

## Calpain-Like Activity Correlates With Photoreceptor Cell Death in the rd1 Mouse

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**Purpose:** Several mouse models, including the rd1-mouse, display inherited retinal degeneration and therefore allow studies of the mechanisms behind the blinding disease retinitis pigmentosa (RP). Activation of calpain has been suggested to play an important role in apoptotic cell death in various systems, however, little is known about the activity of calpain during inherited retinal degeneration. This study compares the transcription, expression, and activity of different calpain isoforms and the endogenous calpain inhibitor calpastatin between wild type and rd1-mouse retinæ.

**Methods:** Transcription and expression levels of various calpain genes were assayed using microarray and proteomic techniques. The expression of certain calpain isoforms and calpastatin were detected immunohistochemically on sections of mouse retinæ. Transcription and expression levels were then compared to calpain activity using an enzymatic assay that allows for a resolution of calpain activation at the cellular level. In addition to the rd1-mouse, activity levels of calpain were investigated in other animal models of inherited retinal degeneration.

**Results:** We were able to identify substantial differences in the transcription, expression and activity of proteins related to the calpain system, particularly in photoreceptor cells. Calpastatin transcription is markedly reduced in rd1-retinæ, whereas calpain activity is substantially increased in rd1 photoreceptors. Calpain activity peaks at PN11, together with rd1-photoreceptor cell death.

**Conclusions:** Activation of calpain isoforms could play an important role in rd1-photoreceptor cell death. Calpain inhibitors might be effective in preventing photoreceptor degeneration.

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