

Targeting Myocardial Fibrosis with a Novel Nanotherapeutic System

RuizdelRio J.¹, Aires A.², Cortajarena A.L.², Villar A.V.¹

¹Universidad de Cantabria Instituto de biomedicina y biotecnología, Cantabria, Spain.

²CIC biomaGUNE, Parque tecnológico de San Sebastián, Spain
ruizdelrioj@unican.es

A novel anti-fibrotic therapeutic peptide-nanocluster cTPR390-Nluc particle[1,2] is utilized to be incorporated to fluorescent nanocarriers to study its arrival to the heart inside engineered manipulated extracellular vesicles (f-EVs) to treat directly cardiac fibrosis. F-EVs from NIH-3T3 cells were selected to promote addressing them to the heart. Fibroblasts will be the target of the therapeutic system, due to their augmented presence in the pathological situation of myocardial fibrosis.

f-EVs were isolated by differential centrifugation and characterized by flow cytometry, western blot, dynamic light scattering, electron and confocal microscopy. The nanocluster was encapsulated by electroporation and the procedure was verified by flow cytometry. Fluorescence and bioluminescence *in vivo* imaging was used to visualize the therapeutic system in an animal model of cardiac fibrosis based on Angiotensin-II administration.

At 2 hours after administration, f-EV fluorescence and cTPR-Nluc bioluminescence were co-localized in the heart and lungs. After 6 days after administration, f-EV fluorescence was only visualized in the liver, stomach and intestine.

We conclude that the antifibrotic nanosystem composed by f-EVs and cTPR-Nluc is a fine system to reach the heart of fibrotic mice and a potential theragnostic complex molecule to be translated to clinics.

References

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Figures

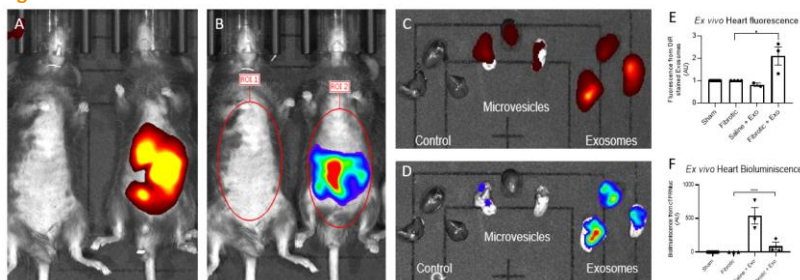


Figure 1: A.: *In vivo* fluorescence detection of f-EVs (exosomes) loaded in cTPR-Nluc after 2 hours of i.p. administration (control left mouse; treated right mouse). B.: *In vivo* bioluminescence detection of cTPR-Nluc loaded in exosomes after 2 hours of i.p. administration (control left mouse; treated right mouse). C.: *Ex vivo* detection of f-EVs fluorescence in the heart (top) and lungs (bottom) after 2 hours of i.p. administration. D.: *Ex vivo* detection of cTPR-Nluc bioluminescence in the heart (top) and lungs (bottom) after 2 hours of i.p. administration. E.: *Ex vivo* quantification of fluorescence detection of f-EVs (exosomes) loaded with cTPR-Nluc after 2 hours of i.p. administration. F.: *Ex vivo* quantification of bioluminescence detection of cTPR-Nluc loaded in exosomes after 2 hours of i.p. administration.