# MARIO LEBENDIKER, Ph.D.

## November 2017

#### CURRICULUM VITAE

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| 1954         | Born in Buenos Aires, Argentina   |
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| 1971-77      | Biochemistry Studies (Equivalent to B.Sc. and M.Sc.) at the Faculty of Pharmacy and Biochemistry, Buenos Aires University.  |
| 1978         | Assistant in the Biology Department at the Faculty of Pharmacy and Biochemistry, Buenos Aires University.   |
| 1979-82      | Ph.D. in Biochemistry, Animal Virology Center (CEVAN), Buenos Aires<br>University. Recipient of the Fellowship of the National Research Council,<br>Argentina.  |
|              | Thesis: "Analysis of the Macromolecular Components of Foot-and-Mouth<br>Disease Virus. Localization and Identification of the Endonuclease of Virions".<br>Under the Guidance of Dr. Jose La Torre.   |
| 1983-85      | Postdoctoral Fellow at the Department of Molecular Virology, Hadassah<br>Medical School, The Hebrew University of Jerusalem. Sponsor: Professor<br>Raymond Kaempfer. Subject: Translational Control of Eukaryotic Gene<br>Expression.   |
| 1985-1994    | Researcher and Group Leader in the Protein Department of Makor<br>Chemicals, a Local Subsidiary of the Sigma, Aldrich, Fluka Corporation.<br>Jerusalem. <u>Subject</u> : In charge of research, development and production of<br>more than 100 fine biochemical products that became an integral part of<br>Sigma catalogue. The development of each project includes: search out<br>library for valuable new products, estimation of potential markets,<br>development of an industrial strategy for purification; physico-chemical and<br>biological stability of the products; development of a biological assay, and<br>scaling-up. |
| 1994-1996    | Research Assistant at the Department of Microbiological and Molecular Ecology,<br>Life Science Institute, The Hebrew University of Jerusalem. Sponsor<br>Professor Shimon Shuldiner. <u>Subject</u> : Structural information by NMR and X-<br>Ray Crystallography of a membrane transporter.  |
| 1997-Present | In charge of the Protein Purification Facilities at the Wolfson Centre for Applied<br>Structural Biology, Life Science Institute, The Hebrew University of<br>Jerusalem. <u>Subject</u> : the research in our group focuses in how to obtain large<br>quantities of highly purified and biologically active proteins that is necessary<br>for structural and biochemical studies.   |

- 2000-Present Two week Course for graduate students on Expression and Purification of Recombinant Proteins (Registerd Courses 72682, 72681 and 72695).
- 2008-Present Faculty member for Structural Biology in the Experimental Biophysical Methods section of Faculty of 1000 Biology Reports: articles evaluations

#### SCIENTIFIC EXPERIENCE

**Ph.D.:** In my doctorate thesis, conducted under the guidance of Dr. La Torre, I have been studying the internal endoribonuclease of Foot-and-Mouth Disease Virions; it's purification and characterization. Activation of the endoribonuclease inside the virions. See publications 1-4 and 10.

As a result of these studies we have formulated an experimental vaccine: inactivation of a vaccine virus strain by activation of the virus-associated endonuclease. (Patent: Acta No. 283355/80 Direccion Nacional de Propiedad Industrial Argentina).

**Postdoc:** During my postdoctoral fellowship under the guidance of Professor Raymond Kaempfer, the focus of my studies concentrated on the translational control of eukaryotic gene expression.

1. Differential modulation of binding and interaction of eukaryotic initiation factor 2

(eIF-2) with double stranded RNA, Met-tRNAf, mRNA, ATP and GTP.

2. Superinduction of the human immune interferon gene.

See publications 5-9 and 11-12.

**Industry:** Researcher and a group leader in the protein department of Sigma Chemicals. I was in charge of the research, development and production of more than 100 fine biochemical products that became an integral part of Sigma catalogue. The development of each project includes: search out library for valuable new products; estimation of potential markets; development of an industrial strategy for purification; physico-chemical and biological stability of the products; development of a biological assay and scaling-up for final processing. The result of this work were:

- 1. Most of the lectins and lectins conjugated to agarose in Sigma catalogue. For example: Wheat Germ Agglutinin, Phytohemagglutinin PHA-P, Leucoagglutinin PHA-L, Ricinnus Toxin, Soybean Agglutinin, Pea Lectin, Galanthus Nivalis, Datura Stram, Vicia Faba, Artocarpus Integrifolia, etc.
- 2. Ribosomal Inhibitor Proteins, like: Ricin A, Abrin, Deglycosylated Ricin A, Gelonin, Momordin, Trichosanthin, etc. These kind of proteins are widely used for preparation of immunotoxins.
- 3. Bacterial toxins as: Cholera Toxin, Pseudomona Exotoxin A, Staphylo Alpha-Toxin. Superantigens as: Staphylo Enterotoxin A, B and Toxic Shock Syndrome Toxin I, etc.
- 4. Proteins of animal and venom origin like Annexins, Desintegrins, Heparan Sulfate Proteoglycans, Cyclophilin, etc.

**<u>Research Assistent:</u>** During my work in the Laboratory of Professor Shimon Schuldiner, the focus of my studies concentrated on a transporter protein. I have purified a very unusual membrane protein. We tried to obtain structural information by NMR and X-Ray Crystallography. I had use techniques of molecular biology such as site directed mutagenesis, DNA sequence, etc.; techniques of purification of membrane proteins and liposome reconstitution of the activity. See publications 13-20.

**Present Work:** In charge of the Protein Purification Facilities in the Wolfson Center for Applied Structural Biology, Life Science Institute, The Hebrew University of Jerusalem. Elucidation of the nature, function and organization of proteins relies significantly on structural studies. While collaborating on different projects with other units, the research in our group focuses in how to obtain large quantities of highly purified and biologically active proteins that is necessary for crystallization or NMR studies. The Protein Purification Facilities are accessible for students and staff of the University and from biotech Industries, that are interested in over-expression and purification of various proteins, under the guidance of the unit's personal.

#### PATENTS

Patent Number: 4,471,054 United States Patent Process for Inactivating Foot-and-Mouth Disease Virus Lattore Jose; Denoya Claudio; Scodeller Eduardo; Vasquez Cesar; **Lebendiker Mario**; Dubra Maria S. and Crespo Oscar Date: Sept. 11 1984

#### LIST OF PUBLICATIONS

- Dubra, M.S., Lebendiker, M.A., Grigera, P.R., Tisminetzky, S.G., Costa Giomi, M.P., Sagedhal, A., La Torre, J.L., and Vasquez, C.(1981) Biologia Molecular del Virus de la Fiebre Aftosa. *Medicina* 41: 221-229.
- 2. La Torre, J.L., Underwood, B.O., **Lebendiker, M.A**., Gorman, B.M., and Brown, F. Application of RNAase (1982) T1 one and two-dimensional analysis to the rapid identification of Footand-Mouth Disease viruses. *Infection and Immunity 36: 142-147.*
- 3. Scodeller, E.A., **Lebendiker, M.A**., Dubra, M.S., Basarab, O., La Torre, J.L., and Vasquez, C.(1982). An experimental vaccine for Foot-and-Mouth Disease Virus. *Proceedings of the 16th Conference of Foot-and-Mouth Disease Virus of the International Organization of Epizaotes* 45-55.
- 4. Scodeller, E.A., **Lebendiker, M.A**., Dubra, M.S., Crespo, D.A., Basarab, O., La Torre, J.L., and Vasquez, C.(1984).Inactivation of FMDV vaccine strains by activation of virus associated endonuclease. *J. of General Virology, 65(9): 1567-1573*.
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- 6. Kaempfer, R., Gonsky, R., and **Lebendiker, M**. (1986). Binding of ATP to eIF-2 induces modulation of its Met-tRNAf-and mRNA-binding activities. *In: Translational Control (M. Mathews, ed.), Cold Spring Harbor, N.Y. pp. 58-62.*
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- 11. Gonsky, R., **Lebendiker, M.A**., Harary, R., Banai, Y., and Kaempfer, R. (1990) Binding of ATP to eukaryotic initiation factor 2: differential modulation of mRNA-binding activity and GTP-dependent binding of Met-tRNAf. *J. Biol. Chem.* 265: 9083-9089.
- 12. Kaempfer, R., Sayar, D., **Lebendiker, M**., Arad, G., Gerez, L., and Ketzinel, M. (1990) Posttranscriptional regulation of the human gene encoding the p55 alpha-subunit of the IL-2 receptor. *J. Leukocyte Biol. Suppl.* 1, 16.
- 13. Yerushalmi, H., **Lebendiker, M.A**., and Schuldiner, S. (1995) EmrE, an Escherichia coli 12kDa Multidrug Transporter, Exchanges Toxic Cations and H+ and Is Soluble in Organic Solvents. J. Biol. Chem. 270:6856-6863
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- 44. Buch M., Wine Y., Dror Y., Rosenheck S., Lebendiker M., Giordano R., Leal R., Popov A., Freeman A and Frolow F. (2014) Protein Products Obtained by Site-Preferred Partial Crosslinking in Protein Crystals and "Liberated" by Redissolution. *Biotechnology and Bioengineering DOI 10.1002/bit.25186*
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### Website - Journals

- Network manager and founder of the Protein Purification Facility website of The Wolfson Centre in The Hebrew University: This site includes a plethora of information in the protein production field, used by students and researchers of many Universities. *More than 72,000 entries since September 2006* <u>http://www.ls.huji.ac.il/~purification/</u>
- 2) Network manager of the Protein Production and Purification Partnership in Europe (P4EU) network since October 2011: A platform for the exchange of information, know-how and materials between core facility labs in the field of protein expression and purification. In construction http://www.structuralbiology.eu/networks/p4eu?tab=contacts
- 3) Neubig R, and Roman D, (2004) Sites of interest on the World Wide Web Mol. Interv.4: 298
- 4) Lederman L. (2009) Protein Isolation and Purification Tech News BioTechniques 46:87-89

http://www.biotechniques.com/BiotechniquesJournal/2009/February/Protein-Isolation-and-Purification/biotechniques-92073.html?service=print

- 5) F1000, Faculty of 1000, Faculty Member (contributor) since 2008 (http://f1000.com/my)
- 6) Editorial Board of F1000 Research since May 2012 (http://f1000research.com)
- 7) GE Healthcare Life Sciences: External Links Resources for Tagged Protein purification http://sciencedirect.verticalsearchworks.com/EN/Microsites/1/GE+Healthcare/Home

8) Pure Pursuits: Techniques for simpler, cheaper, and better antibody purification. By Katherine Bagley. The Scientist May, 1<sup>st</sup>, 2012 http://the-scientist.com/2012/05/01/pure-pursuits/

### Courses in The Hebrew University

- 1) PURIFICATION & EXPRESSION OF RECOMBINANT PROTEIN #72681 Mario Lebendiker and Tsafi Danieli: Theoretical course two hours per week during one semester Years: 2002, 2003, 2005, 2007, 2009, 2010, 2012
- WORKSHOP ON PROTEIN PURIFICATION #72695
   Mario Lebendiker: two practical courses, one week each one, 45 hours each course Years: 2002, 2003, 2005, 2007, 2009, 2010, 2012
- 3) PROTEIN CHEMISTRY ADVANCED BIOPHYSICAL METHODS #69703 Assaf Friedler: 1hour talk
- 4) BIOCHEMISTRY : ADVANCED LEVEL #72339 Dudy Engelberg: 2 hour talk
- 5) Theoretical Course: Protein Production for Biophysical and Biochemical Studies (#92632) – Hebrew University of Jerusalem, Israel. Nov-Dec 2014 (~28hours course, four days. Participation of near 50 students from all the Hebrew University Campus, Tel Aviv University, Haifa University, Technion and Weizzman Institute)
- 6) Practical Course: Protein Production for Biophysical and Biochemical Studies (#92638)
   Hebrew University of Jerusalem, Israel. February 2015 (~24hours course, three days. Participation of six students from the Hebrew University and Haifa University)
- 7) Theoretical Course: Protein Production for Biophysical and Biochemical Studies (#92632) Hebrew University of Jerusalem, Israel. Oct 2014 to Jan 2016 (2 weekly hours course, first semester. Participation of near 16 students from all the Hebrew University Campus and 1 from SIGMA)

## **Congress, Meetings and External Courses**

- 1) PEGS 4<sup>th</sup> Annual Protein Process Development Conference and 10<sup>th</sup> Annual Protein Expression Conference, January 2007, San Diego, USA, (Poster)
- 2) NMR-Life Workshop meeting: "Protein expression and isotope labeling for structural biology" July 2008, BNMRZ, Garching, Germany TALK: Protein Sample Preparation for Structural and Biophysical Studies - Personal Experience Handling Some Difficult Proteins (1hour talk)
- 3) PEGS Europe Protein Engineering Summit, September 2009 Hannover, Germany (participation)
- 4) Meeting of European Protein Expression Facilities, May 2010 Heidelberg, Germany and Helmholtz Center for Infection Disease in Brawnschweig, Germany *TALK: Protein Sample Preparation for Structural and Biophysical Studies - Personal Experience Handling Some Difficult Proteins (1hour talk)*
- 5) GE-Healthcare Innovation day, Tel Aviv, January 2011, 2 days (participation)
- 6) Ilanit / FISEB 2011, February 7-10, 2011, Eilat, Israel (participation)

- First P4EU Meeting (<u>P</u>rotein <u>p</u>roduction and <u>p</u>urification <u>p</u>artnership for E<u>u</u>rope) Halle, Germany 23/2/2011 TALK: Protein Aggregation Problems (20 min talk) <u>Meeting Organizer</u>
- 8) 4th Halle Conference on Recombinant Protein Production Halle, Germany 24-26/2/2011
- TALK: A simple platform for addressing protein aggregation during protein expression and purification steps (40 min talk)
- 9) PROTEIN PRODUCTION WORKSHOP 2011 July 6-7, 2011 Oxford, England *TALK: Protein Refolding (40 min talk)*
- 10) P4EU Workshop on Eukaryotic protein expression platforms, Copenhagen Nov29th 2011 (participation)
- 11) Difficult to Express Proteins- 8<sup>th</sup> ANNUAL PEGS Boston, USA May 1<sup>st</sup> 2012
   TALK: A Simple Platform for Addressing Protein Aggregation During Protein Expression and Purification Steps (30 min talk)
   MODERATOR: Strategies to tackle aggregation problems during purification (90 min talk)
- 12) P4EU Protein Purification Workshop in IRB Barcelona, Spain June 4<sup>th</sup>, 2012 TALK: A difficult to produce RNA binding protein. On-column refolding (30 min talk)
- 13) Fifth Annual Protein Purification & Recovery PEPTALK, The Protein Science week, Palm Spring, California, USA 20/23 January 2013 (Invited for a 40 min talk) TALK: How to Deal with Aggregation Problems of IDPS:"Intrinsically Disordered Proteins" MODERATOR: Strategies to Tackle Aggregation problems during Purification
- 14) Fifth Annual Protein Purification & Recovery PEPTALK, The Protein Science week, Palm Spring, California, USA 20/23 January 2013 (Invited for a 180 min course) TALK: Buffer Optimization for Purifying Proteins
- 15) 4<sup>th</sup> P4EU Meeting IMBC, Porto, Portugal Nov 11-12, 2013 *Talk: Ion exchange: some applications* (30 min talk)
- 16) 4<sup>th</sup> P4EU Meeting IMBC, Porto, Portugal Nov 11-12, 2013 *Talk: Encouraging data publication for reliability assessment (30 min talk)*
- 17) Israel Society for Biotechnology Engineering (ISBE) December 1, 2013, Dan Hotel, Tel-Aviv Talk: How to deal with aggregation problems of IDPs "Intrinsically disorder proteins" and other prone to aggregated proteins (30 min talk)
- 18) Protein expression and characterization workshop. Weizmann Institute of Science, May 11-12, 2014, *Talk: Production of prone-to-aggregate proteins (30 min talk)*
- 19) CTLS 2014 Pan-European Core Technologies for Life Science Congress Institute Pasteur, Paris, France 2-5 June 2014
- 20) 5<sup>th</sup> P4EU meeting at Institute Pasteur June 5-6 2014, *Talk: Reproducing irreproducible results: A love story for a robust Kinase crystallization (30 min talk)*
- 21) Advisory Board Meeting for the Protein Expression & Purification Facility (SFAB) Max Planck Institute of Molecular Cell Biology and Genetic - Dresden – GERMANY. July 15-16 2014
- 22) Max Planck Institute of Molecular Cell Biology and Genetic Dresden GERMANY July 17<sup>th</sup> 2014. Talk: How to deal with the production of IDPs "Intrinsically disorder proteins" and other prone to aggregated proteins (70 min talk + 120 minutes discussions)

- 23) PepTalk: The Protein Science Week. Protein Purification and Recovery, Streamlining Processes.
   19<sup>th</sup> to 23<sup>rd</sup> January 2015 in San Diego, USA
   Talk: Reproducing Irreproducible Results: A Case Study for Robust Kinase Crystallization (30 min talk)
- 24) PepTalk: The Protein Science Week. Protein Purification and Recovery Streamlining Processes. 19<sup>th</sup> to 23<sup>rd</sup> January 2015 in San Diego, USA <u>Short Course:</u> Protein Purification Strategies: Dealing with Proteins that Are Prone to Aggregate (180 min course)
- 25) LSU Training course from Wyatt in the use of SEC/MALS & Quasi-Elastic Light Scattering Santa Barbara, USA January 26<sup>th</sup> to 29<sup>th</sup> 2015 (*Participation 3 days course*)
- 26) Immunologic Molecular Center (CIM) La Havana, Cuba, 7<sup>th</sup> to 9<sup>th</sup> April, 2015. Protein Purification Course (15 hours course – Three days). Participants: 53 profesionales from: Centro de Inmunología Molecular (CIM), Centro de Ingeniería Genética y Biotecnología (CIGB), Instituto Finlay, Centro de Química Biomolecular (CQB), Centro de Investigación y Desarrollo de Medicamentos (CIDEM), Universidad de la Habana & Centro Nacional de Investigaciones Científicas (CNIC)
- 27) 8th P4EU Meeting and Joint session with ARBRE network organized by the Max Planck Institute of Molecular Cell Biology and Genetic - Dresden – Germany July 17-18<sup>th</sup> 2015 *Talk: Quality control from a protein production perspective (20 min talk)*
- 28) 7<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Protein Purification Technologies -Lisbon 11/2015 Talk: IDPs "Intrinsically disorder proteins", difficult to produce, but with a significant role in cellular pathways. Case studies (30 min talk)
- 29) 7<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Protein Purification Technologies -Lisbon 11/2015 Short Course: *Protein Purification Strategies: Dealing with Proteins that Are Prone to Aggregate (3hr course)*
- 30) 9<sup>th</sup> P4EU Meeting of the European Core Facilities in Protein Production 30<sup>th</sup> November to 1<sup>st</sup> December 2015 in Munich Germany Max-Planck-Institute of Biochemistry
- 31) P4EU and AEBRF First Joint meeting *December 1-2, 2015* (Max-Planck-Institute of Biochemistry) Working group Proposal Guidelines on Protein Quality for Biological Experiments. *Coordinator of the group*
- 32) Advanced Methods in Protein Purification 09-13 May, 2016 Max-Planck-Institute of Biochemistry - Munich Germany .*Main guest Speaker and Trainer 5 days course (theoretical and practical lab course for post-docs)*
- 33) 12<sup>th</sup> P4EU Meeting– organized by the European Molecular Biology Laboratory (EMBL) -Heidelberg – GERMANY
- 34) P4EU and AEBRF Joint meeting for Protein Quality 16<sup>th</sup> (evening) June 2016 in Heidelberg Germany - European Molecular Biology Laboratory (EMBL)
- 35) EMBO Course: Protein expression, purification, and characterization (PEPC10) 12 to 20 September 2016 | Hamburg, Germany. *Guest Speaker and Trainer 10 days course (theoretical and practical lab course for post-docs)*
- 36) 8<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Lisbon: Basic Technologies in a Core Protein Expression Lab: Basic Principles in Protein Purification Strategies. Two days Training Seminar 31/10 to 1/11/2016
- 37) 8<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Protein Purification Technologies -Lisbon 3/11/2016 Talk: Improving the time-efficiency and quality of your results (30 min talk)

- 38) 8<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Protein Purification Technologies -Lisbon 3/11/2016 Short Course: Protein Purification Strategies: Dealing with Proteins that are Prone to Aggregate (3hr course)
- 39) 8<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Protein Purification Technologies Lisbon 4/11/2016 Talk: <u>Case Study</u>: Human Kinase Crystallization Phosphatase Co-Expression (30 min talk)
- 40) 13<sup>th</sup> P4EU Meeting– organized by Weizmann Institute of Science, Israel 7/8 Dec 2016 Column chromatography strategies for Adeno Associated Viruses (AAVs) purification (Hadar Amarteli 30min talk)
- 41) ILANIT Eilat 20-23/2/2017 <u>In charge of the Early Bird Session</u>: Reproducing Irreproducible Results -What Can We Do For Recombinant Proteins? <u>Talk:</u> Quality Control of Recombinant Protein: Best Practice Recommendations (30 min talk)
- 42) 10<sup>th</sup> March 2017 Université libre de Bruxelles Meeting: "Challenges and opportunities in Protein Analytics". *Talk:* : "*The Protein Purification Facility*": *case studies in phosphorilation and glycosilation heterogenicity and others (30 min talk)*
- 43) Advanced Methods in Protein Purification 06-10 November, 2017 Max-Planck-Institute of Biochemistry - Munich Germany .*Main guest Speaker and Trainer 5 days course (theoretical and practical lab course for Core Facilities personnel from P4EU)*
- 44) 9<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Lisbon: *Basic Technologies in a* Protein Production Lab. Two days Training Seminar 13/11 to 14/11/2017 (6hr course)
- 45) 9<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Protein Purification Technologies -Lisbon 15/11/2016 Short Course: Protein Purification Strategies: Dealing with Proteins that are Prone to Aggregate (3hr course)
- 46) 9<sup>th</sup> PEGS EUROPE Protein & Antibody Engineering Summit Protein Purification Technologies Lisbon 17/11/2017 Talk: Human Heparanase: Lessons Learned from a Self-Destructing Project (30 min talk)
- 47)

### **Courses in ISRAEL Biotech Companies**

- 1. January 2009 12hr course organized by Danyel Biotech for different biotech
- 2. December 2010 12hr course organized by Danyel Biotech for different biotech
- 3. April 2011 12hr course OMRIX
- 4. January 2012 12hr course INSIGHT
- 5. February 2012 12hr course KAMADA
- 6. March 2012 12hr course organized by Bioforum for different biotech companies
- 7. December 2012 12hr course SIGMA
- 8. April 2017 12hr course BTG / FERRING Holding
- 9. November 2017 12hr course BTG / FERRING Holding
- 10.

### **MEMBERSHIPS:**

- 1) Active member and one of the founders of P4EU: Protein Production Partnership for Europe. **Executive Board Members since December 2016**
- 2) Member of the recently founded CTLS: Core Technologies for Life Science