

to prevent light of wavelengths beyond the range of approximately 400-500 nm from being transmitted to the subject retina **30**. The filtered light **88a** may then be directed to a dichroic reflector **90**, such as the 495 nm long-pass dichroic reflector discussed above, for redirection towards the subject retina **30**.

The redirected filtered light **88b** may then pass through an optics stage **92** which may include a microscope objective **94** and a contact lens **96** or a fundus or slit-lamp camera apparatus. The microscope objective **94** and the contact lens **96** may act to focus, align and magnify the redirected filtered light **88a** onto a desired area of the subject retina **30**. It will be understood that under some test conditions, an applanation means such as a flat, optically clear lens or plane may be used to flatten or deform the cornea **20** to a desired shape to thereby allow better or more accurate imaging. Alternatively, an appropriate contact lens for fundus viewing may be employed.

The focused redirected light **88c** illuminates the retina thereby causing auto-fluorescence of the associated flavoproteins (FPs). The generated FP auto-fluorescence **82a** may be directed away from the subject retina **30** and through the components of the optics stage **92**, and the dichroic reflector **90** to an emission filter **98** such as, for example, an OMEGA OPTICAL® Model No. XF3003 (520DF40). The emission filter **98** may be selected to prevent wavelengths that do not correspond to FP auto-fluorescence wavelength, (e.g., wavelengths of or around 530 nm) from passing through its structure. The filtered FP auto-fluorescence **82b** may then pass through a focusing lens **100** which focuses FP auto-fluorescence **82c** on the still camera or CCD camera **82**. At this point the filtered FP auto-fluorescence **82b** may be displayed on a video display unit **104** such as a LCD or cathode ray tube for visual evaluation, or may be communicated to a personal computer **106** for analysis, storage or other desired image processing.

The CCD camera **82** may further include and cooperate with an image intensifier **102** to magnify the brightness of the focused FP auto-fluorescence **82c** to facilitate analysis of the captured image. The image intensifier **102** will likely be selected such that the gain, which is the ratio between the signal captured by the detector of the CCD camera **82** and the corresponding output signal, represents an increase of 100 to 1000 times the original image intensity. The image can be acquired, for example, by using a high-speed PRINCETON ST-133 interface and a STANFORD RESEARCH SYSTEMS® DG-535 delay gate generator with speeds ranging from 5 nsec to several minutes. The delay gate generator cooperates with the CCD camera **82** and the image intensifier **102** to synchronize and control the operation of these components. It will be understood that this captured image represents only the focused FP auto-fluorescence **82c** in an intensified form, the unwanted auto-fluorescence information or noise having been minimized by the operation of the excitation filter **86** and the emission filter **98**. In this manner, the resulting single image captured by CCD camera **82** has a high S/N ratio and provides a clear and detailed image representing the FP auto-fluorescence **82a-82c**.

The components of the retinal evaluation apparatus **80** described herein may be used in a stand alone fashion, wherein alignment is accomplished via manual clamping and securing of the individual components. However, the imaging, excitation and optical components of the retinal evaluation apparatus **80** may be integrated into any known desktop or handheld ophthalmoscope, slit-lamp, or fundus camera, to allow easy upgrade to the testing equipment described herein. Specifically, the CCD camera **82**, the excitation light source

**84**, the optics stage **92**, and the associated components may each be equipped with an adaptor (not shown) designed to allow each of the individual components of the retinal evaluation apparatus **80** to be mated with the ophthalmoscopes and other devices discussed above. In this case, the standard ophthalmoscope, fundus, or slit-lamp light may be replaced with the excitation means **84** affixed to the ophthalmoscope frame using a bracket or adaptor and the light output by the excitation means **84** may be filtered to produce the desired excitation light **84a**. An image detection device may be attached to the frames of the devices and aligned opposite the retina **30** to detect a single image representing the FP auto-fluorescence generated in response to the excitation light **84a**. In this manner, existing devices can be retrofitted to allow known diagnostic equipment to be used to excite and evaluate retinal auto-fluorescence.

Although certain retinal evaluation systems and methods have been described herein in accordance with the teachings of the present disclosure, the scope and coverage of this patent is not limited thereto. On the contrary, this patent is intended to cover all embodiments of the teachings of the disclosure that fairly fall within the scope of the permissible equivalents.

What is claimed is:

1. A method of measuring characteristics in the eye, including the retina, by:
  - configuring an apparatus to excite, detect, and measure ocular auto-fluorescence of flavoproteins;
  - using the apparatus to excite, detect, and measure ocular auto-fluorescence of flavoproteins related to metabolic activity; and
  - detecting activation of apoptotic mediators, based on the measurement of auto-fluorescence, which detected release of apoptotic mediators indicates the presence of apoptotic activity linked to at least one of metabolic dysfunction, mitochondrial dysfunction, and loss of mitochondrial integrity, and
  - identifying activation of one or more apoptotic signaling pathways causing selective degeneration of ocular tissue.
2. The method of claim 1, wherein measuring ocular auto-fluorescence includes measuring retinal auto-fluorescence.
3. The method of claim 1, wherein measuring ocular auto-fluorescence includes measuring optic nerve auto-fluorescence.
4. The method of claim 1, further including diagnosing at least one of metabolic dysfunction and mitochondrial dysfunction to allow for diagnosis and treatment of at least one disease associated with apoptotic activity.
5. The method of claim 4, wherein diagnosing at least one of metabolic dysfunction and mitochondrial dysfunction allows for diagnosis of the at least one disease is prior to substantial tissue damage occurring.
6. The method of claim 4, wherein the at least one disease includes at least one of cytomegalovirus, retinitis pigmentosa, and light induced blindness.
7. The method of claim 1, wherein measuring ocular auto-fluorescence includes measuring auto-fluorescence of excited flavoproteins.
8. The method of claim 7, wherein measuring ocular auto-fluorescence includes measuring auto-fluorescence of excited flavoprotein within ocular mitochondria.
9. The method of claim 1, further including analyzing an ocular auto-fluorescence signal to determine a contrast change or pattern; and comparing contrast change or pattern readings over time to monitor progression or regression of metabolic and/or mitochondrial dysfunction.