Application for Institute Status

The Vision Institute
Randall J. Olson, MD
Director

Request (section 1)

The leadership team of the John A. Moran Eye Center requests the establishment of the Vision Institute (VI). This proposal is a result of the growing realization that seemingly disparate diseases share common etiologies and thus, the study of disease diagnostics and therapeutics must combine the expertise of multiple disciplines and clinical groups. The establishment of the VI will allow the broadening of the JMEC mission beyond ophthalmology, and into the arena of translational medicine. The VI will embrace a multidisciplinary, multi-department approach to the study of diseases focusing on immune system dysregulation and vascular diseases and will serve as an additional campus wide resource for the exploration of translational medicine.

Forming the VI will include establishment of the Moran Center for Translational Medicine (MCTM). The goal of the proposed MCTM would be the acceleration of the translation of basic scientific discoveries to clinically effective diagnostics and therapies for the treatment of devastating eye disorders such as age-related macular degeneration and glaucoma, as well as other diseases with shared etiologies. The MCTM will house a clinically-based research effort combining clinical observation/phenotyping and the collective strengths and expertise of an interdisciplinary, collaborative team of cell biologists, molecular immunologists, geneticists, microbiologists, pathologists to create new diagnostics and therapeutics, primarily focused on immunologic and vascular dysfunction mechanisms common to many progressive diseases. The unique resources, clinical acumen and scientific expertise of the MCTM will complement the core competencies of collaborating corporate and academic partners to insure its success. In establishing the MCTM the VI would combine the motivation of the Moran Eye Center and expand it beyond ophthalmology creating a new mission focused on learning in the clinic and using that knowledge to guide research in creating new diagnostic tools and treatments in diseases that share etiologies with common ocular diseases.

The proposed Vision Institute Mission Statement:

The John Moran Institute at the University of Utah is dedicated to serving our patients and the greater public health community by creating a broad-based organization focused on clinical care, care-giver education, and basic and translational research. Using a multidisciplinary approach we encourage learning from our patients and using that knowledge to create effective educational and research programs with the goal of creating new, widely available treatments for diseases shared by our patients and the global health community.
A Brief History of the John A. Moran Eye Center

Evolving from a surgical division in 1979 and a department in the School of Medicine in 1981, the John A. Moran Eye Center opened in July 1993, marking the beginning of a new era for the patients and patrons of the University of Utah Department of Ophthalmology and Visual Sciences. In 1993, the Center included three fully equipped operating rooms, a clinical floor with 25 exam rooms, minor procedure rooms, laser suites, a pharmacy, and the Utah Lions Eye Bank. Specialties included cornea and external eye disease, ophthalmic plastic and reconstructive surgery, refractive surgery, glaucoma, cataract, neuro-ophthalmology, pediatric ophthalmology, macular disease, vitreoretinal disease, uveitis and ocular infections, immunologic disease, and contact lenses.

In 2005 the new John A. Moran Eye Center was designed and built based on input from focus groups consisting of individuals with varying levels of sight abilities. It is now home to more than 450 faculty, staff and students, including one of the top retinal research teams in the world and boasts among its accomplishments:

- Faculty involved in more than 30 active clinical trials, compared to three in 1993. These studies involve more than 2,700 clinical visits each year.
- Annual research grants from the National Institutes of Health exceeding $6.5 million dollars, placing the Center 6th in the nation.
- A graduate physician training program that has been ranked among the top 10 residency programs in the country.
- The Utah Lions Eye Bank, which provides donor tissue for vision-restoring corneal transplants to more than 500 recipients in Utah and around the U.S. every year.
- Private funding, by patient care and research grants, requiring less than 1 percent of the center's budget from the State of Utah.
- 11 satellite clinics that host more than 120,000 clinic visits each year.
- Surgeons that perform more than 6,500 surgical procedures annually.
- More than 150 articles published annually in a wide variety of different medical and research publications.
- One of the top ophthalmology training centers in North America receiving over 300 applications from top medical graduate students for only three residency positions.
- More than 15,000 free eye screenings throughout the Wasatch Front.
- “The Highest Patient Satisfaction” award from University of Utah Health Care. This is the highest of 33 clinics specialty clinics. The Moran Eye Center scored in the top 90th percentile nationally for treating our patients extraordinarily well.

Individually, our faculty and staff have received numerous awards and honors including:

- Utah State Ophthalmology President for 2009
- President, American Society of Cataract and Refractive Surgery
- Outstanding Humanitarian Service Award by the American Academy of Ophthalmology (AAO)
- Distinguished Service Award of the North American Neuro-Ophthalmology Society (NANOS.) This is the highest award offered by NANOS.
- President of The Ophthalmic Photographers’ Society (OPS).
- Distinguished Alumni Award, University of Utah, School of Medicine
- Dala Lama’s Unsung Heroes of Compassion Award
- Guinness Book of World Records - Youngest Physician
- (2) Utah Governor’s Medal for Science and Technology
- 100 - 100 Top Entrepreneurs in Utah
- Stoel-Rives Utah Innovation Award (both finalists and winners)

An Expanding Mission

In 2010, the JMEC is focusing on the future. Our research and clinical findings and those of others worldwide has shown that many of the most serious blinding diseases, age-related macular degeneration, geographic atrophy, glaucoma, and others are often accompanied by a distinct set of comorbidities. Genetic analyses of the various diseases and their respective comorbidities also point to diseases of the eye being systemic in nature rather than limited to the ocular tissues. To understand these diseases our research and clinical missions must expand and reach out to a variety of other research disciplines and clinical specialties. It is with this new mindset that we request establishment of the Vision Institute and the Moran Center for Translational Medicine.

In its initial instantiation the VI will encompass two unique centers and their activities:

1. **The John Moran Eye Center (JMEC)**
   Under the direction of Chairman Randy Olson, Medical Director Norm Zabriskie, Research Director Robert Marc, and Clinical Research Director Paul Bernstien the JMEC will continue its focus on Clinical Ophthalmology, Education in Clinical Ophthalmology, Clinical Research in Vision Sciences, Basic Research in Vision Sciences, and training in the area of Vision Sciences research.

2. **The Moran Center for Translational Medicine (MCTM)**
   The MCTM will focus on research toward the creation of therapeutic targets for diseases that share small vessel and immune system etiologies. The MCTM will be intrinsically multi-disciplinary and encompass clinical phenotyping, systems biology analysis, statistics, and genetics. The broadening of mission that the addition of the MCTM represents is significant in bringing multiple disciplines together to study disease and potential diagnostics and therapeutics. The overarching leadership will embrace the idea of translational medicine. Where clinical findings heavily influence basic and translational research, in turn providing new therapies, treatments, procedures, and even preventative strategies improving patient care and patient’s lives. The Director’s Council (illustrated in
The above organizational chart represents the mixing of research and clinic at the leadership level with the VI Director, JMEC Medical Director, JMEC Research Director, JMEC Clinical Research Director, and MCTM Director all sitting on the panel - a mix of clinicians and researchers directing the VI.

Need (section II)

Translational Medicine Requires a Multidisciplinary Approach

A common goal of biomedical research, whether in ophthalmology, radiology, oncology or any other area of clinical activity, is the actualization of significant impact of its research discoveries. In translational medicine this is generally conceived as clinical impact. With this goal in mind, it will be important to focus on all aspects of translational research including: 1) Discovery; 2) Laboratory Testing; 3) Clinical Testing; and
4) **Translation into the Market and Clinic.** As simple as these four steps may seem, assembling individuals and teams that hold expertise in each area is complex. Often, experts in Discovery are different than experts in Laboratory Testing and this is true for every step in the translational chain.

Thus, primary needs in actualizing translational medicine include assembling a collaborative group of experts with a shared goal and providing the group with resources to accomplish that shared goal. Resources are often conceived as material in nature (e.g. personnel, supplies and equipment). Translational medicine certainly requires the typical resources, but the needs also extend into “atypical” resources such as expertise in intellectual property, corporate partnering, regulatory compliance, marketing, and finance. Thus, an institute committed to expanding its mission to include translational medicine must provide an environment that reaches out to atypical communities, at least for a university entity. Following this thought, a multidisciplinary team takes on an expanded meaning, not only including scientific and medical disciplines such as genetics, molecular biology, and cardiovascular but also including disciplines in regulatory navigation, research ethics, intellectual property, finance, etc.... The need is for cross-campus interactions, from the school of medicine to the business school, and collaborations that extend outside the University and include other academic institutions and corporate partners. The VI would be an institute built specifically with the idea of fostering these types of collaborations.

**Building an Awareness of Translation Medicine**

While generally recognized as one of the most efficient methods of building large, complex projects, team-based science is difficult to organize. There is a need for ongoing training, discussion, and “brainstorming” on the emerging field of translational medicine and, in general, team-based science. As with the actual work of translational medicine, the training and discussion of translational medicine also requires engaging individuals with diverse expertise ranging from University scientists to administration. Training must include bringing the next generation of scientists, clinicians, and other experts into the fold of translational medicine or more broadly team-based science. There is a need on campus for the assembly of groups that heighten the general community awareness around translational medicine and can also serve as general resources and champions in this area. Ultimately, research funding mechanisms and academic advancement concepts must also evolve rapidly to meet the objectives of translational research. While the central campus entity that focuses on the agenda of Clinical and Translational Science is the NIH-sponsored Center for Clinical and Translational Sciences (CTSS) which works in the border area of building on the University's strengths in genetics and bioinformatics to translate promising bench science into practices that improve human health. The MCTM would look to partnering with the CTSS and its other partners in increasing the visibility, volume, and quality of participatory research by focusing on the study of the common etiologies of eye disease and other diseases involving the immune and vascular systems. Essentially, the MCTM would serve as a node in the translational science network at the University.

**Institutional Impact (section III)**

**John A. Moran Eye Center at the Crossroads**

The John A. Moran Eye Center at the University of Utah has accomplished a series of important milestones that positions it for expansion into a strong translational research institute. The Center is in a solid position to make significant contributions due to its extensive resources; expertise in genetics, molecular biology, morphology, biochemistry, cell physiology, and pathobiology; its extraordinary sample collection, which numbers over 4,000 samples; and its demonstrated leadership in the diagnosis and treatment of ocular disease. This unique combination of resources, knowledge, talent and a desire of the faculty and staff to
work as a team represents an unprecedented opportunity for the Center to expand its mission and undertake a mission directed towards elucidating the biology of disease, identifying key pathways that lead to human disease and devising pharmaceutical strategies for the diagnosis and treatment of these devastating conditions.

We are fortunate to have a marvelous facility with over 100,000 square feet (sf) dedicated to research. This 210,000 sf facility includes clinical care, eye banking, education, as well as all elements of a first-class research facility. As evidence for the quality of the facility, the University of Melbourne in Australia, in reviewing changes for their own facility, sent a crew of architects and clinicians to all the major centers in the world and notified us that they had concluded the John A. Moran Eye Center was the best thought out, laid out, as well as the most functional facility, that they had a chance to review in their international travels. This is a huge asset.

We are also blessed with an expanding, talented and collaborative research faculty. We have superb leadership and staff dedicated to the expanded mission that would be formed with the establishment of the VI. Critically, we have a mix of researchers including several holding both MD’s and PhD’s, with a foot in both the clinical and research camps, such as Drs. Paul Bernstein (Director of Clinical Research), Bradley Katz, and Bala Ambati, as well as internationally recognized researchers and endowed Professors such as Dr. Robert Marc, Director of Research, Dr. Wolfgang Baehr, and Dr. Gregory Hageman, who would serve as the Director of the Center for Translation Medicine. We have a very active experimental pathology group under the able leadership of Dr. Nick Mamalis. Dr. Randall Olson would lead the VI and Mr. Wayne Imbrescia serve as our administrative lead. The team’s combined expertise in operations, entrepreneurial activity and great vision will chart our path forward.

With all of these elements in place, there is also an entrepreneurial spirit and a desire to exploit synergies. There is a palpable enthusiasm and excitement about the potential future of the VI.

The initial membership of the VI would be the faculty of the Department of Ophthalmology and Vision Sciences:

- Balamurali Ambati
- Alessandra Angeluci
- Wolfgang Baehr
- Paul Bernstein
- Meg Deangelis
- Jeanne Frederick
- Yingbin Fu
- Sabine Fuhrmann
- Gregory Hageman
- Mary Elizabeth Hartnett
- Bryan Jones
- Brad Katz
- David Krizaj
- Edward Levine
- Nick Mamalis
- Robert Marc
- Ning Tian
- Liliana Werner
- Jun Yang

Additionally faculty with other home departments would be offered positions within the VI structure based on the mission and collaborative community of the VI being an enabling factor in that faculty member’s work.

**Impact Across Campus**

*Campus-Wide Collaboration*

As the VI forms we will seek a variety of collaborations across the campus. In fact, many Moran Eye Center-campus collaborations exist today. An example of the type of collaborations we envision in the VI is
the recent high-throughput transmission electron microscopy collaboration between Dr. Robert Marc's laboratory and the groups of Drs. Tolga Tasdizen and Ross Whitaker at the Scientific Computing and Imaging (SCI) Institute. From slow, manual exploration and image capture (typically 10-50 images/day), we now have the ability to automatically collect 5,000 micrographs per day, seven days a week, in which all distortion is computationally compensated and 3-dimensional images volumes automatically assembled. In addition, the data is electronically archived. This allows new computational correlations between research and clinical specimens, which could only have been dreamed of even a few years ago. This is an example of what can happen when multidisciplinary teams work together on complex issues. The software and data generated by this collaboration are being used nationwide (Stanford, UC Santa Barbara, UC Davis, U Texas / Houston, and others) and is being discussed with an industry partner. This work has resulted in both grant applications or grant awards in departments ranging from the Departments of Biology and Electrical and Computer Engineering to the Brain Institute. Additionally, the collaboration has also aided in generating a new class offering in microscopy that is cross-listed with both the Department of Biology and the School of Computing.

The VI, via the Center for Translation Medicine will also pursue and foster collaborations focused on translation of the research into the marketplace. In this area we have had a number of successful collaborations and have recently formed several potential high impact projects. Examples of collaborations based on the translational mission include a collaboration that was formed after a chance meeting in 1996 between newly arrived Moran faculty member Paul Bernstein, MD, PhD and members of the University of Utah physics department. Dr. Bernstein and Professor Werner Gellermann realized that resonance Raman spectroscopy could be used in a novel manner to assess nutritional status in the living human retina by measuring the amounts of the carotenoids lutein and zeaxanthin in the macula. This technology has been successfully used in eye research projects around the world, and has resulted in numerous grants, patents, and publications. In the early stages of the project, one of Dr. Bernstein's laboratory technicians noted that when he put his hand in the path of the eye instrument's laser, he could also quantify the carotenoid levels in his skin. This skin Raman technology was patented and licensed to NuSkin/Pharmanex who developed the BioPhotonic Scanner as a marketing tool for its multi-level marketing vitamin distributors. Over 15,000 units are currently in use worldwide, yielding millions of dollars of royalties to the University of Utah and recent induction to the Technology Commercialization Office’s Hall of Fame.

An example of new collaboration that has significant potential of finding a place in the market is a technique known as Computational Molecular Phenotyping. This work is being moved toward commercialization in the area of drug discovery. The plan for going forward was developed through a collaboration with a student team from the Pierre and Claudette MacKay Lassonde New Venture Development Center. This work provides a unique educational experience in new business development of the students and has resulted in a business plan that the students have used to compete in several national business competitions. Additionally, this work is the recipient of a 2010 Stoel-Rives Utah Innovation Award.

Another example of translational collaborations that would be fostered by the VI is that between the laboratories of Drs. Bala Ambati and Bruce Gale (Mechanical Engineering), which has potential for a large clinical impact. Using his clinical experience in cataract surgery and his research experience in neovascularization of the cornea, Dr. Ambati initiated a collaboration with the Center for Biomedical Microfluidics (led by Dr. Gale) to develop a validated prototype drug delivery device that would alleviate the need for monthly injections into the eyes of patients suffering from macular degeneration. This device has been introduced to the FDA via a pre-IND meeting and the Ambati laboratory is currently preparing an
investigational new drug (IND) application that would allow the device to be introduced into phase I clinical trials.

This collaboration has gained recognition as a new State of Utah Center of Excellence and is the foundation of a new company, iVeena, that was awarded as a finalist in the 2010 Stoel-Rives Utah Innovation Award Program.

Ongoing interdepartmental collaborations include the Departments of Human Genetics (Hageman/Leppert); Neurobiology and Anatomy (Krizaj/Vetter); Physics (Bernstein/Gellermann); Biochemistry (Baehr/Hill); Mechanical Engineering (Ambati/Gale); Obstetrics and Gynecology (Hageman/Varner); and the SCI Institute (Marc/Tadizen/Whitaker).

These limited examples show the impact of the expanding mission of the JMEC. With the establishment of the VI the mission will be formalized and accelerated. We envision impact to be campus wide with example interactions shown in the accompanying graph.

**Educational Impact**

*An Expanded Educational Mission*

The JMEC has always had a strong educational component that is well represented in both the clinical and research areas. In regards to training, the JMEC boasts a graduate physician training program that is consistently ranked in the top 10 residency programs in the country. The fellows program at JMEC is also a consistent high performer and nationally recognized. On the research side, JMEC trains over 15 graduate students from a variety of departments and programs including molecular biology, neuroscience and computer science. Additionally, the JMEC has a number of undergraduates serving roles throughout its laboratories including Ms. Heather Fillerup, a member of the Fu laboratory and recipient of a 2010 NIH/NIDDK Step-up program undergraduate participation grant.

Expansion of our mission as the JMI would also expand our educational mission. Keeping in mind the campus-wide need for the assembly of groups that heighten the general community awareness around translational medicine the JMI will establish, in collaboration with groups such as the Technology Commercialization Office, Eccles School of Business, CTSA, and other relevant groups, a seminar series on translational medicine and best practices on moving basic research to the clinic. It is expected that as we pull collaborations together that we, with our partners, will discovery a variety of educational opportunities to train both the new scientists and clinicians and also the established scientists and clinicians.

In addition, as the VI we will look toward the potential of partnering with groups such as genetics, internal medicine, and computer science to create granted training programs for the next generation of scientists and clinicians. These training programs would be at the graduate, post-doctoral, and fellow levels and focused on clinical findings influencing basic research direction and research both basic and clinical influencing the standard of clinical care.
The collaborative graph: This graph shows a subset of the areas of collaboration envisioned as part of the VI. Areas of collaboration are associated with various departments and outside partners that would be involved in the collaborations.
**Current Funding:** The JMEC is funded using a five-pronged strategy of clinical revenue; federal funding; private foundation funding, corporate research, and benefactor funding. JMEC also receives a limited part of its funding from the State of Utah (less than 2% of the total budget). This model has shown success in the past as the operational research budget has seen steady growth and projections show continued financial success, for instance the research budget shown in the table shows both historical growth and projected growth.

**Future Funding - Success Breeds Success...**

The VI would follow the same funding strategy with a soon to be announced partnership with a large pharmaceutical partner being an example of the corporate funding possible in translational medicine. This partnership will bring in roughly $800K per year in research and $400K in indirect funding. In addition to creation of a marketable therapeutic, success in this partnership would result in meaningful revenues for several years via both milestone payments and royalties. In addition to corporate partnerships, the VI will pursue moving technology and discovery to the market via licensing and new company spin-outs. Examples are PerfectVision, FlickerFusion, iVeena, LLC and Metaboview, Moran spin-offs that are aggressively moving Moran technology to the market. State funding, which makes up roughly 2% of the Moran Eye Center will continue to directly fund the Moran Eye Center.

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**Budget and 5-Year Comparison for JMEC Research**

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