

# CURRICULUM VITAE

## **María del Carmen Clapp Jiménez L**

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## **EDUCATION/TRAINING**

B.S.: Biology. Metropolitan University (UAM), México, DF (1974-1978).

M.S.: Physiology, National University of Mexico (UNAM), México City (1980-1983).

Ph.D.: Physiology, National University of Mexico (UNAM), México City (1982-1984).

Post-doc: Physiology-Anatomy, University of California Berkeley, California, USA (1985-1988)

## **CURRENT POSITION (since 2002)**

Professor, Institute of Neurobiology, UNAM, Querétaro, México; National System of Research, top level III (Member since 1984)

**HONORS:** Biotechnology Career Fellowship. Rockefeller Foundation (1989-1995); Fellow "John Simon Guggenheim Memorial Foundation (1994); Research Award of the Mexican Academy of Science (1995); Young researcher award UNAM (1995); International Research Scholar of the Howard Hughes Medical Institute (1997-2002); José Santos Ophthalmology Award (2001 and 2007); GEN award for research on defects at birth (2005 and 2008); Medical Research Award "Dr. Jorge Rosenkranz" Grupo ROCHE-SYNTEX (2006); Biennial Research Award on Ophthalmology (2006); Research award by the Mexican Chamber of Pharmaceutical Laboratories (CANIFARMA) (2008). Research Award in Diabetic Retinopathy, Mexican Health Foundation (2011). Lifetime Scientific Achievements Award, Queretaro University (2013). UNAM Award in Natural Sciences 2016 (PUN 2016). Clinical Investigation Award 2017, Foundation Miguel Alemán Valdés. Award by the Program of Patent and Innovation (PROFOPI) 2020, UNAM. Mexican Women Scientist Award L'Oréal-UNESCO-AMC, 2021. Emeritus Scientist of the National System of Researchers (2022-). Pharmaceutical Innovation Award 2021, 6a. Edition from Mexican Pharmaceutical Council and Health Foundation.

**EDITORIAL BOARD:** American Journal of Physiology: Regulatory, Integrative & Comparative Physiology ( 2008-); European Journal of Cell Biology (2010-), Frontiers in Vascular Physiology (2011-), Endocrinology (2020-), Frontiers in Endocrinology (2022-).

## **PATENT:**

Invention: Oligopeptide that inhibits angiogenesis and vascular function. Submitted in Mexico on November 20, 2019 (MX/E/2019/079075) and in the European Union on July 7, 2020 ( PCT/EP2020/069154).

Published on May 27, 2021 (WO2021098996 ).

<https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2021098996>

Aplications in EUA (US17/778,396; Exp. P2022/13828US), Japón (Exp. P2022/13827JP), China (Exp. P2022/13825CN) and Europe (EP20740261.1; Exp 109205320).

## **SCIENTIFIC SOCIETIES (8)**

**THESIS:** B.S. (14), M.S. (32), Ph.D. (28)

**SYMPOSIA (82)**

**ABSTRACTS (354)**

**PUBLICATIONS** Articles: 162 (average impact: 4.6); Book chapters: 20; Citations: 6313 (July 2023)

## **ARTICLES (71 in last 10 years; 33 in the last 3 years):**

162. Zamora M, Harris D, Müller N, Ebnet J, Radermacher P, Brucker C, Waller C, Robles JP, Bertsch T, Clapp C, Triebel J. Immunometric and functional measurement of endogenous vasoinhibin in human sera. *Frontiers in Endocrinology*, 2024. En prensa.

161. Vázquez-Carrillo DI, Ocampo-Ruiz AL, Báez-Meza A, Ramírez-Hernández G, Adán-Castro E, García-Rodríguez JF, Dena-Beltrán JL, de Los Ríos EA, Sánchez-Martínez MK, Ortiz MG, Martínez de la Escalera G, Clapp C, Macotela Y. Dopamine D2 receptor antagonist counteracts hyperglycemia and insulin resistance in diet-induced obese male mice. *PLOS ONE*, 2024. En prensa
160. Robles JP, Zamora M, García-Rodrigo JF, Perez AL, Bertsch T, Martínez de la Escalera G, Triebel J, Clapp C. Vasoinhibin's apoptotic, inflammatory, and fibrinolytic actions are in a motif different from its antiangiogenic HGR motif. *Endocrinology* 165: 1-12, 2023. <https://doi.org/10.1210/endocr/bqad185>
159. García Rodrigo JF, Ortiz G, Martínez-Díaz OF, Furuzawa-Carbasseda J, Ruiz-Herrera X, Macias F, García-Colunga MG, Martínez de la Escalera G, Clapp C. Prolactin inhibits or stimulates the inflammatory response of joint tissues in a cytokine-dependent manner. *Endocrinology* 164, 1-14, 2023, doi.org/10.1210/endocr/bqad156.
158. Robles JP, Zamora M, García-Rodrigo JF, Perez AL, Bertsch T, Martínez de la Escalera G, Triebel J, Clapp C. The apoptotic, inflammatory, and fibrinolytic actions of vasoinhibin are in a motif different from its antiangiogenic HGR motif. *BioRxiv* preprint doi: <https://doi.org/10.1101/2023.08.18.553934>
157. Núñez-Amaro CD, López M, Adán-Castro E, Robles-Osorio ML, García-Franco L, García-Roa M, Villalpando-Robles Y, Ramírez-Neria P, Pineiro N, Rubio-Mijangos JF, Sánchez J, Ramírez-Hernández G, Siqueiros-Márquez L, Díaz-Lezama N, López-Star E, Bertsch T, Martínez de la Escalera G, Triebel J, Clapp C. Levosulpiride for the treatment of diabetic macular oedema: A phase 2 randomized clinical trial. *EYE*. In press. 2023.
156. Ruiz-Herrera X, Ruiz-Herrera X, Luzardo-Ocampo I, Martínez de la Escalera G, Clapp C, Macotela Y. Differentiated mouse adipocytes in primary culture: A model of insulin resistance. *J. Vis. Exp.* (192). E63979, doi:10.3791/63979 (2023)
155. Luzardo-Ocampo I, Dena-Beltrán JL, Martínez de la Escalera G, Clapp C, Macotela Y. Obesity-derived alterations in the lactating mammary gland: focus on prolactin. *Molecular and Celular Endocrinology* 559:111810, 2023. FI: 4.102
154. Macotela Y, Ruiz-Herrera X, Vázquez-Carrillo DI, Ramírez-Hernández G, Martínez de la Escalera G, Clapp C. The beneficial metabolic actions of prolactin. *Frontiers in Endocrinology* 13;1001703, 2022. FI: 6.055
153. Triebel J, Bertsch T, Clapp C. Prolactin and vasoinhibin are endogenous players in diabetic retinopathy revisited. *Frontiers in Endocrinology* 13:994898, 2022. FI: 6.055
152. Clapp C, Ortíz G, García-Rodrigo JF, Ledesma-Colunga MG, Martínez-Díaz F, Adán N, Martínez de la Escalera G. Dual actions of prolactin and vasoinhibin in inflammatory arthritis o Vasoinhibin, as its precursor prolactin, play dual roles in inflammatory arthritis. *Frontiers in Endocrinology* 13:905756, 2022. Doi: 10.3389/fendo.2022.905756. FI: 6.055
151. Triebel J, Robles JP, Zamora Z, Clapp C, Bertsch. New horizons in specific hormone proteolysis. *Trends in Endocrinology and Metabolism* 33:371-377, 2022. FI: 12.015
150. Ortíz G, Ledesma-Colunga MG, Zhijian Wu Z, García-Rodrigo JF, Adán N, Martínez-Díaz F, de Los Ríos EA, López-Barrera F, Martínez de la Escalera G, Clapp C. Vasoinhibin is generated and promotes inflammation in mild antigen-induced arthritis. *Endocrinology* 163(5):1-12 2022. FI: 5.045
149. Martínez de la Escalera G, Macotela Y, Clapp C. A new experimental tool towards understanding the regulation of human prolactin secretion and functions. *Endocrinology* 163(4):1-2, 2022. FI: 5.045

148. Robles JP, Zamora M, Martínez de la Escalera G, Clapp C. The spike protein of SARS-CoV-2 induces endothelial inflammation through integrin  $\alpha 5\beta 1$  and NF- $\kappa$ B signaling. *Journal of Biological Chemistry* 298(3):101695, 2022. FI: 4.238
147. Leuchs A, Davies N, Friedrich C, Trier S, Clapp C, Bertsch T, Triebel J. A comparative phylogenetic analysis of prolactin cleavage sites for the generation of vasoinhibin in vertebrates. *General and Comparative Endocrinology* 320:114011, 2022. FI: 2.88
146. Markl-Hahn H, Neugebauer L, Lenke L, Ecker S, Merz T, McCook O, Khouder n, Bruckeer C, Radermacher P, Waller C, Clapp C, Bertsch T, Triebel J. Human placental tissue contains a placental lactogen derived vasoinhibin. *Journal of the Endocrine Society* 6:1-14, 2022. FI: 3.49
145. Hernández-Soto R, Adán-Castro E, Clapp C, Peña-Ortega F. Main olfactory bulb reconfiguration by prolonged passive olfactory experience correlates with increased brain-derived neurotrophic factor and improved innate olfaction. *European Journal of Neuroscience* 55:1141-1161, 2022. FI: 3.386
144. Adán-Castro E, Siqueiros-Márquez L, Ramírez-Hernández G, Díaz-Lezama N, Ruiz-Herrera X, Nuñez FF, Nuñez-Amaro CD, Robles-Osorio ML, Bertsch T, Triebel J, Martínez de la Escalera G, Clapp C. Sulpiride-induced hyperprolactinemia increases retinal vasoinhibin and protects against diabetic retinopathy in rats. *Journal of Neuroendocrinology: Translational and Clinical Neuroendocrinology* 34:e13091, 2022. doi:[10.1111/jne.13091](https://doi.org/10.1111/jne.13091). FI: 3.627
143. Robles JP, Zamora M, Siqueiros-Marquez L, Adan-Castro E, Ramirez-Hernandez G, Nuñez FF, Lopez-Casillas F, Millar RP, Bertsch T, Martínez de la Escalera G, Tiebel J, Clapp C. The HGR motif is the antiangiogenic determinant of vasoinhibin: implications for a therapeutic orally active oligopeptide. *Angiogenesis* 25:57-70, 2022. Doi: 10.1007/s10456-021-09800-x. FI: 9.78
142. Ruggiero C, Altieri B, Arnold E, Siqueiros-Marquez L, Doghman-Bouguerra M, Detomas M, Durand N, Jarjat M, Chatonnet F, Fassnacht M, Deutschbein T, Clapp C, Lalli E. Integrative genomic analysis reveals a conserved role for prolactin signalling in the regulation of adrenal function. *Clinical and Translational Medicine* 11: e630, 2021. Doi: <https://doi.org/10.1002/ctm2.630>, FI: 11.492
141. Robles JP, Zamora M, Martínez de la Escalera G, Clapp C. The spike protein of SARS-CoV-2 induces endothelial inflammation through integrin  $\alpha 5\beta 1$  and NF- $\kappa$ B. *BioRxiv*, Preprint Registrado, Doi: <https://doi.org/10.1101/2021.08.01.454605>, 2021.
140. Friedrich C, Neugebauer L, Zamora M, Robles JP, Martínez de la Escalera G, Clapp C, Bertsch T, Triebel J. Plasmin generates vasoinhibin-like peptides by cleaving prolactin and placental lactogen. *Molecular and Cellular Endocrinology*, 538:111471, 2021. FI: 4.102
139. Zamora M, Robles JP, Aguilar MB, Romero-Gómez SJ, Bertsch T, Martínez de la Escalera G, Tiebel J, Clapp C. Thrombin cleaves prolactin into a potent 5.6 kDa vasoinhibin: Implication for tissue repair. *Endocrinology* 162: 2021. Doi:10.1210/endocr/bqab177. FI: 5.045
138. Müller N, Robles JP, Zamora M, Ebnet J, Markl-Hahn H, Martínez de la Escalera G, Clapp C, Bertsch, Tiebel J. Development of vasoinhibin-specific monoclonal antibodies. *Frontiers in Endocrinology* 12:645085, 2021. DOI: 10.3389/fendo.2021.645085. FI: 3.675
137. Ramírez-Hernández G., Adán-Castro E., Díaz-Lezama N., Ruiz-Herrera X, Martínez de la Escalera G., Macotela Y, Clapp C. Global deletion of the prolactin receptor aggravates streptozotocin-induced diabetes in mice. *Frontiers in Endocrinology* 12:619696, 2021. DOI: 10.3389/fendo.2021.619696. FI: 3.675
136. Nuñez-Amaro C.D., Moreno-Vega A.I., Adan-Castro E., Zamora M., García Franco R., Ramirez-Neria P., Garcia-Roa M., Villalpando Y, Robles J.P., Ramirez-Hernandez G., Lopez M., Sanchez J., Lopez-Star E., Bertsch T., Martínez de la Escalera G., Robles-Osorio M.L., Triebel J., Clapp C. Levosulpiride increases the levels of prolactin and antiangiogenic vasoinhibin in the vitreous of patients with proliferative diabetic retinopathy. *Translational Vision Science & Technology (TVST)* 9:27, 2020.

135. Ortiz G, Ledesma-Colunga M.G., Wu Z., Garcia-Rodrigo JF, Adan N, Martinez de la Escalera G, Clapp C. Vasoinhibin reduces joint inflammation, bone loss, and the angiogenesis and vasopermeability of the pannus in murine antigen-induced arthritis. *Laboratory Investigation* 100:1068-1079, 2020.
134. Macotela Y, Triebel J, Clapp C. Time for a new perspective on prolactin in metabolism. *Trends in Endocrinology and Metabolism* 31:276-286, 2020. FI: 11.64
133. Vazquez-Membrillo M, Sigueiros-Marquez L, Nuñez FF, Diaz-Lezama N, Adan-Castro E, Ramirez-Hernandez G, Adán N, Macotela Y, Martinez de la Escalera G, Clapp C. Prolactin stimulates the vascularization of the retina in newborn mice under hyperoxia conditions. *J. Neuroendocrinology*, e12858, 2020. <https://doi.org/10.1111/jne.12858>
132. Ponce AJ, Galván-Salas T, Lerma-Alvarado RM, Ruiz-Herrera X, Cardenas LE, Hernandez T, Valencia R, Martínez de la Escalera G, Clapp C, Macotela Y. Low prolactin levels associate with visceral adipocyte hypertrophy and insulin resistance in humans. *Endocrine* 67:331-343, 2020. FI: 3.878
131. Triebel J, Schauer N, Zamora M, Moreno-Vega AI, Martínez de la Escalera G, Clapp C, Bertsch T. Matrix Metalloproteases and cathepsin D in human serum do not cleave prolactin to generate vasoinhibin. *Clinical Laboratory*. 66:877-866, 2020
130. Aroña RM, Arnold E, Macías F, López-Casillas F, Clapp C, Martínez de la Escalera G. Vasoinhibin generation and effect on neuronal apoptosis in the hippocampus of late mouse embryos. *American J Physiol: Regulatory, Integrative, Comparative Physiology* 318:R760-R771, 2020. FI: 3.529
129. Lemke L, Martínez de la Escalera G, Clapp C, Bertsch T, Triebel J. A dysregulation of the prolactin/vasoinhibin axis can contribute to preeclampsia. *Front Endocrinol (Lausanne)* 10:893, 2020
128. Arnold, E., Thébault, S., Aroña, R.M., Martínez de la Escalera, G., Clapp, C. Prolactin mitigates deficiencies of retinal function associated with aging. *Neurobiology of Aging* 85: 38-48, 2019. FI: 5.153
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126. Moreno-Carranza, B., Robles, J.P., Cruces-Solís, H., Ferrer-Ríos, M.G., Aguilar-Rivera, E., Yupanki, M., Martínez de la Escalera, G., Clapp, C. Sequence optimization and glycosylation of vasoinhibin: Pitfalls of recombinant production. *Protein Expression and Purification* 161: 49-56, 2019. FI: 1.338
125. Clapp, C., Díaz-Lezama, N., Adan-Castro, E., Ramírez-Hernandez, G., Moreno-Carranza, B., Sarti, A.C., Falzoni, S., Solini, A., Di Virgilio, F. Pharmacological blockade of the P2X7 receptor reverses retinal damage in a rat model of type 1 diabetes. *Acta Diabetologica Acta Diabetologica* 56:1031-1036, 2019. FI: 6.206
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123. Melo, Z., Castillo, X., Moreno-Carranza, B., Ledesma-Colunga, M.G., López-Casillas, F., Ruiz-Herrera, X., Clapp, C., Martínez de la Escalera, G. Vasoinhibin suppresses nerve growth factor-induced differentiation and survival of PC12 pheochromocytoma cells. *Neuroendocrinology* 109:152-164, 2019. Doi: 10.1159/000499507. FI: 5.024

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120. Robles-Osorio, L., García-Franco, R., Núñez-Amaro, D., Mira-Lorenzo, X., Ramírez-Neria, P., Hernández, W., López-Star, E., Bertsch, T., Martínez de la Escalera, G., Triebel, J., Clapp, C. Basis and design of a randomized clinical trial to evaluate the effect of levosulpiride on retinal alterations in patients with diabetic retinopathy and diabetic macular edema. *Frontiers in Endocrinology* 9: 242, 2018. DOI 10.3389/fendo.2018.00242. FI: 3.675
119. de los Ríos, E.A., Ruíz-Herrera, X., Tinoco-Pantoja, V., López-Barrera, F., Martínez de la Escalera, G., Clapp, C., Macotela, Y. The effect of maternal high fat feeding during lactation on offspring metabolism involves altered PRL action on the mammary gland and reduced milk PRL levels. *FASEB J* 32: 3457-2470, 2018. DOI: 10.1096/fj.201701154R. FI: 5.595
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117. Triebel, J., Robles-Osorio, M.L., Garcia-Franco, R., Martínez de la Escalera, G., **Clapp, C.**, Bertsch, T. From bench to bedside: translating the prolactin/vasoinhibin axis. *Frontiers in Endocrinology*, doi:10.3389/fendo.2017.00342. FI: 3.675
116. Zepeda-Romero, L.C., Vázquez-Membrillo, M., Adán-Castro, E., Gómez-Aguayo, F., Gutiérrez-Padilla, J.A., Angulo-Castellanos, E., Barrera de León, J.C., González-Bernal, C., Quezada-Chalita, A., Meza-Anguiano, A., Díaz-Lezama, N., Martínez de la Escalera, G., Triebel, J., **Clapp, C.** Higher prolactin and vasoinhibin serum levels associate with incidence and progression of retinopathy of prematurity. *Pediatric Research*, 81:473-479. FI: 2.76.
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113. Triebel, J., **Clapp, C.**, Martínez de la Escalera, G., Bertsch, T. Commentary: Prolactin alters blood pressure by modulating the activity of endothelial nitric oxide synthase. *Frontiers in Endocrinology* 8: 105, 2017. FI: 3.675
112. Arredondo-Zamarripa, D., Noguez-Imm, R., Bautista Cortés, A.M., Vázquez-Ruiz, O., Bernanrdini, M., Fiorio Pla, A., Gkika, D., Prevarskaya, N., Prevarskaya, N., López-Casillas, F., Liedtke, W., **Clapp, C.**, Thebault, S. Dual contribution of TRPV4 antagonism in the regulatory effect of vasoinhibins on blood-retinal barrier permeability: diabetic milieus makes a difference. *Scientific Reports* 7: 13094-13109, 2017. FI:5.525
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110. Castillo, X., Melo, Z., Varela-Echevarría, A., Tamáriz, E., Aroña, R.M., Arnold, E., **Clapp, C.**, Martínez de la Escalera, G. Vasoinhibins suppresses the ability of NGF and VEGF to stimulate neurite growth in rat primary sensory neurons. *Neuroendocrinology* 2017. DOI:10.1159/000477768. FI: 4.373.
109. Triebel, J., **Clapp, C.**, Martínez de la Escalera, G., Bertsch, T. Vasoinhibin serum levels are required to demonstrate their role in peripartum cardiomyopathy etiopathology. *ASAIO Journal* 63: e50, 2017. FI: 2.291

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107. Ruiz-Herrera, X., de los Ríos, E.A., Díaz, M.M., Lerma-Alvarado, R.M., Martínez de la Escalera, L., López-Barrera, F., Lemini, M., Arnold, E., Martínez de la Escalera, G., **Clapp, C.**, Macotela, Y. Prolactin promotes adipose tissue fitness and insulin sensitivity in obese males. *Endocrinology*, accepted 2016. FI: 5.045
106. **Clapp, C.**, Adán, N., Ledesma-Colunga, G.M., Solís-Gutiérrez, M., Triebel, J., Martínez de la Escalera, G. The role of the prolactin/vasoinhibin axis in rheumatoid arthritis: An integrative overview. *Cellular and Molecular Life Sciences*. 73:2929-2948, 2016. FI: 5.808. DOI 10.1007/s00018-016-2187-0.
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104. Díaz-Lezama, N., Wu, Z., Adán-Castro, E., Arnold, E., Vázquez-Membrillo, M., Arredondo-Zamarripa, D., Ledesma-Colunga, M.G., Moreno-Carranza, B., Martínez de la Escalera, G., Colosi, P., **Clapp, C.** Diabetes enhances the efficacy of AAV2 vectors in the retina: therapeutic effect of AAV2 encoding vasoinhibin and soluble VEGF receptor 1. *Laboratory Investigation* 96: 283-295, 2016. FI: 4.453
103. Triebel, J., Bertsch, T., Bollheimer, C., Ríos-Barrera, D., Pearce, C.F., Hüfner, M., Martinez de la Escalera, G., **Clapp, C.** Principles of the prolactin/vasoinhibin axis. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*. 309: R1193-R1203, 2015. FI: 3.529
102. Lemini ,M., Ruiz-Herrera , X., Ledesma-Colunga, M.G., Díaz-Lezama, N., De los Ríos, E.A., Lopez-Barrera, F., Méndez. I., Martinez de la Escalera, G., Macotela, Y., and **Clapp C.** Prolactin anterior pituitary expression and circulating levels are reduced in obese and diabetic rats: Role of TGF $\beta$  and TNF $\alpha$ . *American Journal of Physiology- Regulatory, Integrative and Comparative Physiology*. 308:R792-R799, 2015. FI: 3.59
101. Triebel, J., Bertsch, T., Martínez de la Escalera, G., and **Clapp, C.** On the path towards classifying hormones of the vasoinhibin-family. *Frontiers in Endocrinology* 6:1-2, 2015
100. Triebel, J., Moreno-Vega, A.I., Vázquez-Membrillo, M., Jeziorski, M.C., García-Franco, R., López-Star, E., Baldivieso-Hurtado, O., Ochoa, D., Macotela, Y., Bertsch, T., Martínez de la Escalera, G., **Clapp, C.** High prolactin excretion in patients with diabetes mellitus and impaired renal function. *Clinical Laboratory*, 61:709-716, 2015. FI:1.084
99. **Clapp, C.**, Thebault, S., Macotela, Y., Moreno-Carranza, B., Triebel, J., Martínez de la Escalera, G. Regulation of blood vessels by prolactin and vasoinhibins. *Advances in Experimental Medicine and Biology* 846: 83-95, 2015. FI: 2.020.
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97. Zamorano, M., Ledesma-Colunga, M.G., Adán, A., Vera-Massieu, C., Lemini, M., Méndez, I., Moreno-Carranza, B., Neumann I.D., Thebault, S., Martínez de la Escalera, G., Torner, L., **Clapp, C.** Prolactin-derived vasoinhibins increase anxiety- and depression-related behaviors. *Psychoneuroendocrinology*. 44: 123-132, 2014. FI: 5.926
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