



# E3B

The Elements of  
Bioremediation,  
Biomanufacturing  
& Bioenergy

## Metals in Biology



Biotechnology and  
Biological Sciences  
Research Council

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# Potential anti-viral and therapeutic activities of the enzymatic degradation products of pharmaceutical polysaccharides modulated by metal ions

**“This Business Interaction Voucher has been vital in advancing our project and enables us to focus on the key anti-viral target molecules for future development,” University of Liverpool**

**PROJECT AIMS:** Fragments of larger sugar molecules derived from the blood thinner heparin and its precursors have promising anti-viral activity and also diminish the symptoms of viral infection such as inflammation. The aim of this study was to produce a panel of novel heparin-derived fragments and identify those with improved potential anti-viral activities and the ability to modulate the immune response. The fragments will then undergo further testing and development in subsequent studies.

**RESULTS:** Heparinase enzymes (hI, hII and hIII) were purified from *Bacteroides spp.* and used to digest heparin and precursor polysaccharides in the presence of associated metal ions.

This process generated a panel of active heparin fragments that had diverse cation forms (Na, K, Mg, Ca, Zn, Cu(II), Mn(II)).

The heparin fragments were then assayed for interactions with viral proteins; namely the SARS-CoV-2 spike protein (S1) and Dengue and Zika virus envelope proteins.

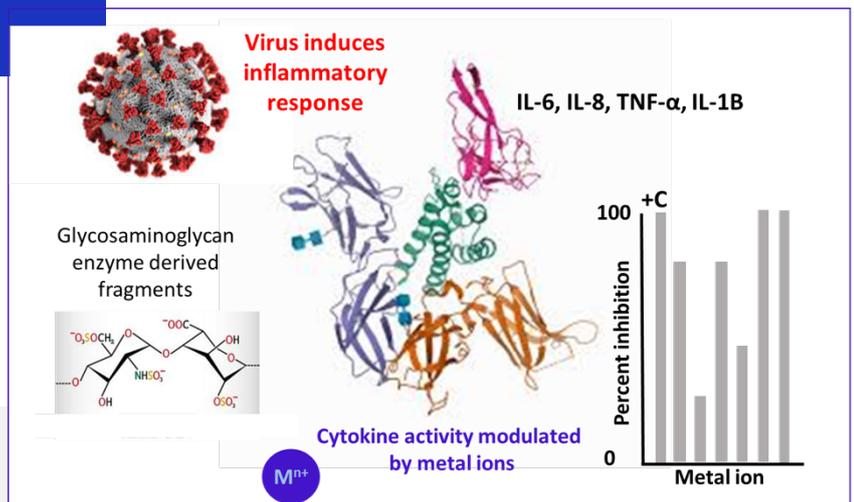
Next, the heparin fractions with the strongest binding to the viral proteins (the top 10 %) were assayed for potential anti-inflammatory activity in cytokine-binding assays (interleukin (IL)-6, IL-8, tumour necrosis factor- $\alpha$ , IL-1B).

This resulted a panel of scores of heparin fragments with potential antiviral and anti-inflammatory activity that will be tested in future studies.

Change in technology readiness level: 1/2 to 2/3

### OUTCOMES & NEXT STEPS:

- More detailed studies of the interaction between the heparin fragments and viral proteins will be carried out by the academic and industry partners, as well as an assessment of the potential of the fragments as therapeutics and anti-inflammatory agents against SARS CoV-2, Dengue and Zika virus infections.
- Parts of this work featured in a talk entitled ‘Heparin inhibits cellular invasion by SARS CoV-2’, at the 28<sup>th</sup> Symposium on Glycosaminoglycans, in San Servolo, Venice, September 2021.



Metal cations modulate the anti-inflammatory activity (measured by cytokine analysis) of enzyme-derived glycosaminoglycan fragments.