

RUBEN GARCIA MARTIN, PHD

Department of Immunology and Oncology,
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TRAINING AND EDUCATION

- Principal Investigator, Assistant Professor *From Jan 2023.*
Department of Immunology and Oncology,
Centro Nacional de Biotecnología, Madrid, Spain

- Postdoctoral Research Fellow, *May 2016-Aug 2022*
Department of Integrative Physiology and Metabolism,
Joslin Diabetes Center/Harvard Medical School, Boston, USA
Supervisor: *Dr. C. Ronald Kahn*
Main Project: *Role of circulating miRNAs in metabolic diseases*

- Postdoctoral Research Fellow, *May 2015-Feb 2016.*
Department of Clinical Pathobiochemistry, Dresden University of Technology/University Clinic Carl
Gustav Carus, Dresden, Germany
Supervisor: *Dr. Triantafyllos Chavakis.*
Main Project: *Role of HIF2 α in fatty liver disease.*

-Doctor of Philosophy (Ph.D.), *Nov 2010-May 2015.*
Department of Clinical Pathobiochemistry, Dresden University of Technology/University Clinic Carl
Gustav Carus/ Max Planck Institute, Dresden, Germany
Supervisor: *Dr. Triantafyllos Chavakis.*
Thesis title: *The role of HIF2 α in obesity-related metabolic dysregulation*
Thesis mark: *summa cum laude* (highest distinction).

- International Graduate Fellow, *Sep 2009-Oct 2010.*
Ontario Cancer Institute/University of Toronto, Toronto, Canada
Supervisor: *Dr. Minna Woo*
Main Project: *Hepatocyte deletion of JAK2 protects against diet-induced steatohepatitis and glucose intolerance.*

- Undergraduate Fellow, *Oct 2007-June 2009.*
Department of Animal Physiology, Complutense University of Madrid, Madrid, Spain.
Supervisor: *Dr. Gustavo Barja*
Main Project: *Effect of dietary restriction of amino acids on mitochondrial oxidative stress.*

- Bachelor & Master of Science (Licenciatura), *Oct 2004- June 2009.*
Complutense University of Madrid, Madrid, Spain.
Mark: *2.98 out of 4.*

GRANTS, HONORS AND AWARDS

- Proyectos Generación Conocimiento 2022**, 250.000 € 2023-2026
Awarded by Spanish Ministry of Science and Innovation.
- Ideas Semilla 2023**, 20.000 € 2023-2025
Awarded by Spanish Agency Against Cancer (AECC)
- Ramon y Cajal Fellowship 2021**, 236.350 € 2022-2027
Awarded by Spanish Ministry of Science and Innovation to support early independence group leader position.
- Atraccion Talento CSIC/Ayuda Incorporación 2021**, 100.000 € 2023-2026
Awarded by CSIC to support early independence group leader position
- Atracción de Talento Fellowship 2022**, 337.255 € 2022-2027
Awarded by Comunidad Autonoma of Madrid to support recruitment of young investigators to independence group leader position. Had to decline due to incompatibility with Ramon y Cajal Fellowship.
- La Caixa Junior Leader Fellowship**, 305.100 € 2022-2025
Awarded by La Caixa Foundation to support early independent career position at CNB, Spain. Had to decline due to incompatibility with Ramon y Cajal Fellowship
- DFG fellowship**, 110.200 € 2017-2019
Awarded by Deutsche Forschungsgemeinschaft (DFG) to support 2 years of postdoctoral work.
- Travel Award**, 1.000 \$ 2018
Awarded by the Joslin Fellow Council for attending ISEV meeting, Barcelona, Spain.
- DZD award**, 1.000 € 2015
Awarded by the Deutsches Zentrum für Diabetesforschung (DZD) to the best talks presented in internationally recognized meetings for my talk in the Keystone Symposium “Diabetes and Metabolic dysfunction”, Santa Fe, NM, USA.
- Travel award**, 1.000 € 2014
Awarded by DIGS-BB PhD program (Max Planck Institute, Dresden) to attend the Keystone Symposium “Diabetes and Metabolic dysfunction”, Santa Fe, NM, USA, Jan-Feb 2015.
- National Grant of Research II**, 20.000 € 2009
Awarded by Ibercaja Foundation (Spain) to support a one-year international fellowship in the laboratory directed by Dr. Woo, Ontario Cancer Institute, Toronto, Canada.
- Becas JAE**, 67.000 € 2009
Awarded by Spanish Ministry of Education to the best marks during Licenciature studies to cover PhD studies in Spain. Finally I had to decline due to incompatibility with Ibercaja

Foundation fellowship.

- **Grant for Collaboration**, 2.700 € 2008/2009
Awarded by Spanish Ministry of Education, to support one-year internship in the laboratory directed by Dr. Barja, Complutense University of Madrid, Spain.

TEACHING

- **Supervision of a visiting PhD student at Kahn lab** Aug 2017-Sept 2018
- **Mentoring of PhD and Master students, IMFAHE Initiative** Sept 2017-June 2018
- **Workshop from CSIC “Supervision PhD students: improving their skills”** April 2023

PATENTS

Title: *Targeting Mirnas for Exosomal Delivery or Cellular Retention*
Inventors: C. Ronald Kahn and Ruben Garcia Martin
US Application No. PCT/US2019/043469

MEMBERSHIP:

-Spanish Society of Extracellular Vesicles (GEIVEX), since June 2022.

PUBLICATIONS:

H-index: 17 (August 2023)
Total citations: ~3,000 (August 2023)

-Rubin de Celis MF, **Garcia-Martin R**, Syed I, Lee J, Aguayo-Mazzucato C, Bonner-Weir S and Kahn BB, 2022, “PAHSAs reduce cellular senescence and protect pancreatic beta cells from metabolic stress through regulation of Mdm2/p53”. *Proc Natl Acad Sci USA*, Nov 22;119(47):e2206923119.

-**Garcia-Martin R***, Brandao BB, Thomou T, Altindis E, Kahn CR, 2022, “Tissue differences in the exosomal/small extracellular vesicle proteome and their potential as indicators of altered tissue metabolism”. *Cell Reports*, 38(3):110277. *Equal contribution.

-**Garcia-Martin R**, Wang G, Brandao BB, Zanutto TM, Shah S, Patel SK, Schilling B, Kahn CR., 2022, “MicroRNA sequence codes for small extracellular vesicle release and cellular retention”, *Nature* 601(7893):446-451. Comment on *Cell*, 2022, by Amy H. Buck: “Cells choose their words wisely”, *Mar* 31;185(7):1114-1116. doi: 10.1016/j.cell.2022.03.010.

-Srinivasa S*, **Garcia-Martin R***, Torriani MD, Fitch KV, Carlson A, Kahn CR, Grinspoon SK. Altered Pattern of Circulating miRNAs in HIV Lipodystrophy Perturb Key Adipose Differentiation and Inflammation Pathways. *JCI Insight* 2021, 6(18):e150399. doi: 10.1172/jci.insight.150399. * **Equal contribution**

-Gomez Salazar M, Prunonosa Cervera I, French K, **Garcia-Martin R**, Bluher M, Schofield C, Chavakis T, Ratcliffe P, Jennings LL, Gudnason V, Morton NM, Emilsson V, Michailidou Z. Targeted deletion of the oxygen sensor PHD2 in adipocytes maintains brown adipose tissue function in thermoneutrality. Manuscript on preparation.

-Cai W, Zhang X, Batista TM, **Garcia-Martin R**, Softic S, Wang G, Ramirez AK, Konishi M, O'Neill BT, Kim JH, Kim JK, Kahn CR. Peripheral insulin regulates a broad network of gene expression in brain. *Diabetes*, 2021 Aug;70(8):1857-1873. doi: 10.2337/db20-1119.

-Mori M, Ludwig R*, **Garcia-Martin R***, Brandao BB*, Kahn CR. Extracellular miRNAs: From Biomarkers to Mediators of Homeostasis and Disease. *Cell Metabolism*, August 2019. 30(4):656-673. doi: 10.1016/j.cmet.2019.07.011. * **Equal contribution**

-Batista T, **Garcia-Martin R**, Cai W, Konishi M, O'Neill BT, Sakaguchi M, Kim JH, Jung DY, Kim JK, Kahn CR. Multi-dimensional transcriptional remodeling by physiological insulin in vivo, *Cell Reports*, 2019, Mar 19;26(12):3429-3443. Made a Research Highlights section in *Nature Reviews Endocrinology*, 2019 <http://doi.org/10.1038/s41574-019-0206-6>.

-Troullinaki M, **Garcia-Martin R**, Sprott D, Klotzsche-von Ameln A, Grossklaus S, Mitroulis I, Chavakis T, Economopoulou. 53BP1 deficiency promotes pathological neovascularization in proliferative retinopathy, *Thrombosis and Haemostasis*, 2019 Mar;119(3):439-448.

- Chung KJ, Chatzigeorgiou A, Economopoulou M, **Garcia-Martin R**, Alexaki VI, Mitroulis I, Nati M, Gebler J, Ziemssen T, Goelz SE, Phieler J, Lim JH, Karalis KP, Papayannopoulou T, Blüher M, Hajishengallis G, Chavakis T, A self-sustained loop of inflammation-driven inhibition of beige adipogenesis in obesity. *Nature Immunology* 2017 Jun;18(6):654-664. doi: 10.1038/ni.3728.

- Thomou T, Mori MA, Dreyfuss JM, Konishi M, Sakaguchi M, Wolfrum C, Rao TN, Winnay JN, **Garcia-Martin R**, Grinspoon SK, Gorden P, Kahn CR. Adipose-derived circulating miRNAs regulate gene expression in other tissues. *Nature* 2017 Feb 23; 542(7642): 450-455.

- Sakaguchi M, Fujisaka S, Cai W, Winnay JN, Konishi M, O'Neill BT, Li M, **García-Martín R**, Takahashi H, Hu J, Kulkarni RN, Kahn CR, Adipocyte dynamics and reversible metabolic syndrome in mice with an inducible adipocyte-specific deletion of the insulin receptor, *Cell Metab* 2017 Jan 4. pii: S1550-4131(16)30641-6.

- **García-Martín R.**, Alexaki VI, Qin N, Rubín de Celis MF, Economopoulou M, Ziogas A, Gercken B, Kotlabova K, Phieler J, Ehrhart-Bornstein M, Bornstein SR, Eisenhofer G, Breier G, Blüher M, Hampe J, El-Armouche A, Chatzigeorgiou A, Chung KJ and Chavakis T. Adipocyte-specific HIF2 α deficiency exacerbates obesity-induced brown adipose tissue dysfunction and metabolic dysregulation. *Mol Cell Biol* 2015 Nov 16;36(3):376-93. (Cover page).

-Rubin de Celis M.F, **Garcia-Martin R**, Wittig D, Valencia GD, Enikolopov G, Funk RH, Chavakis T, Bornstein SR, Androutsellis-Theotokis A, Ehrhart-Bornstein M. Multipotent glia-like stem cells mediate stress adaptation. *Stem Cells*, 2015; 33(6):2037-2051.

-Chatzigeorgiou A, Chung KJ, **Garcia-Martin R**, Alexaki VI, Klotzsche-von Ameln A, Phieler J, Sprott D, Kanczkowski W, Tzanavari T, Bdeir M, Bergmann S, Cartellieri M, Bachmann M, Nikolakopoulou P, Androutsellis-Theotokis A, Siebert G, Bornstein SR, Muders MH, Boon L, Karalis KP, Lutgens E, Chavakis T. Dual role of B7 costimulation in obesity-related nonalcoholic steatohepatitis and metabolic

dysregulation. *Hepatology*. 2014;60:1196-1210.

-Chatzigeorgiou A, Seijkens T, Zarzycka B, Engel D, Poggi M, van den Berg S, van den Berg S, Soehnlein O, Winkels H, Beckers L, Lievens D, Driessen A, Kusters P, Biessen E, **Garcia-Martin R**, Klotzsche-von Ameln A, Gijbels M, Noelle R, Boon L, Hackeng T, Schulte KM, Xu A, Vriend G, Nabuurs S, Chung KJ, Willems van Dijk K, Rensen PC, Gerdes N, de Winther M, Block NL, Schally AV, Weber C, Bornstein SR, Nicolaes G, Chavakis T, Lutgens E. Blocking CD40-TRAF6 signaling is a therapeutic target in obesity-associated insulin resistance. *Proc Natl Acad Sci USA*. 2014;111:2686-2691.

-Qin N, de Cubas AA, **Garcia-Martin R**, Richter S, Peitzsch M, Menschikowski M, Lenders JW, Timmers HJ, Mannelli M, Opocher G, Economopoulou M, Siegert G, Chavakis T, Pacak K, Robledo M, Eisenhofer G. Opposing effects of HIF1alpha and HIF2alpha on chromaffin cell phenotypic features and tumor cell proliferation: Insights from MYC-associated factor X. *Int J Cancer*. 2014;135:2054-2064.

-Phieler J, Chung KJ, Chatzigeorgiou A, Klotzsche-von Ameln A, **Garcia-Martin R**, Sprott D, Moisidou M, Tzanavari T, Ludwig B, Baraban E, Ehrhart-Bornstein M, Bornstein SR, Mziaut H, Solimena M, Karalis KP, Economopoulou M, Lambris JD, Chavakis T. The complement anaphylatoxin C5a receptor contributes to obese adipose tissue inflammation and insulin resistance. *J Immunol*. 2013;191:4367-4374.

-Phieler J*, **Garcia-Martin R***, Lambris JD, Chavakis T. The role of the complement system in metabolic organs and metabolic diseases. *Semin Immunol*. 2013;25:47-53. ***Equal contribution**

-Shi SY*, **Garcia Martin R***, Duncan RE, Choi D, Lu SY, Schroer SA, Cai EP, Luk CT, Hopperton KE, Domenichiello AF, Tang C, Naples M, Dekker MJ, Giacca A, Adeli K, Wagner KU, Bazinet RP, Woo M. Hepatocyte-specific deletion of Janus kinase 2 (JAK2) protects against diet-induced steatohepatitis and glucose intolerance. *J Biol Chem*. 2012;287:10277-10288. ***Equal contribution**

-Caro P, Gomez J, Sanchez I, **Garcia R**, Lopez-Torres M, Naudi A, Portero-Otin M, Pamplona R, Barja G. Effect of 40% restriction of dietary amino acids (except methionine) on mitochondrial oxidative stress and biogenesis, AIF and SIRT1 in rat liver. *Biogerontology*. 2009;10:579-592.

Updated full list available at:

https://www.ncbi.nlm.nih.gov/sites/myncbi/1H_jfsrERoWwBN/collections/55265201/public/

PUBLICATIONS TO THE GENERAL PUBLIC

- "Descifrado el código que utilizan las células para enviarse mensajes a distancia", Science section of *El Pais* Newspaper (Most read Spanish newspaper), February 9th 2022.

- "Descubren cómo se comunican las células en la distancia", National Geographic Spanish Edition, February 21st, 2022.

- "La Comunidad de Madrid eliminó las ayudas para 85 científicos de élite en plena pandemia", Science section of *El Pais* Newspaper, March 11th 2022.

CONFERENCE PARTICIPATIONS

ORAL PRESENTATIONS:

- "Manipulation of microRNA distribution with EXO- and CELLmotifs as a novel approach against atherosclerosis". 6th edition Spanish Extracellular Vesicle Society (GEIVEX), Santiago de Compostela, Spain. Oct 2022.
- "Defining the miRNA Codes Controlling Exosomal Secretion vs. Cellular Retention". Keystone meeting on *Small Regulatory RNAs: From Bench to Bedside*. Santa Fe, NM, USA, May 1st-4th 2022.
- "Cell-type specific repertoire of exosomal cargo and its implications in metabolism". Invited speaker at the Initiative for RNA Medicine organized by Harvard Medical School (June, 2019).
- "Characterization of the exosomal proteins and their potential as regulators of systemic metabolism". 7th *International Meeting of the International Society for Extracellular Vesicles (ISEV)*. Barcelona, Spain. May 2nd-6th, 2018.
- "Adipocyte, but not macrophage or endothelial HIF2 protects from whitening of the brown adipose tissue and metabolic dysregulation in the course of diet-induced obesity". 3rd *International Conference on Immunometabolism: Molecular and Cellular Immunology of Metabolism*. Crete, Greece. Sept 24th-29th, 2015.
- "Adipocyte HIF2 α protects from whitening of the brown adipose tissue and metabolic dysregulation in the course of diet-induced obesity". *Diabetes and Metabolic Dysfunction, Keystone Symposia Conference*, Santa Fe, NM, USA. Jan 27st-Feb 1st, 2015.
- "Adipocyte HIF2 α protects from whitening of the brown adipose tissue and metabolic dysregulation in the course of diet-induced obesity". *2nd Annual Helmholtz-Nature Medicine Diabetes conference*, Munich September 21st-23rd, 2014.

POSTER PRESENTATIONS:

- "Adipocyte, but not macrophage or endothelial HIF2 protects from whitening of the brown adipose tissue and metabolic dysregulation in the course of diet-induced obesity". 3rd *International Conference on Immunometabolism: Molecular and Cellular Immunology of Metabolism*. Crete, Greece. Sept 24th-29th, 2015
- "Adipocyte HIF2 α protects from whitening of the brown adipose tissue and metabolic dysregulation in the course of diet-induced obesity". *Diabetes and Metabolic Dysfunction, Keystone Symposia Conference*, Santa Fe, NM, USA. Jan 27st-Feb 1st, 2015
- "Protective role of hypoxia-inducible factor 2 in diet-induced obesity in mice", *DGE March 2014*, Dresden, Germany. Poster presentation.

-“Liver-specific deletion of JAK leads to profound fatty liver but suppression of inflammation and protection against systemic insulin resistance”. *American Diabetes Association 7st Scientific Sessions*. June 2010. San Diego, CA, USA.

PARTICIPATION IN ASSESMENT OR ADVISORY TASK:

Reviewed articles for the following journals: *PNAS*, *JEV*, *FASEB J*, *European J. of Cell Biology*, *Cell. and Mol. Life Science*, *J. of Nanobiotechnology*, *J. of Innate Immunity*, *Molecular Metabolism*, *Adaptative Medicine*, *Int. J. of Obesity*, *Cell Systems*, and others.