BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Nemeth, Elizabeta	**Professor of Medicine**
eRA COMMONS USER NAME (credential, e.g., agency login) NEMETH2	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Belgrade, Belgrade, Yugoslavia	B.S.	10/1993	Molecular Biology & Physiology
University of Hawaii, Honolulu, HI	Ph.D.	08/1998	Cell, Molecular & Neurosciences (Premature Birth)
University of Hawaii, Honolulu, HI	Postdoc	1998-1999	Cell & Mol Biology (Premature Birth)
Cedars-Sinai Medical Center, Los Angeles, CA	Postdoc	1999-2001	Cell & Mol Biology (Ovarian Cancer)

A. Personal Statement

For the last 15 years, I have studied the function of the hepatic peptide hormone hepcidin and its receptor/iron transporter ferroportin in iron metabolism. I characterized the regulation of hepcidin production by iron, inflammation and erythropoiesis, described the role of hepcidin in different iron disorders including hereditary hemochromatosis, β-thalassemia and anemia of inflammation, elucidated the mechanism of action of hepcidin as the ligand of ferroportin, and developed novel hepcidin-targeted candidates for the treatment of iron disorders. My work has achieved international prominence, and its inclusion in medical textbooks and medical school curricula attests to its high relevance. I am also dedicated to translation of basic research and to this end have co-founded three biotechnology startups: one focused on developing hepcidin diagnostics, another focused on developing hepcidin mimics for the treatment of iron overload diseases, and the third focused on targeting hepcidin suppressor erythroferrone for treatment of iron-restricted anemias. The current research goal of my laboratory is to understand in molecular detail how hepcidin and ferroportin contribute to the pathogenesis of iron disorders, and to develop applications that will improve the diagnosis and treatment of human diseases associated with iron dysregulation.

The following research papers illustrate the high impact of my work (citations from Web of Science):

1. **Nemeth E**, Tuttle MS, Powelson J, Vaughn MB, Donovan A, Ward DM, Ganz T*, Kaplan J*. Hepcidin regulates cellular iron efflux by binding to ferroportin and inducing its internalization. Science 306:2090-3, 2004. (*co-corresponding authors) — **1911 citations**

2. **Nemeth E**, Rivera S, Gabayan V, Keller C, Taudorf S, Pedersen BK and Ganz T. Interleukin-6 mediates hypoferremia of inflammation by inducing the synthesis of the iron-regulatory hormone hepcidin. J Clin Invest 113:1271-1276, 2004. — **1070 citations**

B. Positions and Honors

Positions and Employment

1998-1999 Postdoctoral fellow, Dept. of Anat. & Reproductive Biology, Univ. of Hawaii, Honolulu, HI
1999-2001 Postdoctoral fellow, Dept. of OB/GYN, Cedars-Sinai Medical Center, Los Angeles, CA

2001-2004 Staff Research Associate III, Dept. of Medicine, UCLA, Los Angeles, CA
2004-2005 Assistant Researcher I, Dept. of Medicine, UCLA, Los Angeles, CA
2005-2009 Assistant Professor, Dept. of Medicine, UCLA, Los Angeles, CA
2009-2013 Associate Professor, Dept. of Medicine, UCLA, Los Angeles, CA
2013-present Professor, Dept. of Medicine, UCLA, Los Angeles, CA

Honors

1993 Graduated first in class with highest grade point average in programs history, Faculty of Biological Sciences, University of Belgrade
1994-95 Kotobuki scholarship, University of Hawaii
2005 Junior Faculty Award, UCLA Department of Medicine Research Day
2007 Junior Faculty Award, UCLA Department of Medicine Research Day
2007 Grace Goldsmith Award, American College of Nutrition, for significant contributions to the field of nutrition

Entrepreneurial Activity

U.S. Patent no. 7,524,636B2. Methods for diagnosing and treating pre-term labor. Bryant-Greenwood GD, Tashima LS, Ognjanovic S, Nemeth E, Millar LK.
U.S. Patent no. 8,435,941. Mini-hepcidin peptides and methods of using thereof. Ganz T, Nemeth E, Preza G, Ruchala P.
2006- Co-founded Intrinsic LifeSciences, LLP, La Jolla, CA, engaged in the development of iron-related diagnostics
2011- Co-founded Merganser Biotech, Newtown Square, PA, engaged in the development of minihepcidins for the treatment of iron-loading anemias
2014- Co-founded Silarus Therepeutics, La Jolla, CA, engaged in the development of erythroferrone agonists and antagonists for the treatment of anemias and iron overload

Other Experience and Professional Memberships

2003-present Member, International BioIron Society
2005-present Member, American Society of Hematology
2007-present Founder and director of the UCLA Center for Iron Disorders
2007-2011 Member and Chair, the Scientific Committee on Iron and Heme, American Society of Hematology
2008-2011 Member, Editorial Board of American Journal of Hematology
2012-2017 Member, Editorial Board of Blood
2012-2015 President, East-to-West Iron Club
2013-2017 Member, Board of Directors of the International BioIron Society
2011-2013 Ad-hoc reviewer, Molecular and Cellular Hematology Study Section, NIH
2013-2019 Standing member, Molecular and Cellular Hematology Study Section, NIH

C. Contributions to Science

1. Fetal membrane distention and initiation of labor

Working with Prof. Bryant-Greenwood (my PhD supervisor) we searched for genes that were involved in sensing and signaling fetal membrane distention and the initiation of labor. We identified several candidate genes by subtractive hybridization of distended and resting membranes and of a related resting and stretched cell line monolayer. Among the genes, two encoded cytokines, interleukin-8 and pre–B-cell colony-enhancing factor (PBEF), that were newly identified as involved in the initiation of labor. The work had important implications for understanding the pathogenesis of premature labor in inflammatory states and resulted in two prominent publications and a U.S. Patent.

3. **Nemeth E**, Tashima LS, Yu Z, Bryant-Greenwood GD. Fetal membrane distention: I. Differentially expressed genes regulated by acute distention in amniotic epithelial (WISH) cells. Am J Obstet Gynecol. 2000 Jan;182(1 Pt 1):50-9. PMID: 10649156

4. **Nemeth E**, Millar LK, Bryant-Greenwood G. Fetal membrane distention: II. Differentially expressed genes regulated by acute distention in vitro. Am J Obstet Gynecol. 2000 Jan;182(1 Pt 1):60-7. PMID: 10649157

2. Regulation of hepcidin (also note reference 2)

Hepcidin is the iron-regulatory peptide hormone discovered by my postdoctoral mentor, Dr. Tomas Ganz. I made essential contributions to understanding the regulation of hepcidin during inflammation, and I also demonstrated that the inflammatory regulation of hepcidin was dependent on IL-6 (references 2 and 5). In addition to IL-6, BMP-2 is a strong regulator of hepcidin in the pathological setting of multiple myeloma. I also co-directed studies that identified growth factors EGF and HGF as regulators of hepcidin, and discovered the long-sought erythroid regulator of hepcidin, erythroferrone. As reflected by their high citation rates (see ref. 2), these contributions are considered fundamental in the field of iron homeostasis.

5. **Nemeth E**, Valore EV, Territo M, Schiller G, Lichtenstein A and Ganz T. Hepcidin, a putative mediator of anemia of inflammation, is a type II acute-phase protein. (Plenary Paper). Blood 101: 2461-2463, 2003
6. Maes K, **Nemeth E**, Roodman GD, Huston A, Esteve F, Freytes C, Callander N, Katodritou E, Tussing-Humphreys L, Rivera S, Vanderkerken K, Lichtenstein A, Ganz T. In anemia of multiple myeloma, hepcidin is induced by increased bone morphogenetic protein 2. Blood 116:3635-44, 2010. PMCID: PMC2981483
7. Goodnough JB, Ramos E, **Nemeth E***, Ganz T* (*equal contributors). Inhibition of hepcidin transcription by growth factors. Hepatology. 2012 Jul;56(1):291-9. PMID:22278715; PMCID:PMC3362690
8. Kautz L, Jung G, Valore EV, Rivella S, **Nemeth E**, Ganz T. Identification of erythroferrone as an erythroid regulator of iron metabolism. Nat Genet. 2014 Jul;46(7):678-84.

3. Structure-function analysis of the hepcidin-ferroportin interaction (also note reference 1)

We showed that ferroportin is the receptor for hepcidin as well as the sole cellular iron exporter. Hepcidin controls ferroportin display on cell membranes by binding to ferroportin and inducing its endocytosis and degradation. The hepcidin-ferroportin interaction is the key event in systemic iron homeostasis (reference 1). We also established the structural determinants of this ligand-receptor interaction (references 9-11).

9. **Nemeth E**, Preza GC, Jung C, Kaplan J, Waring AJ and Ganz T. The N-terminus of hepcidin is essential for its activity: structure-function study. Blood 107:328-33, 2006 PMCID: PMC1895343
10. Fernandes A, Preza GC, Phung Y, De Domenico I, Kaplan J, Ganz T, **Nemeth E**. The molecular basis of hepcidin-resistant hereditary hemochromatosis. Blood 2009, 114:437-43. PMCID: PMC2714214
11. Qiao B, Sugianto P, Fung E, del-Castillo-Rueda A, Moran-Jimenez MJ, Ganz T, **Nemeth E**. Hepcidin-induced endocytosis of ferroportin is dependent on ferroportin ubiquitination. Cell Metab. 2012 Jun 6;15(6):918-24. PMID:22682227; PMCID:PMC3372862.

4. Hepcidin, a mediator of iron disorders and target for therapeutics

Simultaneously with the exploration of the basic biology of hepcidin and ferroportin, we initiated a translational program to understand their role in the pathogenesis of anemias, atherosclerosis and iron overload disorders, and to develop diagnostic and therapeutic applications of this new biology. This program resulted in the formation of three biotechnology startups (Intrinsic LifeSciences for diagnostics, and Merganser Biotech and Silarus Therapeutics for the development of new medications for anemia and iron overload).

12. Kautz L, Gabayan V, Wang X, Wu J, Onwuzurike J, Jung G, Qiao B, Lusis AJ, Ganz T, **Nemeth E**. Testing the iron hypothesis in a mouse model of atherosclerosis. Cell Reports. 2013; Dec 5. PMID: 24316081
13. Kim A, Fung E, Parikh SG, Valore EV, Gabayan V, **Nemeth E**, Ganz T. A mouse model of anemia of inflammation: complex pathogenesis with partial dependence on hepcidin. Blood 2014 Feb 20;123(8):1129-36.
14. Preza GC, Ruchala P, Pinon R, Ramos E, Qiao B, Peralta MA, Sharma S, Waring A, Ganz T, **Nemeth E**. Minihepcidins are rationally designed small peptides that mimic hepcidin activity in mice and may be useful for the treatment of iron overload. J Clin Invest. 2011 Dec;121(12):4880-8. PMID:22045566 PMCID: PMC3225996.

15. Fung E, Sugianto P, Hsu J, Damoiseaux R, Ganz T, **Nemeth E**. High Throughput Screening of Small Molecules Identifies Hepcidin Antagonists. Mol Pharmacol. 2013 Mar;83(3):681-90. PMID: 23292796

5. The role of hepcidin in infection

I recently initiated a research program in the lab focused on defining the role of hepcidin and iron in innate immunity. We demonstrated that by causing hypoferremia during infection, hepcidin is essential for host defense against siderophilic pathogens (reference 13, and another manuscript in submission), and that hepcidin agonists can be used to prevent high mortality caused by siderophilic pathogens in iron overload conditions. We are currently exploring the role of hepcidin and iron in clinically more common infections (K. pneumoniae, E. coli and M. tuberculosis).

16. Arezes J, Jung G, Gabayan V, Valore E, Ruchala P, Gulig PA, Ganz T, **Nemeth E***, Bulut Y* (*co-senior authors). Hepcidin-induced hypoferremia is a critical host defense mechanism against the siderophilic bacterium Vibrio vulnificus. Cell Host Microbe. 2015 Jan 14;17(1):47-57. PMID: 25590758, PMCID: PMC4296238
17. Ganz T, **Nemeth E**. Iron homeostasis in host defence and inflammation. Nat Rev Immunol. 2015 Aug;15(8):500-10. Review. PMID: 26160612, PMCID: PMC4801113

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/elizabeta.nemeth.1/bibliography/40316497/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

R01DK107209 Nemeth (multi-PI) 07/01/2015-06/30/2020
NIDDK
Ferroportin structure and function
The proposal is focused on determining the crystal structure of the iron transporter ferroportin, the mechanism of iron export through ferroportin, and structural determinants of hepcidin-ferroportin interaction. The proposal received the perfect score (10) and was **ranked at 1%**.
Role: Principal Investigator

2R01DK065029 Ganz (PI) 07/01/2013-06/30/2018
NIDDK
The role of erythroferrone in iron homeostasis and in iron-loading anemias
The project explores how a novel bone marrow-derived hormone, erythroferrone, regulates hepcidin and iron homeostasis. The role of erythroferrone in beta-thalassemia is also studied. The proposal was **ranked at 1%**.
Role: Co-investigator

Completed

Silarus Therapeutics Nemeth (PI) 11/01/2015-5/31/2016
Effects of erythroferrone agonists in mice
The project explores the utility of recombinant hormone erythroferrone in treating anemia of inflammation in mouse models
Role: Principal Investigator

The Iris Cantor-UCLA Women's Health Center Nemeth (PI) 07/01/2014-06/30/2015
Regulation of maternal and fetal iron status during pregnancy

The project explores iron homeostasis in hepcidin knockout and wild-type mice to determine the role of maternal and fetal hepcidin in regulating iron transfer across placenta.
Role: Principal Investigator

R01DK090554 Nemeth, Rivella (multi-PI) 12/01/2010-06/30/2015
NIDDK
Hepcidin therapy for iron overload and hematologic disorders
The proposal aims to use rational design to develop peptide hepcidin agonists for the treatment of iron disorders including hereditary hemochromatosis and beta-thalassemia. The proposal was **ranked at 3%**.
Role: Principal Investigator

American Society of Hematology Bridge Grant Nemeth (PI) 03/01/2014-02/28/2015
Ferroportin function and regulation
The project focused on identifying ferroportin interactome triggered by hepcidin binding.
Role: Principal investigator

R01HL 091531 Ganz (PI) 6/15/2007-5/30/2011
NHLBI
The role of inflammation in anemia of the elderly
The project explores the contribution of inflammation to anemia in the elderly in both human subjects and in animal models.
Role: Co-investigator

R21 HL106374 Nemeth (PI) 12/1/2010-11/30/2012
NHLBI
The role of iron in atherosclerosis: application of new iron biology
Using a novel mouse model, the proposal explores the role of iron in the development of atherosclerotic plaques. The proposal received the perfect score (10) and was **ranked at 1%**.
Role: Principal Investigator

R01 DK 082717 Nemeth (PI) 9/30/2008-8/31/2013
NIDDK
The hepcidin-ferroportin axis in anemia of inflammation: mechanisms and targets.
The project analyzes the role of hepcidin and ferroportin in anemia of inflammation, and proposes a high throughput screen for hepcidin antagonists as lead drug candidates for anemia of inflammation.
Role: Principal Investigator

R01 DK 065029 Ganz (PI) 7/1/2003-6/30/2013
NIDDK
Hepcidin, ferroportin and iron disorders
The major goal of this project is to analyze the role of hepcidin and ferroportin in the pathogenesis of iron disorders.
Role: Co-investigator