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Supplementary Information

Dendrimer-Tesaglitazar Conjugate Induces a Phenotype Shift of Microglia and Enhances β-amyloid Phagocytosis

Louis DeRidder[1,2], *Anjali Sharma*[1], *Kevin Liaw*[1,2], *Rishi Sharma*[1], *John John*[1,3], *Sujatha Kannan*[4,5], *Rangaramanujam M Kannan*[1,2,5*]

Author Affiliations:

[1] Center for Nanomedicine, Department of Ophthalmology, Wilmer Eye Institute Johns Hopkins University School of Medicine, Baltimore, MD 21231, USA

[2] Department of Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore, MD, 21218, USA

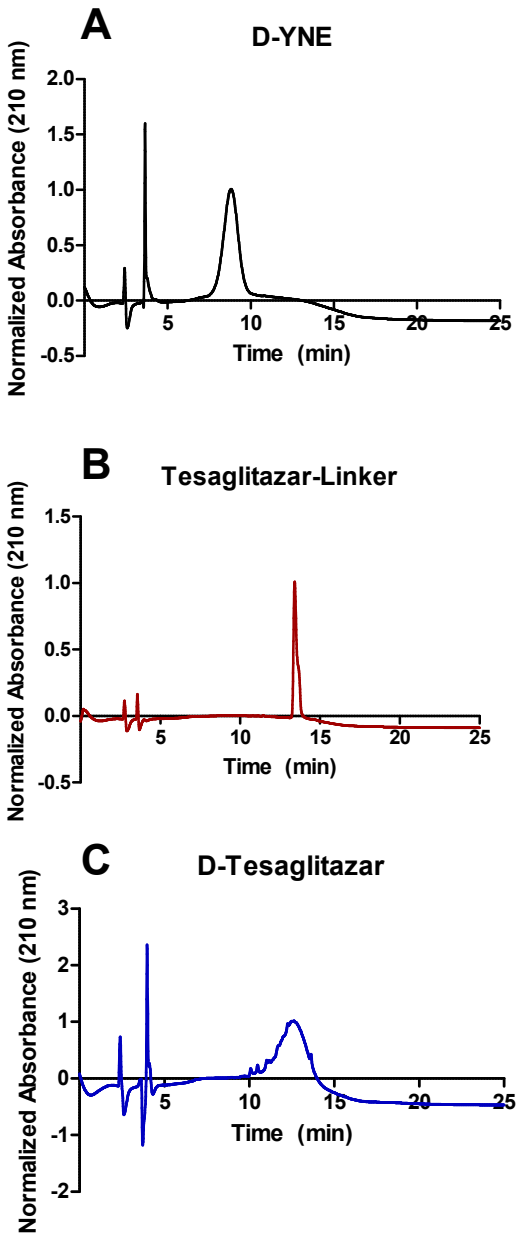
[3] Department of Biomedical Engineering, Johns Hopkins University, Baltimore, 21218, USA

[4] Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA

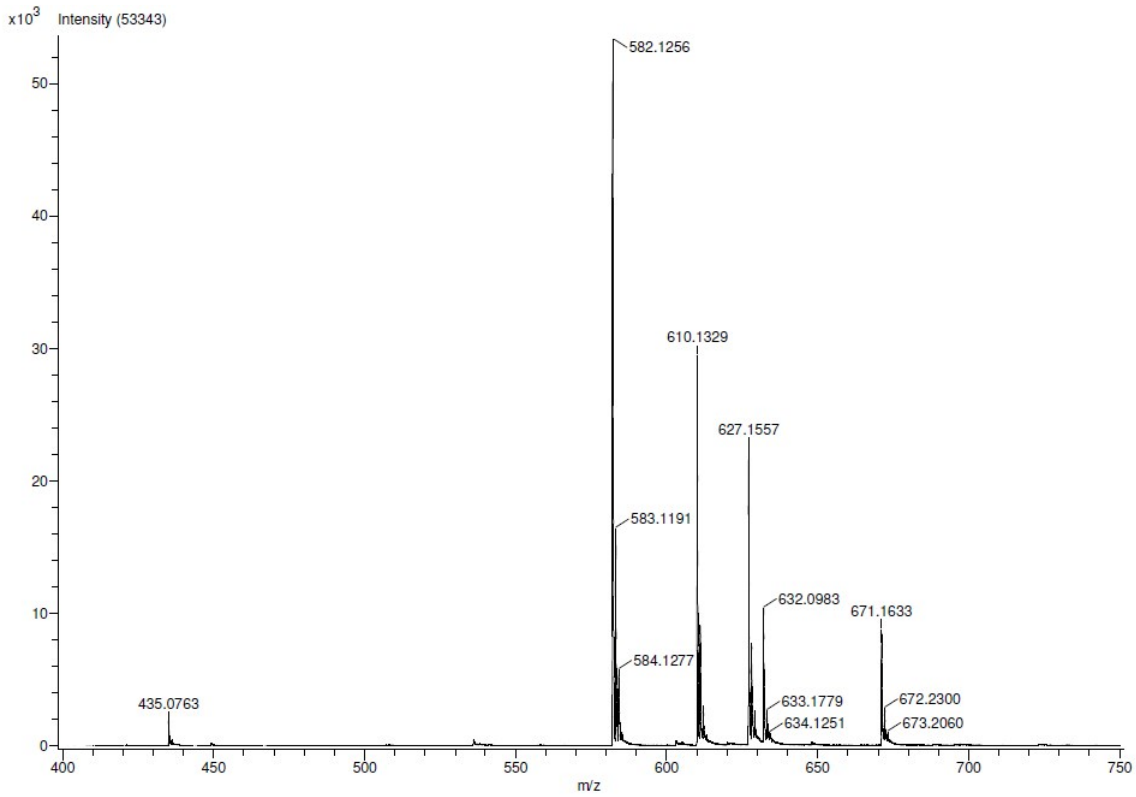
[5] Hugo W. Moser Research Institute at Kennedy Krieger, Inc., Baltimore MD, 21205, USA

* Corresponding author: E-mail: krangar1@jhmi.edu. Phone: +1-443-287-8634. Fax: +1-443-287-8635.

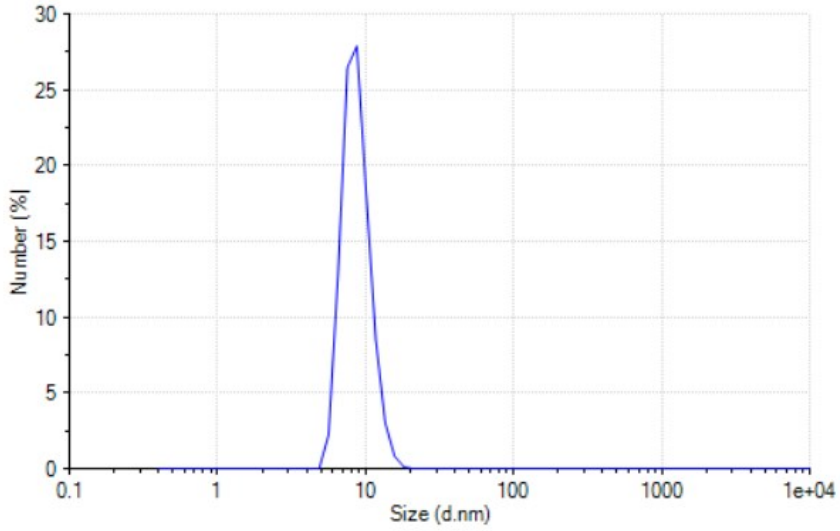
Supplemental Figures:



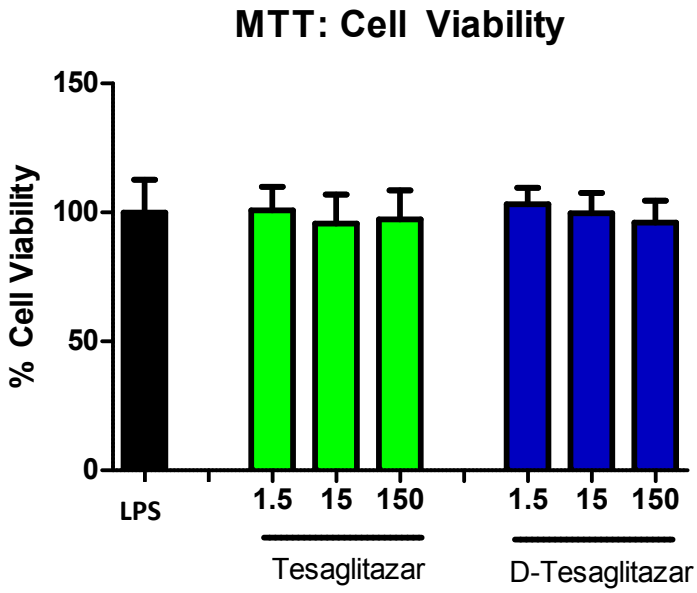
Supplemental Figure 1. HPLC of (A) D-YNE, (B) Tesaglitazar-linker and (C) D-Tesaglitazar. Purities were 99.8%, 99.2%, and 98.6%, respectively. The retention times were 8.9, 13.4, and 12.6 minutes, respectively.



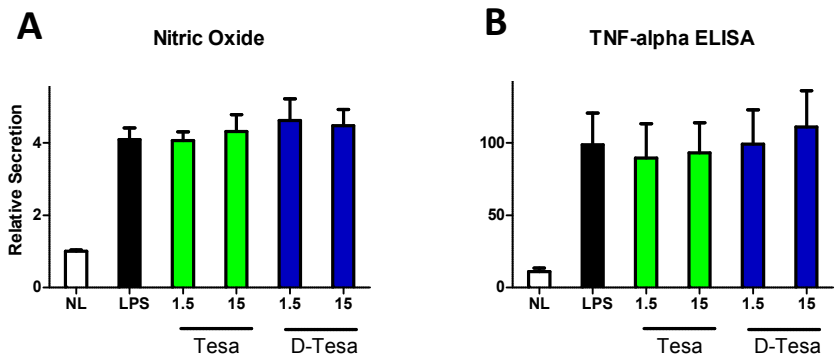
Supplemental Figure 2. Mass spectrum of Tesa-TEG-azide (3).



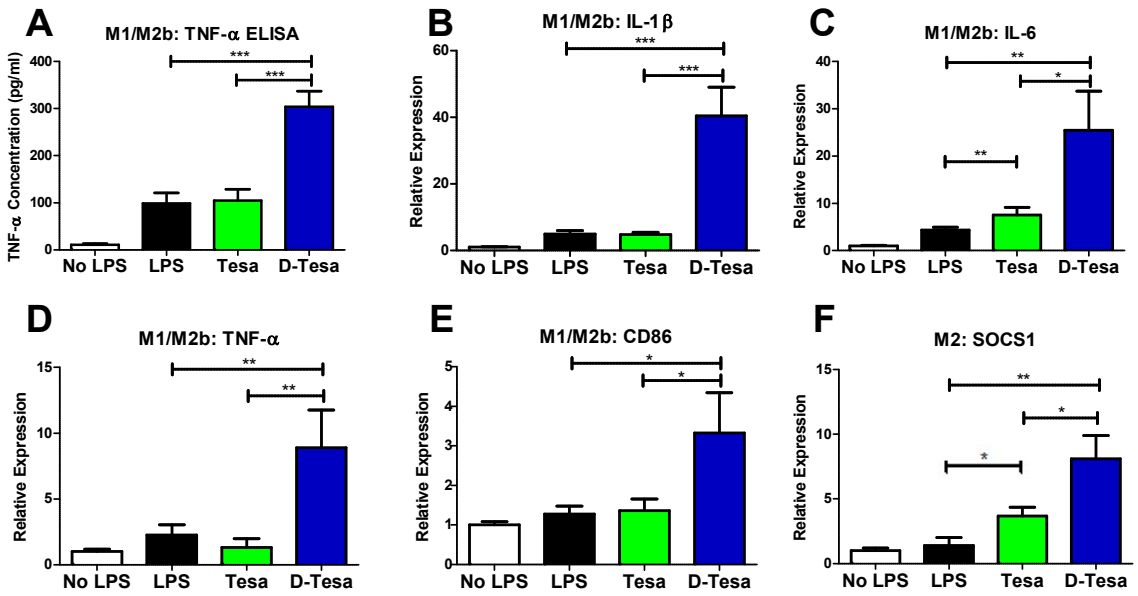
Supplemental Figure 3. Dynamic Light Scattering (DLS) size distribution of D-Tesaglitazar. A representative size distribution graph of D-Tesaglitazar dissolved in water at a concentration of 0.2 mg/ml.



Supplemental Figure 4. MTT Cytotoxicity Assay. BV2 microglia cells were treated with LPS (100 ng/ml) for 3 hours, and then they were co-treated for 48 hours with LPS (100 ng/ml) and free tesaglitazar or D-Tesaglitazar at 1.5, 15, and 150 µM on a drug basis. LPS-only treated cells served as the control vehicle, as all drug solutions were made in 100 ng/ml LPS media. Then the MTT assay was run according to the manufacturer's protocol. Data is mean + SEM (N=3).



Supplemental Figure 5. Low and medium doses of Tesa and D-Tesa do not significantly alter nitric oxide or TNA-α levels. BV2 microglia cells were treated with LPS (100 ng/ml) for 3 hours, and then they were co-treated for 48 hours with LPS (100 ng/ml) and free tesaglitazar (Tesa) or D-Tesaglitazar (D-Tesa) at 1.5, 15, and 150 µM on a drug basis. Cells that were neither treated with LPS nor drug (NL) and LPS-only treated cells (LPS) served as the controls. The supernatant was collected, (A) nitric oxide levels were measured with the Griess reagent, and (B) TNF-α levels were measured via ELISA. Data is mean + SEM (N=3).



Supplemental Figure 6. M1/M2b markers and M2 marker SOCS1 are upregulated with D-Tesaglitazar treatment. BV2 microglia cells were treated with LPS (100 ng/ml) for 3 hours, and then they were co-treated for 48 hours with LPS (100 ng/ml) and free tesaglitazar (Tesa) or D-Tesaglitazar (D-Tesa) at 150 µM on a drug basis. Cells that were neither treated with LPS nor drug (No LPS) and LPS-only treated cells (LPS) served as the controls. (A) Supernatants were collected, and TNF-α levels were measured via ELISA. (B-F) qRT-PCR analysis of: (B) IL-1β, (C) IL-6, (D) TNF-α, (E) CD86, and (F) SOCS1. All data is mean + SEM (N=3). *p<0.05, **p<0.01, ***p<0.001 (Bonferroni corrected).