Fondazione Don Carlo Gnocchi Onlus

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LABION LABORATORY OF NANOMEDICINE AND CLINICAL BIOPHOTONICS

Blood-derived Extracellular Vesicles are potential biomarkers of response and recovery after stroke

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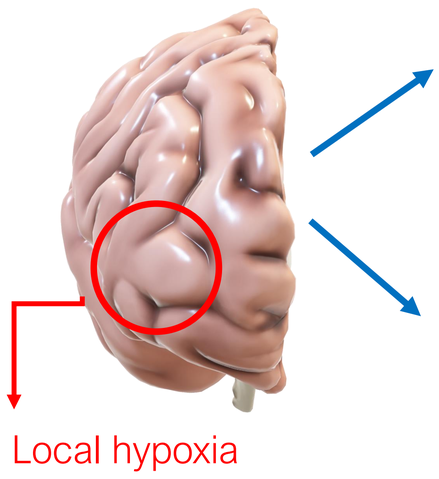


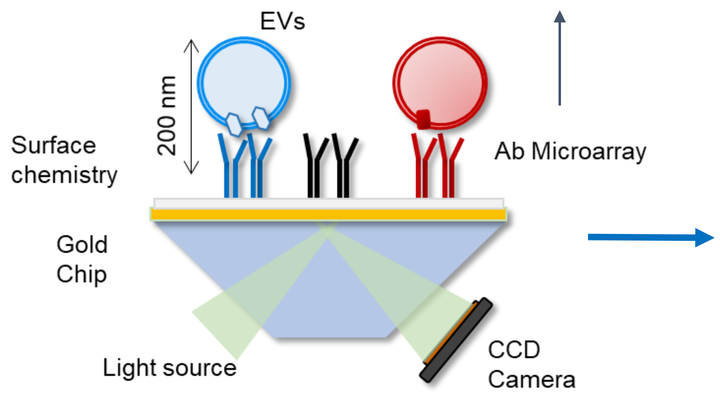
Hemorrhagic strokes
Caused by the rupture of a blood vessel inside the brain

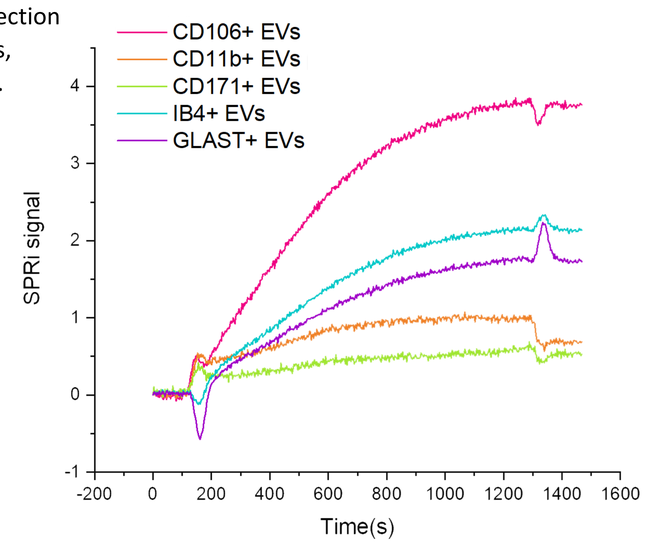
Ischemic strokes
Caused by the blockage of an artery inside the brain

INTRODUCTION

The local hypoxia induced by stroke **damages the brain tissue**. The patients that survive after the event may present **disabilities**, consequently the **rehabilitation phase is fundamental**. However, recovery after stroke is difficult to predict, and the **clinicians need specific predictive biomarkers** for the design of optimal and personalized therapeutic strategies.

Multiplexing biosensor [1,2] optimized for the detection of EVs with different cellular origin (neurons, astrocytes, microglia and endothelial cells).





AIM OF THE STUDY

Exploit the potentiality of **Extracellular Vesicles (EVs)** as **biomarkers** of recovery [3] after stroke to be used as decision support tool for the personalization of stroke therapy and rehabilitation using the **Surface Plasmon Resonance imaging (SPRi) technique.**

METHODS

Serum collection from stroke patients (ST, n=9) at the beginning (T0) and at the end (T1) of the rehabilitation program and from control subjects (CTRL, n=20).
ST: Barthel index at admission and discharge (after rehabilitation).

STROKE EVENT
Ischemic or Hemorrhagic

15 – 30 days

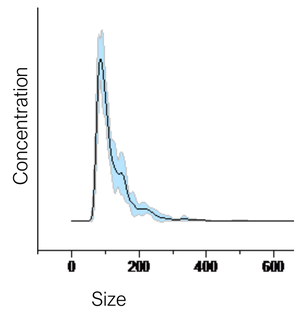
T0 REHABILITATION
Started at Fondazione Don Carlo Grocchi

2 months

T1 HOSPITAL DISCHARGE
Clinical evaluation

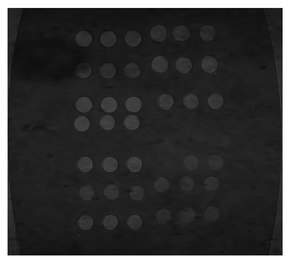
EVs isolation and characterization:

1 SEC



2 Nanoparticle Tracking Analysis

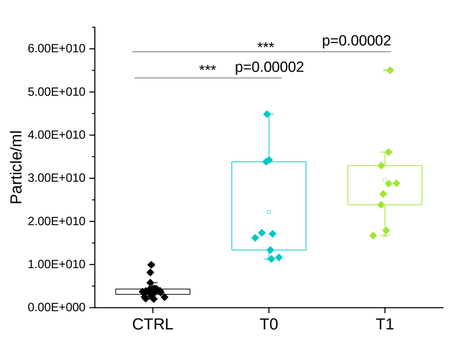
3 ImmunoAssay: ELLA and ELISA

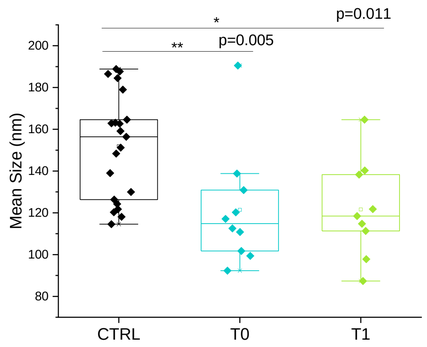


4 SPRi biosensor

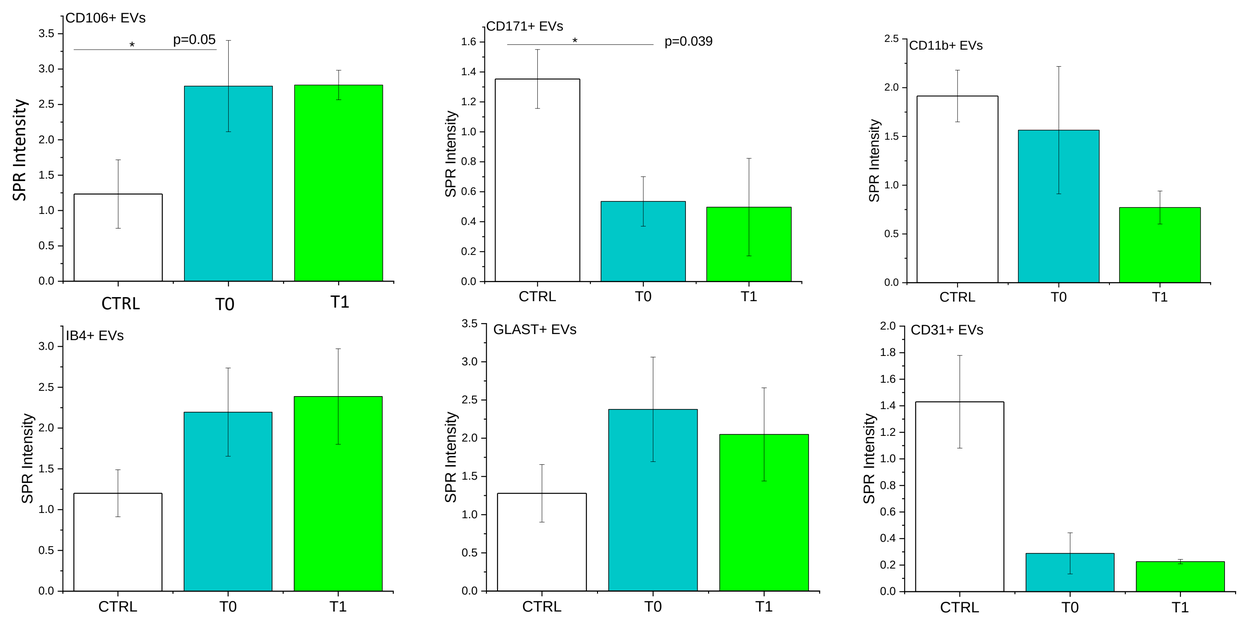
PRELIMINARY RESULTS

1
- **Higher concentration of EVs** in stroke patients (T0 and T1) compared to controls
- **Smaller size of EVs** in stroke patients (T0 and T1) compared to controls

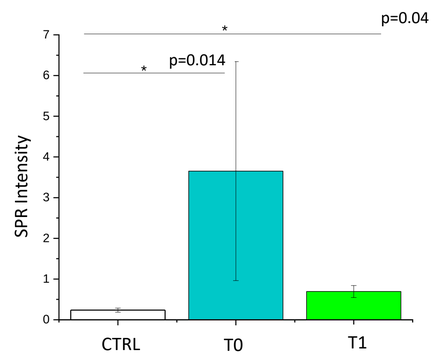




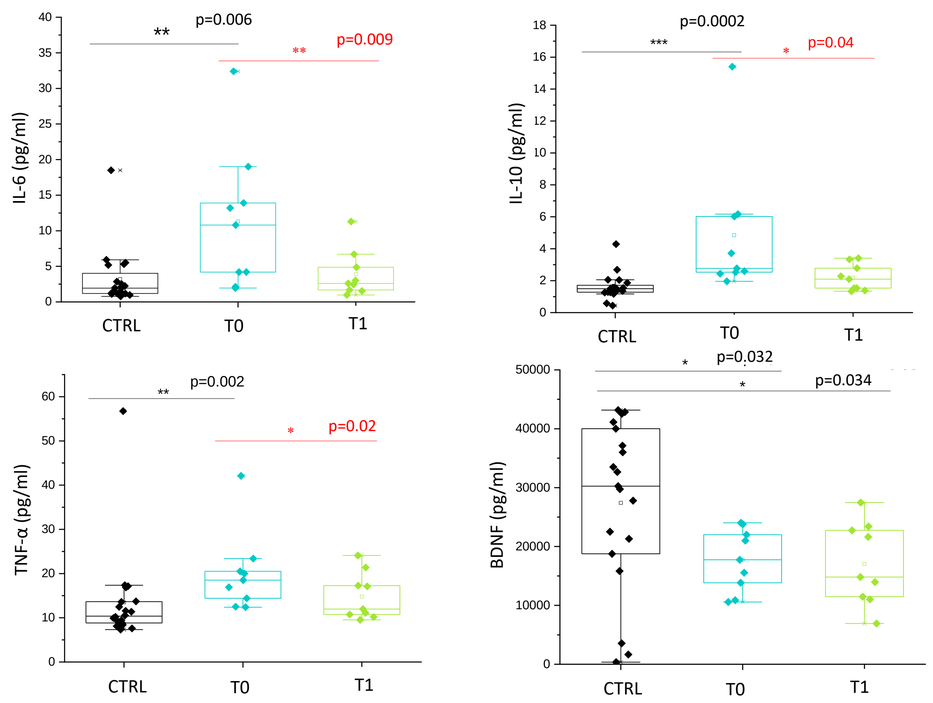
2 The statistical analysis of the SPRi results found significant differences in the following data:
- **Higher concentration of EVs from endothelial cells (CD106+)** in stroke patients (T0 and T1) compared to controls
- **Higher concentration of EVs from neuronal cells (CD171+)** in controls compared to stroke patients (T0 and T1)



3 **Higher expression** of **TSPO** receptor on **microglia EVs (CD11b+)** in stroke patients (T0 and T1) compared to controls. It tends to decease after rehabilitation.



4
- Soluble cytokines **IL-10, IL-6 and TNF-α** are **more concentrated** in stroke patients at T0 compared to T1 and controls
- Soluble **BDNF** is **more concentrated** in controls compared to stroke patients (T0 and T1)



- Mann-Whitney test
- Paired sample Wilcoxon signed rank test

CONCLUSIONS

- SPRi is a useful and versatile tool to characterize EVs with different cellular origins
- Stroke event increases the circulation of small EVs in blood
- Circulating EVs from neurons, microglia and endothelial cells are the most altered by stroke event in the considered cohort
- Cerebral injury at T0 leads to the activation of microglia (CD11b+) EVs and the release of pro and anti-inflammatory factors

[1]Picciolini S et al., JPBA 2021
[2]Picciolini S et al., Analytical Chemistry, 2018
[3]Gualerzi A et al., Biology, 2021

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