Sustained GDNF delivery via PLGA nanoparticles

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INTRODUCTION

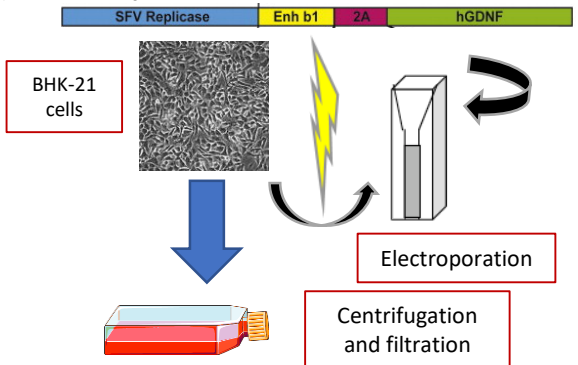
Glial cell line-derived neurotrophic factor (GDNF) is a protein with remarkable trophic actions on dopaminergic neurons which is under investigation for Parkinson's disease (PD) therapy[1,2]. It is a highly glycosylated biopharmaceutical in which the composition of attached glycans potentially influences drug efficacy and immunogenicity[2]. Hence, the use of recombinant GDNF from mammalian cells is essential to avoid safety issues[2]. Moreover, although several approaches to deliver this protein to the brain have been described[3], a promising strategy would be the use of nanoparticles (NPs) containing GDNF in the dopamine-depleted brain areas.

The objective of this work **is to develop and characterize biodegradable NPs loaded with recombinant GDNF produced in mammalian cells for brain tissue engineering.**

RESULTS

hGDNF expression and purification

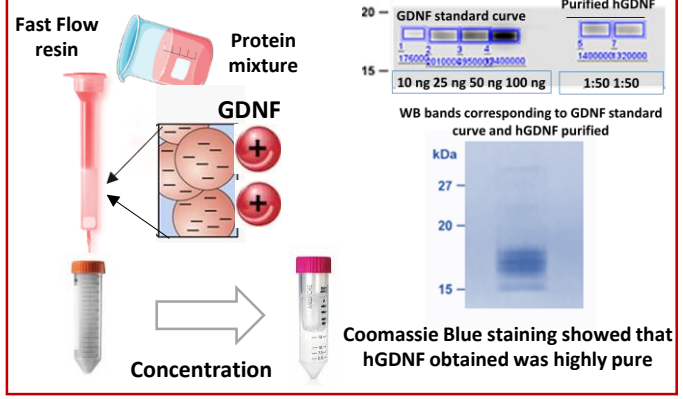
A) hGDNF expression in BHK cells



B) hGDNF purification

Cation exchange chromatography

WB analysis

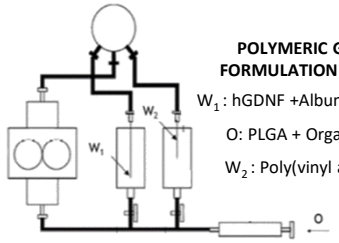


Coomassie Blue staining showed that hGDNF obtained was highly pure

hGDNF-loaded NPs preparation and characterization

A) hGDNF-loaded NPs preparation

hGDNF-NPs were formulated by double emulsión solvent evaporation using One Recirculation Machine (TROMS) Technology



POLYMERIC GDNF-NPs FORMULATION (W_1/O/W_2)

W_1 : hGDNF +Albumin +PEG + PBS

O: PLGA + Organic solvent

W_2 : Poly(vinyl alcohol) 1%

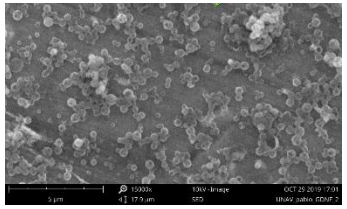
Scheme of TROMS Technology

B) NPs characterization

B1 **Size, PDI and EE**

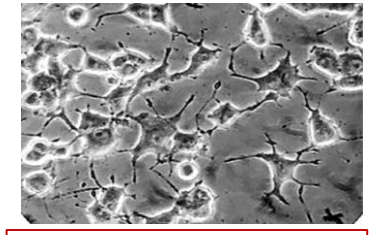
PLGA	MEAN SIZE	PDI	EE%
NPs (n=3)	405.5 ± 2.9 nm	0.08 ± 0.03	61.65 ±7

B2 **SEM analysis**



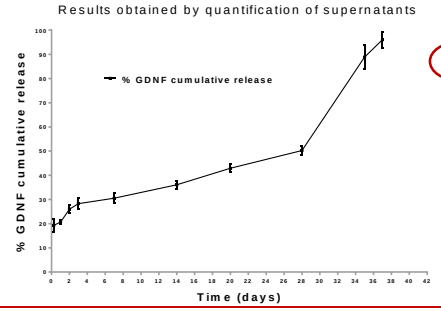
Spherical particles.
Uniform size distribution of NPs.
No aggregation.

B3 **Bioactivity**



PC12 cell-based bioassay showed that GDNF remains bioactive after its nanoencapsulation.

B4 **In vitro release study of GDNF from NPs**



GDNF released within the first 24 hours was 19.10 ± 3.5%, followed by a phase of sustained-release with 50.6 ± 3.1% of GDNF being released within 28 days.

Future perspectives

- A two-component hydrogel based on HA functionalization with adamantane (guest) and β-cyclodextrin (host) will be prepared and characterized.
- GDNF-NPs will be included in the hydrogel for its local brain administration.

CONCLUSIONS

- **GDNF-loaded NPs were successfully prepared by W1/O/W2 emulsion/extraction process using TROMS technology with a high drug entrapment efficiency.**
- **The developed nanosystem has great potential for brain tissue engineering applications.**

REFERENCES

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ACKNOWLEDGEMENTS

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