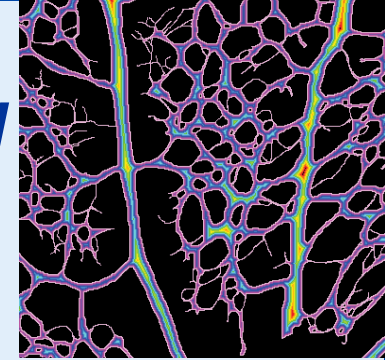


## *Innovative Research & Discovery Tool*

# NASA's VESsel GENeration Analysis (VESGEN) Software



Human Retina

Mouse Retina

## **Vascular Patterning Analysis by VESGEN 2D/3D with Bioinformatics: Updates for Rodent Tissues**

P. Parsons-Wingerter<sup>1</sup>, D. Kao<sup>1</sup>, H. Valizadegan<sup>2</sup>, R. Martin<sup>1</sup>, M.B. Vickerman<sup>3</sup>, M.C. Murray<sup>4</sup>, S. Ramesh<sup>4</sup>, S. Sekaran<sup>4</sup>, E. Ma<sup>4</sup>, A. Adranly<sup>4</sup>, V. Reffato<sup>5</sup>, C. Theriot<sup>5</sup>, S.B. Zanello<sup>6</sup>, X.M. Mao<sup>7</sup>, H.C. Reinecker<sup>8</sup>

<sup>1</sup> NASA Ames Research Center, Mountain View, CA <sup>2</sup>University Space Research Association, NASA Ames Research Center, Mountain View, CA <sup>3</sup> NASA Glenn Research Center, Cleveland, OH <sup>4</sup>Blue Marble Space Institute, NASA Ames Research Center, Mountain View, CA <sup>5</sup>University of Texas Medical Branch, Galveston, TX <sup>6</sup>[University Space Research Association, NASA Johnson Space Center, Houston, TX](#) <sup>7</sup>School of Medicine, Loma Linda University, Loma Linda, CA <sup>8</sup>Gastrointestinal Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA

VESGEN Patent Pending



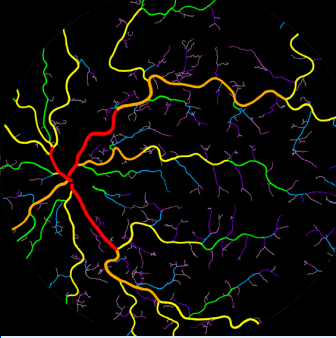
Space  
Biosciences  
NASA AMES RESEARCH CENTER



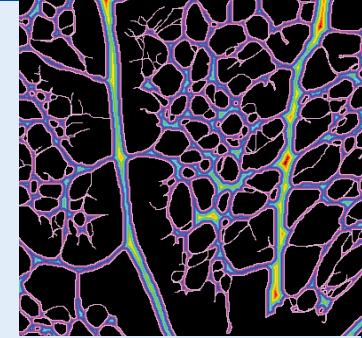
A photograph of an astronaut in a white spacesuit floating in space. The astronaut is wearing a helmet with a communication device and is holding a small white card with a black triangle on it. The background shows the curved horizon of Earth and a bright sun with a starburst effect.

## NASA's VESGEN Vascular Analysis

- Astronaut health risks
- Terrestrial medicine
- Rodent and other vertebrate vascular studies



Human Retina



Mouse Retina

# VESGEN

## Translational Mapping and Quantification of Fractal-Based Vascular Pattern

### Vascular Trees

Human Retinal Disease, Mouse/Avian Coronary Vessels, CAM, Yolksac

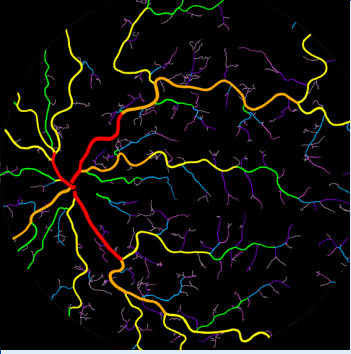
### Vascular Networks

Mouse Intestinal Inflammation, CAM Lymphatic Vessels, Abnormal Mouse Corneal Angiogenesis, Drosophila (Fruitfly) Wing

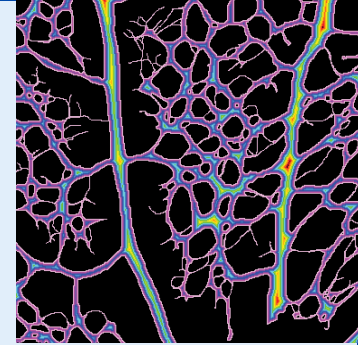
### Vascular Tree-Network Composites

Mouse Postnatal Retina, Early Embryonic Coronary Vessels, Arabidopsis Leaf Venation





Space  
Biosciences  
NASA AMES RESEARCH CENTER



# Vascular Mapping Analysis

Human Retina

Mouse Retina

## Long-Term Research Hypothesis

‘Fingerprint’ vascular patterns offer integrative read-outs of dominant molecular signaling pathways important for astronaut, terrestrial health

## Vascular Physiological Branching Rules

Vascular fluid mechanics, molecular/cell biology (angiogenesis), experimental observations

## Mapping and Quantification by Multiparametric Weighted Analysis

Fractal Dimension,  $D_f$

Vessel Number Density,  $N_v$

Vessel Length Density,  $L_v$

Vessel Diameter,  $D_v$

Branchpoint + Endpoint Densities,  $Br_v + E_v$



# Vascular Patterning Research

Biomedical Translation from Experimental Models to Terrestrial Human and Astronaut Studies



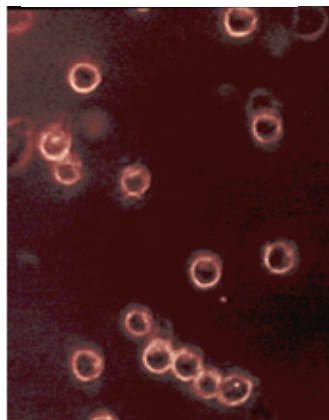
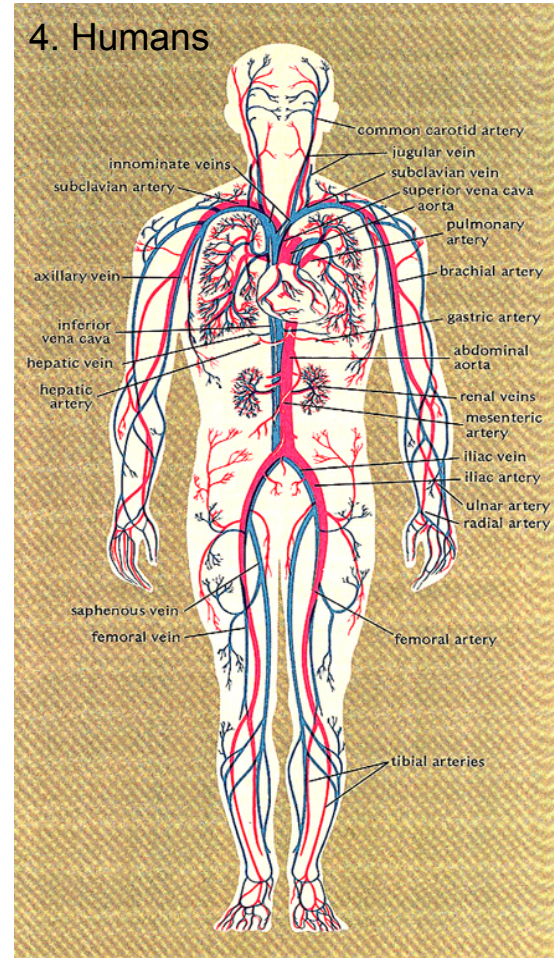
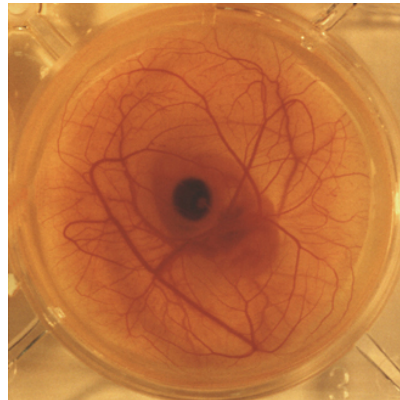
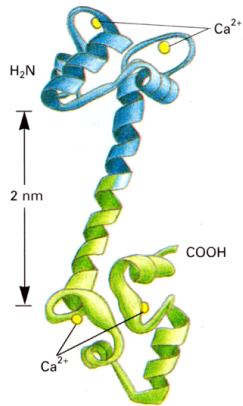
1. Molecules *in Vitro*

*in Vivo*

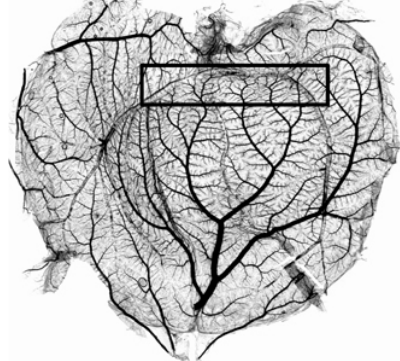
2. Avian CAM

3. Rodents

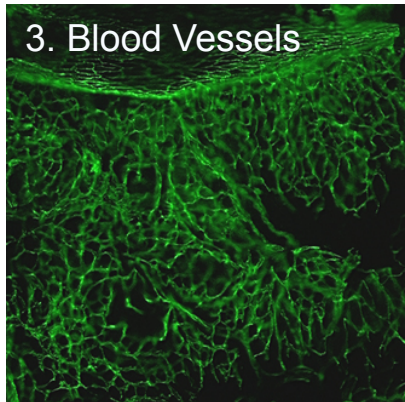
4. Humans



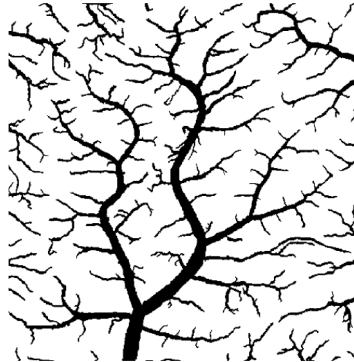
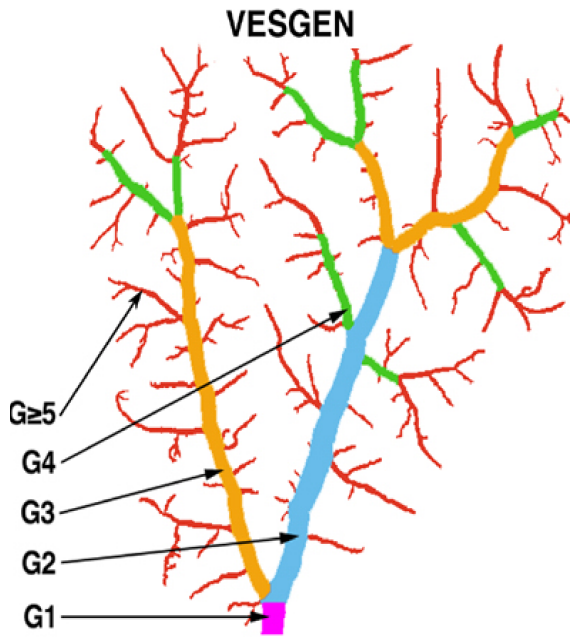
2. Blood Vessels



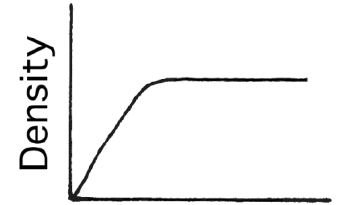
3. Blood Vessels



# Fundamental Hypothesis 'Fingerprint' or 'Signature' Vascular Pattern as Useful Integrative Readout of Complex Molecular Signaling Pathways



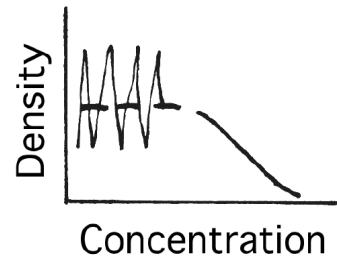
bFGF as Simple Stimulator  
*Arterio Thromb Vasc Biol 20 (2000)*



VEGF as Vascular Complexity Factor: Phenotypic Readout with eNOS Signaling  
*Microvascular Research 72 (2006)*



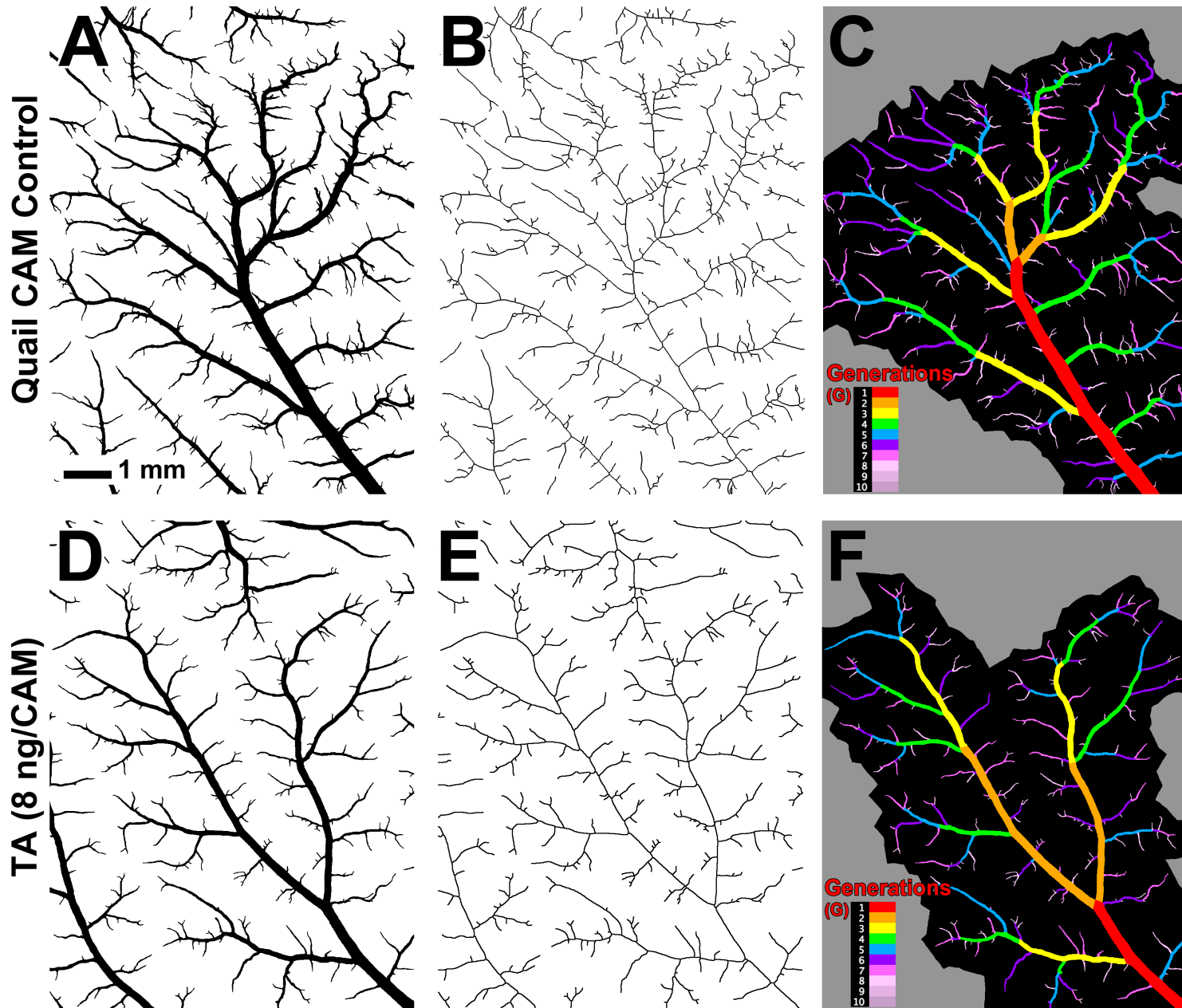
TGF- $\beta$ 1 as Simple Inhibitor but Complex Potentiator  
*Microvascular Research 59 (2000)*



The **form** of an object is a 'diagram of **forces**'

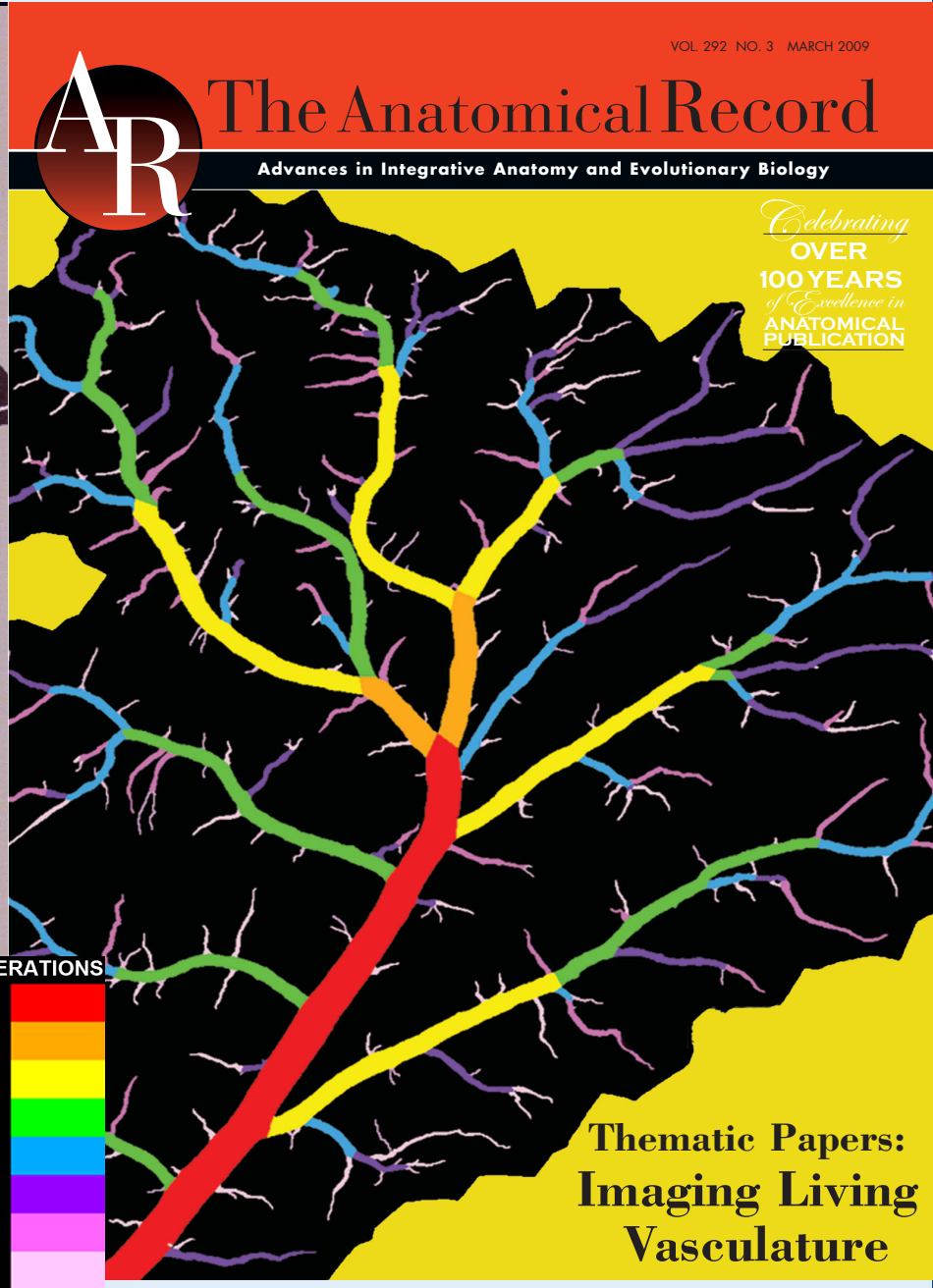
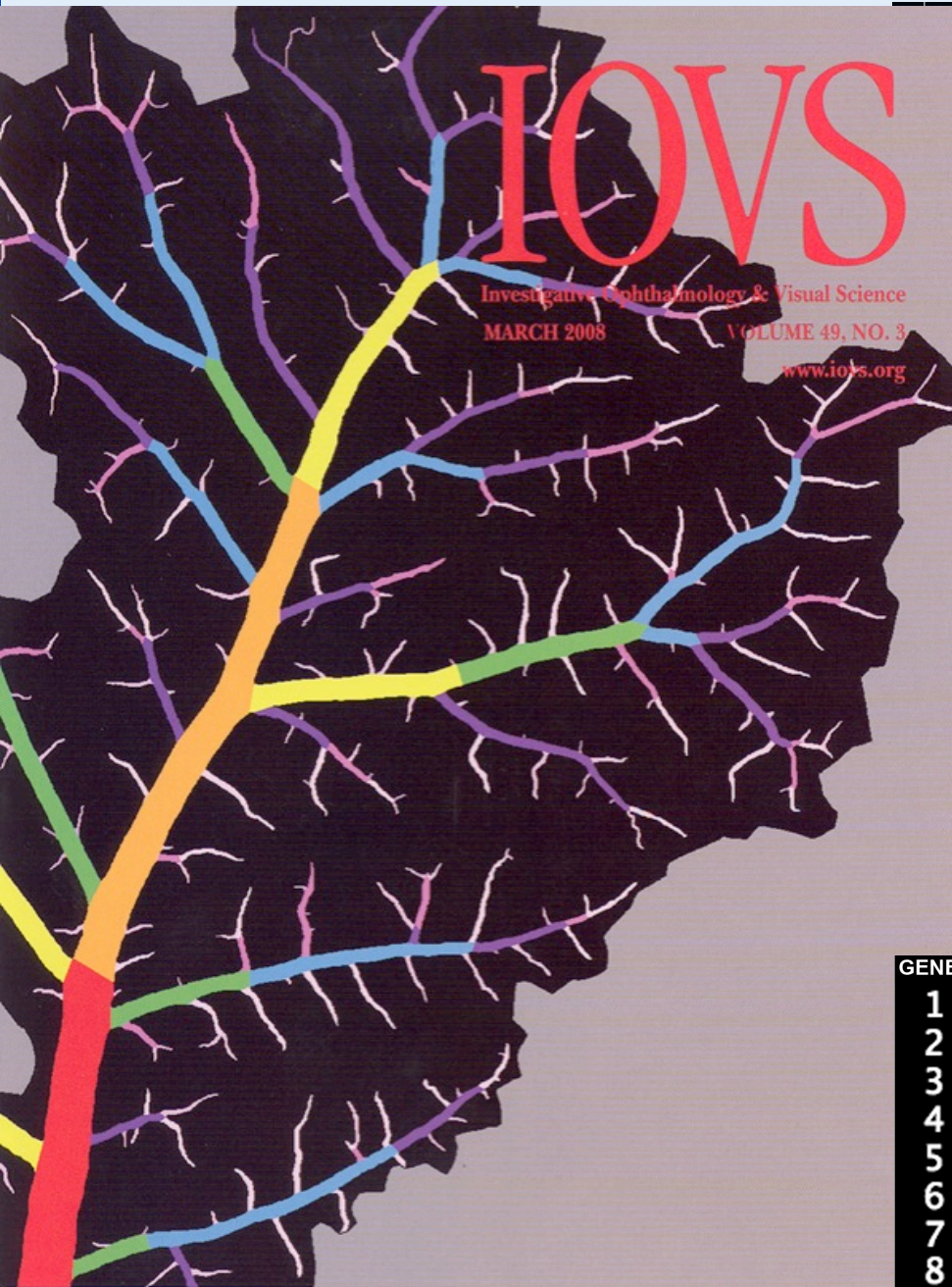
**Physiologist**  
**D'Arcy Thompson**

# Clinical Steroid TA Inhibits and Thins Vessels in Vascular Tree



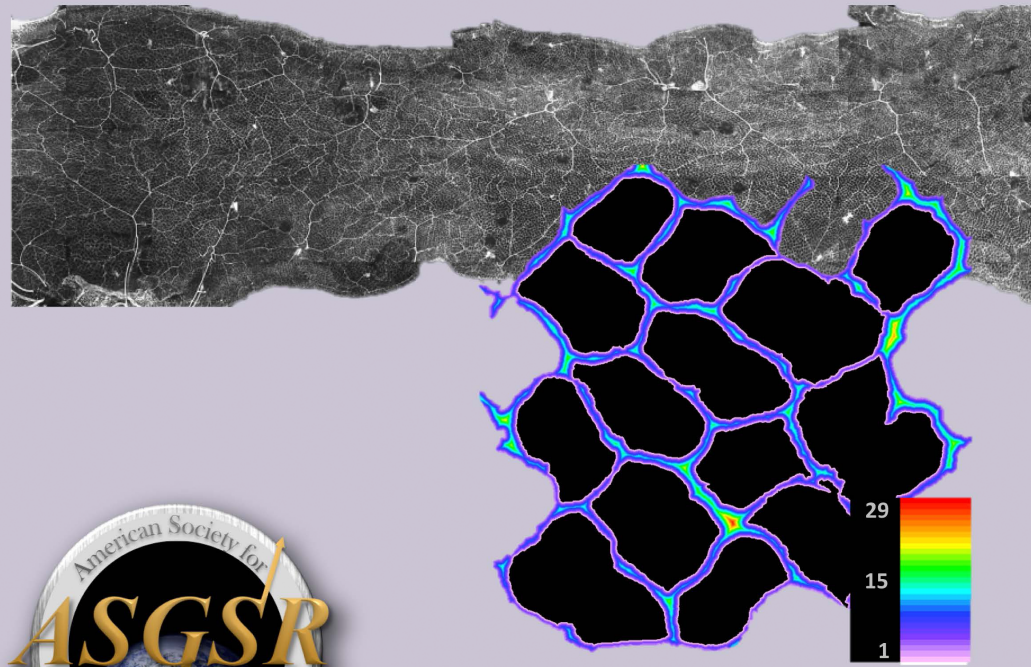
Reviewed in *Anatomical Record* 2009; *Investigative Ophthalmology & Visual Science* 2008





# Gravitational and Space Biology

Publication of the American Society for Gravitational and Space Research

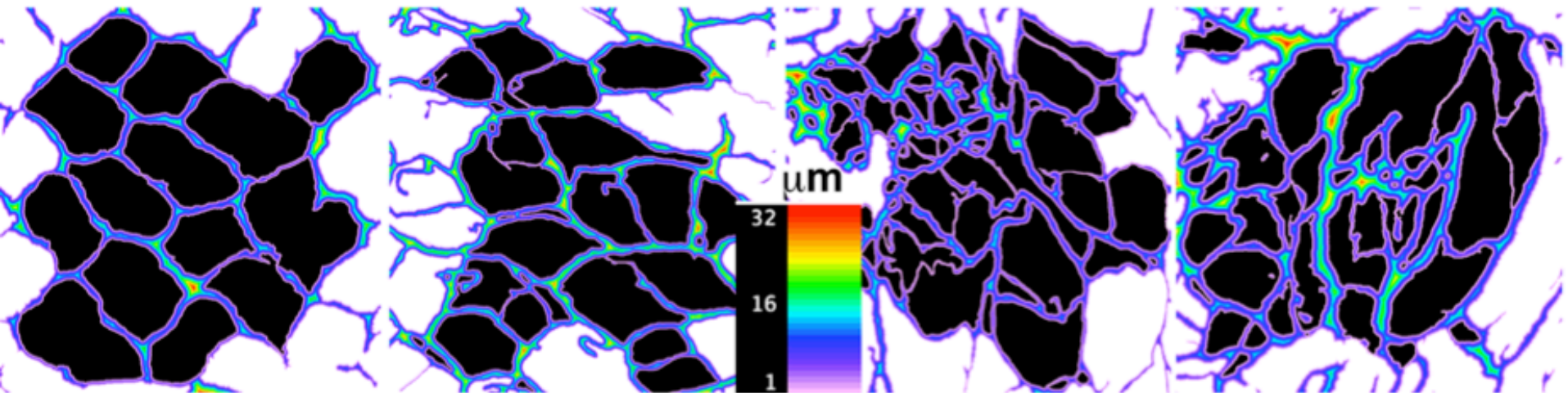
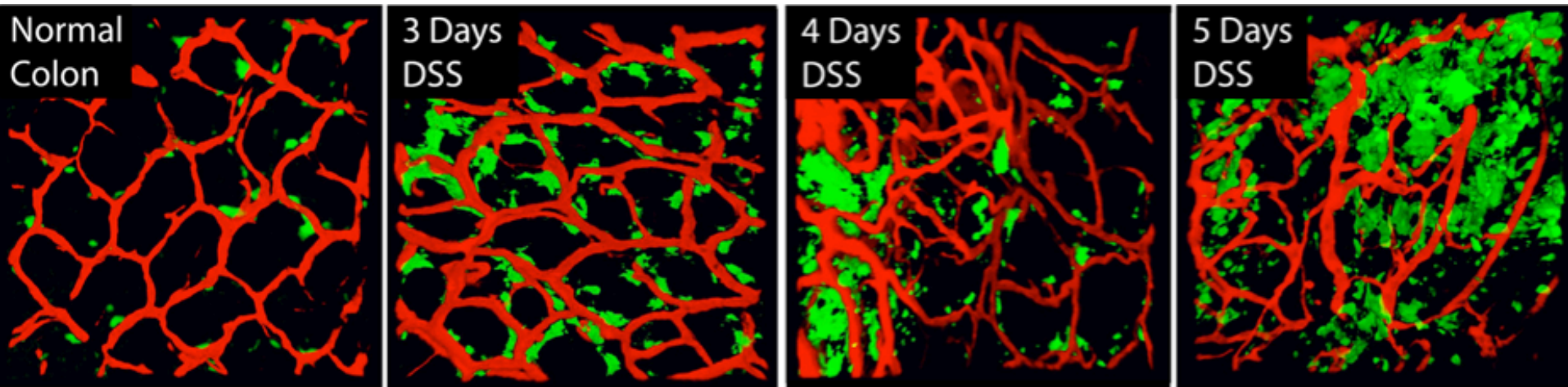


<https://www.asgsr.org/index.php/publications>



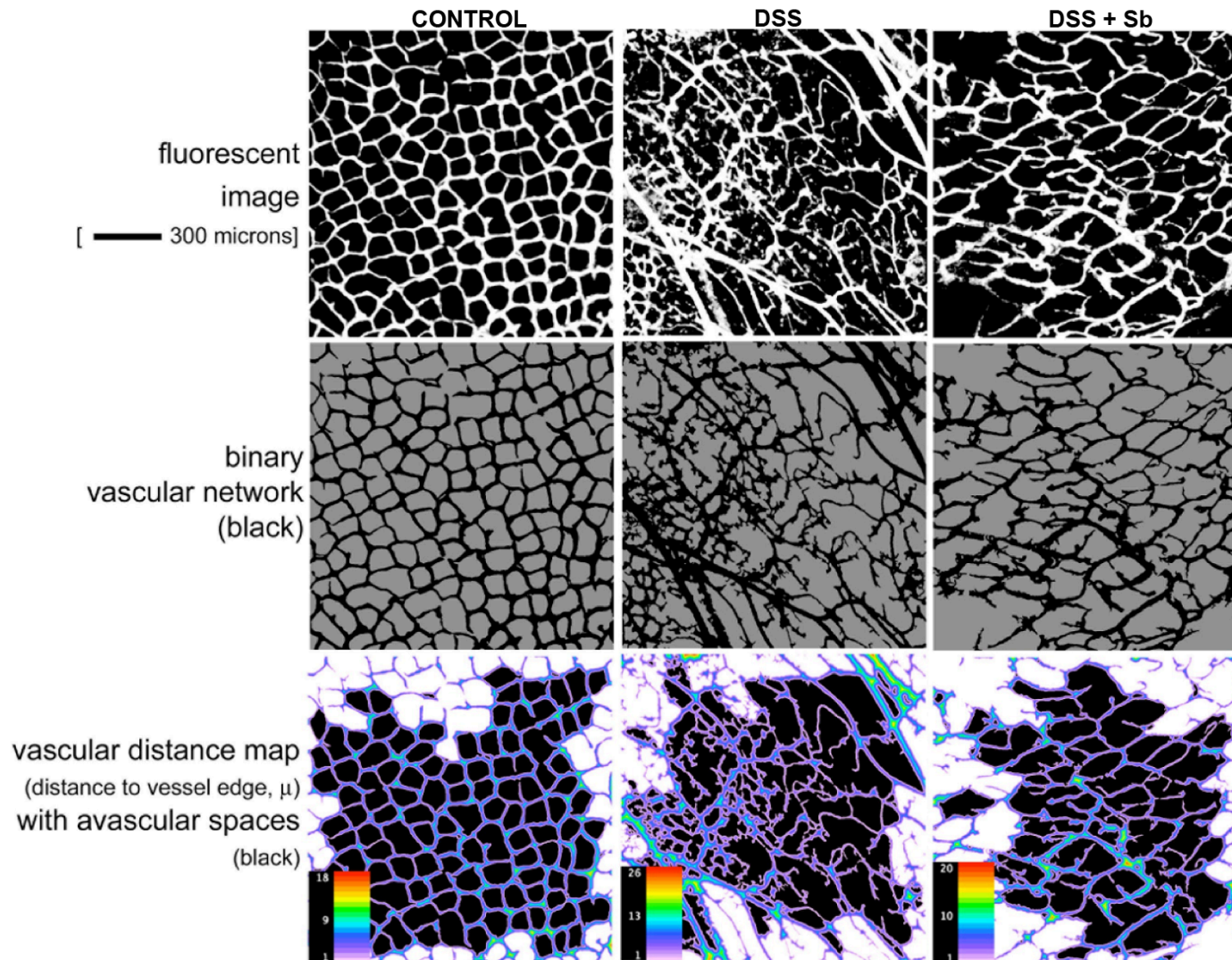
***Translational Research Tool for ROS, oxidative stress, persistent radiation damage***

**VESGEN mapping of progressive GI inflammation in mice with probiotic protection**



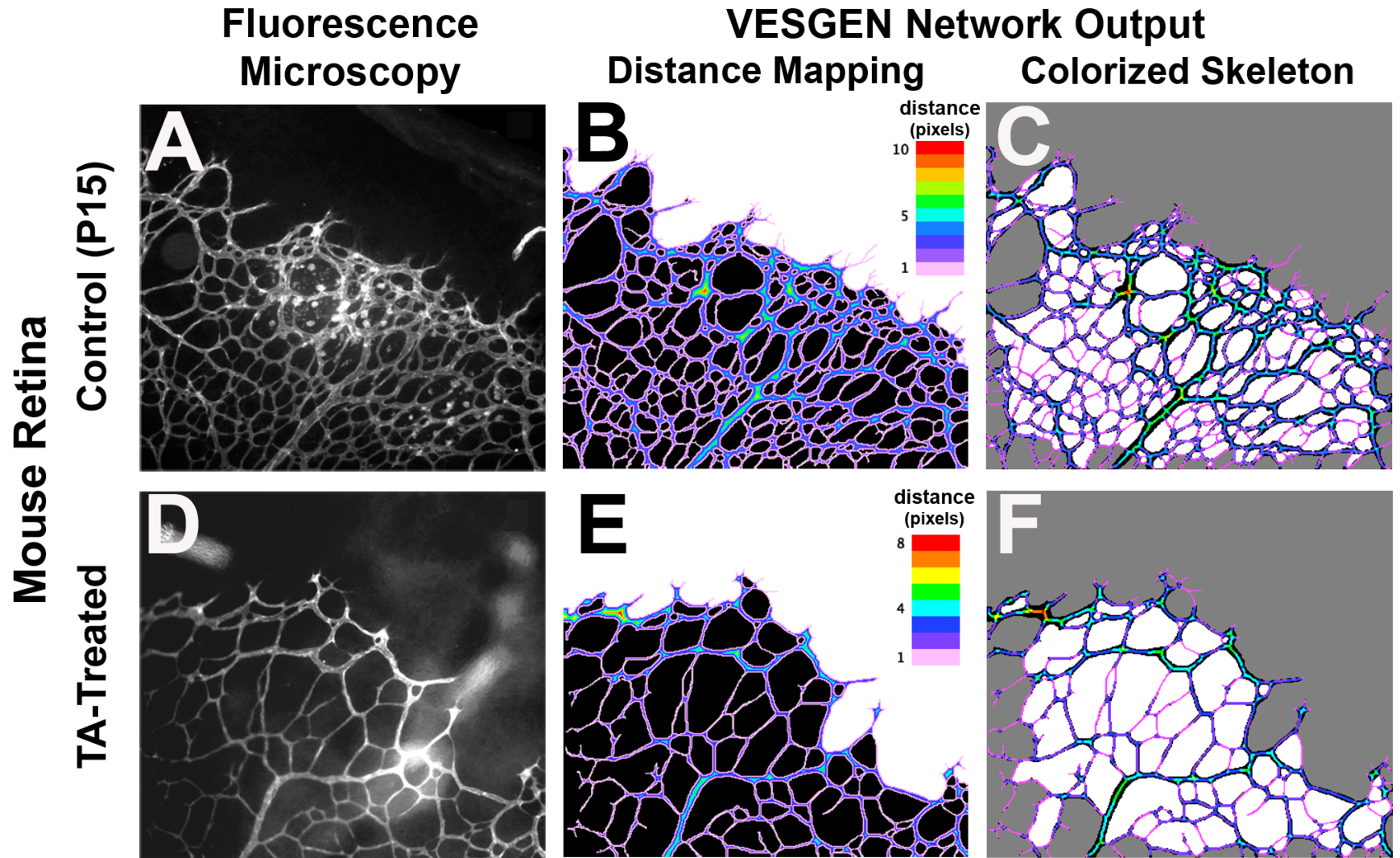
# Collaborative Study of Probiotic Inhibition of VEGF

## VESGEN mapping of progressive GI inflammation in mice with probiotic protection



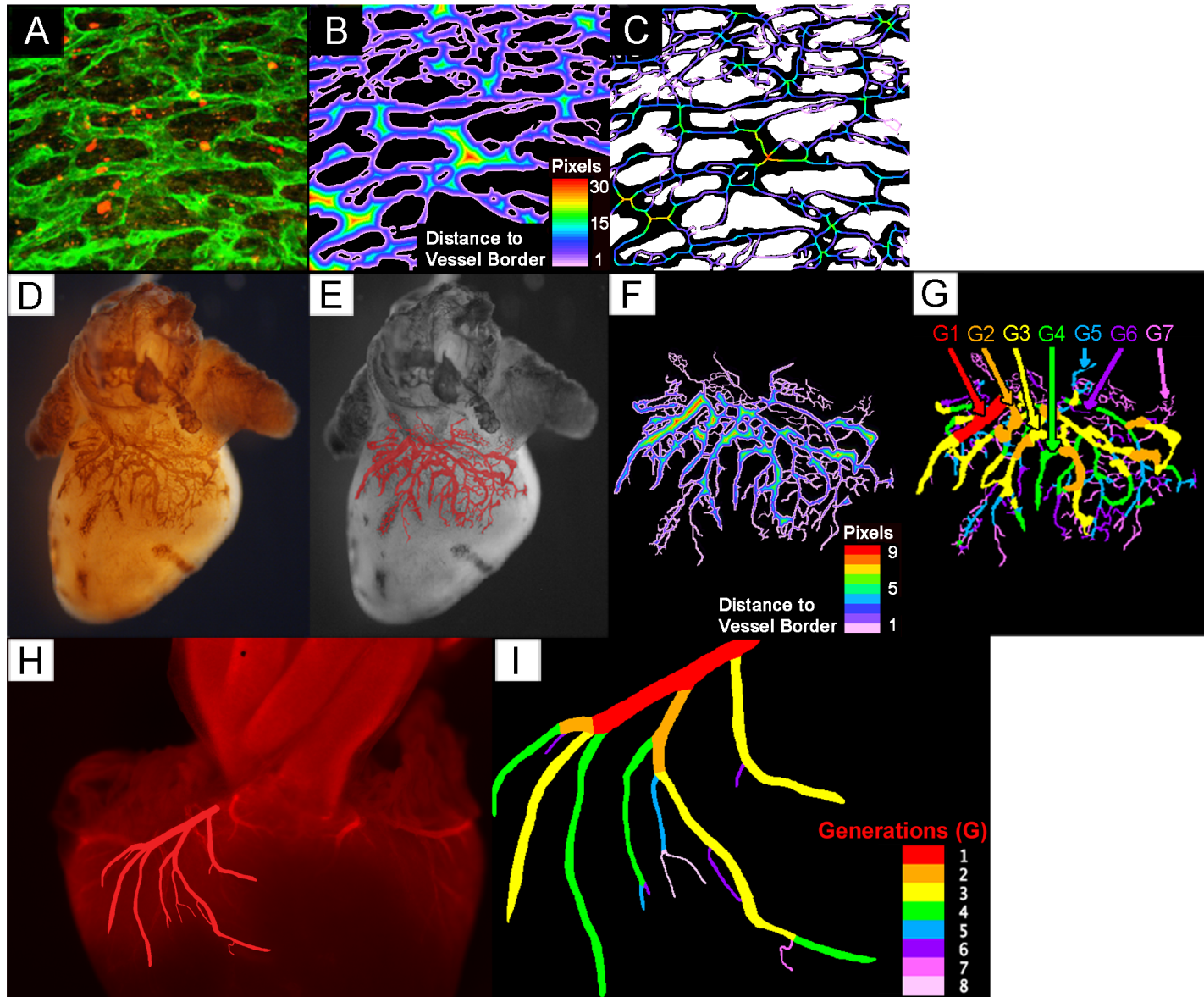


# Vascular Networks in Transgenic Mouse Retina

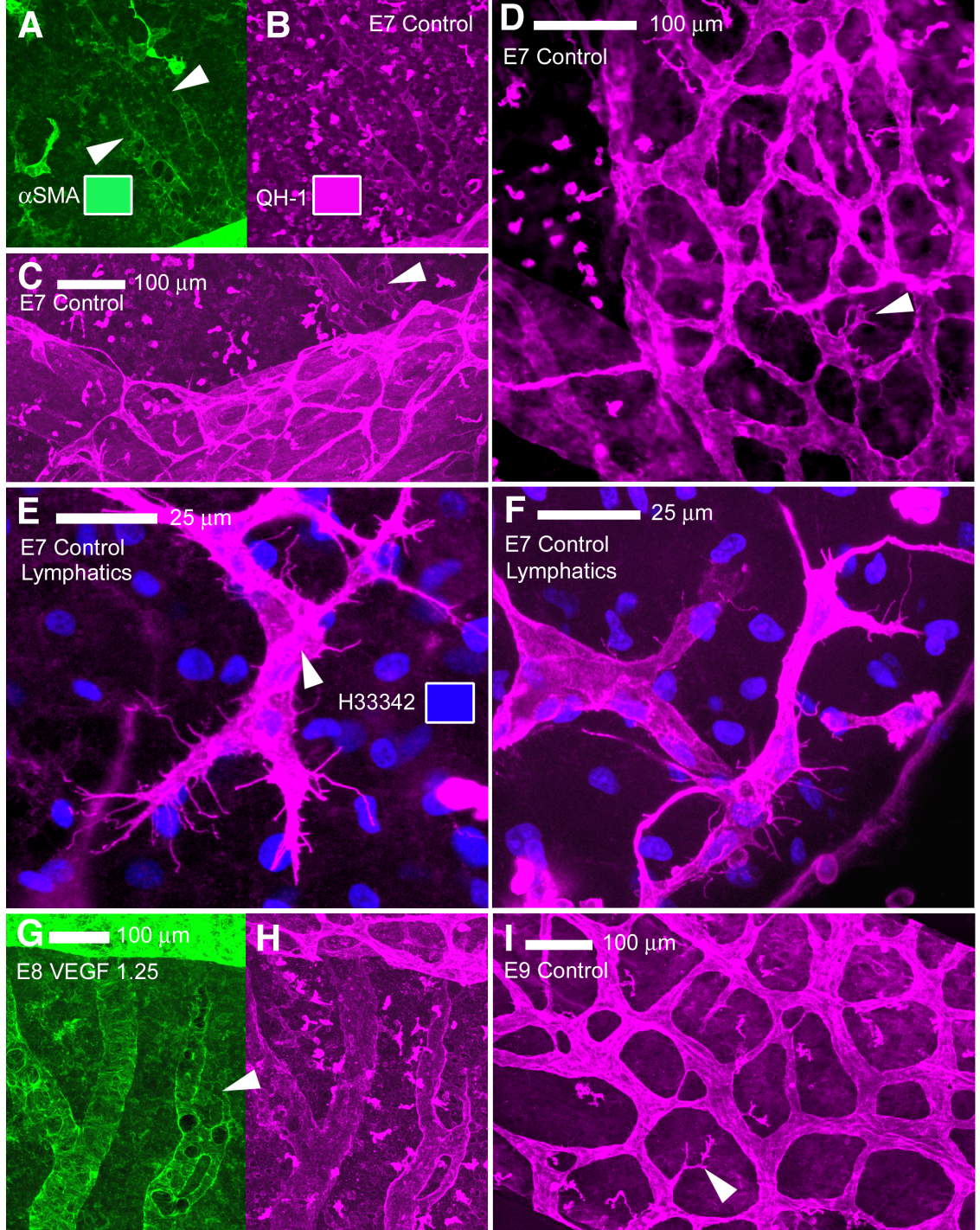


with J Sears & Q Ebrahim (Cole Eye Institute), from Vickerman et al, *Anatomical Record A* 292(3), 2009

# Coronary Vessel Network-to-Tree Transitions









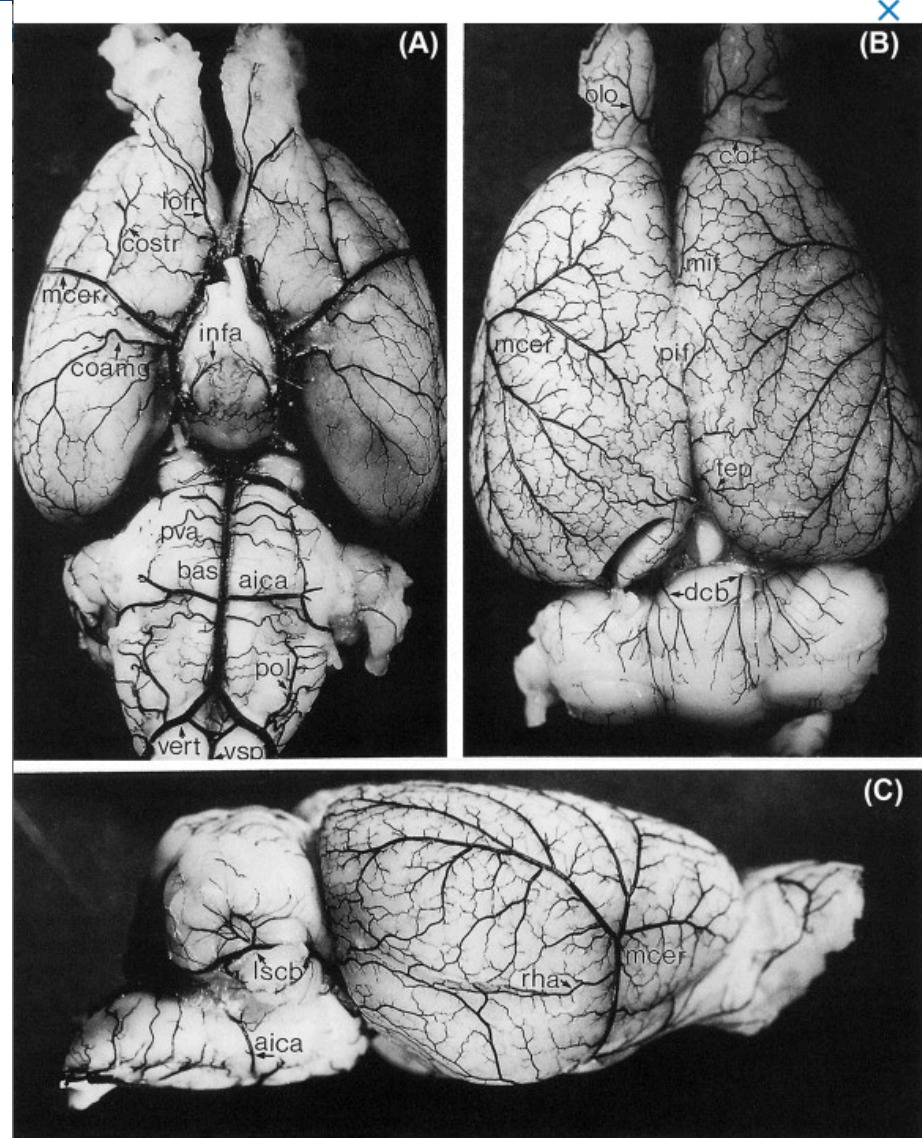
# Heart, Brain

- Superficial, other branching trees
- Small laminar networks

## Cerebral Vascular System

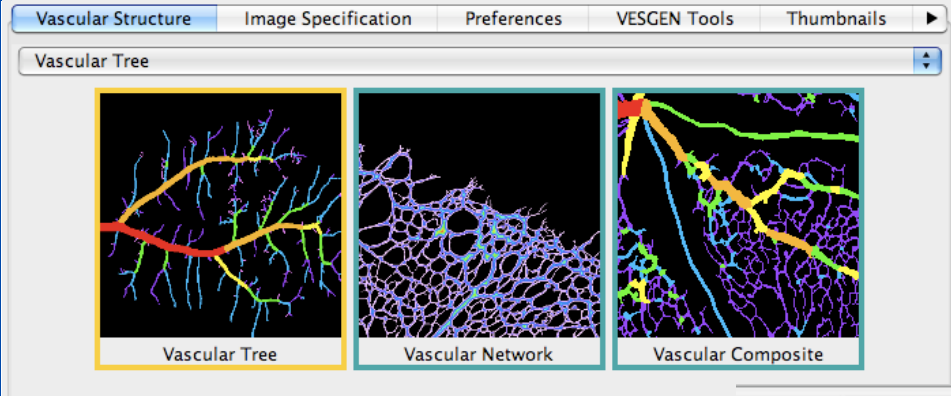
Oscar U. Scremin, in *The Rat Nervous System (Fourth Edition)*, 2015.

Pial Arterial Network

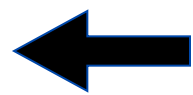


**FIGURE 3**

Ventral (top left), dorsal (top right), and lateral (bottom) views of the superficial cerebral arteries of a rat brain treated by selective arterial injection with a neoprene latex-black ink mixture.



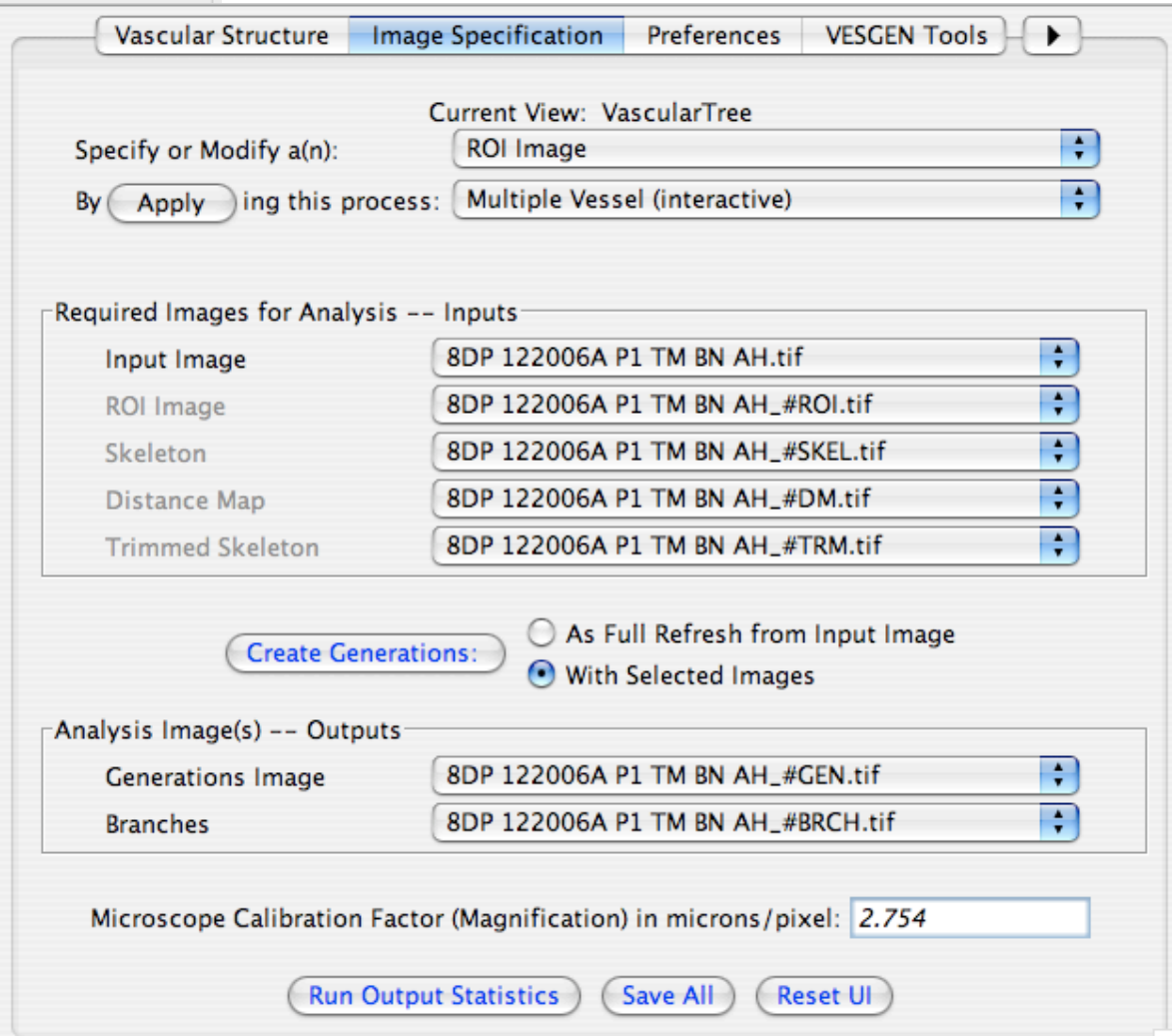
# Mature, Beta-Level VESGEN



Panel to specify vessel type

Main panel 

- Image specification
- Algorithm selection
- Process initiation



# Vascular 2D Image Binarization

Hamed Valizadegan, PhD

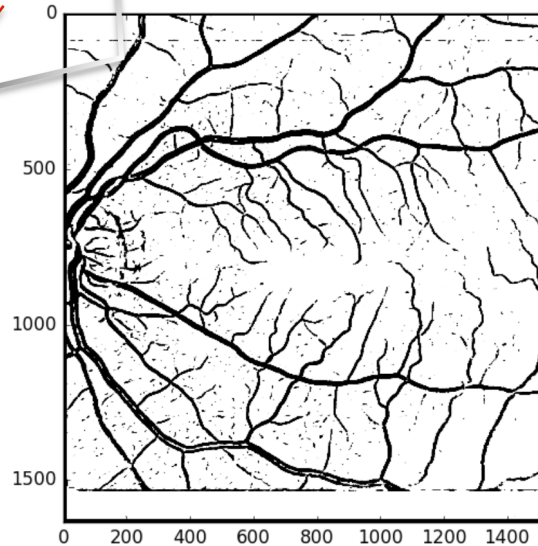


Automation  
result of CIF  
efforts  
(Unsupervised  
binarization)



Automation  
Ongoing  
work:  
Supervised  
Binarization

Semi-automated  
binarization:  
requires 2- 15  
hours per image



- **Involves:** (1) Preprocessing, (2) Segmentation, and (3) Postprocessing
- It reduces time for semi-automated manual extraction, a worldwide technical challenge for biomedical grayscale images
  - But very small vessels are still very difficult to extract
  - Sensitive to the setting of parameters in preprocessing, segmentation and post-processing

## Deep Neural Network (DNN)

- Given the existing manually labeled images, we can utilize the state of the arts supervised learning techniques for binarization.
- Each pixel and its class label (foreground or background) is the training example
- Our preliminary results with DNN shows that this is the right direction to pursue
- This is an ongoing work

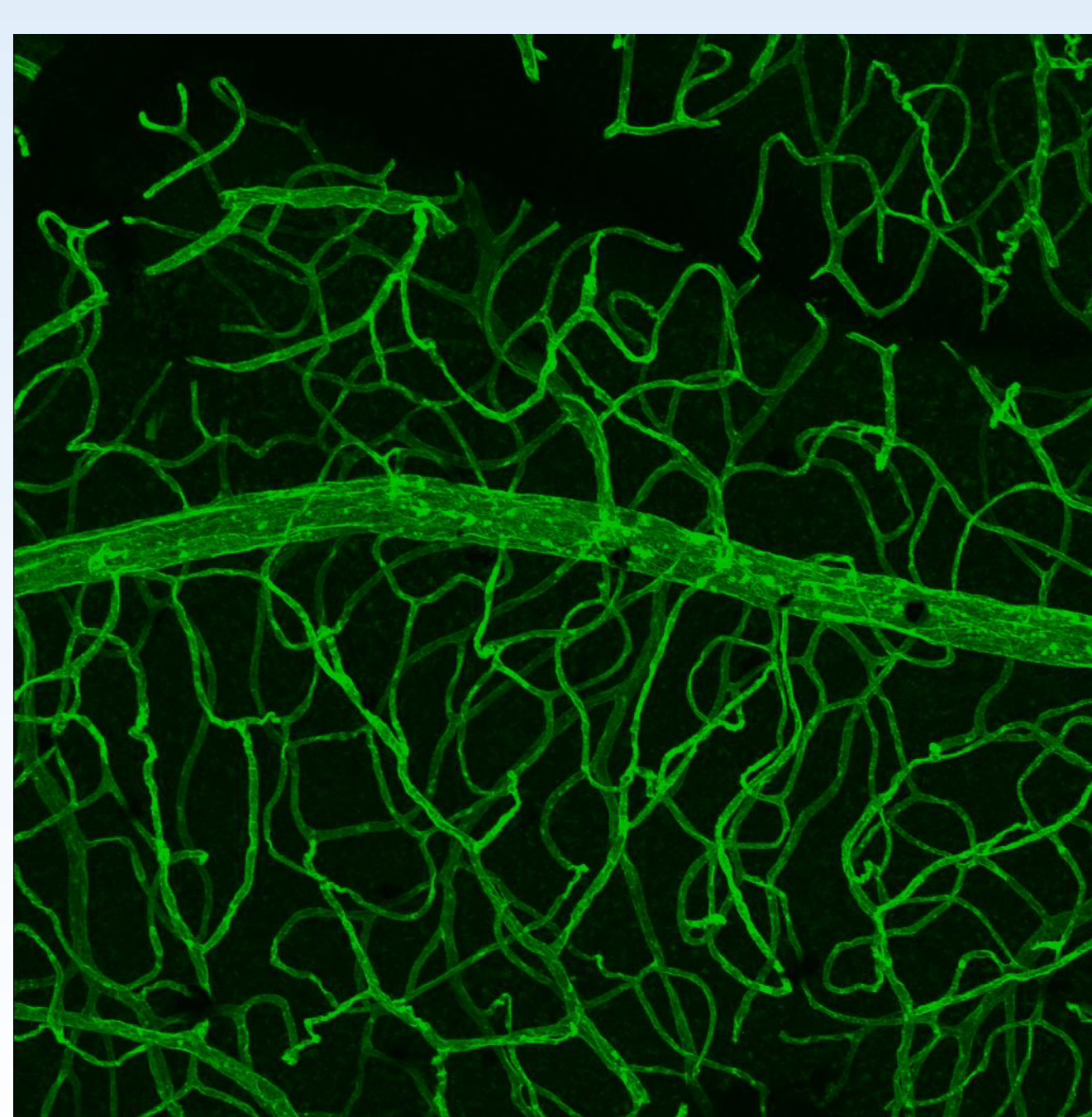


David Kao PhD

## **VESGEN 3D Development**

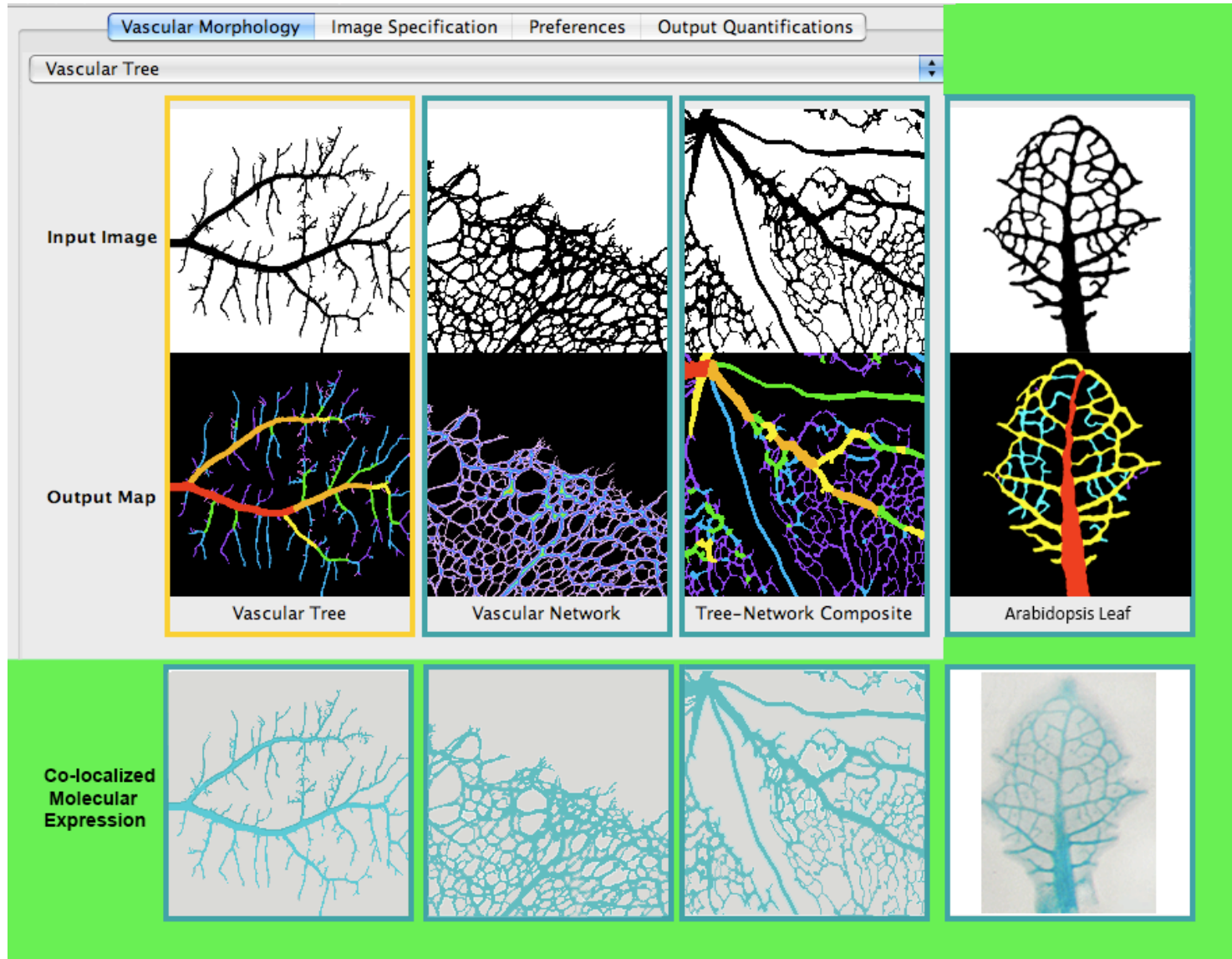
- 3D visualization
- 38 slices
- 1024x1024 resolution

Mouse retina,  
Xiao-Wen Mao PhD



# VESGEN Bioinformatics XD Analysis

## Structure-Function Relationships for Omic Correlations





# Mapping of Progressive Diabetic Retinopathy by VESGEN

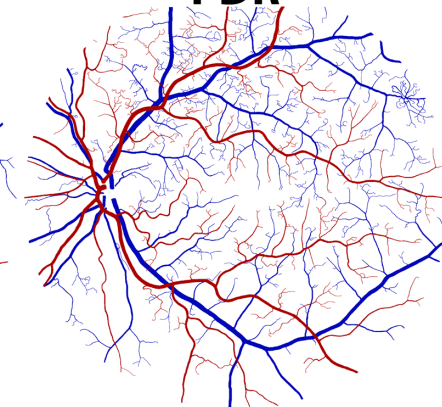
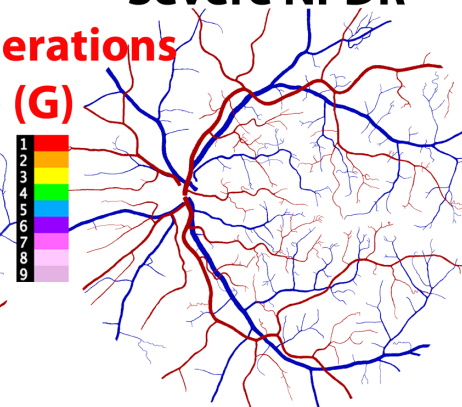
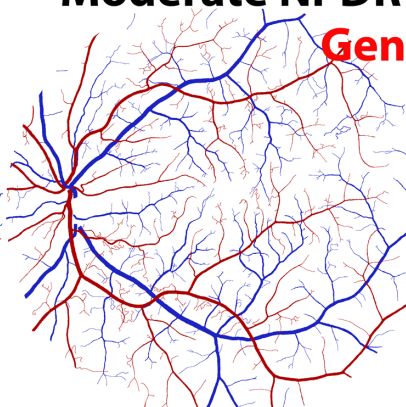
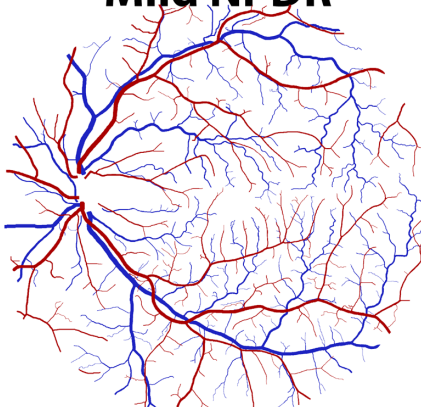
Mild NPDR

Moderate NPDR

Severe NPDR

PDR

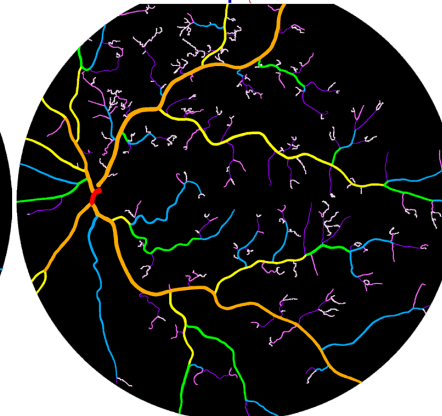
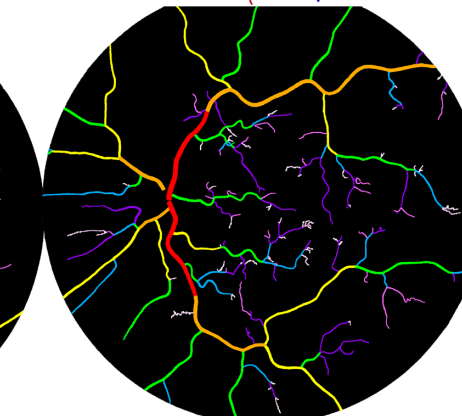
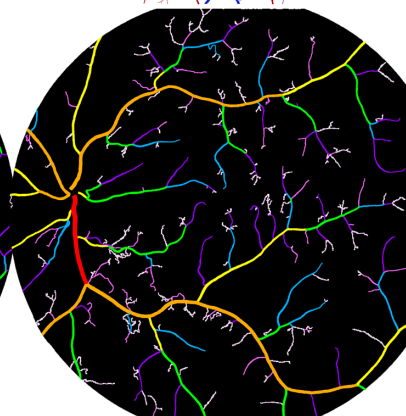
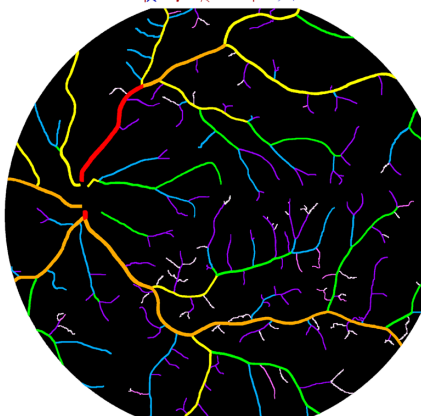
Vascular Trees



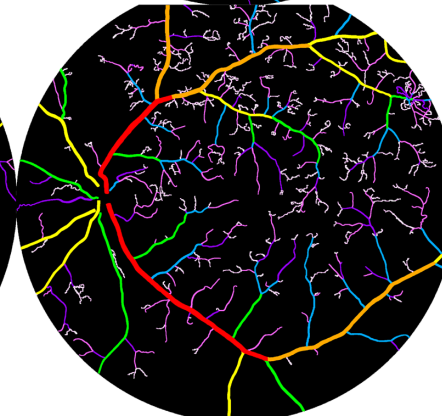
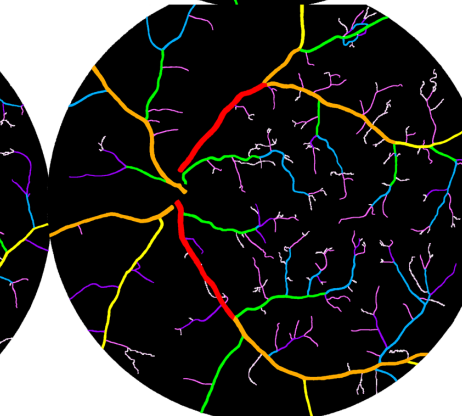
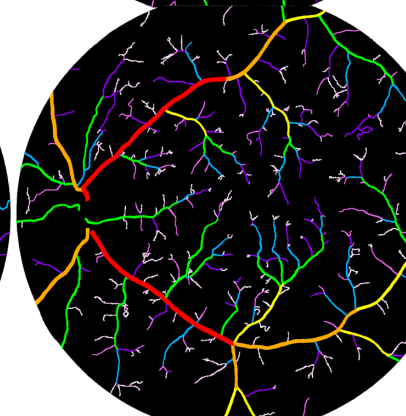
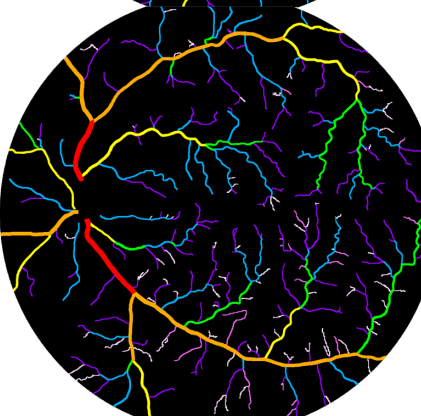
Generations



Arteries

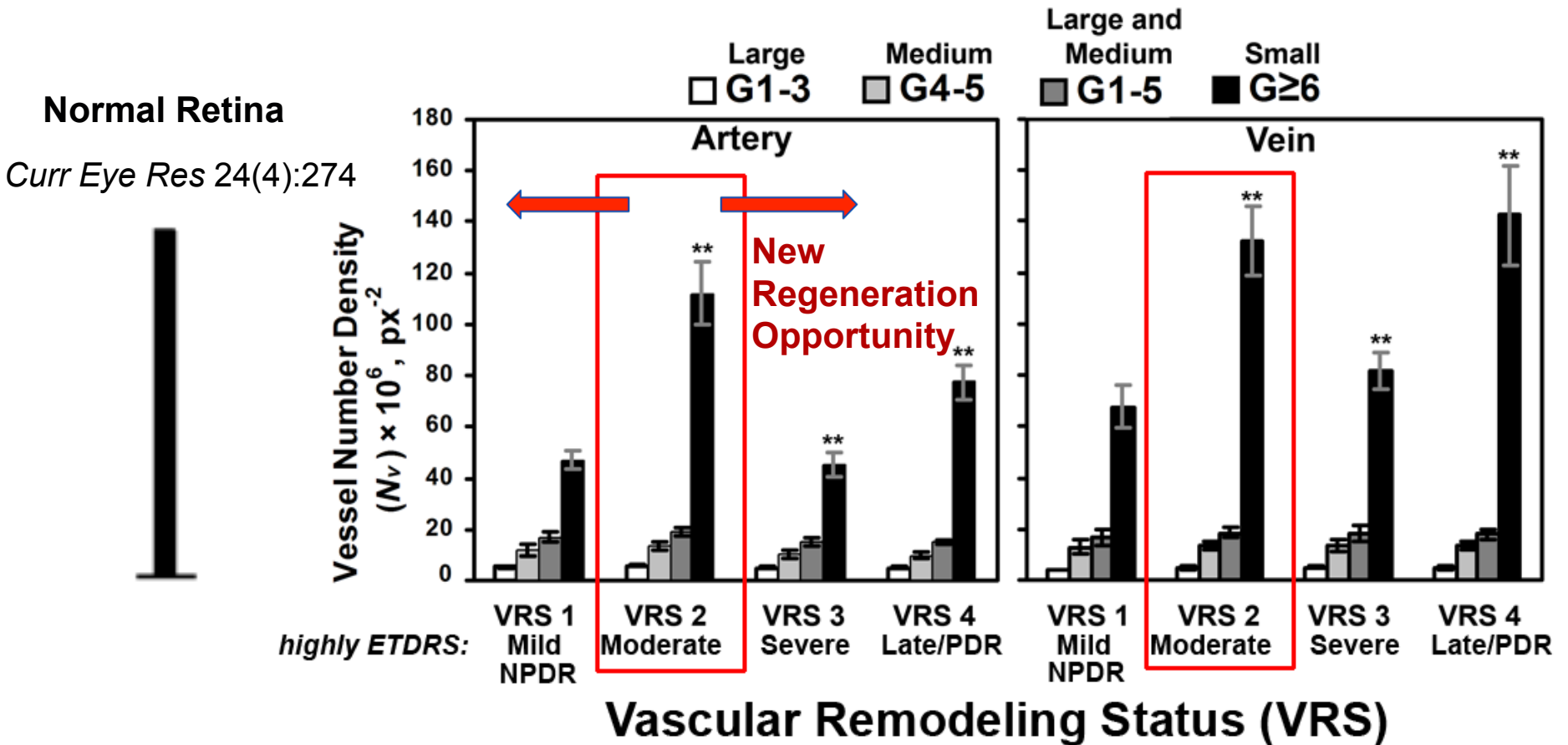


Veins



# Surprising, Innovative Paradigm Shift by VESGEN

Alternation [**Homeostatic Oscillation**] of Vascular Dropout with Vascular Growth (Angiogenesis) during Progression of Diabetic Retinopathy



A photograph of an astronaut in a white space suit floating in space. The astronaut is looking towards the right. In the background, the Earth's blue and white horizon is visible against the blackness of space. A bright star with a lens flare is in the upper right. The astronaut's suit has an American flag patch on the sleeve.

# **Vascular Patterning Analysis by VESGEN 2D/3D with Bioinformatics: Updates for Rodent Tissues**

*How can we work together for future space exploration  
and colonization?*