**Alcohol abuse drug can be repurposed to treat a blinding disorder**

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Disulfiram prevents scars forming in a mouse model of scarring conjunctivitis and returns human scarring cells from people with the condition back to normal

New research has identified a gene that drives scarring in the UK’s most common cause of blinding conjunctivitis. The results also show that the drug disulfiram returns human and mouse scar-making cells to normal and prevents scarring in a mouse version of the condition. The research took place at University College London, Moorfields Eye Hospital and Duke University School of Medicine with funding from Fight for Sight, UCL Business, and Moorfields Eye Charity.

Scarring conjunctivitis is a major cause of long-term pain and sight loss. The conjunctiva is the membrane that lines the eyelid and covers the white of the eye.

When it’s healthy the conjunctiva helps to lubricate and protect [the eye](http://www.fightforsight.org.uk/about-the-eye/anatomy-of-the-eye/). But when it’s not, inflammation can quickly trigger severe scarring.

**Destructive scarring**

This can happen in conditions such as [ocular mucous membrane pemphigoid](http://www.fightforsight.org.uk/about-the-eye/a-z-eye-conditions/ocular-mucous-membrane-pemphigoid/) (ocular pemphigoid), severe eye allergy, Stevens-Johnson syndrome, and trachoma. The scarring process often continues after the inflammation has gone and can destroy the conjunctiva’s ability to protect the eye.

Ocular pemphigoid was chosen for the current study because mucous membrane pemphigoid is a classic example of this type of condition. It’s also the most common scarring conjunctival condition in the UK that’s controlled by the immune system.

Standard treatment for ocular pemphigoid is to suppress the immune system. This controls inflammation when it works (it doesn’t always), but there are unpleasant side effects and it has little effect on scarring. Approximately 1 in 5 people with the ocular form go blind.

In this study, the research team looked for genetic activity linked to scarring in conjunctival tissue, and in the scar-making cells (fibroblasts) grown from this conjunctiva. The aim was first to find a target for treatment and then to be able to test the effect of treating the target.

**Disulfiram blocks vitamin A pathway**

Results show that a family of molecules known as aldehyde dehydrogenase 1 (ALDH1) is more active in tissue and fibroblasts from people with ocular pemphigoid compared to controls. ALDH1 is critical for one step in the process of turning vitamin A into retinoic acid – a key protein in immunity, inflammation and scarring.

Disulfiram is a drug that’s licensed for treating alcohol abuse. It works by blocking ALDH activity, including ALDH2, which processes alcohol. Treatment with disulfiram eye drops reduced eye surface inflammation in mice with a version of the condition and prevented scarring compared to controls. The drug was also used successfully to treat scarring cells from patients.

**Closer to the clinic**

Fight for Sight’s Director of Research, Dr Dolores M Conroy said:

“This is very important work given the devastating impact of progressive scarring on the eye and other organs. There is currently just one licensed drug for fibrosis and that is for lung disease. Mucous membrane pemphigoid affects the eye in 7 in 10 people with the condition, with 1 in 5 going blind. The potential for disulfiram as an effective treatment is very exciting, particularly as we know that it may be closer to the clinic than a drug developed from scratch, and especially if it can also find an application in trachoma, which affects 40 million people around the globe.

Dr Sarah Ahadome at UCL Institute of Ophthalmology is the study’s first author and did the research for her Fight for Sight-funded PhD. Professor John Dart and Professor Julie Daniels, both of NIHR Moorfields Biomedical Research Centre and the UCL Institute of Ophthalmology, were joint research leads, together with Professor David Abraham at UCL Royal Free Campus. The study is [published in the *Journal of Clinical Investigation Insight*](http://insight.jci.org/articles/view/87001).

Read the full release ([PDF](http://www.fightforsight.org.uk/media/1646/ommp-2016-08-04-aldh-inhibition-with-disulfram.pdf)) ([text](http://www.fightforsight.org.uk/media/1647/ommp-2016-08-04-aldh-inhibition-with-disulfram.txt)).

Find out more about the research project: