ANA PAULA ARRUDA

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EDUCA	ATION						
2004-2 2003-2 1999-2	004	Biochemistry Biochemistry Biological Sciences	Ph.D. M.Sc. B.Sc.	Federal University of Rio de Janeiro, RJ Brazil Federal University of Rio de Janeiro, RJ, Brazil State University of Sao Paulo, SP, Brazil			
PROFE	SSION	AL TRAINING					
2010-2	015	Metabolism	Post-Doctoral	Harvard TH Chan School of Public Health, Boston			
2008-2	010	Physiology	Post-Doctoral	State University of Campinas, SP, Brazil			
ACADE	EMIC A	PPOINTMENTS					
2017-Present		Research Scientist		Harvard TH Chan School of Public Health, Boston			
2015-2017		Research Associate		Harvard TH Chan School of Public Health, Boston			
ACADE	EMIC L	EADERSHIP					
2017-Present		Coordinator of the Sabri Ülker Center Imaging Lab - Harvard TH Chan School of Public Health, Boston					
2015-2017		Coordinator of the Seminar series entitled "Research in Progress" at the Department of Genetics and Complex Diseases, (now "Department of Molecular Metabolism") at Harvard TH Chan School of Public Health, Boston					
HONOI	RS ANI	DISTINCTIONS					
2019	Best Po	Best Poster Award, "Molecular Membrane Biology" Gordon Research Conference, MA, USA.					
2010	PEW I	PEW Latin American Fellow in Biomedical Sciences, The Pew Charitable Trusts.					
2008	Best PhD thesis from the Biological Chemistry Institute, Federal University of Rio de Janeiro, R Brazil.						
2006							
2005	Travel Assends for Verra Scientist Society of Comput Physiology, Woods Ho			of Comment Dharmintons Woods Hale MA LICA			

Travel Awards for Young Scientist, Society of General Physiology, Woods Hole, MA, USA.

2004 Young Investigator Basic Sciences, Brazilian Endocrine Society, Vitoria, ES, Brazil.

2004 Best Poster Presentation Awards, Brazilian Society of Biochemistry and Molecular Biology meeting, Caxambu, MG, Brazil.

2000 Selected to be part of the "Special Training Program (PET)" directed to students who have demonstrated outstanding performance during undergrad studies. Fellowship: Capes/Sesu.

GRANTS

2010-2012 2008-2010	PEW Post-doctoral fellowship, Harvard School of Public Health, USA. Fapesp Post-doctoral fellowship, University of Campinas, Sao Paulo, Brazil.
2004-2008	Faperj grade 10 predoctoral fellowship, Federal University of Rio de Janeiro, Brazil
2003-2004 2000-2002	Capes fellowship at Institute of Medical Biochemistry, Federal University of Rio de Janeiro Capes/Sesu fellowship at State University of Sao Paulo, Botucatu, Brazil.

2020

American Heart Association- Career Development Award – <u>Revised version to be resubmitted</u> <u>on Feb 2021.</u>

PUBLICATIONS

As of January 2021:

Total citations : Google Scholar : 1832 h-factor: Google Scholar : 21

Manuscript in preparation:

1. **Arruda, A.P.***, Parlakgul, G.*, Cagampan, E., Min, N., Xu, S., Pang, S., Hess, H. and Hotamisligil, G.S. Distinct structural signatures of hepatic-ER mitochondria interactions in fasting and obesity. *These authors contributed equally to this work *Corresponding author. *Manuscript in preparation*.

Summary: In this manuscript we examined how nutritional fluctuations such as fasting, feeding and obesity impact physical and functional interaction between ER and mitochondria in the liver. We combined transmission electron microscopy (TEM) with large volume Focused Ion Beam Scanning Electron Microscopy (FIB-SEM), followed by machine learning-based segmentation in order to resolve the ER- mitochondria interaction in 3 dimensions. We found that in lean mice, fasting induces a special type of ER architecture where a single, continuous and uniform rough ER sheet surrounds the mitochondria like an envelope at a 50-80nm distance. Interactions through this type of structure are significantly reduced in the course of chronic overnutrition, which is characterized by enrichment of tight (10-25nM) ER-mitochondria contact sites. In addition to physical distance, the molecular signatures of the contacts are distinct in the settings of fasting, feeding and obesity.

Manuscripts in revision:

- 1. Parlakgul, G.*, **Arruda, A.P.*,** Cagampan, E., Xu, S., Pang, S. Guney, E., Lee Y., Hess H. and Hotamisligil, G.S. High resolution 3D imaging of liver reveals a central role for subcellular architectural organization in metabolism*These authors contributed equally to this work. *Manuscript in revision in Nature*. *BioRxiv.* https://doi.org/10.1101/2020.11.18.387803. Videos associated with this paper can be accessed at https://www.youtube.com/playlist?list=PLpzquMkvsJ9XZvqAKyHcz62iDQkoKxmpx

First and Co-first author Publications (in chronological order):

- 1. **Arruda, A.P.*,** Pers, B.M.*, Parlakgul, G., Güney, E., Goh, T., Cagampan, E., Lee, Y.G., Goncalves, R.L., Hotamisligil, G.S. Defective STIM-mediated store operated Ca²⁺ entry in hepatocytes leads to metabolic dysfunction in obesity. *eLife*, Dec 15;6, 2017. *These authors contributed equally to this work.
- 2. **Arruda, A.P.**, Hotamisligil, G.S. Organelle calcium homeostasis in metabolic disease. *Cell Metabolism*, 22:381-97, 2015.
- 3. **Arruda A.P.*** Pers B.M.*, Parlakgul G., Guney E., Inouye K., Hotamisligil G.S. Chronic enrichment of hepatic endoplasmic reticulum-mitochondria contact leads to mitochondrial dysfunction in obesity. *Nature Medicine*, 20:1427-35, 2014. *These authors contributed equally to this work (Cover of the Nature Medicine's December 2014 issue)

- 4. **Arruda, A.P.,** Milanski, M., Coope, A., Torsoni, A.S., Ropelle, E., Carvalho, D.P., Carvalheira, J.B., Velloso, L.A. Low-grade hypothalamic inflammation leads to defective thermogenesis, insulin resistance and impaired insulin secretion. *Endocrinology*, 152:1314-26, 2011.
- 5. **Arruda, A.P.,** Milanski, M., Romanatto, T., Solon, C., Coope, A., Alberici, L.C., Festuccia, W.T., Hirabara, S.M., Ropelle, E., Curi, R., Carvalheira, J.B., Vercesi, A.E., Velloso, L.A. Hypothalamic actions of tumor necrosis factor provide the thermogenic core for the wastage syndrome in cachexia. *Endocrinology*, 151: 683-94, 2010.
- 6. Nigro, M.*, **Arruda**, **A.P.***, Meis, L. Ca2+ transport and heat production in vesicles derived from the sarcoplasmic reticulum terminal cisternae: regulation by K+. <u>Biochimica et Biophysica Acta.</u> Biomembranes. 1788:1517-22, 2009. *These authors contributed equally to this work.
- 7. **Arruda, A.P.***, Ketzer, L.A.*, Nigro, M., Carvalho, D.P., Galina, A., Meis, L. Cold tolerance in hypothyroid rabbits: role of skeletal muscle mitochondria and Ca²⁺ ATPase (SERCA 1) heat production. *Endocrinology*, 149: 6262-71, 2008. *These authors contributed equally to this work
- 8. **Arruda, A.P.**, Nigro, M., Oliveira, G.M., Meis, L. The heat production by Ca ATPase from heavy sarcoplasmic reticulum: The role of ryanodine Ca Channel. <u>Biochimica et Biophysica Acta.</u> *Biomembranes*, 1768:1498-05, 2007.
- 9. **Arruda, A.P.**, Oliveira, G.M., Carvalho, D.P., Meis, L. Thyroid Hormone differentially regulate the distribution of skeletal muscle Ca-ATPases (SERCA) isoforms in light and heavy sarcoplasmic reticulum fractions. *Molecular Membrane Biology*, 22: 529 -37, 2005
- 10. **Arruda**, **A.P.**, Da-Silva, W.S., Carvalho, D.P., Meis, L. Hyperthyroidism increases the uncoupled ATPase Activity and heat production by the sarcoplasmic reticulum Ca²⁺-ATPase. *Biochemical Journal*, 375:753 -60, 2003.

Co-author Publications (in chronological order):

- 1. Tirosh, A., Tuncman, G., Calay, E.S, Yalcin, A. Lee, Y, **Arruda, A.P.** and Hotamisligil, G.S. Connexin 43 mediates the propagation of obesity-induced endoplasmic reticulum stress in the liver. *Manuscript accepted for publication in Cell Metabolism, 2020.*
- Bartelt, A.*, Widenmaier, S.B.*, Schlein, C., Johann, K., Goncalves, R.L.S.P., Eguchi, K., Fischer, A.W., Parlakgül, G., Snyder, N., Nguyen, T.P., Bruns, O.T.P., Franke, D., Bawendi, M.G., Lynes, M.D., Leiria, L.O., Tseng, Y.H., Inouye, K.P., Arruda, A.P., Hotamisligil, G.S. Brown adipose tissue thermogenic adaptation requires Nrf1-mediated proteasomal activity. *Nature Medicine*, 24:292-303, 2018. *These authors contributed equally to this work
- 3. Widenmaier, S.B., Snyder, N.A., Nguyen, T.B., Arduini, A. Lee, Y.G., **Arruda, A.P.**, Saksi, J., Bartelt, A., Hotamışlıgil, G.S. Identification of Nrf1 as an ER cholesterol sensor guarding immunometabolic homeostasis. *Cell*, 171:1094-1109, 2017.
- 4. Charles, K.N.,* Li, M.*, Engin F, **Arruda**, **A.P**., Inouye K., Hotamisligil GS.. Uncoupling of metabolic health from longevity through genetic alteration of adipose tissue lipid binding proteins. *Cell Reports*, 21:393-402, 2017. * These authors contributed equally to this work
- 5. Fu, S., Yalcin, A., Lee, G.Y., Fan, J., **Arruda, A.P.**, Pers, B.M., Yilmaz, M., Eguchi, K., Hotamisligil, G.S. Novel phenotypic assays lead to identification of a small molecule modulator of the unfolded protein response with potent anti-diabetic activity. *Science Translational Medicine*, 7:292-298, 2015.
- 6. Ignacio-Souza, L.M., Bombassaro, B., Pascoal, L.B., Portovedo, M.A., Razolli, D.S., Coope, A., Victorio, S.C., de Moura, R.F., Nascimento, L.F., **Arruda, A.P.,** Anhe, G.F., Milanski, M., Velloso, L.A. Defective regulation of the ubiquitin/proteasome system in the hypothalamus of obese male mice. *Endocrinology*, 155:2831-44, 2014.
- 7. Solon C.S., Franci D., Ignacio-Souza L.M., Romanatto T., Roman E.A., **Arruda A.P.**, Morari J., Torsoni A.S., Carneiro E.M., Velloso L.A. Taurine enhances the anorexigenic effects of insulin in the hypothalamus of rats. *Amino Acids*. 42:2403-10, 2012.
- 8. Milanski, M., **Arruda, A.P.,** Coope, A. Souza, L.M., Roman, E.A., Romanatto, T., Pascoal, L.B., Caricilli, A.M., Torsoni, M.A., Prada, P.O., Saad, M.J., Velloso, L.A. Inhibition of hypothalamic inflammation reverts diet-induced insulin resistance in the liver. *Diabetes*, 2011.

- 9. Breder, I., Coope, A., **Arruda, A.P.**, Razolli, D., Milanski, M., Dorighello, G., de Oliveira, H., Velloso, L.A. Reduction of endoplasmic reticulum stress- A novel mechanism of action of statins in the protection against atherosclerosis. *Atherosclerosis*, 212:30-1, 2010.
- 10. Ketzer, L.A., **Arruda, A.P.**, Carvalho, D.P., Meis, L. Cardiac sarcoplasmic reticulum Ca2+-ATPase: heat production and phospholamban alterations promoted by cold exposure and thyroid hormone. *American Journal of Physiology. Heart and Circulatory Physiology*, 297:H556-63, 2009.
- 11. Meis, L., Arruda, A.P., Guimaraes, J. The impact of science in Brazil. *IUBMB Life*, 59: 227-34, 2007.
- 12. Meis, L., **Arruda**, **A.P.**, Costa, R.M., Benchimol, M. Identification of a Ca2+-ATPase in brown adipose tissue mitochondria: regulation of thermogenesis by ATP and Ca2+. *The Journal of Biological Chemistry*, 281:16384-90, 2006.
- 13. Meis, L., **Arruda**, **A.P.**, Carvalho, D.P. Role of sarco/endoplasmic reticulum Ca2+-ATPase in thermogenesis. *Bioscience Reports*, 25: 181-190, 2005
- 14. Meis, L., Oliveira, G.M., **Arruda, A.P.**, Santos, R., Costa, R.M., Benchimol, M. The thermogenic activity of rat brown adipose tissue and rabbit white muscle Ca²⁺⁻ ATPase. *IUBMB Life*, 57:337 45, 2005.
- 15. Meis, L., **Arruda**, **A.P.**, Da-Silva, W.S., Reis, M., Cavalho, D.P. The thermogenic function of the sarcoplasmic reticulum Ca2+-ATPase of normal and hyperthyroid rabbits. *Annals New York Academy Science*, 986: 481 -88, 2003.

Book chapters:

- 1. **Arruda, A.P.**, Geloneze, S., Geloneze, B. Tecido Adiposo In: Tratado de Obesidade, Rio de Janeiro:Guanabara Koogan, 2010.
- 2. **Arruda, A.P.,** Carvalho, D.P. Doenças da Tireóide. In: Carvalho-Alves, P.C.; Da Poian, A.T.; Abrahão, A. (Org.). Bases Moleculares em Clínica Médica. Rio de Janeiro: Editora Atheneu, 2010.
- 3. **Arruda, A.P.,** Meis, L. ATPases de Transporte. In: Margarida de Mello Aires. (Org.). Fisiologia. 3 ed. Rio de Janeiro: Guanabara Koogan, 2006.

TALKS IN CONFERENCES AND EVENTS

Invited lectures:

- 1. Signal Transduction Department Seminar Series, NIH/NIEHS, Chapel Hill, NC, USA, March 2019. "Defective endoplasmic reticulum calcium handling in metabolic diseases."
- 2. EMBO Membrane Contact-sites meeting, Arosa, Switzerland, September 2018. "Regulation of ER-mitochondria contact sites by nutritional fluctuations."
- 3. International Meeting of the European Calcium Society, Hamburg, Germany, September 2018. "Defective endoplasmic reticulum calcium handling in metabolic diseases."
- 4. International Mitochondria Meeting (Mito-meeting), Guape, Minas Gerais, Brazil, July 2018. "Regulation of hepatic ER-mitochondria structure and calcium homeostasis in obesity."
- 5. Metabolism and Cancer Symposium, Harvard and iBG Joint Meeting" Izmir, Turkey, May 2016. "Endoplasmic reticulum dysfunction in obesity."
- 6. Experimental Biology meeting, San Diego, California, USA, 2014. "Physical and functional interactions between endoplasmic reticulum and mitochondria."
- 7. 39a Reunião Anual da Sociedade Brasileira de Bioquímica, Foz do Iguaçu -Brazil, May 2010. "Central control of thermogenesis by TNFalpha: Implications for metabolic diseases."
- 8. 9 Congresso Paulista de Diabetes e Metabolismo, Águas de São Pedro, SP, Brazil, 2010. "Hypothalamic inflammation induces peripheral insulin resistance and reduce thermogenesis."

- 9. III Encontro sobre Mecanismos Celulares e Moleculares Envolvidos na Secreção e Ação da Insulina e no Controle Metabólico, Cuiabá, MT, Brazil, 2009.
 - "Control of thermogenesis by central nervous system: Implications for metabolic diseases."
- 10. XIII Latin American Thyroid Congress Gramado, CT, Brazil, 2009. "Central control of thermogenesis by TNFalpha: Implications for metabolic diseases."

Short talks and seminars:

- 11. Pew Fellows Reunion, Costa Rica, March 2014. "Endoplasmic Reticulum and Mitochondria Interactions in Obesity."
- 12. Keystone meeting "Adipose tissue biology: Keystone, Colorado USA, January 2013. "Altered Mitochondria-Associated ER Membranes Links ER Stress to Mitochondrial Dysfunction in Obesity."

TEACHING AND MENTORING EXPERIENCE

Lecturing:

- 1. "Biochemistry of Muscle Contraction" for medical students Federal University of Rio de Janeiro, (24 hours) 2006.
- 2. "Physiology" for medical students- Federal University of Rio de Janeiro (16 hours), 2004.
- 3. "Biochemistry and Bioenergetics" for medical students Federal University of Rio de Janeiro (30 hours), 2003.

Trainees:

2004-2006	Gaya Oliveira	Biomedical science UFRJ, Brazil	Undergrad thesis
2006-2008	Mariana Mattos	Biology, UFRJ, Brazil	Master's thesis
2007-2008	Anderson Santos	Biology, UFRJ, Brazil	Undergrad thesis
2011-2015	Gunes Parlakgul	Harvard School of Public Health	Research fellow
2011-2015	Ekin Guney	Harvard School of Public Health	Research fellow
2015-2017	Ted Goh	Harvard School of Public Health	Research Assistant
2017-2019	Erika Cagampan	Harvard School of Public Health	Research Assistant
2019- Present	Nina Min	Harvard School of Public Health	Research Assistant

SCIENCE OUTREACH

- 1. Organizer: Summer course "The Cell" for teachers and high school students. Medical Biochemistry Institute, Federal university of Rio de Janeiro, RJ, Brazil. (80 hours), 2006.
- 2. Organizer: Summer course "The Cell" for teachers and high school students. Medical Biochemistry Institute, Federal university of Rio de Janeiro, RJ, Brazil. (80 hours), 2005.
- 3. Organizer: Summer course "Thermogenesis and Obesity" for teachers and high school students. Medical Biochemistry Institute, Federal university of Rio de Janeiro, RJ, Brazil. (80 hours), 2004.
- 4. Organizer: Summer course "Muscle Contraction" for teachers and high school students. Medical Biochemistry Institute, Federal university of Rio de Janeiro, RJ, Brazil. (80 hours), 2003.
- 5. Participation in a play entitled "The scientific method" presented at high-schools, universities and scientific meetings, 2004-2008.
- 6. Organizer: National symposium "Science, Art and Education in postmodernity" for high-school and undergraduate students, State University of Sao Paulo, Botucatu, SP, Brazil, 2001.

CONTACT INFORMATION FOR LETTERS OF RECOMMENDATION

1-Gokhan S Hotamisligil, M.D., Ph.D.

James S Simmons Professor of Genetics & Metabolism

Director, Sabri Ulker Center for Metabolic Research

Department of Molecular Metabolism

Associate Member, Harvard-MIT Broad Institute, Harvard Stem Cell Institute

Harvard TH Chan School of Public Health

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2-Denise P. Carvalho, M.D., Ph.D.

President of Federal University of Rio de Janeiro

Professor of Endocrinology

Institute of Biophysics Carlos Chagas Filho

Federal University of Rio de Janeiro

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3-Jörg Heeren, Ph.D.

Heisenberg Professor of Immunometabolism.

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4-Harald Hess, Ph.D.

Senior group leader

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Ashburn, VA 20147, USA.

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5-William B. Mair, PhD

Associate Professor of Molecular Metabolism

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