

# Gap Junctions as Therapeutic Targets for the Treatment of Degenerative Disorders of the Retina

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## Technology description

Neurodegenerative diseases of the retina, such as retinitis pigmentosa, glaucoma, and ischemia, lead to the death of ganglion cells and the progressive loss of vision. In addition to the intrinsic mechanisms underlying primary cell death, intercellular communication appears to play a major, but presently unclear, role in so-called secondary cell death. Our recent experimental findings indicate that a primary disease or insult leads to the death of a limited cohort of vulnerable cells, which, in turn, pass toxic molecules via gap junctions to coupled neighbors that leads to secondary death. Cells that are clustered and can thereby communicate via gap junctions tend to die en masse under a broad range of neurodegenerative conditions.

We have found that pharmacological blockade of gap junctions either before or after induction of an insult to the retina results in an increase in the survivability of ganglion cells by up to 70%. In addition, genetic deletion of select connexins, the subunits that form gap junctions, can also significantly increase the survivability of ganglion cells under a number of pathological conditions. Moreover, we found that secondary cell death in the retina is mediated by different cohorts of gap junctions, based on the connexin proteins they express, depending on the type of initial insult. Targeting specific gap junction connexins may thus offer a novel therapeutic approach to reduce the progressive cell loss in the retina seen under different neurodegenerative conditions.

We propose that intraocular injection of selective gap junction blockers can significantly reduce the progressive loss of ganglion cells under different degenerative conditions such as glaucoma, retinitis pigmentosa, diabetic retinopathy, and ischemia. The pharmacological blockade of gap junctions may also protect cells that are lost following traumatic injury to the head. Since different cohorts of gap junctions play a role in secondary death dependent on their connexin makeup and the type of insult, development of drugs that target specific connexin proteins is called for.

**Keywords:** apoptosis, retina, bystander effect, cell death, excitotoxicity, ischemia



# Connexin Inhibitors

## Inventor:

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## Patents:

Title: Methods of  
Using Gap Junctions  
as Therapeutic  
Targets for the  
Treatment of  
Degenerative  
Disorders of the  
Retina

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## OVERVIEW

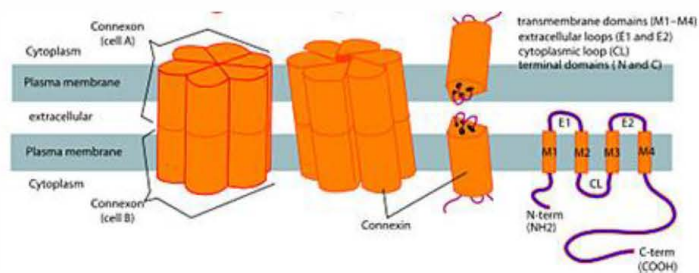
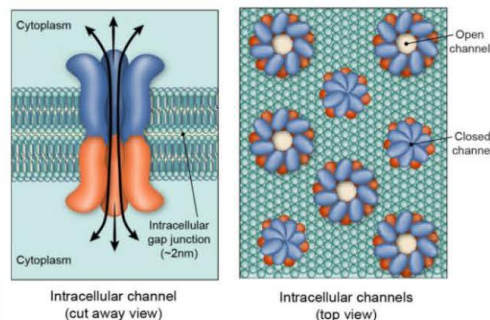
Irreversible blindness from retinal cell loss results from many common neurodegenerative eye disorders: glaucoma, retinitis pigmentosa, diabetic retinopathy, and assorted neovascular diseases. Dr. Stewart Bloomfield, SUNY College of Optometry, aims to discover and develop novel compounds that inhibit connexin proteins in the retina. Such drugs can function as non-specific blockers of connexin 36 and connexin 45 to protect the retina and the optic nerve cells from dying, preventing blindness.

## KEY FEATURES

- Retinal neuroprotection
- Can prevent vision loss in patients with glaucoma
- Derived from known, non-specific inhibitor base compounds using cell-based assay systems

## HOW IT WORKS

- Cells have the ability to communicate through gap junctions. Small molecules pass between adjacent cells through channels known as connexins
- Connexins can spread toxins that kill neighboring cells – the cause of loss of vision
- Connexin inhibitors preserve retinal cell structure and function



Institution

[State University of New York](http://www.suny.edu)

## Inventors

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