

**Neuroscience Center of Excellence  
LSU Health Sciences Center School of Medicine,  
New Orleans**

**SEMINAR**

**Genetic and Epidemiological Factors Contributing to Risk of  
Age-related Macular Degeneration**

**Margaret M. DeAngelis, Ph.D.  
Department of Ophthalmology  
Harvard Medical School**

Age-related macular degeneration (AMD) is the most common form of legal blindness in the United States as well as other developed countries. The Eye Disease Prevalence Group estimates that 1.75 million United States citizens have advanced AMD in at least one eye. Approximately 10% of the population aged 43 and older is affected with some form of the disease and 30% of the population aged 75 and older is affected. As the population lives longer this number will likely increase. It is estimated that 2.95 million individuals in the US will have advanced AMD by the year 2020.

Currently available treatments are directed against neovascular AMD, which is an advanced stage of the disease, and accounts for the majority of severe debilitating vision loss associated with AMD. Although the newest treatments offer some chance of visual improvement, they require invasive delivery methods and have limited ability to prevent or reverse vision loss. Assessment of an individual's risk of developing advanced AMD is based on ocular findings in those who already have the early stages. Methods have yet to be developed that determine risk of vision loss due to AMD prior to the development of any signs of the disease.

Previous studies of genetic and epidemiologic factors have not been in agreement as to predictors of AMD. Cigarette smoking appears to be the only epidemiologic risk factor generally accepted as being associated with an increased risk for AMD, while an allelic variant in the complement factor H gene (CFH) appears to be the strongest genetic risk factor. Specifically, several independent reports have shown the CFH Y402H functional polymorphism as well additional variants to be associated with increased risk of both early and late stages of AMD (both neovascular and geographic atrophy) These findings further suggest that the histidine allele, or disease allele, contributes to almost half of all cases of AMD in the population. Although having these factors may increase one's risk of disease, there are still many individuals who both smoke and have the CFH associated disease variant but have no signs of AMD. Additionally smoking is a risk factor for many disorders such as cardiovascular disease. Moreover, some of CFH variants (or a combination of them) including Y402H are

associated with increased risk for other diseases such as myocardial infarction, hemolytic uremic syndrome (HUS), and membranoproliferative glomerulonephritis (MPGN). This suggests that, although smoking and CFH play an important role in the pathophysiology of AMD, there are other environmental and genetic risk factors that influence AMD progression. This underscores the importance of examining common variation in multiple susceptibility genes as well as contributing environmental factors simultaneously to better estimate individual risk of AMD. Currently, several groups, including our laboratory, have begun to do this with respect to the contribution of smoking and CFH along with other reported genetic and epidemiological risk factors.

Our group, in conjunction with collaborators from diverse disciplines, is using novel approaches to discover precisely which genes and epidemiological factors contribute to the risk of AMD. These risk factors could provide targets that could be modifiable through therapeutic or behavioral interventions, thereby reducing or preventing the incidence of this disease.

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2020 Gravier Street**