VDI Vision

Georgia Health Sciences University

Vision Discovery Institute

HIGH IMPACT RESEARCH AND DISCOVERY RELATED TO VISUAL FUNCTION AND DISEASES...WITH FAR REACHING CLINICAL APPLICATIONS FOR PATIENTS SUFFERING FROM BLINDNESS AND VISUAL DISORDERS

SUMMER 2012

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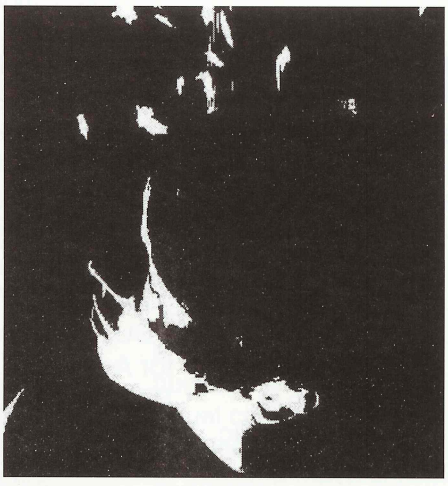
Romancing Vision, the 'Make-Do' Artist

Research into how we see is a wellspring of wonders great and small. One of the more slowly emerging surprises in the last decade or so, through the work of hordes of talented researchers around the world, has been the realization that we actually see more than we're given to see, even when our eyes are in perfectly good order. What makes this finding about healthy vision truly wondrous is that it is imbued with enormous future potential for rehabilitating vision when it is not in good working order.

We generally don't realize it, but the image of the outer world that forms on the retina is surprisingly noisy. Yet, the visual system accomplishes the magical feat of making sense of it all. For instance, can you see a face in the black-and-white picture below? It is probably rather hard to see anything in this picture, because there is so little to see. Perhaps your visual system needs a little help. Now look at the color picture on the back page of this newsletter. Can you see a face in the black-and-white picture now?



This illustrates both the formidable task the visual system is faced with, and how deftly it faces it. The image of the world that forms in the retina is unbelievably threadbare and ambiguous, much like this black-and-white picture. The visual system initially has trouble with this particular picture, because it doesn't quite know how to make sense of it. Once it learns how to make sense of it, though, the visual system is undaunted by the lack of information in this picture. Note also how little it takes for the visual system to catch on. The color picture is also quite hard to see, but the visual system already knows how to cope with this type of ambiguity. It uses these abilities to make sense of the color picture, and carries that information over to help itself make sense of the black-and white picture. Really, when you think about how much the visual system makes do with whatever little help it gets wherever it gets it, you just can't help falling madly in love with this little engine that could!

It is the aforementioned counterintuitive insight -- that the visual system has to make do with surprisingly little reliable information, and that the 'bag of tricks' it uses to make do with – that has radically reshaped how we think about the process of seeing.

But what is so clinically promising about all this? After all, the fact that the healthy visual system has very little to work with sounds like bad news, because it would mean that it has even less to work with when vision is impaired. But the promise lies in the fact that the visual system knows how to cope with such situations; it is a make-do artist with a bag of myriad tricks that it can bring to bear on the task. Sometimes, though, it needs a little help. In case of the black-and-white picture, for instance, it did better once it learned what it was supposed to look for. The 'trick', in this case, was to gain familiarity with a visual image. Thus, by understanding and augmenting the visual system's bag of tricks, researchers can use its innate ability to cope with impoverished incoming information to help it cope with even more impoverished information. Of course, this approach will not be a panacea for all visual ills. But given how fundamental the underlying coping mechanisms are to vision itself, this approach does open a promising new front in

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Romancing Vision

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our fight against visual impairments.

This is the focus of research in the laboratory of Jay Hegdé, an Assistant Professor in the Department of Ophthalmology, Vision Discovery Institute, and the Brain and Behavior Discovery Institute. His group uses a large variety of research methodologies to understand how the healthy visual system makes sense of information that comes in through the eyes and to use this toward developing new strategies for rehabilitating visual impairments.

To understand how the visual system manages ambiguous information, Dr. Hegdé tests how it reacts to cases of extreme ambiguity such as camouflage, where an object of interest is hidden in plain view. To recognize any object, camouflaged or otherwise, one has to separate it from its background. Finding your car keys on the coffee table, for instance, means you have to be able to distinguish them from everything else on the coffee table, not to mention from the coffee table itself. If there are hundreds of other irrelevant keys on the coffee table, the ambiguity of the scene greatly increases, and the visual system has to pull out all the stops to find the one key that matters. Camouflage is such an extreme case of ambiguity, as are the stakes of resolving the ambiguity. For example, in warfare, the ability to break enemy's camouflage can be a matter of life and death. Thus, this topic of research, with its aforementioned implications for understanding of vision and treatment of visual impairments, also has practical implications in other fields of human endeavor. Finding a tumor in a mammogram, for instance, involves processes that are very much like recognizing a camouflaged object. In recognition of these facts, this line of research in Dr. Hegdé's laboratory has received funding from the U.S. Army.

Another line of Dr. Hegdé's research that has received external funding, in this case from the National Science Foundation, is how we recognize an object when it is occluded, or blocked, from view by another object. This is another instance of underappreciated ambiguity that the visual system tackles in the visual world. But understanding how we recognize occluded objects also has clinical implications. A healthy person sees a complete, clear image. But in a person with macular degeneration, the same scene appears as though the portion of the image where the eyes are gazing is blocked. Thus, it should be possible, in principle, to coax the visual system to bring to bear its mechanisms of coping with blocked objects to cope with the 'blocking' that results from macular degeneration.

Dr. Hegdé's laboratory has also recently started another line of research to study visual function directly in patients with macular degeneration. The goal of this project is to understand which 3-D vision visual faculties, especially the ones we use for walking, driving, reading and reaching, are relatively spared in macular degeneration, so that such spared faculties can be used to help rehabilitate patients in the future.

More information about Dr. Hegdé's research can be found on his laboratory's website at www.hegde.us.

Awards and Recognitions

The following won Travel Awards to attend the Association for Research in Vision and Ophthalmology (ARVO) meeting held in Ft. Lauderdale, FL, May 6-10, 2012:

- Priya Narayanan, Ph.D. from the lab of Dr. Ruth Caldwell. Dr. Narayanan presented *"Arginase 2 Deficiency Reduces Hyperoxia-induced Retinal Neurodegeneration through the Regulation of Polyamine Metabolism."*
- Wen Chen, Wuhan Student in the lab of Dr. Sally Atherton. Ms. Chen presented *"Apoptosis and Expression of Antiviral Response Genes during Ocular HSV-1 Infection in TNFR1 or TNFR2 Knockout Mice."*
- Karishma Choksi, Graduate Student in the lab of Dr. Mohamed Al-Shabrawey. Ms. Choksi's presentation was titled *"Interrelation between NADPH Oxidase and BMP2/SMAD Pathway in Diabetic Retinopathy."*
- Barbara Mysona, Ph.D. from the lab of Dr. Azza El-Remessy. *Dr. Mysona's presentation was "Inflammatory Role of ProNGF/p75NTR in Müller cells of the Diabetic Retina."*

Graduate Student Folami Lamoke from Dr. Manuela Bartoli's lab has received the 2012/UNCF/Merck Graduate Science Research Dissertation Fellowship.

Graduate Student Steven Walker from Dr. Jeffrey Mumm's lab has been awarded the Kirschstein NRSA Fellowship award from the National Institutes of Health (NIH). His project is titled *"Genetic Circuitry of Cell-specific Retinal Neuron Regeneration."*

Dr. Azza El-Remessy, Associate Professor, Program in Clinical and Experimental Therapeutics, University of Georgia College of Pharmacy (Augusta) and Adjunct Assistant Professor of Pharmacology and Toxicology, Graduate Studies and Ophthalmology and a member of the VDI has received an RO1 grant for a 5 year period from the National Eye Institute (NEI).She is an expert in the area of diabetic retinopathy and optic neuropathy with a special emphasis in studies of angiogenesis and retinal inflammation and how it culminates in cell death. Her studies have particular relevance to the retinal diseases diabetic retinopathy`, retinopathy of prematurity and glaucoma. Her work for the RO1 is entitled *"Molecular Mechanisms of Diabetic Retinopathy."* Diabetic retinopathy (DR), the leading cause of blindness in working age adults in the US, is characterized by neurodegeneration, glial reactivity, inflammation and acellular capillary formation that eventually lead to retinal neovascularization and blindness. Given the limited and invasive treatments available only for advanced stages of DR, there is a great need to identify novel molecular targets for earlier therapeutic intervention. Her long-term goal is to identify targets by probing relationships between glial inflammation and vascular injury. She hopes to understand how disruption of nerve growth factor (NGF) homeostasis in diabetes can lead to accumulation of its precursor proNGF and upregulation of the death receptor $p75^{NTR}$, leading to vascular injury. She hypothesizes that the diabetes-upregulated proNGF/$p75^{NTR}$ axis causes acellular capillary formation via direct activation of the apoptotic JNK pathway in endothelial cells that is sustained by paracrine release of proNGF in Muller cells.

To test her hypothesis, Dr. El-Remessy will determine whether diabetes-induced proNGF/$p75^{NTR}$ causes retinal acellular capillaries, whether cleavage of $p75^{NTR}$ release ICD is essential to activate JNK endothelial cells, and whether $p75^{NTR}$ is required for sustained release of proNG and vascular injury.

Recent Graduate

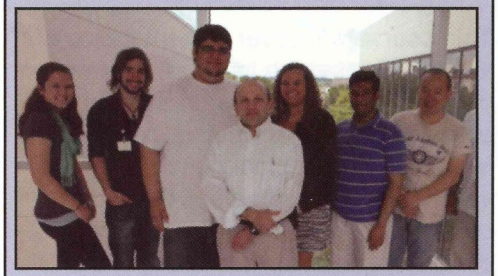
The Departmer of Cellular Biology and Dr. Jeffrey Mumm wish to announce the recent graduation of Junko Ariga, Ph.D. The title of her dissertation was *"Cellular and Molecular Mechanisms of Retinal Bipolar Cell Regeneration in Zebrafish."* Our congratulations to D Ariga!

Emerging Scientist Award

Dr. Jay Hegdé has been honored for his work and has received the **MCGRI Emerging Scientist Award.** This award was presented at the GHSU faculty senate meeting on May 3, 2012.

The award recognizes Dr. Hegdé's multidisciplinary, innovative research program with a clinical focus to study the neural mechanisms of visual function and dysfunction, and to develop rehabilitative treatments for visual impairments.

Dr. Hegdé is also the recipient of a 4 year grant award from the National Science Foundation (NSF). Dr. Hegdé's work is entitled*" Recognition of Occluded Objects as Statistical Inference: A Neurophysiological Study in Awake, Behaving Monkeys."*



Dr. Hedgé and lab members