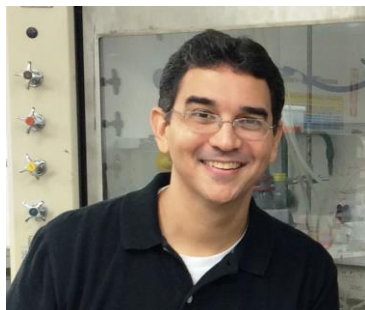


# Faculty

School of Pharmacy  
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## Rank/Discipline

Assistant Professor  
Medicinal Chemistry  
Department of Pharmaceutical  
Sciences

## Education & Specialty Certification

PhD, University of Puerto Rico,  
2006.  
Post-doc, UPR-Medical  
Sciences, 2008.

## Eliud Hernández O'Farrill, Ph.D.

### Research Areas and Active Projects

Design and synthesis of bioactive molecules as anti-invasive breast cancer compounds via docking calculations and medicinal chemistry methodology. In our laboratory, we are currently working in two different projects:

#### **Small molecule inhibitors of Rac1 as anti-invasive breast cancer compounds**

We are interested in the synthesis of small molecule inhibitors of Rac1 as anti-invasive breast cancer compounds. Rho family GTPases are molecular switches that control signaling pathways regulating a myriad of cellular functions. Rac1, a Rho family member, plays a critical role in several aspects of tumorigenesis, cancer progression, and has been associated with the increased proliferation and invasion of several breast cancer cell lines. Since the activation of Rho GTPases is controlled by guanine nucleotide exchange factors (GEFs), inhibition of the interaction of Rac with its GEFs is a targeted strategy for blocking Rac activation. In this research, we used an existing Rac inhibitor NSC23766 to design and develop improved derivatives. We identified EHopp-016 as a Rac inhibitor, with 100-fold more potency than NSC23766, which binds to Rac1 with tighter interaction. The compound EHopp-016 is an effective tool for probing Rac function in different cell lines.

#### **Drug discovery of N-WASP inhibitors in metastatic breast cancer cell lines**

The Wiskott-Aldrich syndrome protein (WASP) family proteins are important regulators of actin polymerization and invadopodia formation. The neural-WASP (N-WASP) is a central regulator of Arp2/3 complex-mediated actin polymerization into invadopodia to initiate cell migration, and thus, cancer metastasis. N-WASP is activated at the cell membrane during invadopodia initiation, thus, implicating N-WASP in the initiation of cell invasion. In this project we are interested in the design and synthesis of small-molecule inhibitors of N-WASP. The new compounds are designed based on

the available structures of known N-WASP inhibitors, visual inspection and docking software. Also, in this project we use virtual screening and docking to identify new molecules with potential to interact and inhibit N-WASP activity in metastatic breast cancer cells.

## Collaborators

**Dr. Suranganie Dharmawardhane** - Department of Biochemistry, School of Medicine, University of Puerto Rico Medical Sciences Campus

**Dr. Cornelis P. Vlaar** - Department of Pharmaceutical Sciences, School of Pharmacy, University of Puerto Rico Medical Sciences Campus

**Dr. Peter Crooks** – University of Arkansas Medical Sciences, Department of Pharmaceutical Sciences

## Publications

Humphries-Bickley T, Castillo-Pichardo L, Corujo-Carro F, Duconge J, **Hernandez-O'Farrill E**, Vlaar C, Rodriguez-Orengo JF, Cubano L, Dharmawardhane S. Pharmacokinetics of Rac inhibitor EHop-016 in mice by ultra-performance liquid chromatography tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci.* (2015) Jan 2; 981-982C:19-26. PubMed PMID: 25594952.

Castillo-Pichardo L, Humphries-Bickley T, De La Parra C, Forestier-Roman I, Martinez-Ferrer M, **Hernandez E**, Vlaar C, Ferrer-Acosta Y, Washington AV, Cubano LA, Rodriguez-Orengo J, Dharmawardhane S. The Rac Inhibitor EHop-016 Inhibits Mammary Tumor Growth and Metastasis in a Nude Mouse Model. *Transl Oncol.* (2014) Oct 24; 7(5): 546-55. PubMed PMID: 25389450

Characterization of EHop-016, Novel Small Molecule Inhibitor of Rac GTPase. Brenda L. Montalvo-Ortiz, Linette Castillo-Pichardo, **Eliud Hernández**, Tessa Humphries-Bickley, Alina De La Mota-Peynado, Luis A. Cubano, Cornelis P. Vlaar, and Suranganie Dharmawardhane. *J. Biol. Chem.* 287, **16**, 13228-13238, (2012).

Novel Inhibitors of Rac1 in Metastatic Breast Cancer. **Eliud Hernández**, Alina De la Mota, Suranganie Dharmawardhane and Cornelis P. Vlaar. *PRHSJ.* 29, **4**, 348-356, (2010).

Synthesis of 1,4-dihydro[d][1,3]oxazin-2-ones from pthalides via an aminolysis-Hofmann rearrangement protocol. **Eliud Hernández**, Jessica M. Vélez and Cornelis P. Vlaar\*. *Tetrahedron Letters* **48**, 8972, (2007).

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Enantioselective Allylboration of *N*-Trimethylsilylketimines. E. Canales, **E. Hernandez**, J. A. Soderquist.\* *Synfacts* **10**, 1052, (2006).

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Asymmetric Propargylation with Trimethylsilyl-9-borabicyclo[3.3.2]decanes. **Hernández, E.**; Soderquist, J. A.\* *Synfacts* **2**, 148, (2006).

Asymmetric synthesis with the robust and versatile 10-substituted 9-borabicyclo[3.3.2]decanes: Homoallylic amines from aldimines. **Hernandez, E.**; Canales, E.; Gonzalez, E.; Soderquist, J. A.\* *Pure Appl. Chem.*, **7**, 1389, (2006).

Nonracemic  $\alpha$ -Allenyl Carbinols from Asymmetric Propargylation with the 10-Trimethyl-9-borabicyclo[3.3.2]decanes. **Hernández, E.**; Soderquist, J. A.\* *Org. Lett.*, **7**, 5397, (2005).

Spectroscopic Characterization of Titanocene Complexes with Thionucleobases. **Hernández E.**; Marrero M.; Rivera C.; Segal A.; Meléndez E.\*. *Inorg. Chim. Acta*, **298**, 178, (2000).

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### Book Chapter

Suranganie Dharmawardhane, **Eliud Hernández**, Cornelis P. Vlaar, "EHop-016, a small molecule inhibitor of Rac", in Inhibitors of the Ras Superfamily of G Proteins, *The Enzymes*, Ed., Fuyuhiko Tamanoi, Elsevier, UK, Vol. 33, Chapter 6, (2013), 117-146.

## Patents

**Hernandez E**, Vlaar C, Dharmawardhane S, inventors; University of Puerto Rico, San Juan, PR (US), assignee. SMALL-MOLECULE INHIBITORS OF RAC1 IN METASTATIC BREAST CANCER. U.S. patent 8,884,006 B2. 2014 November 11.

## Presentations

**Eliud Hernández**, Cornelis Vlaar and Suranganie Dharmawardhane. Drug Discovery and Development of EHop-016: A Small Molecule Inhibitor of Rac. 2014 AACR Annual Meeting Grapevine, TX. July 28, 2014.

Julia I. Medina, Diana M. Soto, Zulma Ramos, Cornelis Vlaar, **Eliud Hernández**. Synthesis of Carbazole Derivatives and their Use as Antiproliferative Compounds. 35th Foro Annual de Investigación y Educación del Recinto de Ciencias Médicas, San Juan, PR, March 25-26, 2015.

Cynthia Agosto, PharmD; Danitza Rodriguez, PharmD; Alexandra Velez, PharmD; **Eliud Hernández-O'Farrill**, PhD. Structure-Based Virtual Screening for the Discovery of P-Rex1 Inhibitors. 35th Foro Anual de Investigación y Educación del Recinto de Ciencias Médicas, San Juan, PR, March 25-26, 2015.

**Eliud Hernández**, Cornelis Vlaar and Suranganie Dharmawardhane. Discovery of EHop-016: A Small Molecule Inhibitor of Rac. American Chemical Society UPR-Bayamon Student Chapter, Bayamon, PR. February 6, 2015.

Structure-Based Virtual Screening Approach to the Discovery of Tiam1 Inhibitors. Lorianne Bermúdez-Rivera, PharmD; Russell Davis-Santos, PharmD; Dariana Ortiz-Torres, PharmD; **Eliud Hernández-O'Farrill**, PhD. Annual Convention of the Colegio de Farmacéuticos de Puerto Rico at El Conquistador Resort in Fajardo, Puerto Rico, August 23-25, 2013.

Computer-based virtual screening to identify lead inhibitors of DOCK9. Kasandra Rodríguez Hernández, Lilliana Ortiz-Acevedo, Denisse M. Marcano-Fernandez, **Eliud Hernández-O'Farrill**. Annual Convention of the Colegio de Farmacéuticos de Puerto Rico at El Conquistador Resort in Fajardo, Puerto Rico, August 23-25, 2013.

Computer-based virtual screening to identify lead inhibitors of DOCK9. Kasandra Rodríguez Hernández, Lilliana Ortiz-Acevedo, Denisse M. Marcano-Fernandez, **Eliud Hernández-O'Farrill**. 33er

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Structural optimization of the Rac GTPase inhibitor EHop-016. Ericka Velez Bonet, Cornelis Vlaar, **Eliud Hernández**. 33er Foro Anual de Investigación y Educación del Recinto de Ciencias Médicas, San Juan, PR, March 13-15, 2013.

Characterization of EHop-016, a Novel Small Molecule Inhibitor of Rac GTPase, as a Potential Inhibitor of Metastatic Cancer. Linette Castillo-Pichardo, Brenda L. Montalvo-Ortiz, **Eliud Hernández**, Alina De La Mota-Peynado, Tessa Humphries-Bickley, Cornelis P. Vlaar, and Suranganie Dharmawardhane. 13th RCMI International Symposium on Health Disparities, San Juan, PR, December 10-13, 2012.

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**Eliud Hernández**, Brenda L. Montalvo-Ortiz, Alina De La Mota-Peynado, Linette Castillo-Pichardo, Tessa Humphries-Bickley, Cornelis P. Vlaar, and Suranganie Dharmawardhane. New Inhibitors of Rac1 in Metastatic Breast Cancer. 43rd IUPAC World Chemistry Congress, San Juan, Puerto Rico, July 31 to August 5, 2011. (Oral presentation).

Janibeth Hernández, Brenda L. Montalvo, Surangani Dharmawardhane, Cornelis P. Vlaar and **Eliud Hernández**. Development of Small Molecule Inhibitors for Rac as Anti Breast Cancer Metastasis Therapy. 31st Puerto Rico Interdisciplinary Scientific Meeting, 46th Junior Technical Meeting, Interamerican University, Bayamón, PR, March 12, 2011.

**Eliud Hernández**, Brenda L. Montalvo, Janibeth Hernández, Surangani Dharmawardhane and Cornelis P. Vlaar. New Inhibitors of Rac1 in Metastatic Breast Cancer. American Chemical Society 241th National Meeting, Anaheim, CA, March 27-31, 2011.

**Eliud Hernández**, Brenda L. Montalvo, Janibeth Hernández, Surangani Dharmawardhane and Cornelis P. Vlaar. Novel Inhibitors of Rac1 in Metastatic Breast Cancer. 31er Foro Anual de Investigación y Educación del Recinto de Ciencias Médicas, San Juan, PR, May 3-6, 2011.

Janibeth Hernández, Brenda L. Montalvo, Surangani Dharmawardhane, Cornelis P. Vlaar and **Eliud Hernández**. Novel Inhibitors of Rac1 in Metastatic Breast Cancer. Sixth Transdisciplinary Research Conference, Conrad Condado Plaza, San Juan, PR, May 5-6, 2011.

**Eliud Hernández**, Brenda L. Montalvo-Ortiz, Alina De La Mota-Peynado, Linette Castillo-Pichardo, Tessa Humphries-Bickley, Cornelis P. Vlaar, and Suranganie Dharmawardhane. New Inhibitors of Rac1 in Metastatic Breast Cancer. 43rd IUPAC World Chemistry Congress, San Juan, Puerto Rico, July 31 to August 5, 2011.

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Small Molecule Inhibitors of Rac1 as Anti-invasive Breast Cancer Compounds. **Eliud Hernández**, Alina de la Mota, Suranganie Dharmawardhane and Cornelis P. Vlaar. Drug Discovery, Development & Clinical Research in Academia Syposium, Caribe Hilton San Juan PR, September 18-19, 2008.

Synthesis of Optically Active Trimethylsilyl-Substituted Tertiary  $\alpha$ -Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**; Soderquist J. A.\*. 41<sup>st</sup> ACS Junior Technical Meeting, University of Puerto Rico Cayey PR, March 11, 2006.

Synthesis of Optically Active Trimethylsilyl-Substituted Tertiary  $\alpha$  - Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**; Soderquist J. A.\*. 20 Years of EPSCOR in Puerto Rico Westin Rio Mar, September, 2005.

Synthesis of Optically Active Trimethylsilyl-Substituted Tertiary  $\alpha$  - Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**; Soderquist J. A.\*. 229<sup>th</sup> ACS National Meeting, San Diego CA, March 13-17, 2005.

Synthesis of Optically Active Trimethylsilyl-Substituted Tertiary  $\alpha$  - Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**;

Soderquist J. A.\*. 2<sup>o</sup> Presentación de Afiches del Programa AGEP, UPR Río Piedras PR, July 15, 2004.

Synthesis of Optically Active Homoallylic Amines *via* Asymmetric Allylboration with *B*-Allyl-10-TMS-9-borabicyclo[3.3.2]decane. **Hernández E.**; Canales E.; Soderquist J. A.\*. 227<sup>th</sup> ACS National Meeting, Anaheim CA, March 28-April 1, 2004.

Synthesis of Optically Active 2<sup>o</sup> and 3<sup>o</sup> Alkyl Homoallylic Amines *via* Asymmetric Allylboration. **Hernández E.**; Canales E.; Soderquist J. A.\*. 27<sup>th</sup> ACS Senior Technical Meeting, Quebradillas PR, November 7, 2003.

Synthesis of Optically Active Trimethylsilyl-Substituted  $\alpha$ -Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**; Soderquist J. A.\*. 1<sup>er</sup> Encuentro de Estudiantes de Química Río Piedras PR, April 12, 2003.

Synthesis of Optically Active Trimethylsilyl-Substituted  $\alpha$ -Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**; Soderquist J. A.\*. 225<sup>th</sup> ACS National Meeting, New Orleans LA, March 23-27, 2003.

Synthesis of Optically Active Trimethylsilyl-Substituted  $\alpha$ -Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**; Soderquist J. A.\*. External Advisory Board, PRSG-Consortium NASA, Río Piedras PR, February 7, 2002.

Synthesis of Optically Active Trimethylsilyl-Substituted  $\alpha$ -Allenic Alcohols *via* Asymmetric Propargylboration. **Hernández E.**; Soderquist J. A.\*. 1<sup>st</sup> Congress on Integrating NASA Research and Education Projects in PR, Dorado PR, November 14-17, 2001.

Phenylsulfonyl-Methylenation of Aldonolactones. **Hernández E.**; Mangual E.; Prieto J. A.; Alzérreca A.\*. 215<sup>th</sup> ACS National Meeting, Dallas TX, March 29-April 2 1998.

Phenylsulfonyl-Methylenation of Aldonolactones. **Hernández E.**; Mangual E.; Prieto J. A.; Alzérreca A.\*. 33<sup>th</sup> ACS Junior Technical Meeting, Carolina PR, March 1998.