

# Researchers uncover genetic link to age-related cataracts

July 31 2009, by Susan Lampert Smith

---

(PhysOrg.com) -- Bing-Cheng Wang, Ph.D., Case Western Reserve University School of Medicine professor of pharmacology and senior staff scientist at MetroHealth Medical Center, and Sudha K. Iyengar, Ph.D. professor of genetic and molecular epidemiology at Case Western Reserve University School of Medicine, have discovered the first gene associated with the formation of age-related cataracts, a leading causes of blindness.

Their research is part of a large-scale collaborative investigation involving 10 different laboratories from the United States, United Kingdom and Australia. The study, entitled "EphA2 is associated with age-related cortical cataract in mice and humans," will be published in the July 31 issue of [PLoS Genetics](#).

Millions of Americans suffer from Age-Related Cataract or ARC and an estimated 4 billion dollars are spent to treat the disease in the U.S. each year. ARC is known to be highly heritable, yet even after decades of research, little is known about the genetic causes for ARC.

The lens of the eye is normally clear, allowing the transmission of focused light onto the retina. Cataracts occur when proteins in the lens become damaged and clump together - causing the lens to become cloudy and obscure vision. Researchers say EphA2 encodes an enzyme which plays a role in the repair of those damaged proteins.

Expression of the EphA2 protein occurs naturally in human and mice. It

decreases with age, providing a possible explanation for age-related cataract formation. The protein, an enzyme called a tyrosine kinase, is responsible for the transfer of phosphate groups to other proteins in the lens, a process known as phosphorylation that is a common step in cell signaling. When EPHA2 is absent, unphosphorylated proteins accumulate that indicate high levels of cellular stress. Researchers believe that these underphosphorylated proteins become sticky, bunch up, and cause damaged proteins to form clusters that damage the structure and impair the clarity of the lens.

The discovery was serendipitous," explained Dr. Wang. Initially Dr. Wang's group was interested in testing the hypothesis that EphA2 was involved in preventing tumor formation. So his lab obtained a line of mice in which EphA2 gene had been deleted. Supporting their hypothesis, the mice without EphA2 gene became much more susceptible to tumor development, which was reported in the journal *Cancer*

Research two years ago. Interestingly, in addition to increased tendency to develop tumors, the mice formed cataracts as they became older. This was an exciting but totally unexpected observation. Co-incidentally, around the same time, Dr. Iyengar's group reported in *Proceedings of National Academy of Science* that the same gene region was linked to human age-related cataract. By another amazing coincidence, Dr. Wang and Dr. Iyengar had offices next door to each other in the late 1990's when they first came to Cleveland as independent scientists. They have been friends and colleagues ever since.

"After many excited phone calls and emails, a collaboration was initiated, and the rest was history," said Wang.

So far, the groups have managed to identify several specific mutations in human EphA2 that are associated with ARC. In the future, the groups

plan to search for additional mutations. They believe that this effort will allow them to better understand the specific cellular processes by which EphA2 helps maintain lens clarity.

The hope is that the identification of the underlying causes for ARC will point researchers in the direction of new treatments and preventions for ARC. Dr. Wang's lab at Cleveland's MetroHealth Medical Center is developing such agents.

"Our mutant mice will provide a unique platform to find out which specific molecules or cellular processes are affected by EphA2 deletion. Meanwhile, studies of human mutant EphA2 could also verify if the same molecules or cellular processes are affected in human lens," said Wang.

By age 80, more than half of Americans will have a cataract or have had cataract surgery. Researchers say that as the population ages, ARC is becoming an increasingly large problem. Delaying the development of ARC could have a huge medical impact, both by alleviating the suffering of affected individuals and their families and by saving health care costs.

Source: Case Western Reserve University ([news](#) : [web](#))

Citation: Researchers uncover genetic link to age-related cataracts (2009, July 31) retrieved 25 April 2024 from

<https://medicalxpress.com/news/2009-07-uncover-genetic-link-age-related-cataracts.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--