ROLE OF THE EXTRACELLULAR MATRIX IN PROGRESSION OF RETINAL DEGENERATIVE DISORDERS

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Abstract:
Progressive inherited retinal degenerative disorders (PIRDDs) are the leading cause for blindness in the developed countries with age-related macular degeneration (AMD) and retinitis pigmentosa (RP) constituting the majority of PIRDDs. Currently, over 8 million Americans have PIRDs and that number is estimated to drastically increase by the end of this decade. Although a mutant protein is expressed starting early during retinal development in PIRDDs patients, symptoms of retinal degeneration manifest much later. Current research focuses on understanding the role a mutation plays in the function of a protein. However, it remains unknown why the disease manifests much later in life even though cells are dying throughout early and middle life. Our research offers a potential explanation to the presence of a time point when the degenerative process is accelerated. This point is defined by structural disruptions of the extracellular matrix (ECM). Death of a critical number of ECM-maintaining mutant protein-expressing retinal cells contributes to that break point in the degenerative process. It is, therefore, important to understand the changes occurring at the ECM during PIRDs and to take that in account when therapeutic approaches are designed.