characterized by foot pain, as well as gangrene. CLTI is a significant risk for amputation of the leg and has a quality of life equivalent to a terminal cancer patient.

Surgical interventions have provided excellent results in treating CLTI however, up to 30% of patients with CLTI will not be candidates for angioplasty or bypass and the only treatment option for relief of pain or removal of an infected ulcer, is amputation. The number of amputations in the US gas increased by over 50% in the last decade and currently over 153,000 amputations are performed each year. The American Heart Association has declared lower extremity amputations a national health care crisis with a call to reduce amputation rates by 20% by the year 2030.

Diabetic patients are especially at risk for limb amputation due to infection and more extensive hardening of the arteries. The incidence of diabetes and its vascular complications continues to rise each and every year.

Current Research - With the support of the CMMRF, the Indiana School of Medicine is addressing the critical need for effective therapies to prevent amputations.
With research funds they have created a diabetic mouse model of CLTI and are testing new stem cell types and preparations able to regenerate skeletal muscle in the diabetic mice with limb ischemia. Further, it has been discovered that mice treated with mesenchymal stem cells grown in clusters (called spheroids) have complete return of muscle function and limb function. This is a discovery that does and will lend itself to clinical trials in the near future.

They are collaborating with Harvard University, who has developed a gel material that can envelope the stem cell and then be injected into the muscle of a leg with PAD. The reason that this is significant is that it protects the mesenchymal stem cells until they are introduced into the targeted area. Also, with the utilization of CMMRF funds, the University of Indiana Medical School has been able to purchase a “Buchi Encapsulator”. This device encapsulates cells which protects them from getting cleared by the recipient’s immune system, yet still allows the cells to secrete growth factors that stimulate new blood vessels to grow. With new blood vessel development, oxygen is restore to the afflicted area, and the chronic pain is reduced, or eliminated.

A recent paper in Nature Medicine showed that encapsulated human islet cells, when injected into a diabetic mouse survived for 175 days and controlled the mouse’s blood sugar.

They plan to use this encapsulating shield for their MSC spheroids. If the cells can survive longer they may be more effective in restoring blood flow to the leg and promote wound healing.

Furthermore the Buchi device allows them to package other cargo in capsules such as growth factors or genes, which can target diseased tissue.

The Indiana University School of Medicine is leading the field in adult stem cell biology to treat PAD by developing an induced pluripotent stem cells (iPSC) that can directly grow into a functioning blood vessel when injected into muscle. This iPSC mesodermal cell is a discovery of Dr. Mervin Yoder at IU and a close collaborator of the Indiana University School of Medicine. We are currently assessing these iPSCs in our mouse models of limb ischemic and plan to move this novel cell population into a clinical trial.

They are now using induced pluripotent stem cells that have been genetically modified to lack expression of what are called major histocompatibility antigens. Because these cells lack these antigens they can be transplanted into an unrelated patient without the patient's immune system recognizing them and thus they will be more effective as they will last longer.

In essence they have the ability to take a bone marrow derived stem cell and convert it into an embryonic like state, that is undefined, and then differentiate it into a specific type cell such as a heart muscle cell. This ability to re-designate a cell into something other then what it was, allows for the creating of targeted stem cells be introduced into other organs for repair.

On Going and Future Developments - Critical Limb Threatening Ischemia (CLTI) is the most severe form of peripheral arterial disease caused by atherosclerotic occlusion (a build up of fats and cholesterol) of blood vessels to the lower extremities. It is often associated with excruciating pain and leads to the development of skin ulcers or gangrene.

The Indiana Center For Regenerative Medicine and Engineering has been at the national forefront in developing cutting-edge approaches to treat "no option" for revascularization CLTI patients. The Cryptic Masons Medical Research Foundation funding has been actively used to focus on cell-based approaches for cardiovascular disease for over the past 20 years, and will continue to do so.

Dr. Murphy conducted the first trial in the U.S. using a patient's own bone marrow cells to prevent amputations. His pioneering work culminated in the MOBILE (Marrow Stem Treatment of Limb Ischemia in Subjects with Severe Peripheral Arterial Disease) trial—a randomized, placebo-controlled trial that assessed the ability of intra-muscular injection of a patient's own bone marrow cells to prevent amputation.

The MOBILE study demonstrated that cell therapy was safe; however there was not a significant difference in amputation rates at one-year between the cell treated and placebo.

Further research in this area will be conducted to improve the results and determine why the therapy appears to be blocked in patients suffering from diabetes. The ultimate goal is to treat the patient with stem cell therapies that will preclude the need for further amputations of limbs and to relieve the chronic pain that is experienced by those suffering with PAD.

3. Condition Under Study – HEART FAILURE

Description – Heart failure occurs when the heart muscle doesn't pump blood as well as it should. Blood often backs up and causes fluid to build up in the lungs (congest) and in the legs. The fluid buildup can cause shortness of breath and swelling of the legs and feet. Poor blood flow may cause the skin to appear blue (cyanotic). Ultimately, heart failure can be terminal as it leads to heart attacks and organ failure.

Current Research – The Indiana University School of Medicine has participated in the CONCERT-HF trial and the SENECA trials through the Cardiovascular Cell Therapy Research Network. This is a consortium of 7 centers in the US recognized for their expertise in stem cell research. The SENECA study was a Phase I trial that recruited 60 patients with heart failure after receiving chemotherapy for cancer. Unfortunately the chemotherapy, besides killing cancer cells, also kills heart muscle cells and at times patients survive their cancer but end up with heart failure. SENECA was designed to assess the effects of mesenchymal stem cells injected into the heart muscle of these patients. The study reached completion and the results show that the stem cells improved all 7 measures of heart function and plans are underway for a larger and more definitive Phase II trial.

The CONCERT-HF trial was designed to assess the ability of stem cells in improving heart function in patients with heart failure after a heart attack. In this study patients underwent a biopsy of their heart muscle and also a bone marrow aspiration. Both tissue samples were sent to the University of Miami where stems cells called “c-kit” positive cells were grown from the heart muscle and mesenchymal stem cells were grown from the bone marrow. Then the cells were sent back to the respective medical center the combination of c-kit and MSCs were injected into the heart muscle.

On-Going and Future Development – The CONCER-HF trial has completed enrollment and all follow-up evaluations. They will be meeting in February to review the results of this exciting study.

Using a 3D bioprinter to create scaffolds onto which heart cells can be implanted, it is anticipated that a “beating” scaffold can then be used to surgically replace parts of the heart that have been damaged from a heart attack. (Scaffolds are materials that have

been engineered to cause desirable cellular interactions to contribute to the formation of new functional tissues for medical purposes.) Cells are often 'seeded' into these structures capable of supporting three-dimensional tissue formation.

Further, they are working with Stanford University to develop new approaches to treating heart failure. It has been shown that induced pluripotent heart muscle cells produce small microvesicles that contain mitochondria. Mitochondria are small organelles that are in every cell and they make ATP, which is the energy source for the cell to survive. When these microvesicles are injected into a pig heart with an infart they are able to rescue injured heart cells.

They will be creating microbeads with the Buchi encapsulating device that will be loaded with mitochondria, which will be injected into the pig model. In other words, they are progressing into Phase 2 studies with the goal of introducing stem cells into a heart that has suffered a heart attack and restoring the damaged muscle cells, while generating new blood supplies and providing the energy necessary for normal heart cells to survive.

4. Condition Under Study – DIABETES

Description - Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves.

There are four main types of diabetes: Type 1 diabetes, Type 2 diabetes, gestational diabetes, and a condition known as prediabetes, in which you have higher-than-normal blood glucose levels but not quite high enough (yet) to qualify as Type 2 diabetes. Type 2 being the most common in US society, mainly due to diet and weight issues.

Current Research - The current focus is on treating Type 1 diabetes with islet cell transplants from donors has not been successful as the patient's immune system recognizes the islet cells as foreign and clears the cells from the patient's body. Islets are cells found in clusters throughout the pancreas. They are made up of several types of cells. One of these is beta cells, which makes insulin. Insulin is a hormone that helps the body use glucose for energy. Islet cell transplantation transfers cells from an organ donor into the body of another person A recent publication in Nature Medicine has shown that encapsulation of human islet cells with "aliginate" (which is a complex carbohydrate found in seaweed), a hydrogel approved for clinical use; protected the human islet cells from the mouse immune system and corrected the diabetes.

On-Going and Future Development - Thanks to CMMRF support the Indiana University School of Medicine, they were able to purchase the Buchi encapsulation device that can make a clinical grade capsule. They plan to begin encapsulating human islet cells and test their ability to control blood sugar levels in thier polygenic diabetic mouse model, the "TALLY-HO" mouse strain. This genetic diabetic mouse more closely duplicates the human diabetic condition then that used in the Nature Medicine paper.

Furthermore if they are able to demonstrate success they will be able to move this to a clinical trial in patients as the materials they are using are FDA approved.

The goal of this research is to allow cells in the pancreas to stimulate insulin production, thus improving the quality of life for those that suffer with diabetes.

5. Condition Under Study – CANCER

Description - Cancer is the uncontrolled growth of abnormal cells in the body. Cancer develops when the body's normal control mechanism stops working. Old cells do not die and instead grow out of control, forming new, abnormal cells. These extra cells may form a mass of tissue, commonly known as a tumor.

Current Research - The Indiana Center for Vascular Biology has teamed up with the IU Center for Immunotherapy, based on mutual interests in modulating the patient's immune system to fight disease and also because the Indiana University School of Medicine is building a cell manufacturing facility.

The Center for Immunotherapy needs expertise in creating antigen specific T cells to fight cancer, what is known as CAR-T cells. Their group has developed the technology to create antigen specific regulatory cells to prevent inflammation in cardiovascular disease and they will be working with other colleagues in oncology in creating CAR-T cells.

Note – "Chimeric antigen receptor" or (CAR) T - cell therapy is a type of immunotherapy that modifies a person with cancer's immune system so it is more effective at finding and destroying cancer cells. A person's immune system is very complex and involves many different types of cells and systems throughout the body.

On-Going and Future Development - This joint venture between the Indiana Center for Vascular Biology, IU Center for Immunotherapy and Indiana University School of Medicine will continue its research to hopefully create an antigen specific T cell, which will provide a new treatment protocol for those afflicted with cancer.

6. Condition Under Study – STROKE

Description - A stroke is defined as a loss of blood flow to part of the brain, which damages brain tissue. Strokes are caused by blood clots and broken blood vessels in the brain. Symptoms include dizziness, numbness, weakness, paralysis, on one side of the body, and problems with talking, writing, or understanding language.

Generally speaking, there are three types of strokes which can affect a person, which have various degrees of severity. These there forms are as follows:

- Ischemic stroke. Most strokes are ischemic strokes.
- Hemorrhagic stroke. A hemorrhagic stroke happens when an artery in the brain leaks blood or ruptures (breaks open).
- Transient ischemic attack (TIA or "mini-stroke")

Current Research – The Veterans Administration Research Consortium has asked the Indiana University School of Medicine to develop new approaches to improving outcomes after a stroke. Key to recovery after a stroke is "rescuing" those brain cells that are injured but not dead.

They are working with colleagues in Neurosurgery in a rat stroke model in which they can inject regulatory T cells that they are creating in their lab directly into the injured part of the brain.

On-Going and Future Development – Future research is designed to save damaged brain cells from further damage or death of the cell. Laboratory research on rats will continue to develop the techniques that will hopefully lead to phase 1 and phase 2 studies. The ultimate goal is to save as many brain cells as possible after a stroke event has occurred. By doing this, the stroke victim will be allowed to have further brain function, then would normally occur after such an event.

7. Condition Under Study – ARTHRITIS

Description - Arthritis is the swelling and tenderness of one or more joints. The main symptoms of arthritis are joint pain and stiffness, which typically worsen with age. The most common types of arthritis are osteoarthritis and rheumatoid arthritis.

The 5 Common Types of Arthritis are:

- Osteoarthritis.
- Rheumatoid Arthritis.
- Psoriatic Arthritis.
- Gout.
- Lupus.

Current research – The Veterans Administration also has called for new innovative approaches in treating arthritis of the knee and hip. They have designed a clinical trial in which patients will be treated with mesenchymal stem cells with injections directly into the knee space.

They are awaiting FDA approval and final funding from the VA for this multi-center study.

On-Going and Future Development - Once FDA approval has been obtained, clinical trials will be initiated with the anticipation that the introduction of mesenchymal stem

cells will begin to repair damaged and lost cartilage, thus restoring some degree of mobility and improved quality of life to the patient.

8. Condition Under Study – PANCREATITIS

Description - Pancreatitis is inflammation of the pancreas. The pancreas is a large gland behind the stomach, close to the first part of the small intestine, called the duodenum. The pancreas has two main functions—to make insulin and to make digestive juices, or enzymes, to help you digest food.

When the pancreas is inflamed, the powerful digestive enzymes it makes can damage its tissue. The inflamed pancreas can cause release of inflammatory cells and toxins that may harm your lungs, kidneys and heart.

Current Research - Each year 37,000 people are diagnosed with pancreatitis, a debilitating disease associated with significant pain and requiring frequent admissions to the hospital.

The Indiana University School of Medicine has one of the largest pancreatitis programs in the U.S.

They plan a phase I clinical trial, similar to the aortic aneurysm trial, in which they will treat patients with pancreatitis with MSCs.

On-Going and Future Development - Once the Phase 1 studies begin, their goal will be to introduce stem cells into the pancreas, and allow for it to decrease inflammation as well as excessive production of toxins. This will lead to a normalization of pancreas function and elimination of pain.

Conclusion - Much of the ongoing research sponsored by CMMRF has cross application into multiple areas. As one can see, the Indiana University School of Medicine has been developing tools (mainly through the use of adult stem cells) to be able to provide new treatment protocols across a broad range of medical conditions that affect each of us on a daily basis.

In science, often times; minor discoveries are made that lead up to a major treatment protocol or cure. Most of the above mentioned medical conditions have plagued humans over the course of our history. Because of discoveries such as those made by the Indiana University School of Medicine, advancements have been made that are leading to real cures. However, what is very exciting, is that their research is leading to treatments that will be affective in allowing a patient that is afflicted by one of these conditions, to have an improved quality of life. Those who have debilitating conditions that leave them at

home with a loss of mobility and in chronic pain, have a chance at leading a more normal life by gaining increased mobility and a minimization of pain.

The future for the victims with chronic conditions such as PAD, is becoming brighter due to the advancements that are being made. Our continued and reliable support to the CMMRF program will bring a hope and promise of giving these afflicted people a better life, with a lot less pain involved. Think of the joy in a person who has lived with chronic and debilitating pain, being given adult stem cell therapies, thus removing their pain. Think of the immediate improvement in their quality of life both physically and psychologically. This is what we as Cryptic Masons are supporting. This is truly something to be proud of.

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