

# Structural Function of MIP/Aquaporin 0 in the Eye Lens; Genetic Defects Lead to Congenital Inherited Cataracts

Ana B. Chepelinsky

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**Abstract** Aquaporin 0 (AQP0) was originally characterized as a membrane intrinsic protein, specifically expressed in the lens fibers of the ocular lens and designated MIP, for major intrinsic protein of the lens. Once the gene was cloned, an internal repeat was identified, encoding for the amino acids Asp-Pro-Ala, the NPA repeat. Shortly, the MIP gene family was emerging, with members being characterized in mammals, insects, and plants. Once Peter Agre's laboratory developed a functional assay for water channels, the MIP family became the aquaporin family and MIP

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A.B. Chepelinsky  
National Institutes of Health, National Eye Institute, Bldg. 31, Room 6A-32, Bethesda,  
MD 20892-2510, USA  
abc@helix.nih.gov

became known as aquaporin 0. Besides functioning as a water channel, aquaporin 0 also plays a structural role, being required for maintaining the transparency and optical accommodation of the ocular lens. Mutations in the AQP0 gene in human and mice result in genetic cataracts; deletion of the MIP/AQP0 gene in mice results in lack of suture formation required for maintenance of the lens fiber architecture, resulting in perturbed accommodation and focus properties of the ocular lens. Crystallography studies support the notion of the double function of aquaporin 0 as a water channel (open configuration) or adhesion molecule (closed configuration) in the ocular lens fibers. The functions of MIP/AQP0, both as a water channel and an adhesive molecule in the lens fibers, contribute to the narrow intercellular space of the lens fibers that is required for lens transparency and accommodation.

## Abbreviations

aa	amino acid
bp	base pair
kD	kilodaltons
AQP0	aquaporin 0
AQP1	aquaporin 1
MIP	major intrinsic protein of the lens
MP26	membrane protein 26
NPA	asparagine-proline-alanine

## 1 Introduction

In the period spanning approximately the last 30 years, MIP, a protein highly expressed in the ocular lens fiber membrane, puzzled investigators because various approaches suggested possible functions without conclusive results. However, contributions from various scientific disciplines have now unraveled the structure and function/s of MIP, now also known as aquaporin 0.

### *1.1 How Major Intrinsic Protein of the Lens MIP became Aquaporin 0*

MIP, MP26, MIP26, and aquaporin 0 are the various names given to the same protein since its discovery as a lens membrane protein up until its characterization as a water channel. MIP (major intrinsic protein of the lens), was first identified biochemically as the most abundant intrinsic membrane protein of the ocular lens fibers (Bloemendal 1982; Bloemendal et al. 1977; Broekhuysen et al. 1976, 1979; Vermorken et al. 1977). It was also called MIP26 or MP26 because of its mobility as a 26-kD polypeptide in electrophoretic studies. However, another band with