Cataractogenesis: Can cataract be delayed or reversed?

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What triggers onset of cataract? The human eye lens contains water soluble, heat stable and fully transparent proteins. Oxidation, dehydration, formylation, fragmentation, misfolding, aggregation could make these proteins insoluble, making the lens cloudy, translucent and finally opaque. αA Crystallin the most abundant protein in the eye lens and plays a critical role in cataractogenesis. It has a chaperoning role and holds a 'misfolded' protein until it refolds to its original state. (“Holdase function”). 3-Hydroxyurenone (& possibly 3-hydroxyanthranilic acid) oxidises αA Crystallin producing hydrogen peroxide in the eye and is implicated in cataractogenesis. Aquaporin 0 and calcium binding control opening/closing of the water channel, creating osmotic pressure, forcing water into the eye lens, leading to cataract. “Proteomic analysis of Age-Related Nuclear Cataracts and Normal Lens Nuclei” (ARNC) is associated with formation of high-molecular weight aggregates in ARNC lens nuclei. Cross linking of wild type αA WT Crystallin and αA-G98R mutant has been compared using a homobifunctional cross linker-mass spectrometry (MALDI-MS, MS/MS) & bioinformatics. A single difference in subunit-subunit interaction sites has been detected between the αA-G98R mutant and the wild type which leads to a conformational change making the mutant protein more prone to aggregation. Studies on congenital cataract on two patients have shown that two mutations (W581R and G588S) in the highly conserved region for lanosterol synthase leads to increased aggregation of the mutant protein. Lanosterol delays and reverses such cataract in rabbits and dogs. Can this result be extended to man?

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