

BIOGRAPHICAL SKETCH

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NAME: Mario Henrique Bengtson

eRA COMMONS USERNAME (credential, e.g., agency login): mhbengtson

POSITION TITLE: Associate Professor at the Department of Biochemistry and Tissue Biology, UNICAMP

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Universidade Estadual Paulista Júlio de Mesquita Filho (UNESP), São Paulo, Brazil	BS	06/1997	Pharmacy and Biochemistry
University of São Paulo, São Paulo, Brazil	SD	02/1998	Biochemistry and Molecular Biology
University of São Paulo, São Paulo, Brazil	PhD	06/2002	Biochemistry and Molecular Biology
Genomics Institute of Novartis Foundation, San Diego, USA	Postdoctoral	02/2006	Molecular Genetics/ Functional Biology
The Scripps Research Institute, San Diego, USA	Postdoctoral	12/2012	Molecular Genetics/ Molecular Biology

A. Personal Statement

I am an Associate Professor in the Department of Biochemistry and Tissue Biology at the State University of Campinas (UNICAMP) in Brazil. I have a broad background in Molecular Biology, with a strong emphasis on Functional Biology and Molecular Genetics, acquired during my postdoctoral training at the Genomics Institute of the Novartis Foundation and The Scripps Research Institute (San Diego, USA). During my postdoc, I discovered a new pathway responsible for the ubiquitination and cotranslational degradation of peptides synthesized from defective mRNAs that stall the ribosome during translation. My main scientific interests include understanding cotranslational quality control mechanisms, elucidating how gene expression is regulated at the translational level to facilitate neuronal differentiation, and exploring how failures in these mechanisms contribute to neurodegenerative diseases.

Upon returning to Brazil, I continued to pursue my research interests and also assumed the role of co-coordinator at the Center for Medicinal Chemistry at UNICAMP (CQMED - www.cqmed.unicamp.br). This multidisciplinary laboratory is dedicated to developing chemical probes for understudied proteins involved in human diseases. In this role, I successfully managed projects, budgets, and collaborations across various projects, resulting in several peer-reviewed publications. Additionally, we are developing chemical inhibitors for proteins involved in the pathway I discovered during my postdoctoral training, both to enhance our understanding of the process and as potential new targets for treating neurodegenerative diseases.

B. Positions, Scientific Appointments, and Honors

- Principal Investigator in the International Consortium "Structural Genomics Consortium" – SGC (<https://www.thesgc.org>), since 2023
- Co-coordinator of the Center for Medicinal Chemistry at UNICAMP (CQMED - www.cqmed.unicamp.br), since 2020
- Associate Professor at the Department of Biochemistry and Tissue Biology, UNICAMP, since December 2012
- FAPESP Doctoral Fellowship, May 1998 - July 2002
- FAPESP Specialization Fellowship, October 1997 - February 1998
- FAPESP Scientific Initiation Scholarship, September 1994 - August 1996

C. Contributions to Science

1. Takarada, Jéssica E. ; Cunha, Micael R. ; Almeida, Vitor M. ; Vasconcelos, Stanley N.S. ; Santiago, André S. ; Godoi, Paulo H. ; Salmazó, Anita ; Ramos, Priscila Z. ; Fala, Angela M. ; de Souza, Lucas R. ; da Silva, Italo E.P. ; **Bengtson, Mario H.** ; Massirer, Katlin B. ; Couñago, Rafael M. . Discovery of pyrazolo[3,4-d]pyrimidines as novel mitogen-activated protein kinase kinase 3 (MKK3) inhibitors. *Bioorganic & Medicinal Chemistry* , v. 98, p. 117561, 2024.
2. de Souza, Lucas Rodrigo ; Silva, Italo Esposti Poly da ; Celis-Silva, Gabriele ; Raddatz, Bruna Winkert ; Imamura, Louise Matiê ; Kim, Edson Yu Sin ; Valderrama, Gabriel Vieira ; Riedi, Halanna de Paula ; Rogal, Sergio Renato ; Almeida, Bernardo Montesanti Machado de ; Figueredo, Marcus Vinícius Mazega ; **Bengtson, Mario H.** ; Massirer, Katlin Brauer . Improved protocol for Bst polymerase and reverse transcriptase production and application to a point-of-care diagnostics system. *Experimental Biology and Medicine* , v. 248, p. 1671-1683, 2023.
3. Lins, Érico Moreto ; Oliveira, Natássia Cristina Martins ; Reis, Osvaldo ; Ferrasa, Adriano ; Heraí, Roberto ; Muotri, Alysson R. ; Massirer, Katlin Brauer ; **Bengtson, Mário Henrique** . Genome-wide translation control analysis of developing human neurons. *Molecular Brain* , v. 15, p. 55, 2022.
4. Oliveira, Natássia Cristina Martins ; Lins, Érico Moreto ; Massirer, Katlin Brauer ; **Bengtson, Mário Henrique** . Translational Control during Mammalian Neocortex Development and Postembryonic Neuronal Function. *Seminars in Cell & Developmental Biology* , v. 1, p. S1084, 2020.
5. Silva, Suélen Fernandes ; Klippel, Angélica Hollunder ; Ramos, Priscila Zonzini ; Santiago, André da Silva ; Valentini, Sandro Roberto ; **Bengtson, Mario Henrique** ; Massirer, Katlin Brauer ; Bilsland, Elizabeth ; Couñago, Rafael Miguez ; Zanelli, Cleslei Fernando . Structural features and development of an assay platform of the parasite target deoxyhypusine synthase of *Brugia malayi* and *Leishmania major*. *PLoS Neglected Tropical Diseases* , v. 14, p. e0008762, 2020.
6. Yonashiro, Ryo ; Tahara, Erich B ; **Bengtson, Mario H** ; Khokhrina, Maria ; Lorenz, Holger ; Chen, Kai-Chun ; Kigoshi-Tansho, Yu ; Savas, Jeffrey N ; Yates, John R ; Kay, Steve A ; Craig, Elizabeth A ; Mogk, Axel ; Bukau, Bernd ; Joazeiro, Claudio AP . The Rqc2/Tae2 subunit of the ribosome-associated quality control (RQC) complex marks ribosome-stalled nascent polypeptide chains for aggregation. *eLife* , v. 5, p. e11794, 2016.
7. Doamekpor, Selom K. ; Lee, Joong-Won ; Hepowit, Nathaniel L. ; Wu, Cheng ; Charenton, Clement ; Leonard, Marilyn ; **Bengtson, Mario H.** ; Rajashankar, Kanagalaghatta R. ; Sachs, Matthew S. ; Lima, Christopher D. ; Joazeiro, Claudio A. P. . Structure and function of the yeast listerin (Ltn1) conserved N-terminal domain in binding to stalled 60S ribosomal subunits. *Proceedings of the National Academy of Sciences of the United States of America* , v. 113, p. E4151-E4160, 2016.
8. Edwards, Aled M. ; Arrowsmith, Cheryl H. ; Bountra, Chas ; Bunnage, Mark E. ; Feldmann, Marc ; Knight, Julian C. ; Patel, Dhavalkumar D. ; Prinos, Panagiotis ; Taylor, Michael D. ; Sundström, Michael ; Barker, Phil ; Barsyte, Dalia ; **Bengtson, Mario H.** ; Bell, Cindy ; Bowness, Paul ; Boycott, Kym M. ; Buser-Doepner, Carolyn ; Carpenter, Christopher L. ; Carr, Andrew J. ; Clark, Kirk . Preclinical target validation using patient-derived cells. *Nature Reviews. Drug Discovery* , v. 14, p. 149-150, 2015.
9. Ossareh-Nazari, Behnam ; Nino, Carlos A. ; **Bengtson, M. H.** ; Lee, J.-W. ; Joazeiro, C. A. P. ; Dargemont, Corinne . Ubiquitylation by the Ltn1 E3 ligase protects 60S ribosomes from starvation-induced selective autophagy. *The Journal of Cell Biology* , v. 204, p. 909-917, 2014.

10. Lyumkis, D. ; Doamekpor, S. K. ; **Bengtson, M. H.** ; Lee, J.-W. ; Toro, T. B. ; Petroski, M. D. ; Lima, C. D. ; Potter, C. S. ; Carragher, B. ; Joazeiro, C. A. P. . Single-particle EM reveals extensive conformational variability of the Ltn1 E3 ligase. *Proceedings of the National Academy of Sciences of the United States of America* , v. 110, p. 1702-1707, 2013.
11. Mitne-Neto, M. ; Machado-Costa, M. ; Marchetto, M. C. N. ; **Bengtson, M. H.** ; Joazeiro, C. A. ; Tsuda, H. ; Bellen, H. J. ; Silva, H. C. A. ; Oliveira, A. S. B. ; Lazar, M. ; Muotri, A. R. ; Zatz, M. . Downregulation of VAPB expression in motor neurons derived from induced pluripotent stem cells of ALS8 patients. *Human Molecular Genetics* , v. 1, p. 1-1, 2011.
12. **Bengtson, M. H.** ; Joazeiro, Claudio A. P. . Role of a ribosome-associated E3 ubiquitin ligase in protein quality control. *Nature* , v. 467, p. 470-473, 2010.
13. Baptista, Márcio S. ; Melo, Carlos V. ; Armelão, Mário ; Herrmann, Dennis ; Pimentel, Diogo O. ; Leal, Graciano ; Caldeira, Margarida V. ; Bahr, Ben A. ; **Bengtson, Mário** ; Almeida, Ramiro D. ; Duarte, Carlos B. . Role of the Proteasome in Excitotoxicity-Induced Cleavage of Glutamic Acid Decarboxylase in Cultured Hippocampal Neurons. *Plos One* , v. 5, p. e10139, 2010.
14. Li*, Wei ; **Bengtson*, Mario H.** ; Ulbrich, Axel ; Matsuda, Akio ; Reddy, Venkateshwar A. ; Orth, Anthony ; Chanda, Sumit K. ; Batalov, Serge ; Joazeiro, Claudio A. P. . Genome-Wide and Functional Annotation of Human E3 Ubiquitin Ligases Identifies MULAN, a Mitochondrial E3 that Regulates the Organelle's Dynamics and Signaling. *Plos One* , v. 3, p. e1487, 2008. *** Authors had equal contributions**
15. Brioschi, Daniela ; Nadalini, Larissa D. ; **Bengtson, Mario H.** ; Sogayar, Mari Cleide ; Moura, Daniel S. ; Silva-Filho, Marcio C. . General up regulation of *Spodoptera frugiperda* trypsin and chymotrypsins allows its adaptation to soybean proteinase inhibitor. *Insect Biochemistry and Molecular Biology* , v. 37, p. 1283-1290, 2007.
16. Bizarro, Cristiano V. ; **Bengtson, Mário H.** ; Ricachenevsky, Felipe K. ; Zaha, Arnaldo ; Sogayar, Mari C. ; Ferreira, Henrique B. . Differentially expressed sequences from a cestode parasite reveals conserved developmental genes in platyhelminthes. *Molecular and Biochemical Parasitology* , v. 144, p. 114-118, 2005.
17. Obashinjo, S ; **Bengtson, M.** ; Winnischofer, S ; Colin, C ; Vedoy, C ; Demendonca, Z ; Marie, S ; Sogayar, M. . Identification of novel differentially expressed genes in human astrocytomas by cDNA representational difference analysis. *Molecular Brain Research* , v. 140, p. 25-33, 2005.
18. Reis, E. M. ... **Bengtson, M. H.** ... and the Head and Neck Annotation Consortium. Large-scale Transcriptome Analyses Reveal New Genetic Marker Candidates of Head, Neck, and Thyroid Cancer. *Cancer Research* , v. 65, p. 1693-1699, 2005.
19. Martins de Lima, Thais ; de Oliveira Rodrigues, Leonardo ; **Henrique Bengtson, Mario** ; Cleide Sogayar, Mari ; Nogueira Alves Bezerra, Camila ; Amaral Rebouças, Nancy ; Curi, Rui. Identification of genes regulated by oleic acid in Jurkat cells by suppressive subtractive hybridization analysis. *FEBS Letters* , v. 576, p. 320-324, 2004.
20. Brentani, H... **Bengtson, M. H.** ... and the Human Cancer Genome Project Sequencing Consortium. The generation and utilization of a cancer-oriented representation of the human transcriptome by using expressed sequence tags. *Proceedings of the National Academy of Sciences of the United States of America* , v. 100, p. 13418-13423, 2003.
21. Camargo, A. A. ... **Bengtson, M. H.** ... de Souza SJ. The contribution of 700,000 ORF sequence tags to the definition of the human transcriptome. *Proceedings of the National Academy of Sciences of the United States of America* , v. 98, p. 12103-12108, 2001.
22. Correa, R ; **Bengtson, M. H.** . Human Semaphorin 6B [(HSA)SEMA6B], A Novel Human Class 6 Semaphorin Gene: Alternative Splicing and All-Trans-Retinoic Acid-Dependent Downregulation in Glioblastoma Cell Lines. *Genomics* , v. 73, p. 343-348, 2001.
23. de Souza, S. J. ; Camargo, A. A. ... **Bengtson MH** ... Simpson, A.J. . Identification of human chromosome 22 transcribed sequences with ORF expressed sequence tags. *Proceedings of the National Academy of Sciences of the United States of America* , v. 97, p. 12690-12693, 2000.
24. Vedoy, C. G. ; **Bengtson, M. H.** ; Sogayar, M. C. . Hunting for differentially expressed genes. *Brazilian Journal of Medical and Biological Research, Ribeirão Preto*, v. 32, n.7, p. 877-884, 1999.

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NAME: Italo Esposti Poly da Silva

eRA COMMONS USER NAME (credential, e.g., agency login): IESPOSTI

POSITION TITLE: PhD Candidate / Research Associate

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Universidade Estadual do Noroeste Fluminense	BS	08/2014	Biology
Universidade Federal de Vicosa	MS	03/2018	Structural and Cell Biology
Universidade Estadual de Campinas	PhD	Present	Genetics and Molecular Biology

A. Personal Statement

I am a final semester PhD student in Genetics and Molecular Biology at Universidade Estadual de Campinas, Brazil. Currently, I am engaged at the CQMED (Center for Medicinal Chemistry), where I contribute to early-stage drug discovery through structural biology-oriented medicinal chemistry. CQMED specializes in fostering public-private partnerships to leverage the synergies between academia and industry. For my PhD project, I am developing tools for understanding the role of the complexities of the ribosome-mediated quality control (RQC) pathway, a crucial mechanism regulating protein translation to prevent the accumulation of abnormal proteins. Our research aims to provide biochemical and structural insights into the Ribosome Quality Control Trigger complex (RQT) and its core helicase, ASCC3, while also seeking to discover new chemical inhibitors. The success of this project could significantly advance early-stage drug development for specific neurodegenerative illnesses, offering promise for more effective treatments and therapeutic interventions. Drawing upon my expertise in virology, molecular biology, and public health, I also serve as a Research Associate at CQMED. In this role, I am involved in a project aimed at achieving national autonomy in the production of enzymes crucial for molecular diagnostics tests targeting tropical and neglected diseases. This initiative was spurred by the 2020 Sars-Cov-2 pandemic, during which the scarcity of reagents posed a significant constraint on mass testing efforts.

Ongoing projects to highlight include:

2022- present.

Structural determination and search for inhibitors of the enzyme deoxyhypusine synthase from eukaryotic organisms causing neglected diseases. Financial Support: FAPESP, CAPES, CNPq. Coordinators: Prof. Mário Henrique Bengtson and Prof. Cleslei Fernando Zanelli.

2021- present.

The Saccharopine Pathway in neurological genetic diseases. Financial Support: FAPESP, CAPES, CNPq. Coordinator: Prof. Paulo Arruda

2021- present.

Development of enzymatic inputs for diagnostic tests in point-of-care system with result delivery using Artificial Intelligence. Financial Support: FAPESP, CAPES, CNPq, EMBRAPA. Coordinators: Prof. Katlin Massirer and Prof. Mário Henrique Bengtson;

2019- present.

Characterizing the Structure of the RNA helicase ASCC3 and Developing Potential Inhibitors for human RQC pathway. Financial Support: FAPESP, CAPES, CNPq. Coordinators: Prof. Mário Henrique Bengtson and Prof. Jon Elkins;

2019- present.

New approaches for MRCK α , MRCK β and MRCK γ protein kinase inhibitors. Financial Support: FAPESP, CAPES, CNPq. Coordinators: Prof. Rafael Counago and Prof. Katlin Massirer;

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2021- present.

Research Associate at Center for Medicinal Chemistry (CQMED), Unicamp (Universidade Estadual de Campinas), Campinas- SP, Brazil.

2019- present.

PHD Candidate, Unicamp (Universidade Estadual de Campinas), Campinas- SP, Brazil.

2018- 2019

Technician, CQMED (Center of Medicinal Chemistry), Unicamp (Universidade Estadual de Campinas), Campinas- SP, Brazil.

2016-2018

Master Degree Student, UFV (Universidade Federal de Viçosa). Viçosa-MG, Brazil.

2010-2016

Health Services Administrative Assistant for Health Secretary of Itaperuna-RJ, Brazil.

Honors and Awards

2024 Travel award for the 2024 Biophysical Society Annual Meeting.

2022 Honourable mention for oral presentation: "Development of reagents for viral diagnosis in artificial intelligence and IoT-based Point-of-Care system"

2022 Second Place for Oral presentation: "Structural determination and searching for small chemical inhibitors of the DNA/RNA helicase ASCC3"

2019 Scholarship for PhD studies at Unicamp. Agency: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, CAPES.

2017 Poster prize for "Evaluation of the antiviral effect and action mechanisms of derivative compounds of xanthenedione against Zika virus". V Symposium of Integration of Programs in Cell Biology from UFU, UFMG and UFV.

2016 Scholarship for MSc studies at UFV. Agency: Fundação de Amparo à Pesquisa do Estado de Minas Gerais, FAPEMIG.

C. Contributions to Science

I have remained fiercely dedicated to applying my research projects to address local issues throughout my academic career. This motivation inspired me to focus on tropical virus research for my master's thesis, where I created protocols and carried out antiviral testing. I then made the decision to further my knowledge of medicinal chemistry at CQMED by emphasizing on target-based drug development. At CQMED, I have had the invaluable opportunity to not only engage in cutting-edge research but also to contribute to teaching both graduate and undergraduate students. Additionally, the center has provided me with exposure to international collaborations and advanced techniques. Leveraging this diverse skill set, I have actively collaborated on various projects.

During the recent pandemics, I had the opportunity to tackle pressing issues, particularly the scarcity of reagents for mass testing. Utilizing my expertise in molecular biology, public health, and virology, I led an effort at CQMED to tackle this problem. By the project's end, we had successfully generated reagents for more than a million tests, garnering praise and honors, as well as an offer to submit a manuscript for publication.

My area of interest has recently changed to structural biology, namely the use of cryo-electron microscopy (Cryo-EM) for structure identification. I've assumed a leadership position in our group to incorporate Cryo-EM into our lab's operations as a supplement to our current emphasis on using X-ray diffraction to determine structure. Currently, as a trainee at the New York Structural Biology Center, I am acquiring and applying skills in single-particle cryo-EM to advance drug discovery efforts, yielding promising results.

Publications

Takarada, Jéssica E. ; Cunha, Micael R. ; Almeida, Vitor M. ; Vasconcelos, Stanley N.S. ; Santiago, André S. ; Gdoi, Paulo H. ; Salmazo, Anita ; Ramos, Priscila Z. ; Fala, Angela N. ; de Souza, Lucas R. ; **da Silva, Ítalo E. P.** ; Bengtson, Mario H. ; Massirer, Katlin B. ; Couñago, Rafael M. . Discovery of pyrazolo[3,4-d]pyrimidines as novel Mitogen-Activated Protein Kinase Kinase 3 (MKK3) Inhibitors. BIOORGANIC & MEDICINAL CHEMISTRY, v. 98, p. 117561, 2023.

de Souza, Lucas & **Silva, Ítalo**; Celis-Silva, Gabriele; Raddatz, Bruna; Imamura, Louise; Valderrama, Gabriel; Kim, Edson; Riedi, Halanna; Almeida, Bernardo; Rogal Jr, Sergio; Figueredo, Marcus; Bengtson, Mario And Massirer, Katlin. Improved protocol for Bst polymerase and reverse transcriptase production and application to a point-of-care diagnostics system. Submitted on June 2023, Experimental Biology and Medicine.

da Silva Rodrigues, João Vitor ; Rodrigues Gazolla, Poliana Aparecida ; da Cruz Pereira, Iago ; Dias, Roberto Sousa ; Poly da Silva, **Ítalo Esposti** ; Oliveira Prates, John Willians ; De Souza Gomes, Isabela ; De Azevedo Silveira, Sabrina ; Costa, Adilson Vidal ; De Oliveira, Fabrício Marques ; De Aguiar, Alex Ramos ; Canedo Da Silva, Cynthia ; Teixeira, Róbson Ricardo ; De Paula, Sérgio Oliveira . Synthesis and virucide activity on zika virus of 1,2,3-triazole-containing vanillin derivatives. ANTIVIRAL RESEARCH , v. 212, p. 105578, 2023.

Fernandes, Luciana S. ; da Silva, Milene I. da ; Dias, Roberto S. ; da S. Lucindo, Marcel S. da S. ; **da Silva, Ítalo E. P.**; Silva, Cynthia C. ; Teixeira, Rbson R. ; de Paula, Sérgio O. de . Evaluation of Antiviral Activity of Cyclic Ketones against Mayaro Virus. Viruses-Basel , v. 13, p. 2123, 2021.

Poly da Silva, Ítalo Esposti; Lopes da Silva, Milene ; Dias, Roberto Sousa ; Santos, Edjon Gonçalves ; Brangioni de Paula, Maria Cecília ; Silva de Oliveira, André ; Costa da Silveira Oliveira, Ana Flávia ; Marques de Oliveira, Fabrício ; Canedo da Silva, Cynthia ; Teixeira, Róbson Ricardo ; Oliveira de Paula, Sérgio . Xanthenedione (and intermediates involved in their synthesis) inhibit Zika virus migration to the central nervous system in murine neonatal models. MICROBES AND INFECTION , v. 22, p. 489-499, 2020.

de Oliveira, André S. ; Gazolla, Poliana A. R. ; Oliveira, Ana Flávia C. da S. ; Pereira, Wagner I. ; de S. Viol, Lívia C. ; Maia, Angélica F. da S. ; Santos, Edjon G. ; **da Silva, Ítalo E. P.** ; Mendes, Tiago A. de Oliveira ; da Silva, Adalberto M. ; Dias, Roberto S. ; da Silva, Cynthia C. ; Polêto, Marcelo D. ; Teixeira, Róbson R. ; de Paula, Sergio O. . Discovery of novel West Nile Virus protease inhibitor based on isobenzonafuranone and triazolic derivatives of eugenol and indan-1,3-dione scaffolds. PLoS One , v. 14, p. e0223017, 2019.

Lima, Ângela ; Teixeira, Róbson ; Silva, Bianca ; Siqueira, Raoni ; **Silva, Ítalo** ; Santos, Edjon ; Fernandes, Maria Cecília ; Gonçalves, Victor ; Bressan, Gustavo ; Mendes, Tiago ; Paula, Sérgio ; Costa, Adílson ; Santos, Marcelo . síntese e avaliação das atividades fotoprotetora, citotóxica e antiviral contra o Zika vírus de derivados triazólicos da benzofenona. QUIMICA NOVA , v. 42, p. 473-484, 2019.

Oliveira, Ana Flávia C. da S. ; de Souza, Ana Paula M. ; de Oliveira, André S. ; da Silva, Milene L. ; de Oliveira, Fabrício M. ; Santos, Edjon G. ; **da Silva, Ítalo Esposti P.** ; Ferreira, Rafaela S. ; Villela, Filipe S. ; Martins, Felipe T. ; Leal, Daniel H. S. ; Vaz, Boniek G. ; Teixeira, Róbson R. ; de Paula, Sergio O. . Zirconium catalyzed synthesis of 2-arylidene Indan-1,3-diones and evaluation of their inhibitory activity against NS2B-NS3 WNV protease. EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY , v. 149, p. 98, 2018.