



Silvia del V. Alonso, PhD

Information:

Full Professor, Senior Scientist Research Career CONICET

Academic Degrees

Chemist, PhD in Chemistry (UNT, Argentina), Postgraduate Molecular Biophysics (UAB, Ala, USA)

Departmental Affiliation

LBM-MPBio Director, Science and Technology

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Research and Professional Experience

Design and biophysical characterization of stabilized vehicles *in vitro* and *in vivo* for drug and gene delivery in physiological conditions.

Properties such as stability of liposomal formulations, protein interaction, cell toxicity, and biodistribution of Drug Delivery Systems (DDS): e.g. liposome formulations as DNA vehicles in gene-therapy protocols were efficiently design. Lipidic DDS containing GM1 and GM type III survive through the gastrointestinal tract, those containing diacetylenic polymerized lipids showed further augmentation of the Hydrophobicity Factor (HF) and size beside phase separation and lower Tt. Diacetylenic polymerized liposomes would serve effectively as oral delivery vehicle and non-polymerized diacetylenic liposomes were selected as possible immunoadjuvants. In collaboration we demonstrated that the interaction of Brucella abortus MFP with phospholipid vesicles promotes *in vitro* membrane fusion. We have shown that DNA association did not alter the hydrophobicity factor (HF) trend for ternary formulations with cationic, neutral or negatively charged mixed with diacetylenic lipids. We also contributed to a better understanding of the interaction between DNA and lipids: more fluid the membrane (higher HF) higher the efficiency of DNA association and DNA conformation changed. Lyophilized DNA/cationic vesicles with high hydrophobicity change conformation into a more condensed form (C form). Non charged vesicles, change conformation from B to a partial A form, suggesting there is direct relationship between hydrophobicity and DNA conformation changes: higher hydrophobicity factor more pronounced the change in DNA to a more condensed form. These conformational changes are related to DNA/liposome-mediated tissue distribution in Balb-c female mice. Non charged liposomes were able to deliver DNA to liver after intraperitoneal (i.p.) inoculation, while polymeric liposomes were able to deliver DNA to kidney by using the same inoculation route. Cationic liposomes were found in a wide range of tissues by the i.p. route (e.g., liver, intestine, kidney, and blood). Subcutaneous inoculation, allowed only cationic liposomes to deliver DNA through the bloodstream. Cell toxicity in general was low for neutral formulations and cell death became present at concentrations higher than 0.5 mg/mL. In the case of non charged and polymeric liposomes, toxicity increased upon interaction with serum proteins. Further studies analyze a molecular biorheology approach to understand the viscoelastic properties related to their oral or i.v. route under air or blood stress bias bench prototypes. Actually we are implementing nanotransporters such as polymeric protein nanoparticles (BSAnano or HSAnano), nanolipopolymers, ultradeformable liposomes and dendrimers to target lungs, brain, and topic use. Design of targeted Albumin nanoparticles used as theranostics vectors combined with Gold nanoparticles.

Breakthroughs

Non viral vector design: Murine melanoma B16F0 cells transfected with SA:DPPC:DOPE (2:1:1 molar ratio) liposomes associated with a plasmid encoding murine IL-12, its expression had a marked effect on *in vivo* growth of B16 melanoma tumors implanted intradermally and developed in the dorsal- region of the foot of mice (significantly retarding their growth and prolonging host survival). Tumor progression compared standard implantation in the flank and dorsal-region model herein introduced is a valuable tool to study the metastatic potential of different cell lines and the microenvironment components affecting tumor growth.

Non viral vector design: Special lipid/protein vector combined with arsenic drug and fluorescent probe induced more apoptosis with no proliferation compared with Trisenox® (drug administered against Acute Promyelocytic Leukemia) in HL60 cell line.

Toxicity and teratogenicity of nanoparticles determine in zebrafish (*Danio rerio*), important vertebrate model organism system for biomedical research: DL50, cardiotoxicity, morphology, comportameental as pre-clinical trials).

Keywords

Drug delivery, lipopolymers, stability, cytotoxicity, toxicity, teratogenicity, biodistribution, immune response, *in vitro* e *in vivo* delivery

Honors and Awards

2007-on: Director Research Program MPBio (Polymeric Materials Biofunctionals)

2000-on: Director LBM (Laboratory of BioMembranes).

2011-on: Principal Investigator Research Council of Argentina (CONICET)

2012- 2014 President of LaFeBS (Latin American Federation of Biophysical Societies)

2006-2008: President Argentinean Biophysical Society (SAB).

2008-2010 Past President Argentinean Biophysical Society

2009 Co-Coordinador Latin American Postgraduate Program of Biophysics (POSLATAM, <http://www.lafebs.org/>)



2006-on IUPAB Argentinean Biophysical Society (SAB) representative.

2013-2016: President of The Latin American Federation of Biophysical Societies (LaFEBS)

Selected Publications

- "Optimization and in vivo toxicity evaluation of G4.5 PAMAM Dendrimer-Risperidone complexes". Prieto, Maria Jimena; del Rio Zabala, Nahuel Eduardo; Marotta, Cristian Hernán; Carreño Gutierrez, Hector; Arévalo Arévalo, Rosario; Chiaramoni, Nadia Silvia; Alonso, Silvia del Valle. Accepted with revisions 20-12-2013. Accepted January 2014. ISSN 1932-6203. PLoS One. 2014 Feb 28;9(2):e90393. Pages 1/10. E-collection 2014. PMID:24587349.
- "Is the amphiphilic carrier structure relevant for α -tocopherol anti-peroxidation efficiency in mitochondrial membranes?". Nadia S. Chiaramoni, Evandro L. Duarte, Marina Marsanasco, M. Julieta Fernandez Ruoco, M. Jimena Prieto, M. Teresa Lamy and Silvia del V. Alonso. American Journal of Biological Chemistry. Vol. 2, No. 1, 2014, pp. 1-7. 3 <http://www.openscienceonline.com/journal/ajbc>.
- "A model based in the radius of vesicles to predict the number of unilamellar liposomes". Jorge A. M. Montanari, Paula L. Bucci, Silvia del V. Alonso. International Journal of Research in Pharmacy and Chemistry. Accepted May 2014. IJRPC 2014, 4(2), 484-489. ISSN: 2231-2781. Available online at www.ijrpc.com.
- "Successful Latin American initiatives in biophysics". Editorial. Marcelo M. Morales & Silvia del V. Alonso. Biophys Rev (2014) 6:1-2. DOI 10.1007/s12551-014-0139-1. Springer. ISSN 1867-2450
- "Estudios biorreológicos de vectores de transporte de acidos grasos esenciales y funcionales". Fernández, Valeria E; Martínez, Luis M.; Marsanasco, Marina; Alonso, Silvia del Valle. Pag 155-168. Publicaciones Reológicas: Primer Congreso Argentino de Biorreología y V Jornada Dr. Rodolfo J. Rasia de Física Aplicada a la Biomedicina. Trabajos completos. 1a ed. Rosario: UNR Editora. Editorial de la Universidad Nacional de Rosario, 2013 (212 páginas, 23x16 cm). ISBN 978-987-702-043-4.
- "G4.5 Pamam Dendrimer-Risperidone: Biodistribution and Behavioral Changes in In Vivo Model", Prieto, Maria Jimena; del Rio Zabala, Nahuel Eduardo; Marotta, Cristian Hernán; Bichara, Dario; Simonetta, Sergio; Chiaramoni, Nadia Silvia and Alonso, Silvia del Valle. J. Nanomedicine Biotherapeutic Discov, 4 (1):121, 2013.
- "Nanoparticle-based therapy for respiratory diseases" Adriana L. Da Silva, Raquel S. Santos, Débora G. Xisto, Silvia Del V. Alonso, Marcelo M. Morales and Patricia R.M. Rocco. Anais da Academia Brasileira de Ciências 2013, 85(1): 137-146. (Annals of the Brazilian Academy of Sciences). www.scielo.br/aabc.
- "Lipid-polymer membranes as carriers for L-tryptophan: molecular and metabolic properties". Fernandez-Ruocco, Maria Julieta; Siri, Macarena; Igartua, Daniela; Prieto, Maria Jimena; Alonso, Silvia del Valle; Chiaramoni, Nadia Silvia. Submission Time: 2013-01-01 03:25:47. OJMC., 2013, 3, 30-39. Paper ID: 1790033. Accepted 02-16-2013.
- "Synthesis of a Fluorescently Labeled Compound for the Detection of Arsenic-induced Apoptotic HL60 Cells". A. Lis Femia, C. Facundo Temprana, M. Silvia Amor, Mariano Grasselli and Silvia del V. Alonso. Med Chem. 2012, 8, 222-229. [Feb 24 2012, Epub ahead of print]. PMID: 22385172. [PubMed - as supplied by publisher].
- "INTRATRACHEAL INSTILLATION OF LIPOPOLYMERIC MICRO-VECTORS AND THE EFFECT IN MICE LUNG PHYSIOLOGY". Debora Xisto, C. Facundo Temprana, Sabrina V. Martini, Soraia Abreu, Johnatas Dutra, Adriana Silva, Julia Crosseti, Patricia R. M. Rocco, Silvia del V. Alonso, Marcelo M. Morales. Cell Physiol. Biochem. 2012, 29, 791-798.
- "Structural effect of cationic amphiphiles in diacetylenic photopolymerizable membranes". C. Facundo Temprana, Evandro L. Duarte, A. Lis Femia, Silvia del V. Alonso, M. Teresa Lamy. Chem. Phys. Lipids. 2012, 165, 589-600. Received 18 April. Revised, 15 June. Accepted, 19 June; on line 3 July 2012. [<http://dx.doi.org/10.1016/j.chemphyslip.2012.06.007>].
- "Arsenic fluorescent compound as a novel probe to study arsenic-binding-proteins". A. L. Femia, C. F. Temprana, J. Santos, M. L. Carbajal, M. S. Amor, M. Grasselli and S. del V. Alonso. Protein J.; 2012 Dec; 31(8):656-66. Received 18 May, accepted with revisions. Jun 24th, in press July 26th. Protein J. 2012 Aug 31. [Epub ahead of print]. PMID:22936492. ISSN: 1572-3887.
- Effect of risperidone and fluoxetine on the movement and neurochemical changes of zebrafish". Maria Jimena Prieto, Hector Carreño Gutierrez, Rosario Arévalo Arévalo, Nadia S Chiaramoni, Silvia del Valle Alonso. Open Journal of Medicinal Chemistry (OJMC), 2012, 2, 129-138. Enviado septiembre 2012, Pub. Date: December 31, 2012. In press Oct- 2012. ISSN Print: 2164-3121. (2), 4 129-138, December 31, 2012.
- "The role of the microenvironment: Models for the study of melanoma". Lucia Speroni, Victoria de los Angeles Bustuobad, Julieta Gasparri, Nadia Silvia Chiaramoni, Silvia del Valle Alonso. (2011) Book Chapter 2, page 33-42. Breakthroughs in Melanoma Research. Book edited by: Dr. Yohei Tanaka. Editorial INTECH Open Access Publisher. ISBN 978-953-307-291-3. <http://www.intechopen.com/articles/show/title/the-role-of-the-microenvironment-models-for-the-study-of-melanoma>.
- "Liposomes as vehicles for vitamins E and C: An alternative to fortify orange juice and offer vitamin C protection after heat treatment" M Marsanasco, AL Marquéz, JR Wagner, S del V Alonso and NS Chiaramoni, Food Res Int, 2011, 44 (9), 3039-3046.
- "Optimization and in vitro toxicity evaluation of G4 PAMAM dendrimer-risperidone complexes" Prieto MJ, Temprana CF, del Rio Zabala NE, Marotta CH, Alonso S. del V. Eur J. Med Chem. 2011 Mar;46(3):845-50. Epub 2010 Dec 22. PMID: 21251731.
- "Ultraviolet irradiation of diacetylenic liposomes as a strategy to improve size stability and to alter protein binding without cytotoxicity enhancement". Temprana CF, Amor MS, Femia AL, Gasparri J, Taira MC, Del Valle Alonso S. J Liposome Res. 2011 Jun;21(2):141-50. Epub 2010 Jun 18. PMID: 20560742.
- "Ultraviolet irradiation of diacetylenic liposomes as a strategy to improve size stability and to alter protein binding without cytotoxicity enhancement". Temprana CF, Amor MS, Femia AL, Gasparri J, Taira MC, Del Valle Alonso S. J Liposome Res. 2011 Jun;21(2):141-50. Epub 2010 Jun 18. PMID: 20560742.
- "Alternative site of implantation affects tumor malignancy and metastatic potential in mice". Lucia Speroni, Victoria de los A Bustuobad, Julieta Gasparri, Nadia S Chiaramoni, María C Taira & Silvia del V. Alonso Cancer Biology & Therapy 2009; 8:4, 373-377; E-pub 15 February 2009.
- "Antitumoral effect displayed by liposome-mediated IL-12 gene transfected into B16F0 cells". Lucia Speroni, Julieta Gasparri, Victoria de los A Bustuobad, Nadia S Chiaramoni, Andrzej Smagur, Stanislaw Szala, María C Taira, Silvia del V Alonso Acta Biochim Pol. 2009; 56(2):249-53. Epub 2009 May 7.
- "Brucella abortus-MFP: A TRIMERIC COILED-COIL PROTEIN WITH MEMBRANE FUSOGENIC ACTIVITY". Carrica, Mariela; Craig, Patricio; Alonso, Silvia del V.; Goldbaum, Fernando; Cravero, Silvio. Biochemistry. 2008 Aug 5; 47(31):8165-75. Epub 2008 Jul 11. PMID: 18616282 .