

A Novel Therapeutic Approach Encapsulating Brain-Derived Neurotrophic Factor in Nanoporous Particles for Treating Sensorineural Hearing Loss

Authors:

F Glynn^{1,2}

J Tan¹

Y Wang²

F Caruso²

RK Shepherd¹

Institutions:

The Bionic Ear Institute¹
384-388 Albert Street
East Melbourne
Victoria 3002

Dept of Chemical and Biomolecular Engineering²
University of Melbourne
Victoria 3010

Submitted for poster presentation

Author details:

fglynn@bionicear.org

Tel: 99298288

Fax: 99631958

INTRODUCTION

The spiral ganglion neurons, target neurons of cochlear implants, gradually degenerate following sensorineural hearing loss, potentially reducing the clinical efficacy of these devices. A means of preventing spiral ganglion nerve degeneration in deafness is therefore of great clinical significance. The neurotrophin, brain-derived neurotrophic factor (BDNF), is known to be important in the development and maintenance of the auditory system and also has been shown to have a protective effect on spiral ganglion neurons in animal models of deafness. Importantly it has been shown that these survival effects are not maintained upon cessation of treatment, therefore it is necessary to develop clinically relevant methods for longer term delivery and thus protection of spiral ganglion neurons following deafness.

AIMS

To use polymer chemistry and templating technique to create nanoporous biodegradable and bio-compatible particles which are able to sequester biologically active BDNF.

METHODS

Nanoporous polyglutamic acid (NPGA) spheres were first created using mesoporous silica as a template. The polymer is infiltrated into the silica particles and covalently crosslinked with cystamine by the catalysis of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride. The silica template is then dissolved using buffered hydrofluoric acid. The polysaccharide heparin sulphate is then infiltrated into the NPGA spheres thus creating a highly negatively charged nanoparticle. BDNF is then adsorbed into the particle through electrostatic interactions between the residual amine group on the protein, the carboxyl group on the polymer and highly sulphated glycosaminoglycan on the heparin salt. The quantity of BDNF released is assessed using an enzyme-linked immuno-adsorbant assay. The biological activity of the released BDNF is assessed by its affect on cultured third generation neuroblastoma SH-SY5Y cell lines.

RESULTS

A sustained delayed release of BDNF was obtained over a period greater than 50 days. The biological activity of the BDNF was confirmed by its survival effects on neurons differentiated from the SH-SY5Y neuroblastoma cell line.

CONCLUSION

BDNF can be successfully sequestered in a biologically active form within nanoporous polyglutamic acid/heparin sulphate nanoparticles. Its release can be prolonged to a period greater than 50 days. While this technique has potential therapeutic application for neural rescue in the auditory system, it also has potential application more broadly in the field of neural degeneration.

This work was supported by the NIH (HHS-N-263-2007-00053-C), the Royal Victorian Eye & Ear Hospital and the University of Melbourne.