| BIOGRAPHICAL SKETCH                       |              |           |                      |  |
|-------------------------------------------|--------------|-----------|----------------------|--|
| NAME: Silvia Muro, Ph.D.                  | POSITION     | ITITLE    |                      |  |
|                                           | Associate    | Professor |                      |  |
| eRA COMMONS USER NAME: silvia             |              |           |                      |  |
| EDUCATION & TRAINING                      | <u>'</u>     |           |                      |  |
| University of Granada. Spain              | B.S.         | 1995      | Sciences - Biology   |  |
| University Autonoma of Madrid. Spain      | Ph.D.        | 1999      | Sciences - Mol.Biol. |  |
| University Autonoma of Madrid. Spain      | PostDoctoral | 2000      | Human Genetics       |  |
| University of Pennsylvania, Philadelphia, | PostDoctoral | 2000-2003 | Drug Delivery        |  |

**A. PERSONAL STATEMENT.** I was trained in cell/molecular biology and drug delivery, and my research program particularly focuses on the development and optimization of strategies of targeting and transport of drug delivery systems into and across the endothelium. My lab was the first to identify CAM-mediated transcytosis across the blood-brain barrier, we have directly compared this pathway to classical clathrin transport at this interface, and we have worked over the years in understanding the role of carrier design parameters (size, shape, valency, combination targeting, etc.) and physiological parameters (inflammatory activation, disease state, shear stress, etc.) in modulating cell-carrier interactions and transport, both in cell cultures and in vivo. I have experience in managing federal grants (NIH, NSF) and other funds, supervising personnel, training students and postdoctoral researchers who have successfully graduated and secured faculty positions, and conducting intra- and extra-mural collaborative efforts.

#### **B. PROFESSIONAL POSITIONS**

| 1997-1998    | Assistant Instructor. Biochemistry. Autonomous University of Madrid. Spain.                  |
|--------------|----------------------------------------------------------------------------------------------|
| 1998-1999    | Assistant Instructor. Molecular Genetics. Autonomous University of Madrid. Spain.            |
| 2003-2005    | Research Associate. Institute for Environmental Medicine (IFEM), University of Pennsylvania. |
|              | Philadelphia.PA.                                                                             |
| 2005-2008    | Research Assistant Professor of Pharmacology, Adjunct Invest. IFEM, and Member Institute for |
|              | Translational Medicine and Therapeutics. University of Pennsylvania. Philadelphia. PA.       |
| 2008-2012    | Assistant Professor. Fischell Department of Bioengineering & Institute for Bioscience and    |
|              | Biotechnology Research (IBBR). University of Maryland (UMD), College Park, MD.               |
| 2012-Present | Associate Professor. Bioengineering & IBBR; Affiliate faculty in Cell Biology and Molecular  |
|              | Genetics. UMD, College Park, MD.                                                             |

#### C. HONORS, AWARDS & PROFESSIONAL ACTIVITIES

**Awards to Muro & her lab**: Summary: 7 international awards; 15 awards from professional societies in the fields of human genetic/lysosomal disorders and pharmacology/drug delivery; 9 achievement/career/leadership awards; 6 best paper awards; 13 best poster/presentation awards; 2 entrepreneurial awards; 14 fellowships; 3 travel awards.

Selected Awards: 1990-1995-National Undergraduate Fellowship Program, Ministry for Education and Science, Spain; 1995-Genetic Engineering & Society Fellowship, University of Granada, Spain; 1996-Highest GPA in Biological Sciences, Academy of Sciences, University of Granada, Spain; 1996-1999-National Graduate Fellowship Program, Ministry for Education & Science, Spain; 1997-International Student Fellowship on Techniques in Cell Biology, Federation of European Biochemical Societies, UK (only one student per country is selected each year); 1998-Best paper, Spanish Society for Inborn Errors of Metabolism; 1999-International Researcher Fellowship Program, Ministry for Education & Science, Spain; 1999-Travel Award, Spanish Society of Biochemistry and Molecular Biology, Spain; 1999-Travel Award, Society for the Study of Inborn Errors of Metabolism, UK; 2000-Best paper, European Society for the Study of Inborn Errors of Metabolism, UK; 2000-National Postdoctoral Fellowship Program, Institutes for Research in Health, Spain; 2000-2002-NATO International Postdoctoral Fellowship Program (relinquished in favor of the following fellowship); 2000-2002-Ramón Areces Foundation Postdoctoral Fellowship, Spain (only 4 fellowships per year in the country are awarded in Biomedical Sciences); 2004-2008-Scientist Development Grant, American Heart Association; 2005-Best paper, Spanish Society for Inborn Errors of Metabolism; 2006-Best presentation, UPenn Medicine Research Symposium: 2007-Best poster, Nanomedicine and Drug Delivery Symposium: 2008-Searle Foundation Award Nominee for UMD; 2009-Best poster, Bioscience Day UMD; 2010-Best poster, AICHE Mid-America; 2010-Best presentation, Graduate Research Interaction Day, UMD; 2011-Best poster,

Nanomedicine and Drug Delivery Symposium; 2012-Best poster, Bioscience Day UMD; 2011-Best presentation, Graduate Research Interaction Day, UMD; 2011-Best paper, Controlled Release Society; 2011-Young investigator and Best poster, American Society of Nanomedicine; 2011-Outstanding Life Sciences Invention of the Year, UMD; 2012-Research Leader, UMD; 2012-Best presentation, Engineering Festival, UMD; 2012-Travel award, World Organization for Rare Lysosomal Disorders; 2012-Best Inventor Pitch, UMD; 2012-Junior Faculty Outstanding Research Award in Engineering, UMD; 2013-Best presentation, Engineering Festival, UMD; 2013-Best poster, Biomedical Engineering Research Day, UMD-Johns Hopkins; 2013-Top 25 Maryland women professors, StateStats Org.; 2013-Board of Scientific Advisors, Spanish & Portuguese Chapter of the Controlled Release Society. 2013-Blavatnik Foundation Award Nominee for UMD. 2013-Young investigator and Best poster, American Society of Nanomedicine; 2014-Outstanding Campus Leader, CampusNewsPublications. 2014-Standing member, NIH NANO Study Section. Three Muro students had Undergraduate Research Fellowships from Howard Hughes Medical Institute, three had Graduate Research Fellowships from the NSF, and one had an NIH Graduate Research Diversity Supplement.

<u>Journal Reviewer (Selected)</u>: ACS Nano, Advanced Drug Delivery & Research, Angewandte Chemie, Annals of Biomedical Engineering, Biomacromolecules, Biomedical Nanotechnology, Cell Biochemistry and Biophysics, Chemistry, Expert Opinions on Emerging Drugs, Expert Opinions on Drug Delivery, Gene Therapy, International Journal of Nanomedicine, Journal of Cell Biology, Journal of Controlled Release, Journal of Gene Medicine, Langmuir, Molecular Pharmaceutics, Molecular Therapy, Nano Letters, Nanomedicine, PLOS One.

**Grant Reviewer (Selected)**: NIH: (1) ZRG1, (2) HLBP1-32 BSTM, (3) 2011/10 GDD, (4) 2012/05 GDD, and (5) 2013/01 NANO; (6) DOD TRN CET A; (7) 2010 Tay-Sachs Foundation; (8) 2011 Italian Telethon Foundation; (9) 2013 Czech Republic Science Foundation; (10) 2014 Vienna Science & Technology Fund; (11) 2014 New Zealand Marsden Fund; (12) Standing member, NIH NANO Study Section, July 2014 – June 2020.

<u>Editor:</u> (1) "New Frontiers in Drug Delivery", Frontiers in Bioscience Encyclopedia; (2) Journal of Nanomedicine and Biotherapeutic Discovery; (3) International Journal of Experimental Medicine; (4) Book "Drug delivery across physiological barriers" Pan Stanford Publishing (in press).

<u>Conference Chair</u>: 2006-New strategies for immunotherapy, Controlled Drug Delivery, Spain; 2008-Session II, International Symposium on Polymer Therapeutics, Valencia, Spain; 2010-Drug Delivery, Southern Biomedical Engineering Conference, College Park, MD; 2012-Organizer, International Conference on Nanotechnology and Nanomedicine, Omaha, NE, USA; 2012-Discussion leader, Drug Carriers-Gordon Conference, Waterville, NH.

## **D. PUBLICATIONS**

Research and Review Articles, and Book Chapters: 67 total (25 in the last 3 years), 37 as corresponding author, 13 highlighted in journal editorials, press release, and/or the journal cover page.

Peer-Reviewed Proceedings & Abstracts: 75 total (23 in the last 3 years).

Other examples of Scholarship: 41 non-peer reviewed abstracts; 53 invited talks; 37 contributed talks.

<u>Citations:</u> Google Scholar: 2,497 (1,287 last 3 years); 37 citations/article, 132 citations/year (399 citation/year last 3 years); 17 articles ≥ 50 citations, 7 articles ≥ 100 citations; 2 article ≥ 200 citations; h-index=27; i-10: 42.

### Fifteen Selected Articles (from a total of 67):(\*corresponding author)

- 1-Hsu J, Hoenicka J, **Muro S\***. (2014) Targeting, endocytosis, and lysosomal delivery of active enzymes to model human neurons by ICAM-1-targeted nanocarriers. Pharm Res. In press.
- 2-Ghaffarian R, **Muro S\***. (2014) Distinct subcellular trafficking resulting from monomeric vs. multimeric targeting to endothelial ICAM-1: implications for drug delivery. Mol Pharm. In press.
- 3-Hsu J, Rappaport J, **Muro S**\*. (2014) Specific binding, uptake, and transport of ICAM-1-targeted nanocarriers across endothelial and subendothelial cell components of the blood-brain barrier. Pharm Res. 31(7):1855-66.
- 4-Hsu J, Bhowmick T, Burks S, Kao J, **Muro S\***. (2014) Enhancing the biodistribution of therapeutic enzymes in vivo by modulating surface coating and concentration of ICAM-1-targeted nanocarriers. J Biomed Nanotech, 10(2):345-354.
- 5-Papademetriou I, Tsinas Z, Hsu J, **Muro S\***. (2014) Combination-targeting to multiple endothelial cell adhesion molecules modulates binding, endocytosis, and in vivo biodistribution of drug nanocarriers and their therapeutic cargoes. J Control Release, 188:87-98.

- 6-Ansar M, Serrano D, Papademetriou I, Bhowmick T, **Muro S\***. (2013) Biological functionalization of drug carriers to bypass size restrictions of receptor-mediated endocytosis independently from receptor targeting. ACS Nano, 7(12):10597-10611.
- 7-Papademetriou I, Garnacho C, Schuchman EH, **Muro S\***. (2013) In vivo performance of polymer nanocarriers dually-targeted to epitopes of the same or different receptors. Biomaterials, 34(13):3459-3466.
- 8-Papademetriou J, Garnacho C, Serrano D, Bhowmick T, Schuchman EH, **Muro S**\*. (2013) Comparative binding, endocytosis, and biodistribution of antibodies and antibody-coated carriers for targeted delivery of lysosomal enzymes to ICAM-1 versus transferrin receptor. J Inherit Metab Dis, 36(3):467-477.
- 9-Ghaffarian R, Bhowmick T, **Muro S**\*. (2012) Transport of nanocarriers across gastrointestinal epithelial cells by a new transcellular route induced by targeting ICAM-1. J Control Release, 163(1):25-33. <u>Featured in journal cover</u>
- 10-Serrano D, Bhowmick T, Chadha R, Garnacho C, **Muro S\***. (2012) Intercellular adhesion molecule 1 engagement modulates sphingomyelinase and ceramide, supporting uptake of drug carriers by the vascular endothelium. Arterioscler Thromb Vasc Biol, 32(5):1178-1185. <u>Journal editorial on this article</u>
- 11-Hsu J, Serrano D, Bhowmick T, Kumar K, Kuo YC, Shen Y, **Muro S\***. (2011) Enhanced endothelial delivery and biochemical effects of α-galactosidase by ICAM-1-targeted nanocarriers for Fabry disease. J Control Rel, 10;149(3):323-31. *Featured in journal cover and editorial*
- 12-Bhowmick T, Berk E, Cui X, Muzykantov V\*, **Muro S\***. (2012) Effect of flow on endothelial endocytosis of nanocarriers targeted to ICAM-1. J Control Rel, 157(3):485-492.
- 13-Calderon A, Bhowmick T, Leferovich J, Burmann B, Pichette B, Muzykantov V, Eckmann D\*, **Muro S\***. (2011) Optimizing endothelial targeting by modulating the antibody density and particle concentration of anti-ICAM coated carriers. J Control Rel, 150(1):37-44.
- 14-Calderon A, Muzykantov V, **Muro S\***, Eckmann D\*. (2009) Flow dynamics, binding and detachment of spherical carriers targeted to ICAM-1 on endothelial cells. Biorheology, 46(4):323-341.
- 15-**Muro S\***, Garnacho C, Champion J, Leferovich J, Gajewski C, Schuchman E, Mitragotri S, Muzykantov V\*. (2008) Controlled endothelial targeting and intracellular delivery of therapeutics by modulating size and shape of ICAM-1-targeted carriers. Mol Ther, 16(8):1450-1458. *Featured in journal cover*
- **E. RESEARCH SUPPORT.** Active & completed awards where Muro is/was PI: ~\$3.14 million (M). Active & completed awards in which Muro is/was involved (PI, co-PI, co-investigator): ~\$25.6 M total (Muro share: ~\$5.3 M).

### **Active Support:**

1-NIH R01 HL098416 Muro (PI) 04/01/10 - 03/31/15 (No cost extension to 03/31/16)

Targeted replacement of defective lysosomal enzymes in the lung and brain.

2-<u>NSF CBET 1402756</u> **Muro (PI)** 06/01/14 - 05/31/17

Engineering a DNA-based nanodevice to enable cytosolic transport of enzymes

3-Seed Grant OCT-UMD Muro (PI) 07/01/14 - 06/30/15

Oral delivery of therapeutic enzymes.

### **Completed Support:**

4-NIH TRND – SAIC 11X178 **Muro (PI)** 09/01/11 – 08/31/13

Development of strategies for treatment of Alzheimer's disease and Niemann-pick disease.

5-AHA 09BGI2450014 **Muro (PI)** 07/01/09 - 06/30/11 Endothelial clearance of fibrin by non-classical endocytic transport

6-<u>Minta Martin Foundation</u> **Muro (PI)** 07/01/09 - 06/30/10

Transport of substances by the vascular endothelium in microgravity

7-<u>NIH R21 HL085533</u> **Muro (PI)** 07/01/06 - 06/30/08

Targeted enzyme delivery systems for treatment of orphan Niemann-Pick disease

8-<u>NIH -UPenn Pilot P30 DK47757-</u> **Muro (PI** UPenn Pilot grant); Wilson (PI P30) 09/01/06 08/31/08

Targeted delivery of lysosomal enzyme therapeutics by multivalent nanocarriers

9-<u>AHA SDG 0435481N</u> **Muro (PI)** 07/01/04 - 06/30/08

Endothelium targeted enzyme replacement therapy for lysosomal storage disorders

10-NIH P01 HL079063 Muro, Co-In; Muzykantov (PI project 4) Fisher (PI P01), 07/11/05 - 04/30/10 Reactive oxygen species and antioxidants in acute lung injury

11-NIH R01 HL073940-01A1 **Muro, Co-In**; Muzykantov (PI) 04/04/04 - 03/31/08

Augmentation of antioxidant defenses by immunotargeting

12-DOD DAMD17-02-1-0197-04 **Muro, Co-PI**; Muzykantov (PI) 04/01/02 - 03/31/07

Targeting of drugs to ICAM for treatment of acute lung injury

13-NIH R01 HL71175-04 **Muro, Co-In**; Muzykantov (PI) 07/01/02 - 06/30/06

Targeting of drugs to ICAM-1

# Support Relinquished due to relocation from U.Pennsylvania to U.Maryland College Park:

14-NIH R01 EB006818A2 **Muro, Co-In**; Eckmann (PI) 07/01/08 - 06/30/13

Targeted microcarrier design and optimization

15-NIH R01 HL087036-01A2 **Muro, Co-In**; Muzykantov (PI) 04/01/08-03/31/12

Targeting carriers with controlled geometry to endothelium\

16-NIH R01 EB007279 **Muro, Co-In**; Vinogradov (PI) 04/01/07 - 03/31/12

Oxygen microscopy by two photon excited phosphorescence

# F. PATENTS & INVENTIONS (\* denotes leading inventor)

- 1-**Muro S\***, Schuchman E, Muzykantov VR. Targeted protein replacement for the treatment of lysosomal storage disorders. US provisional patent application 60/584,648 filed 07/01/04. International patent application PCT/US05/02359 filed 07/01/05. Awarded
- 2-**Muro S\***, Muzykantov VR. Targeted nanocarriers for intracellular drug delivery. US provisional patent application 60/931,552 filed 05/23/07. International Patent Application PCT/US2008/06589 filed 05/22/08; Publication WO2008147526 A1 date 4 Dec 2008; Australian patent issued Nov. 7 2013: UPN-T4312AUSAL (2008257419).
- 3-**Muro S\***, Ming, M, Garnacho C. Peptides for transport of therapeutics and their carriers in mouse models and humans. US provisional patent applications 61/184,657 filed 06/05/09 and 61/220,404 filed 06/25/09. International patent application PCT/US2010/37490 filed 06/04/10. Awarded
- 4-Marugan J\*, Zhang W, **Muro S**. Delivery of a therapeutic protein across the blood-brain barrier for Alzheimer's disease treatment. US provisional patent application 61/286,205 filed 12/14/09. International patent application PCT/US2010/060205 filed 12/14/10.
- 5-**Muro S\***, Ghaffarian R. Targeted carriers for drug delivery across the gastrointestinal epithelium (2010). US provisional patent application 61/330,739 filed 05/03/10, and second provisional patent application 61/481,779 filed 05/03/11. Non-provisional application filed on 5/3/2012 (CIP 13/376362 & 61/481779); Published patent application 201020263652. Issued July 2014. <u>Outstanding Invention of the Year, U. Maryland, MD.</u> Awarded
- 6-**Muro S\***, Serrano D. A new strategy to regulate interaction of leukocytes with endothelium and to potentiate cell transport of therapeutics and their carriers. US provisional patent application 61/393,131 filed 10/14/10, and 61/547687 filed 10/15/2011. Non-provisional patent application filed Fall 2012 10/15/2012 12/652165; Published Patent Application 20130095091

#### G. TEACHING & MENTORING.

<u>Scholarly Training & Mentoring:</u> Trained 5 postdocs (3 hold assistant/associate positions in international universities; 1 works is a consultant firm, 1 works for a DOD contractor); Graduated 4 PhD students (1 is a postdoc in Boston U., 1 works in FDA, 1 went to AAAS, 1 is a postdoc in the National Children's Hospital in DC) and 2 MS students (1 works in industry, 1 went for a PhD degree); Trained 16 undergraduate students (7 are in graduate school) and 6 high school students (all are in university); Currently training 3 PhD students (2 advanced to candidacy), 3 undergraduate students, and 1 high school student. Muro's mentees hold > 30 awards, fellowships, and other professional accolades.

<u>Other Academic Advising</u>: Mentoring ~30 undergraduate advisees/year; Mentored 17 PhD student for lab rotations; served in 5 PhD candidacy committees, 8 PhD proposal committees, and 5 PhD dissertation committees; Mentor/Protégé Program of the Controlled Release Society; Mentor American Heart Association Outreach Program; Mentor of the Science and Technology Eleanor Roosevelt High School Program.