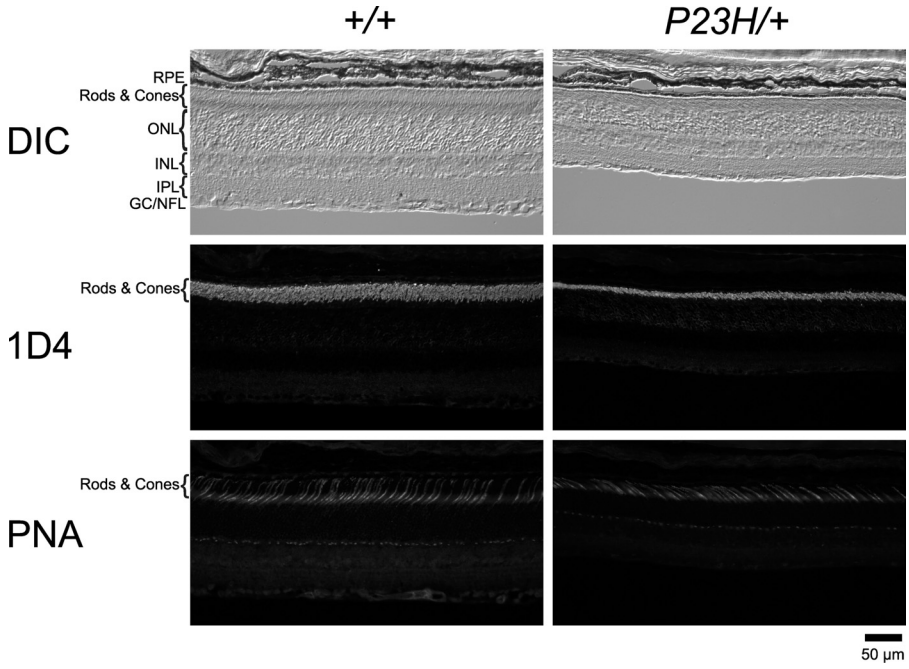
Papers of the Week

Insight into Human Blinding Disease ♦

♦ See referenced article, *J. Biol. Chem.* 2011, **286,** 10551–10567

Probing Mechanisms of Photoreceptor Degeneration in a New Mouse Model of the Common Form of Autosomal Dominant Retinitis Pigmentosa due to P23H Opsin Mutations



P23H/+ mice have significant shortening of rod outer segment structures as compared to wild type mice.

Rhodopsin, the pigment that mediates dim light vision, is composed of the apoprotein opsin and the chromophore ligand 11-*cis*-retinal. A P23H mutation in the opsin gene is one of the most frequent causes of a human blinding disease called autosomal dominant retinitis pigmentosa (adRP). Although there has been considerable interest in developing animal models to study the pathology arising from this mutation, to date none of these models faithfully recapitulates the human disease. In this manuscript, Sanae Sakami and colleagues provide convincing evidence that they have generated a faithful and experimentally useful model for human P23H adRP using a P23H opsin knock-in mouse. The authors' data establish that the P23H protein is inadequately glycosylated and does not accumulate in the rod photoreceptor cell endoplasmic reticulum. Instead, it causes a structural disorganization of rod photoreceptor disk membranes. Furthermore, most of the synthesized P23H protein is degraded, and its retinal cytotoxicity is enhanced by a lack of the 11-*cis*-retinal chromophore during rod outer segment biogenesis. This new animal model will undoubtedly prove very useful for studying the molecular basis of adRP and also for developing new therapeutic strategies for helping human patients.

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