Slide 1: 2010 sees the Moran Eye Center at its most mature, with its highest faculty count, publication rate and federal funding rate. With its largest number of faculty innovations and strongest position for the future of vision research. Traditionally, National Eye Institute targeting policies drives funding. JMEC researchers define those targets ... rather than chase them. (25 sec)
Our research operations address the fundamental mechanisms of ocular disease. The most challenging forms of blindness attack three systems in the signal transmission train: (1) the primary and irreplaceable optic element of the eye ... the cornea; (2) the most complex neural tissue known ... the retina ... and its obligate partner the retinal pigmented epithelium; (3) and the optic projections to the CNS. Corneal disease, vasculopathies, RP, AMD, glaucoma, and other pathologies are a spectrum of complex disorders. JMEC research touches on all these areas. (35 sec)
We have 16 major funded laboratories. Associate Professor Dr. Bala Ambati is the world’s leading expert on the control of vascular growth, especially but not exclusively in cornea, and is developing both molecular tools to regulate vascular pathologies and new drug delivery systems for the eye. He holds two NIH grants. (20 sec)
Wolfgang Baehr is the Ralph and Mary Tuck Professor of Ophthalmology and one of the world’s most renowned molecular biologists. He is exploring the mechanisms of protein trafficking in photoreceptor cells. He is our most prolific mentor, having produced 3 stellar PhD students in two years, and our most prolific scientific author. He holds 2 NIH grants and co-directs the Biochemistry module of our vision core grant.

In collaboration with my lab and Bryan Jones, we are preparing a new gene therapy for autosomal dominant RP. (40 sec)
Usher syndrome is one of the most devastating forms of RP. Assistant Professor Jun Yang is one of our future hopes. She developed the most complete library of animal models for Usher Syndrome where genes interact to corrupt protein trafficking. She is designing viral vectors to reverse the defect.

(20 sec)
Research Assistant Professor Bryan W. Jones is another emerging talent, with funding from RPB and the Thome foundation to study the mechanisms of retinal remodeling in RP and AMD. His collaboration with Mineo Kondo of the University of Nagoya brought the world’s only rabbit model of adRP to the US. The Moran Eye Center is the only breeding facility for it outside Japan. He and Dr. Baehr are collaborating on an RNA-based gene therapy for adRP.
Mary Boesche Professor of Ophthalmology Paul Bernstein is a retinal surgeon and world class biochemist, focusing on the mechanisms of carotenoids in nutritional protection against oxidative stress leading to AMD. (15 sec)
Yingbin Fu is an Assistant Professor who has been developing mouse models of AMD. His most recent successes demonstrates a disease phenotype in mouse more like neovascular AMD than any other group has achieved. (15 sec)
Associate Professor Edward Levine’s NIH funded program is designed to discover how neural stem cells are programmed to become neurons. His most recent exciting findings include changing the proportions of different neuronal types with different combinations of genetic mutations. His goal is to find progenitor populations and molecular rules that can build a true retina.
Assistant Professor Sabine Fuhrmann just received one of the NIH top scores ever for her program to understand the genetic and molecular rules controlling how the RPE develops and is maintained. This is a critical step in the ultimate translational goal of being able to replace the RPE in retinal degenerations such as AMD and some forms of arRP. (25 sec)
Associate Professor Meg DeAngelis represents a new, and more mathematically robust way of mapping the interacting genes in various forms of AMD. Her recent work implicates an previously poorly understood retinoic acid signaling pathway in the cellular deconstructions that accompany AMD.

(20 sec)
John Moran Presidential Professor Gregory Hageman transformed the field of AMD research with his career of detailed and insightful anatomic, molecular and genetic analysis. He established that AMD is an inflammatory disease related to a large array of systemic disorders and will lead our Center for Translational Research on a mission to discover real therapeutics for AMD. (25 sec)
Professor Mary Elizabeth Hartnett is another one of our new researchers focussing on diseases resulting from disordered vascular development, such as retinopathy of prematurity and neovascular macular disease. She brings both expertise as an NIH investigator (with two grants) and as a pediatric retinal surgeon. (20 sec)
Associate Professor David Krizaj has discovered most of the molecular machinery associated with calcium signaling. Calcium fluxes are ionic events by which all cellular signaling is encoded. Calcium is also the key death molecules of cells. And calcium permeant channels, as shown by Dr. Krizaj, are clearly part of a multicellular mechanism that creates ganglion cell axon death in glaucoma. (30 sec)
My lab is all about how retinas are wired and get unwired in disease. Using NIH funding and a generous gift of a state-of-the-art transmission electron microscope from Marth Ann Healy, as well as extensive collaborations with the University of Utah Scientific Computing and Imaging institute, we have built the world’s first retinal connectome ... a volume of tissue containing images of all the retina’s connections. (30 sec)
Associate Professor Ning Tian was the first to show that retinal neurons wire and rewire after birth; after the retina has “developed”. He has recently shown that this rewiring depends on immune signaling pathways very similar to those discovered by Dr. Hageman. This has profound implications for being able to regenerate retinal networks after retinal degenerations. (25 sec)
With the work of Dr. Alessandra Angelucci, supported by NSF and NIH, we move to the challenging area of the organization of the visual cortex, where flows of information are multiplexed into different processing geometries: a true 3D computational system. She and her students have systematically changed the models of how cortex extracts “salient” information. (25 sec)
For many years Dr. Richard Normann has championed the idea that direct drive of cerebral cortex can lead to restoration of sensory and motor function. With his colleague Bradley Greger, they have continually refined the tools with which brain neurons can be both monitored and activated. While true vision is some ways off, it remains one of the biggest hopes for the profoundly blind for whom gene therapy cannot be considered. (30 sec)
No research program can function without students – the lead scientists of our near ... not distant future. In the past two years, the Baehr, Marc, Fuhrmann and Angelucci laboratories have produced highly talented PhD students. Peter Westenskow led the research discovering the control of RPE development in Sabine Fuhrmann’s lab. James Anderson in the Marc lab supervised the construction of the first retinal connectome and single-handedly developed a Google Earth-like tool called Viking to explore it. Postdoctoral fellows take on even more advanced projects and Moran Eye Center fellows have won numerous awards from Fight for Sight and Knights Templar, like Felix and Yanhua (who has 2 PhDs). (60 sec)
The Utah Retinal Connectome RC1

16.5 TB Raw, 50 TB total

The first 3D retinal volume

400,000 TEM images @ 5000/day

371 automosaics of > 1000 tiles each

Archetype for analysis of epilepsy, Alzheimer’s disease, RP & AMD

Wednesday, July 21, 2010

In competition with major labs at Harvard, Janelia Farm, Stanford and Max Planck in Germany, we achieved the first functional connectome assembly by teamwork, cooperation, open standards, good design and persistence. The 50 TB storage requirement is equal to a stack of 200 high-end laptops worth > $0.5 M. The volume contains of 400,000 images – 20 lifetimes worth of work for an electron microscopist. (30 sec)
This is the first time in history that such a dataset could be built. In 1985, when I started my computational lab, the dataset would have cost over $1.5B to store and display. And, at imaging rates prior to our new transmission electron microscope, the imaging work would have taken decades (24–7) and the analysis centuries. (20 sec)
Viking produces high density coded maps of all the real connections. This image displays a set of images that actually changes all of the existing models of how night vision systems operate. (15 sec)
Viking movie – narrated 3 min
The Utah retinal connectome shows how incomplete our existing ideas have been. One of the best mapped networks is the so-called AII cell system. This is its accepted wiring diagram. (15 sec)
This is its correct wiring diagram. The original model was so incomplete as to be meaningless. Connectomics will change all analysis of how retinas and brains work. We are now collaborating with the Capecchi laboratory to understand the wiring mechanisms of “obsessive–compulsive disorder” pathways in mouse brains. (15 sec)
Why is this level of detail important. This is an Intel I7 processor chip – with over 700,000,000 transistors. If 0.5% didn’t work, the system would fail. A 50% error in biological wiring models is worse than useless -- it is dangerous.
The John A. Moran Eye Center Research Profile

therapeutics

connectomics

translational science

Wednesday, July 21, 2010

The new John A. Moran Eye Center houses research programs directed to discovering gene–based, molecular, and cellular therapeutics for blinding diseases. It houses new research tools that will revolutionize neuroscience – like connectomics. And it is poised, by combining these skills with new ventures in translational medicine, led by Dr. Hageman, to identify new ways to prevent, ameliorate or correct debilitating diseases like AMD, heart disease and more. (30 sec)