New Insight into Dry Eye Inflammation

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Dry eye disease (DED) is a common disorder of the tears and ocular surface, affecting some 5 million Americans 50 years of age and older and affecting women disproportionately.¹ Tens of millions more have less severe symptoms typically triggered by adverse factors such as low humidity or contact lens wear.¹ Although the disorder is not life threatening, the symptoms of pain and irritation associated with DED significantly impede daily activities such as driving and reading and reduce overall quality of life.² The prominent role of inflammation in the development and exacerbation of DED is well recognized, but our understanding of the pathogenesis of DED is far from complete.² This has hindered the development of novel treatments, with Restasis remaining the only Food and Drug Administration–approved dry eye pharmaceutical treatment in the United States.

The study by Sonawane et al.³ sheds light on a previously unexplored possible source of inflammation in DED, namely extracellular DNA (eDNA). The authors show that in a severe dry eye patient population there is increased ocular surface eDNA and molecular components of neutrophil extracellular traps (such as cathelicidin, LL-37), a likely consequence of reduced nuclease activity that they also detected in DED patients. Sonawane et al.³ also show increased expression of genes associated with inflammation such as TLR9 and various cytokines in DED patients. Given the ability of LL-37 to bind self-DNA,⁴ as suggested for other inflammatory conditions, one scenario proposed by the authors is that LL-37 binds eDNA, carrying it into ocular surface cells and leading to activation of the TLR9-MyD88 pathway, a type 1 interferon response, and triggering adaptive immunity. This is significant given recent evidence of a prominent role for adaptive immunity in the pathogenesis of dry eye.⁵ It remains to be seen if the findings of Sonawane et al.³ are also applicable to less severe dry eye; nevertheless, their results raise the possibility of novel treatment approaches to reduce DED inflammation, for example by clearing excess eDNA from the ocular surface and/or reducing activation of eDNA signaling pathways.

References