|  |
| --- |
| **Electrospun patch delivery of anti-TNFα F(ab) for the treatment of inflammatory oral mucosal disease** |
| Jake G. Edmans1,2, Bethany Ollington1, Craig Murdoch1, Sebastian G. Spain2, Paul V. Hatton1, Helen E. Colley1 |
| 1The School of Clinical Dentistry, University of Sheffield, Sheffield, United Kingdom; 2Department of Chemistry, The University of Sheffield, Sheffield, United Kingdom |
| **Background:** Chronic ulcerative oral mucosal inflammatory diseases, including oral lichen planus (OLP) and recurrent aphthous stomatitis (RAS), are painful and highly prevalent, yet lack effective clinical management. The pro-inflammatory cytokine TNFα is a key molecule in the pathogenesis of these diseases. The ability to deliver TNFα-neutralising biologics topically to the oral mucosa would greatly expand treatment options. This study aims to evaluate a mucoadhesive patch formulation for the delivery of anti-TNFα-F(ab) antibody fragments to the oral mucosa. |
| **Methods:** Mucoadhesive fibrous polymer patches containing F(ab) antibody fragments were prepared using electrospinning and characterised. Patches containing neutralising anti-TNFα F(ab) were applied to tissue-engineered oral ulcer models containing activated macrophages to measure the effect on pro-inflammatory cytokine concentrations. |
| **Results:** The polymers had a protective effect on F(ab) functionality and facilitated patch fabrication by electrospinning. The F(ab) were rapidly released from the patch in aqueous media (97 ± 5% released within 3h). Neutralising anti-TNF-α F(ab) fragments were generated by papain cleavage and incorporated into patches. Patches containing anti-TNFα F(ab) were found to have TNF-α neutralising activity, as shown by the suppression of TNF-α-mediated CXCL8 release from oral keratinocyte grown as monolayer cultures. Anti-TNFα patch treatment led to reduced levels of active TNFα along with a reduction in the levels of disease-implicated T-cell chemokines (CCL3, CCL5, and CXCL10) to baseline concentrations. |
| **Conclusions:** Topical antibody delivery using this formulation has the potential to change the way debilitating oral diseases such as OLP and RAS are treated in the future, as well as representing a platform technology for the site-specific delivery of antibody fragments to tissue surfaces to treat a wide range of conditions. |