# Sustained GDNF delivery via PLGA nanoparticles

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## INTRODUCTION

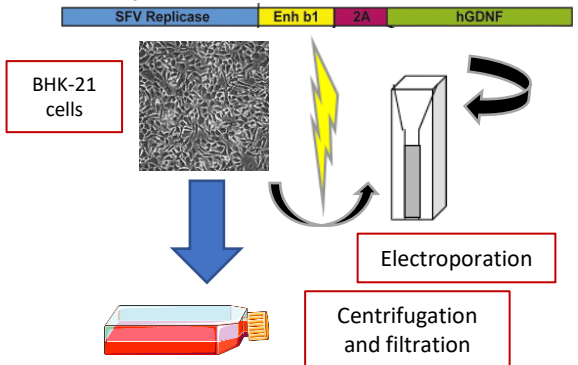
Glial cell line-derived neurotrophic factor (GDNF) is a protein with remarkable trophic actions on dopaminergic neurons which is under investigation for Parkinson's disease (PD) therapy[1,2]. It is a highly glycosylated biopharmaceutical in which the composition of attached glycans potentially influences 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

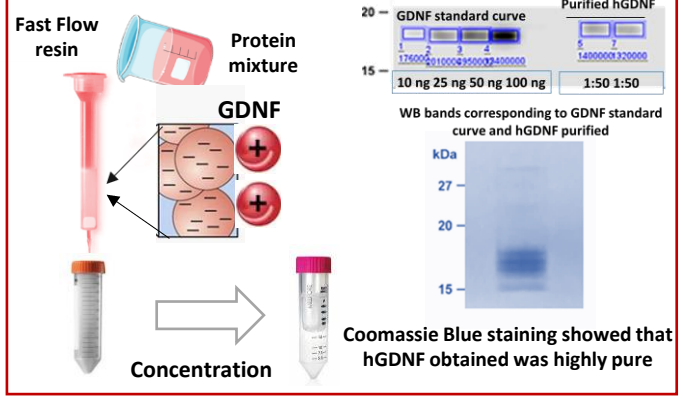
#### A) hGDNF expression in BHK cells




#### B) hGDNF purification

**Cation exchange chromatography**

**WB analysis**

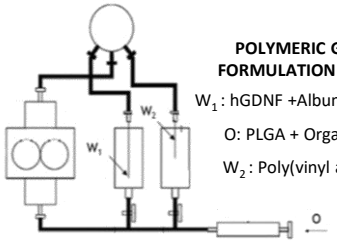



**Coomassie Blue staining showed that hGDNF obtained was highly pure**

### 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%

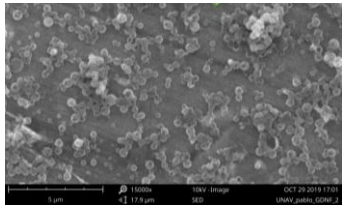
**Scheme of TROMS Technology**

#### B) NPs characterization

**B1** **Size, PDI and EE**

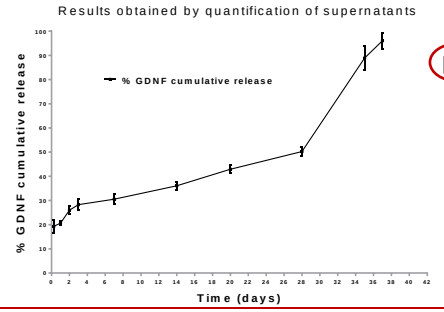
| PLGA | MEAN SIZE | PDI | EE% |
|---|---|---|---|
| NPs (n=3) | 405.5 ± 2.9 nm | 0.08 ± 0.03 | 61.65±7 |

**B2** **SEM analysis**



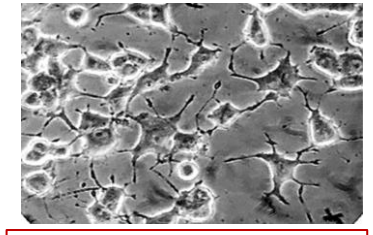
Spherical particles.
Uniform size distribution of NPs.
No aggregation.

**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.

**B3** **Bioactivity**



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

### 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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4. E. Ansorena et al. A simple and efficient method for the production of human glycosylated glial cell line-derived neurotrophic factor using a Semliki Forest virus expression system.

## ACKNOWLEDGEMENTS

This work was supported by the Spanish Ministry of Education (program FPU (FPU17/01212)) and Government of Navarra (2019_66_NAB9).
E. Garbayo is supported by a "Ramon y Cajal Fellowship (RYC2018-025897-I).