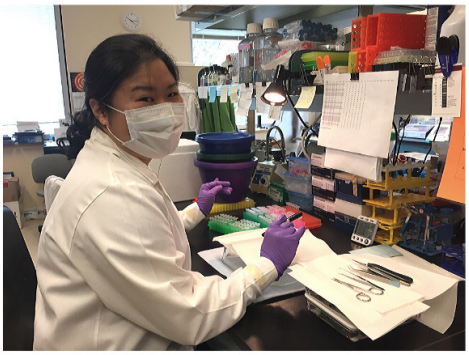
Collins Medical Trust

Medical Research and Education in Oregon

2019 Annual Report



OHSU and OSU Partnering in Portland for Rare Diseases

Collins Medical Trust
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Purpose and History

"The principal and income of the trust fund shall be used (a) to aid, further, promote, develop, encourage and sponsor research, experiment and work in the cause, cure and treatment of human diseases or in any field of medical research, and (b) to aid, further and promote medical education."

The Collins Medical Trust was founded by Truman Collins Sr. in the fall of 1956. He was interested in the medical field and wanted to set up a trust that would contribute to medical research and education taking place in Oregon. Contributions were made to the trust over the next ten years or so, and its assets have grown significantly since that time, largely due to the wise investment decisions of the financial adviser, Jim Miller, over the first forty years of the Trust's existence.

Because the Trust makes relatively small grants—typically in the $25,000 to $30,000 range—our focus for research has primarily been seed funding for projects that, if successful, will go on to apply to the NIH or to other large funders for later-stage funding. We also like to support researchers at a stage where they are gaining their independence in a supportive environment.

Since its inception, the Collins Medical Trust has made grants totaling about $11.6 million.

Trustees and Staff

Shannon Osieczanek	Administrator	(2016 – present)
Truman Collins Jr.	Trustee	(1990 – present)
Dr. Elizabeth Eckstrom	Trustee	(2003 – present)
Dr. Walter McDonald	Trustee	(2005 – present)
Virginia Tilden, Ph.D.	Trustee	(2017 – present)
Timothy Bishop	Treasurer	(1990 – present)

Financial Statements **(Fiscal year ending September 30, 2019)**[1]

Assets and Liabilities

Assets:	2019	2018
Cash	$84,000	$98,000
Stocks	$8,653,000	$9,507,000
Total assets	$8,737,000	$9,605,000
Liabilities	($51,000)	($61,000)
Net Assets	$8,686,000	$9,544,000

Revenue and Expenses

Income:	2019	2018
Income (interest & dividends)	$254,000	$349,000
Realized gains	$172,000	$285,000
Unrealized gains	($763,000)	($232,000)
Total income	($337,000)	$402,000
Taxes & investment expense	($5,000)	($7,000)
Net Investment Income	($342,000)	$395,000
Grants - net	($516,000)	($554,000)
Net revenue	($858,000)	($159,000)

[1] Rounded to the nearest thousand.

2019 Grants (October 1, 2018 – September 30, 2019)

Research

Kei Adachi, Ph.D. **OHSU Foundation** **$30,000**
A functional role of the liver for the prolonged blood clearance of adeno-associated virus type 9

Nuria Marti Gutierrez, Ph.D. **OHSU Foundation** **$30,000**
Correcting inheritable BRCA mutations in the human germline

Ian Martin, Ph.D. **OHSU Foundation** **$30,000**
LRRK2-mediated Neurodegeneration in Parkinson's Disease

Naoki Oshimori, Ph.D. **OHSU Foundation** **$30,000**
Molecular Signature of a Tumor-Promoting Cancer Stem Cell Niche

Khanh P. Nguyen, M.D. **Portland VA Research Foundation** **$30,000**
Investigating the role of platelets in venous thrombus resolution and post-thrombotic vein wall fibrosis

Greg Duncan, Ph.D. **OHSU Foundation** **$30,000**
Promoting Neuronal and Axional Health in Demyelinating Disease

Ferdinando Pucci, Ph.D. **OHSU Foundation** **$30,000**
Genetic approaches to study tumor-derived extracellular vesicles and their role in generating tumor promoting antibodies

Brandon Togioka, M.D. **OHSU Foundation** **$30,000**
Multiple Ascending Dose to Study the Safety, Tolerability, and Pharmacokinetic Effects of Intraperitoneal Chloroprocaine

Brett Walker, M.D. **OHSU Foundation** **$29,999**
Utilizing Circulating Hybrid Cells as a Liquid Biopsy to Distinguish Benign Intraductal Papillary Mucinous Neoplasms from Early Pancreatic Cancer

Molly Burke, Ph.D. **Oregon State University** **$30,000**
Evolving long-lived yeast: developing model populations with postponed aging to identify candidate genes for improving human healthspan

Jonathan Nelson, Ph.D. **OHSU Foundation** **$30,000**
Defining the Role of Mesangial Cell Angiotensin Signaling in Diabetic Kidney Disease

Jonathan Pruneda, Ph.D. **OHSU Foundation** **$30,000**
Prediction of bacterial effectors targeting the host ubiquitin signaling response

Stephen Martin, Ph.D. **Oregon State University** **$30,000**
Mechanistic Regulation of Bone Marrow Mesenchymal Stem Cell PGC-1a Throughout Differentiation and Aging

Terry Medler, Ph.D. **Providence Portland Medical Foundation** **$30,000**
Contribution of the inflammasome to radiation response in pancreatic cancer

Total Research: **$419,999 (82%)**

Education

Linfield School of Nursing **$95,000**
Paquet Scholarship Fund, Half for Endowment and Half for Current Scholarships.

Total Education: **$95,000 (18%)**

Total Grants Approved in 2019: $514,999

Illustrative Prior Grant Recipients — Text Supplied by OHSU

The following grants were made in past years. For each, some context and detail is given for the outcome of the project. The summaries of these grants were provided by OHSU.

OHSU and OSU Partnering in Portland for Rare Diseases

Penelope Hogarth, M.D.
Oregon Health Sciences University
$30,000 awarded in May 2017

Pantothenate kinase-associated neurodegeneration (PKAN) is a rare disease caused by a genetic mutation that impairs metabolism of vitamin B5 in the brain. The body uses this vitamin to make coenzyme A, a compound essential for nearly 10% of all biochemical reactions in the body. PKAN causes profound disability and suffering, resulting in painful involuntary movements, as well as progressive difficulty with speech, swallowing and walking. Children are disproportionately affected, many succumbing to complications of the disease in the first decade of life. There is currently no disease-modifying treatment available.

In 2018, the Collins Medical Trust provided funding to Dr. Hogarth to further development of a potential nutritional treatment for the disease. The proposed therapy is designed to bypass and overcome the metabolic block caused by the genetic mutation. The Collins Medical Trust funding supported several essential steps on the path to a clinical trial: first, studies in a mouse model of the disease, using a disease-relevant biomarker to find the appropriate dose range of the compound for future human trials; second, collection of biosamples from PKAN patients and healthy controls to establish the utility of the biomarker in humans; third, development of a suitable formulation for the compound; and fourth, conduct of shelf-life studies to determine stability of the formulated compound.

As reflected in the project title, the project also resulted in a creative new collaboration between physician-scientists at Oregon Health & Science University and food science faculty at Oregon State University. A team at OSU's Food Innovation Center, an "agriculture experiment station" in Portland that provides development, technical and educational services to the food industry and Northwest communities, developed a strawberry-flavored syrup that not only enhanced stability of the compound, but was also appealing to children and suitable for administration via a feeding tube in advanced patients. The Food Innovation Center staff also contributed their expertise to design and conduct the shelf-life studies.

The work funded by the Collins Medical Trust comprised key background studies for a grant application to the National Institutes of Health to support a national clinical trial of the compound in children and adults with PKAN. This substantial 5-year grant was funded by the Eunice Kennedy Shriver National Institute of Child Health & Human Development on its first submission, and enrollment for the clinical trial opened in December 2019. In a fitting illustration of the success of this 'bench-to-bedside' project, more than a third of the total projected participants had signed up to join the trial in the first three weeks since opening.

Opioid-Use Disorders and HIV infection: A Double-Edged Assault on the Immune System

Christina Lancioni, M.D.
Oregon Health Sciences University
$29,808 awarded in July 2018

People living with Human Immunodeficiency Virus infection (PLHIV) are at significantly higher risk for chronic pain than the general population, with much of this pain originating from direct nerve injury by the virus and the resulting inflammatory response. Like for many Americans, management of chronic pain using opioid medications has led to a crisis of opioid use disorders (OUD) among PLHIV. However, PLHIV are uniquely susceptible to complications resulting from OUD. Indeed, individuals with HIV and substance abuse disorders who receive appropriate treatment with highly active anti-retroviral therapy (ART) still have an increased risk of secondary infections, AIDS, and death that is independent from their compliance with medical care. These epidemiologic findings indicate that PLHIV are particularly vulnerable to the effects that opioids have on the immune system. Studies in animals and using in vitro experimental systems have shown that opioids facilitate HIV replication, interfere with critical pathways controlling inflammation, and cause damage to the intestines allowing for the movement of immune stimulating molecules released from gut bacteria into the body's circulation. This interplay between opioids and HIV may drive what is termed "immune dysregulation," an immunologic phenomenon characterized by exhaustion of the immune system. HIV-infection itself places a large burden on the immune system and can lead to immune dysregulation; in fact, biomarkers of immune dysregulation are strongly related with progression to AIDS and non-AIDS related morbidities and deaths. Understanding how OUD exacerbate HIV-associated immune dysregulation is critical to develop treatments that can treat both the underlying substance abuse disorder, improve immune function, and optimize clinical outcomes.

In 2018, the Collins Medical Trust provided funding to Dr. Lancioni to support a research project to investigate the impact of OUD on the immune system of PLHIV, and to identify mechanisms driving opioid-associated immune dysregulation in this vulnerable population. The aims of this project focused on delineating the impact of OUD on monocytes, a critical cellular component of the innate immune system. Specific investigations focused on determining if OUD were associated with alterations in: the types of monocyte subsets; the functional responses of monocytes to immune stimulation; and the pathways used to regulate monocyte responses to immune stimulation, among PLHIV.

Through her collaboration with Dr. Korthuis (Professor of Medicine, OHSU) Dr. Lancioni was able to access research samples from PLHIV with and without OUD and Hepatitis C co-infection. Here, the novel observation that subtypes of monocytes vary significantly between PLHIV with and without OUD (regardless of Hepatitis C co-infection) was made. This finding has clinical implications, as PLHIV with OUD were found to have expansions in "intermediate" and "nonclassical" monocytes, cellular populations that are associated with advanced HIV disease and HIV-associated neurocognitive disease (HAND). The expression of a molecule termed CD163 was also studied on the surface of monocytes. CD163 is a cell-surface glycoprotein scavenger receptor that is highly expressed on monocytes and tissue macrophages, and serves as a receptor for hemoglobin-haptoglobin complexes. Among PLHIV, levels of soluble CD163 (sCD163) correlate with HIV disease activity, and sCD163 has been proposed as a biomarker of macrophage-mediated HIV disease progression. Here, it was found that PLHIV with OUD and Hepatitis C, specifically, have elevated levels of cell surface and soluble CD163. Among PLHIV with OUD, production of inflammatory signaling molecules called cytokines were also found to be altered in response to multiple different immune stimuli, when compared to PLHIV without OUD. These findings confirm that both the populations of monocytes, and the functional responses of monocytes, are altered among PLHIV with OUD.

Dr. Lancioni's findings are novel and have not been previously reported. These findings are important to the field as populations of intermediate and nonclassical monocytes are more susceptible to HIV-infection and permissive to viral replication when compared to "classical" monocytes. Furthermore, they are associated with

advanced HIV disease, and have been shown to correlate with other marks of chronic systemic inflammation, as well as HIV-associated neurocognitive disease. It should also be noted that as part of her investigations, Dr. Lancioni examined the frequencies and function of different types of CD4+ and CD8+ T cells among PLHIV with and without OUD and Hepatitis C co-infection. In contrast to what was observed among monocyte populations, CD4+ and CD8+ T cell subtypes, and production of T cells cytokines, were comparable between PLHIV with and without OUD once differences in HIV viral load were considered. Thus, Dr. Lancioni has been able to demonstrate that among PLHIV, OUD is associated with dysregulation of innate immunity that is further exacerbated by Hepatitis C co-infection. In addition to access to treatment for OUD, novel therapies to reduce the burden of innate immune activation and restore populations of classical monocytes, should be prioritized among PLHIV suffering from OUD.

The data generated from this Collins Medical Trust award to Dr. Lancioni has been used to support a recently accepted (October 4, 2019) manuscript to the high-impact journal AIDS, entitled "Altered monocyte phenotype and dysregulated innate cytokine responses among people living with HIV and opioid-use-disorder." Moreover, the support provided by this award was critical to Dr. Lancioni's NIH/NIDA R01 proposal entitled "The impact of naltrexone treatment on opioid-induced immune and viral dysregulation during HIV-infection," that was awarded in fall 2018. Here, Dr. Lancioni will have the opportunity to investigate if the medications used to treat OUD among PLHIV correct the dysregulation of innate immunity she has found to be associated with opioid exposure.

Policies and Procedures

The **Collins Medical Trust** was established in 1956 by Truman W. Collins as a tax-exempt charitable trust under the laws of the State of Oregon. It is recognized by the Internal Revenue Service as tax-exempt under Section 501(c)(3) of the Internal Revenue Code and has been classified as a private foundation under Section 509(a) of the Code. The Trust is directed by a Board of Trustees.

Policies
The Original Trust document states that monies from the Trust shall be used:

"To aid, further, promote, develop, encourage and sponsor research, experiment and work in the cause, cure and treatment of human disease or in any field of medical research, and

To aid, further and promote medical education."

With this statement as a guide, and having knowledge of the desires and concerns of the Trustor, Mr. Collins, and applicable laws, the Trustees over the ensuing years have established the following *general guidelines* under which grant requests are considered:

1. Disbursements are made only to organizations which have established their tax-exempt status with the U.S. Treasury Department and are operated exclusively for scientific and/or educational purposes.

2. Preference is given to projects and programs conducted by qualified organizations within the State of Oregon.

3. Funds cannot be paid directly to or for the benefit of any specific individual. This does not preclude grants to qualified institutions for organized scholarship programs. Education is generally geared toward the education of health care professionals.

4. Grants for annual operating budgets or for deficit financing are not favored.

5. Disbursements are normally not made to "Private Foundations", as defined in the Internal Revenue Code.

6. The Trust will not support efforts to influence legislation or other political action.

7. In considering projects or programs involving substantial funds, the Trust prefers to participate with other donors and expects the applicant to seek additional support.

8. Research involving human subjects, animals, or recombinant DNA must be approved by the appropriate institutional review board (IRB/IACUC/IBC). Investigators are encouraged to have this approval in process or completed at the time of application. Note that no funds will be distributed until IRB/IACUC/IBC approval is obtained. Although awards are made, the actual spending only commences upon approval of the relevant institutional review board (IRB/IACUC/IBC).

9. Funds cannot be used for any overhead or indirect expenses associated with the research project.

Preference is given to projects or proposals where the researcher/investigator is newly embarking on their research career and is clearly supported by their respective mentor(s).

Submission Procedures
Requests for information and applications for grants from the **Collins Medical Trust** should be presented in writing. Applications should include an Executive Summary suitably brief to present the necessary facts about the applying organization and the project for which the grant is being sought, supported by sufficient technical detail to present a clear picture of the project and expected outcomes. Project outcomes should be clearly articulated, along with an evaluation plan that will determine how successful the project was in attaining its objectives. Plans for subsequent grant applications for future grants should be stated, and the mentor's support to the project should be spelled out.

The application should include (If the Trustees believe further information is required, they may request an interview with a principal of the applicant and/or a visit to the applicant's facility):

1. The exact name of the organization or agency making application, and the specific date when requested funds will be required.

2. A copy of the letter from the Treasury Department of the United States which grants tax exempt status; also a statement that the applicant is classified as "Not a Private Foundation", as defined in the Internal Revenue Code.

3. The nature of the project for which funds are requested. Projects seeking funding for symposiums, seminars or conferences should contain details regarding course evaluations.

4. Curriculum vitae of the investigator(s). NIH format is preferred.

5. Junior investigators should identify and provide evidence of an established mentor relationship as well as submit a letter of support from their primary mentor(s).

6. MD's should substantiate 'protected' time for research.

7. Bibliography supporting the project.

8. Include the status of approval from the appropriate institutional review board (IRB/IACUC/IBC) for research involving human subjects, animals or recombinant DNA.

9. A budget for the proposed project.

10. Estimated total of funds required for the proposed project and the amount sought from the **Collins Medical Trust**. Should not include indirect or overhead expenses.

11. Anticipated source of balance required in excess of funds requested from the **Collins Medical Trust**.

12. Other sources being approached for financial assistance for the project.

Electronic submission (preferred): via email to CMT@collinsmedicaltrust.org
(.pdf format preferred).

Hard copy submission: Submit the *original and 1 photocopy* of the proposal (including any supporting documentation). Mail to:

Shannon Osieczanek, Administrator
Collins Medical Trust
29100 S.W. Town Center Loop, Suite 300
Wilsonville, OR 97070
(503) 826-5230
CMT@collinsmedicaltrust.org
http://www.collinsmedicaltrust.org/

Replies to Applications
The Trustees meet *three times a year*, in January, May and September. Requests should be submitted by the *last business day of the month preceding* these months to receive timely consideration. It is not possible to react to emergency requests for crash programs. When an application has finally been acted upon by the Trustees, it will be accepted or rejected in writing sent to the mailing address of the applicant by the first week in the following month.

Reports
The organization receiving a grant from the **Collins Medical Trust** has a responsibility to report on the use of the funds granted. Unless otherwise indicated at the time disbursement is made, reports are requested to be made annually until a year after the project has been completed. These reports should cover not only progress, but also evaluate the results being achieved. Additionally, throughout the duration of the project, any substantial changes in scope, personnel, or funds that are re-directed from the original purpose, should be reported to the Administrator of the Collins Medical Trust for approval by the Trustees at their next regularly scheduled meeting. Lastly, the Collins Medical Trust expects acknowledgment, primarily in scientific publications, for their contribution in support of the project.

Trustee Biographies

Walter J. McDonald, M.D., M.A.C.P.

Walter received his undergraduate education at Williams College and his MD degree at the University of Michigan. Following a residency in internal medicine at Oregon Health Sciences University, he returned to Michigan for training in Endocrinology. He is certified in both internal medicine and endocrinology.

Walter was the Chief of Medicine at the Portland Oregon VA Medical Center for 12 years beginning in 1979. He then assumed the role of Associate Dean for Education at the Oregon Health Sciences University. In 1995 he became the CEO of the American College of Physicians. In 2002 he assumed the role of CEO of the Council of Medical Specialty Societies, a position he held until 2008. Walter is the vice president for QHC Advisory, a consulting firm based in New York.

He is a member of Alpha Omega Alpha and has been elected as a Master of the ACP. He has been recognized by Oregon Health Sciences University as Alumnus of the Year (1998) and has been recognized by a number of organizations for both his teaching and leadership skills.

His primary interests include quality improvement, continuing and graduate medical education, and professionalism.

Elizabeth Eckstrom, M.D., M.P.H.

Elizabeth is a geriatrician who specializes in promoting a healthy lifestyle in older adults and in educating all health professionals to be competent in the care of older adults. She is Professor of Medicine and Chief of Geriatrics in the Division of General Internal Medicine & Geriatrics at Oregon Health & Science University in Portland, Oregon. She Co-Directs OHSU's Healthy Aging Alliance.

Her research has focused on interprofessional education, tai chi to improve health in older adults, and fall prevention. She also studies the effectiveness of training primary care faculty in geriatrics, and speaks regionally and nationally on strategies to optimally care for older patients in primary care practice.

Personal interests include travel, windsurfing, telemark skiing, gardening, and piano.

Virginia Tilden, Ph.D., R.N., F.A.A.N.

Virginia is Professor and Senior Associate Dean for Research in the School of Nursing at OHSU. She earned her undergraduate degree in nursing from Georgetown University and her master's and PhD degrees from the University of California San Francisco. Her postdoctoral certificate in Clinical Bioethics is from the University of Washington School of Medicine. She has been principle investigator of four large NIH-funded studies and PI or co-investigator of numerous foundation and professional organization research grants spanning a 35-year research career. She is the author or co-author of 104 scholarly publications primarily focused on improving end-of-life care and clinical teamwork. She is presently a funded investigator with two research teams: as a measurement specialist with the Program Evaluation Center with the VA's Centers of Excellence in Primary Care and as Co-PI of Reaching Rural Residents with IPE, funded by the National Center for Interprofessional Practice and Education. She has a track record of successfully initiating interprofessional education innovations over the last two decades in multiple faculty, associate dean, and dean roles. As Dean of the College of Nursing at the University of Nebraska Medical Center (2003–2011) she was instrumental in bringing UNMC into the invitation-only Health Professions Education Collaborative. To accelerate the national agenda on collaborative care, in the past five years she served on national advisory committees to advance team-based care, care transitions, primary care transformation, and teaching in patient centered medical homes; this service has been to the American Board of Internal Medicine Foundation, the American College of Physicians, Primary Care Progress, the American Academy of Nursing, and the Society for General Internal Medicine.

Truman W. Collins, Jr.
Truman is the son of the founder of the Collins Medical Trust (Truman W. Collins, Sr.), and has been a trustee since 1990. Truman earned his undergraduate degree from Willamette University in 1986 and his Master's degree in Computer Science from Stanford University in 1987. He worked for 25 years as a software developer in the field of electronic design automation.

In addition to serving as Trustee of the Collins Medical Trust, Truman is the President of The Collins Foundation, and a board member of The Collins Companies. He serves as a trustee of Willamette University, and is a board member of Foundations for Better Oregon.

The cover photos were provided by Penelope Hogarth, M.D. from OHSU from the "OHSU and OSU Partnering in Portland for Rare Diseases" research project that we funded in 2017.