Delivery of immobilised NGF and BDNF via a bioactive surface to enhance neurite outgrowth

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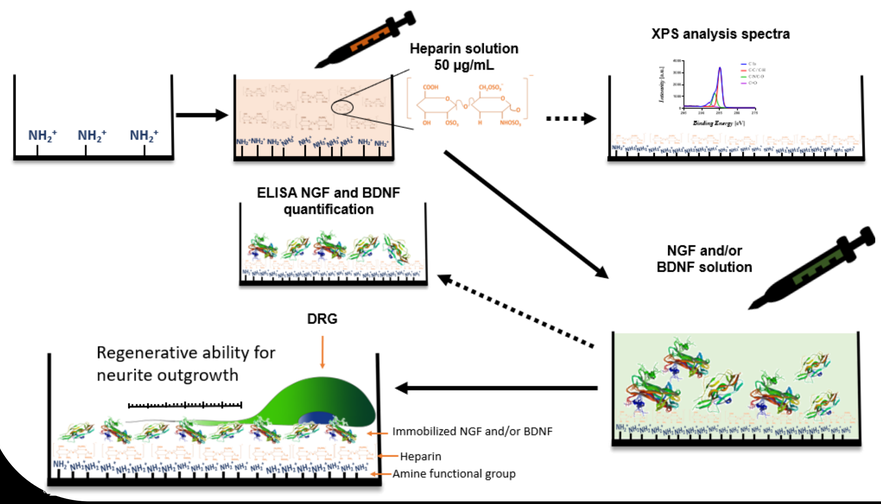
Introduction

Peripheral nerve injury remains a major cause of disability that compromises the life quality and health of 1 in 1000 patients [1]. A novel strategy to improve the performance of NGCs includes the addition of neurotrophins. However, the short half-life of neurotrophins limits the regeneration of the nerve [2][3]. The development of a sustained delivery platform would allow a controlled release of neurotrophins and thus, enhance neurite outgrowth. We present the fabrication of a bioactive surface using electrostatic interactions to bind neurotrophins [4] and improve their release. The aim of this study was to 1) develop a bioactive surface enriched with positive amine groups and in turn heparin. This platform was then loaded with NGF, BDNF, or in combination for local release, and thereafter 2) evaluate their effects in neurite outgrowth.

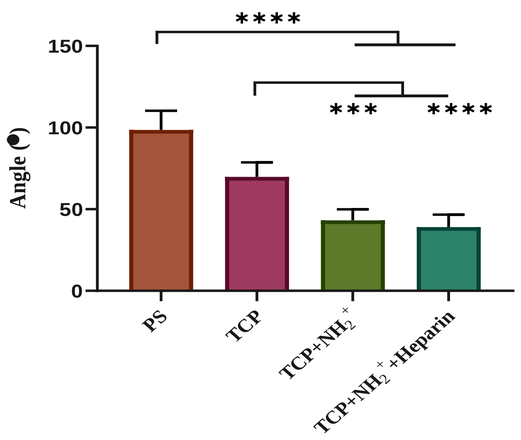
Materials and Methods

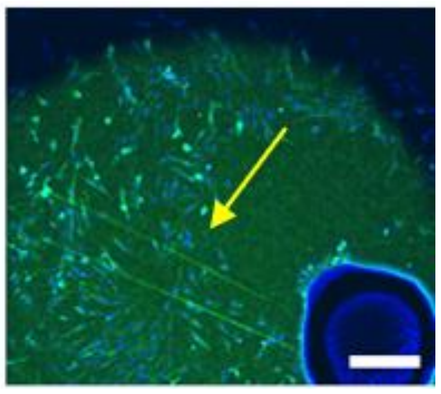


1. To a pre-coated amine 96 well-plate, heparin solution was added and incubated overnight at room temperature.
2. To the amine + heparin surface, NGF, BDNF or NGF plus BDNF were added and incubated for 5 h at room temperature.
3. Surface characterisation: water contact angle, XPS analysis, ELISA assay.
4. Evaluation of biological effects: measurement of neurite length of chick embryonic (EDD 12) DRGs seeded on bioactive surface for 7 days. (Immunolabelling of βIII tubulin).

Results and Discussion

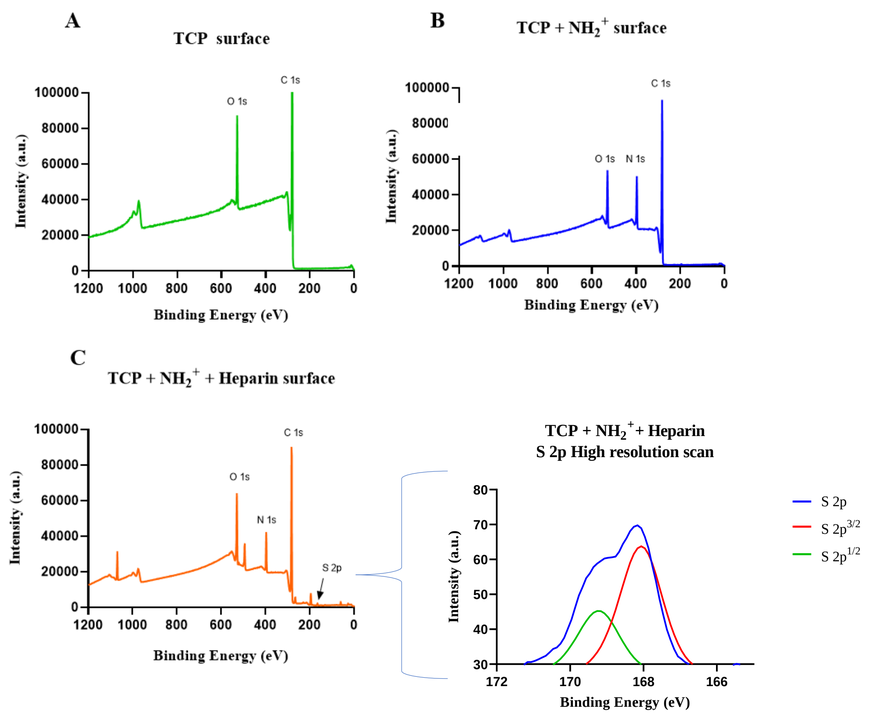
Water contact angle



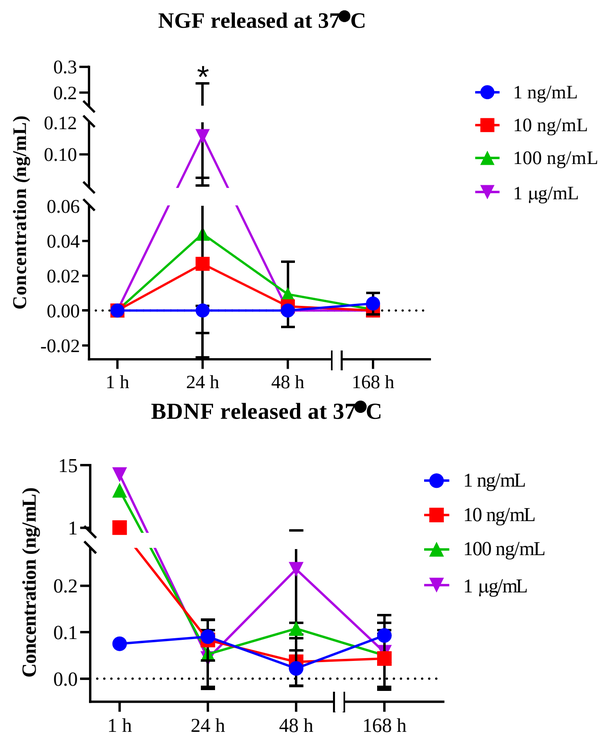


βIII tubulin for neurites = green
DAPI for nuclei = blue
Scale bar = 500 µm

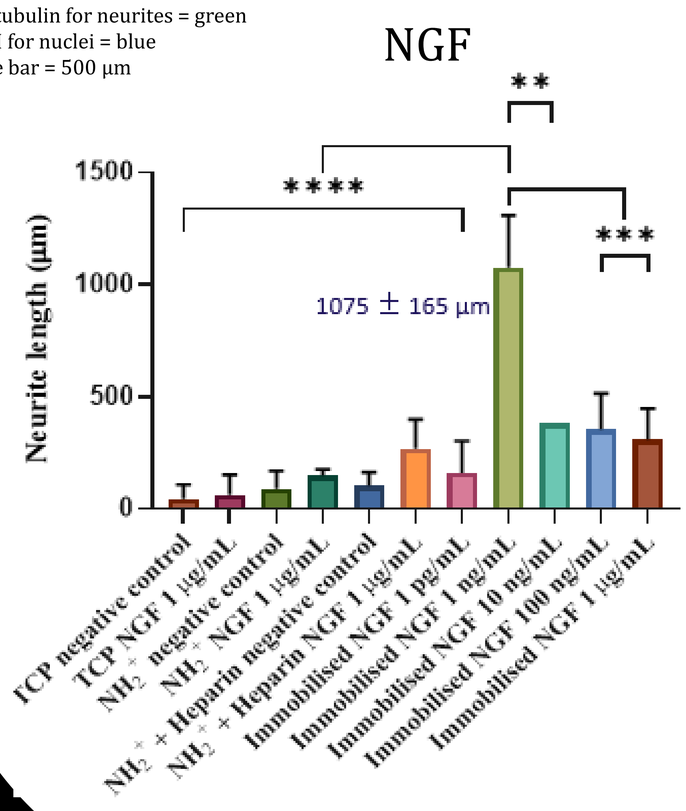
XPS analysis

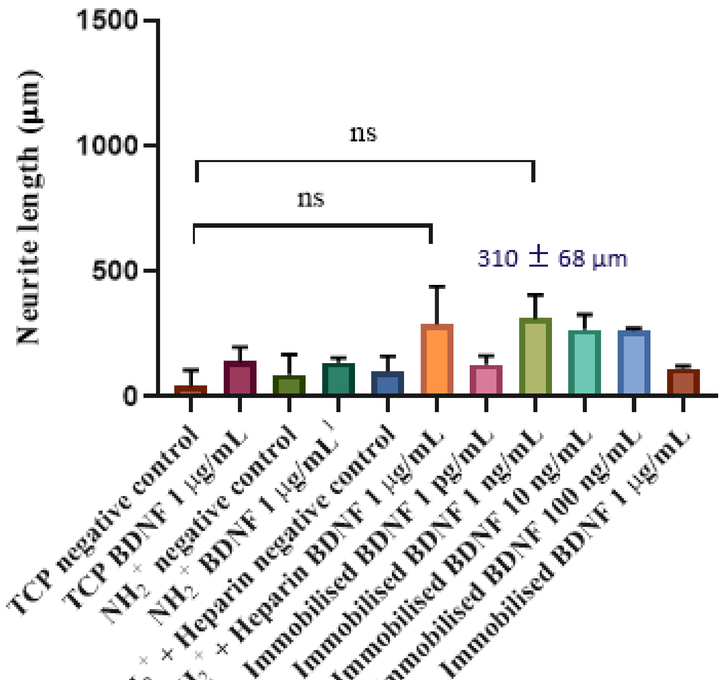


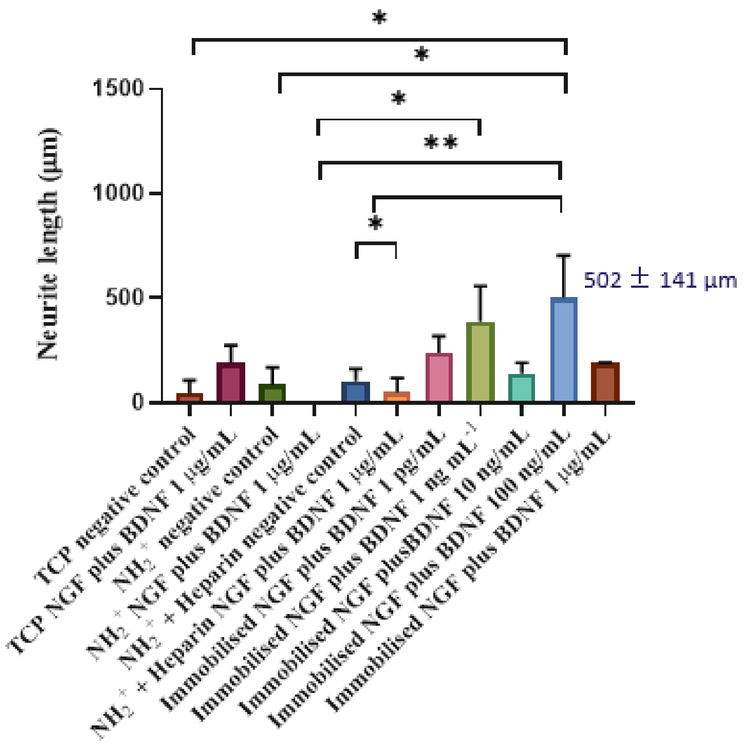
ELISA assay



Effect in neurite outgrowth: DRGs







Conclusion

Our results showed that bioactive surfaces with immobilised NGF at 1 ng/mL supported the largest neurite. In summary, locally delivered neurotrophin surfaces are a promising approach to stimulate nerve regeneration using bioactive nerve guides [5].

References

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