

Scientists discover genetic changes linked to a major risk factor for blinding trachoma

February 16 2016



Overal disease burden of trachoma, 2004. Credit: Lokal_Profil.

Another clue to the workings of trachoma - the world's leading infectious cause of blindness - has been revealed in a new study published in *BMC Infectious Diseases*. Researchers identified markers of genetic regulation present in the early stages of infection that could predispose children to developing the condition in its long-term, severe form.

The study was carried out by a team at the London School of Hygiene &



Tropical Medicine, part-funded by Fight for Sight and The Wellcome Trust, in partnership with colleagues in West Africa.

Trachoma is endemic in 51 countries and is the cause of irreversible blindness in 1.2 million people worldwide.

Mass distribution of antibiotics can successfully treat the initial <u>infection</u> of the conjunctiva with the bacterium Chlamydia trachomatis. The conjunctiva is the mucous membrane that covers the front of the eye and lines the inside of the eyelids. However, children in <u>trachoma</u>-endemic areas can suffer repeated episodes of infection and, in some, this triggers chronic inflammation and scarring of the eyelid.

As the eyelids tighten, eyelashes turn inward and scratch the cornea - a condition called trichiasis - eventually leaving the cornea opaque and causing <u>blindness</u>. Researchers are investigating why only some people in endemic areas go on to experience inflammation and scarring.

The research team has previously found that two microRNAs - known as miR-147b and miR-1285 - are increased in adults with scarring and inflammatory trachoma. MicroRNAs are small molecules that are key controllers of the activity of many other genes. The new study is the first report of microRNA activity in inflammatory trachoma during the initial stage of disease.

The team looked at samples from children with both infection and inflammation compared to samples from children with healthy conjunctiva and no infection. The analysis showed that two microRNAs - miR-155 and miR-184 - have a direct relationship with the degree of inflammation.

Lead author and Fight for Sight PhD student, Tamsyn Derrick from the London School of Hygiene & Tropical Medicine, said: "We found that



miR-155 is increased and miR-184 is decreased as the severity of clinical inflammation goes up. We think this pattern of microRNA expression reflects the activity of immune cells in the conjunctiva. MiR-155 in particular has wide-ranging and profound effects on immune cell development and function, while miR-184 is the only microRNA that is present in significantly different levels between people with inflammatory trachoma that has persisted post-infection, versus uninfected healthy controls."

Dr Martin Holland who led the research group at the London School of Hygiene & Tropical Medicine said: "Our results suggest that the presence of inflammatory cells is required to drive pathological responses in the conjunctiva. They also present in miR-184 a new target with significant therapeutic potential.

"Studies conducted elsewhere have shown that increasing miR-184 prevents abnormal communication between cells in a mouse model of retinal disease and lower levels of miR-184 during acute corneal injury are restored upon healing. Its prolonged low-level state in post-infection inflammatory trachoma could therefore reflect prolonged wound healing and abnormal cell signalling. It may also contribute to thinning of the conjunctiva's outer layer, something we see in trachoma, which could predispose people to repeat infection."

Dr Dolores M Conroy, Director of Research at Fight for Sight, said: "Inflammation is known to be a major risk factor for scarring trachoma and these results give us an important indication of why. One of the priorities for research identified by the Sight Loss and Vision Priority Setting Partnership was to find out whether severe ocular surface diseases in children can be better managed. Knowing who is at risk and how that risk can be reduced is a major step towards better management of this globally devastating condition."



Provided by London School of Hygiene & Tropical Medicine

Citation: Scientists discover genetic changes linked to a major risk factor for blinding trachoma (2016, February 16) retrieved 6 May 2024 from <u>https://medicalxpress.com/news/2016-02-scientists-genetic-linked-major-factor.html</u>

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