Biocompatibility of a Novel Biomaterial for Adult Neural Progenitor Cell Proliferation and Differentiation

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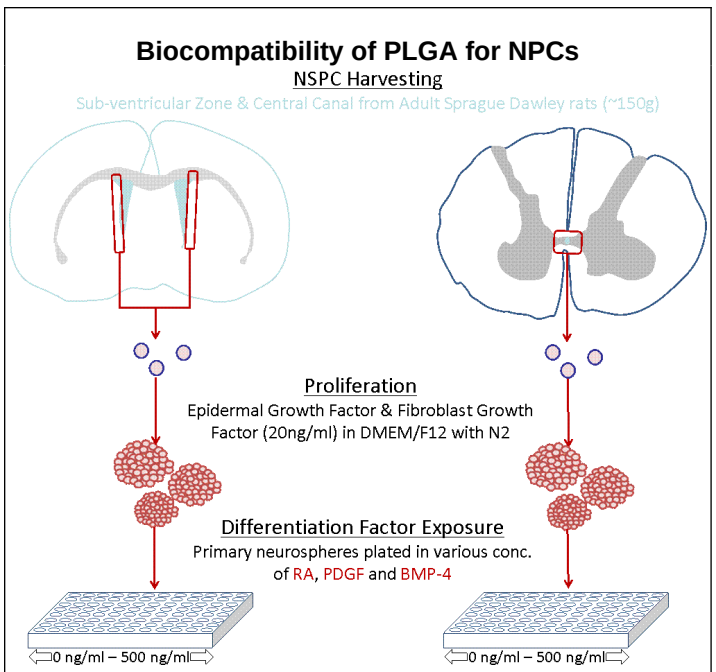
Introduction

We have developed a poly (lactide-co-glycolide) (PLGA) scaffold to act as a therapeutic factor delivery agent following injury to the central nervous system. Our PLGA scaffold can degrade over time while releasing proliferation and differentiation factors for endogenous neural progenitor cell (NPC) recruitment. Prior to in vivo testing, its in vitro effects were profiled. We hypothesized that PLGA would not be toxic to NPCs and would not affect the differentiation of NPCs.

Methods



NPCs were incubated with and without the biomaterial for 7, 14 and 21 days in vitro (div), and then underwent differentiation conditions for 7 more days. The longest exposure time point was 28 div (21 div proliferation + 7 div differentiation). At the end of each time point cells were fixed and stained using standard immunocytochemistry techniques.

Results

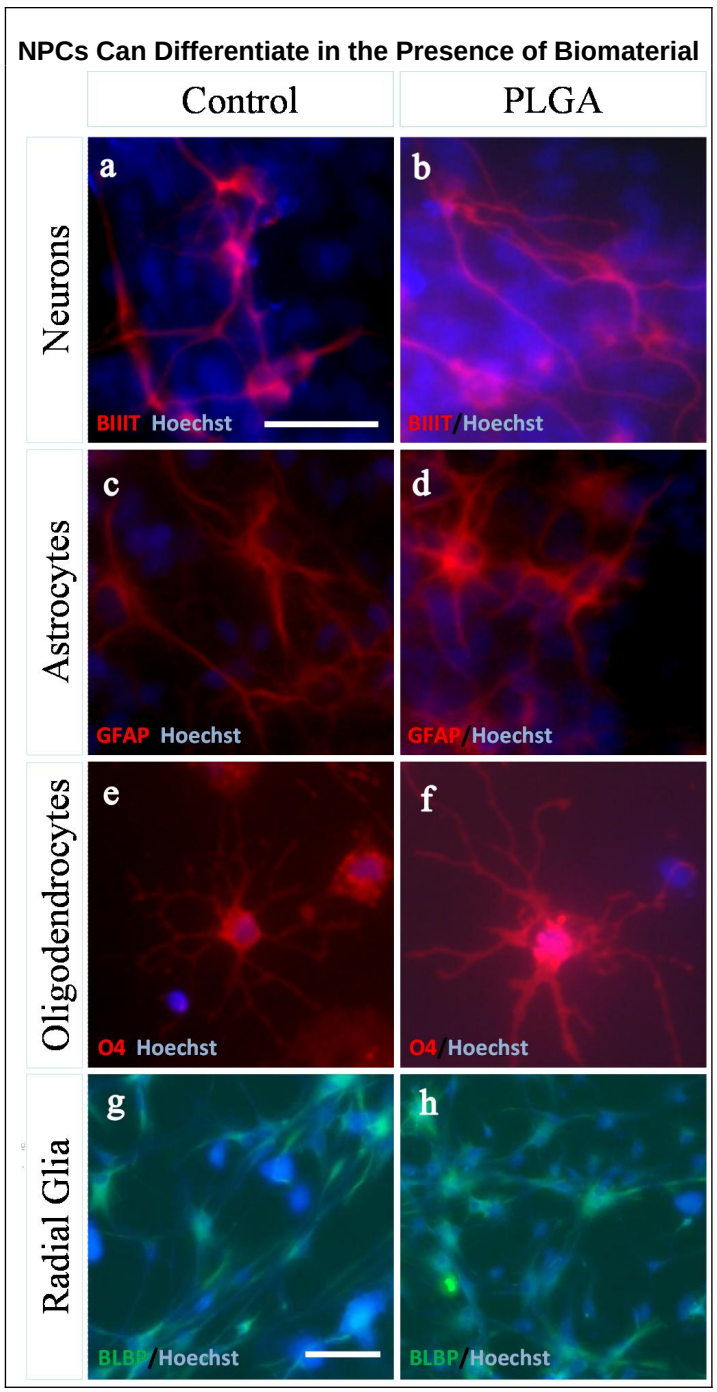


Figure 4: NPCs immunopositive for (a,b) beta-III-tubulin (neurons) (c,d) glial fibril acidic protein (astrocytes) (e,f) O4 (oligodendrocytes) after 7 div. Scale bar = 5 um. SEZ cells immunopositive in vitro for (g,h) brain lipid binding protein (radial glia) after 7 div. Scale bar = 5 um

At both 14 and 21div NPCs survived, proliferated and differentiated in the presence of PLGA with no significant difference compared to control. However, after prolonged exposure (28 div) to PLGA a significant decrease in the degree of proliferation of the NPCs was observed (ANOVA, $p<0.05$). Also, 28 div PLGA exposure led to a substantial increase in the proportion of apoptotic positive cells (ANOVA, $p<0.05$).

Conclusions

The low toxicity and normal proliferation seen at 14 and 21 div but not at 28 div indicate that it is the by-products from the PLGA degradation and not the biomaterial itself that leads to increased toxicity. Therefore, this study reveals the need to control the degradation rate of biomaterials, in order to prevent harmful effects of the by-products of biomaterial degradation.

Learning Objectives

To understand that by-products of biodegradable biomaterials may be toxic to neural stem/progenitor cells and prevent neural stem/progenitor proliferation.