

BIOGRAPHICAL SKETCH

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NAME: Italo Esposti Poly da Silva

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

POSITION TITLE: Research Scientist

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 <i>(if applicable)</i>	Completion Date MM/YYYY	FIELD OF STUDY
Universidade Estadual do Noroeste Fluminense	BS	08/2014	Biology
Universidade Federal de Vicos	MS	03/2018	Structural and Cell Biology
Universidade Estadual de Campinas	PhD	12/2024	Genetics and Molecular Biology

A. Personal Statement

I hold a Ph.D. in Genetics and Molecular Biology from the Universidade Estadual de Campinas, Brazil. Currently, I am a Scientist Researcher at the Center for Medicinal Chemistry (CQMED), where I contribute to early-stage drug discovery with a focus on structural biology-driven medicinal chemistry. CQMED specializes in fostering public-private partnerships that harness the synergy between academia and industry. My main research project focuses on developing tools to better understand the complexities of the ribosome-mediated quality control (RQC) pathway—a key mechanism that regulates protein translation and prevents the accumulation of aberrant proteins. Specifically, our project investigates the Ribosome Quality Control Trigger complex (RQT) and its core helicase, ASCC3, aiming to uncover biochemical and structural insights while identifying novel chemical inhibitors. The success of this work has the potential to accelerate early-stage drug development targeting neurodegenerative diseases, paving the way for more effective therapeutic interventions. In addition to this, and among others, I am also involved in a project aimed at promoting national self-sufficiency in the production of enzymes used in molecular diagnostics for tropical and neglected diseases. This initiative emerged in response to the SARS-CoV-2 pandemic, during which the scarcity of reagents severely limited mass testing capacity. Drawing on my background in virology, molecular biology, and public health, I have actively contributed to this effort at CQMED.

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, EMBRAPII. 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

2024- present.

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

2021- present.

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

2019- present.

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

2018- 2019

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

2016-2018

Master Degree Student, UFV (Universide Federal de Vicoso). Vicoso-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

Throughout my academic career, I have been deeply committed to addressing local and global health challenges through research. This dedication shaped the direction of my master's research, which focused on tropical viruses. During that time, I developed protocols for antiviral assays and conducted in vitro testing of candidate compounds. Later, I joined CQMED to broaden my expertise in medicinal chemistry with an emphasis on target-based drug discovery. At CQMED, I have had the opportunity to participate in cutting-edge research, engage in national and international collaborations, and contribute to the training of undergraduate and graduate students. These experiences have strengthened my scientific foundation and expanded my skill set across disciplines.

During the COVID-19 pandemic, I led a team at CQMED in response to the urgent need for diagnostic reagents. Applying my knowledge of molecular biology, public health, and virology, we successfully produced reagents sufficient for over one million diagnostic tests. This work received significant recognition, including honors and an invitation to publish a manuscript detailing the initiative.

Most recently, my scientific focus has shifted toward structural biology, particularly the application of cryo-electron microscopy (Cryo-EM) for structure-based drug discovery. Following a cross-training program at the New York Structural Biology Center, where I acquired skills in single-particle Cryo-EM, I assumed a leadership role in implementing this technology at CQMED. This complements our existing expertise in X-ray crystallography and has already begun to yield promising results in our drug discovery efforts.

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, 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, 2023.

de Souza, Lucas & **Silva, Italo**; Celis-Silva, Gabriele; Raddatz, Bruna; Imamura, Louise; Valderrama, Gabriel; Kim, Edson; Riedi, Halanna; Almeida, Bernardo; Rogal Jr, Sergio; Figueiredo, 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, **Italo 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, Italo 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, Italo 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, Italo 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, Italo** ; 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, Italo 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.

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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 ; Figueiredo, 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 ; Herai, 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 ; Klippe, 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.