BIOSKETCH – MANUEL COLLADO

Part A. PERSONAL INFORMATION

First name	MANUEL		
Family name	COLLADO RODRÍGUEZ		
Gender (*)	MALE	Birth date	10/04/1969
ID number	51674262R		
e-mail	manuel.collado.rodriguez@sergas.es	URL Web: https://colladolab.com	
Open Research and Contributor ID (ORCID)(*)		0000-0002-0330-0880	

(*) Mandatory

A.1. Current position

Position	INVESTIGADOR I3-SNS		
Initial date	01/06/2020		
Institution	SERGAS		
Department/Center	IDIS CHUS		
Country	SPAIN	Teleph. number	+34981955441
Key words	senescence; cancer; senolytics		

A.2. Previous positions (research activity interruptions, art. 45.2.b)

Period	Position/Institution/Country/Interruption cause
1997-1999	Research Fellow, LICR, London, UK
2000-2000	Research Fellow, NYU Medical School, NYC, USA
2000-2001	Research Associate, MSKCC, NYC, USA
2001-2003	Research Fellow, CNB, Madrid, Spain
2003-2012	Staff Scientist, CNIO, Madrid, Spain
2012-2017-2020	Miguel Servet I-II, SERGAS, Santiago de Compostela, Spain
2022-	I3-SNS Investigator, SERGAS, Santiago de Compostela, Spain

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
BSc	UAM	1992
PhD	UAM	1997

Part B. CV SUMMARY

Scientific contributions: Our laboratory was created officially in June 2012 when I was awarded a Miguel Servet, although laboratory space was not available until February 2013. Since then, we have worked to establish a group within the Health Research Institute of Santiago de Compostela, IDIS, whose main scientific focus has been to advance our knowledge of the cellular senescence process in general, and

specifically to improve cancer treatment. In the last 10 years we have published 36 papers and book chapters.
During these years we have advanced our knowledge on the process of cellular senescence to expand the range of settings in which this response plays crucial roles. For example, we identified developmentally-induced senescence as a crucial morphogenetic player during embryogenesis, an observation that we also made in lower vertebrates such as fish, showing that this process is evolutionarily conserved. We also identified senescence contributing to tissue repair and regeneration using zebrafish and demonstrated how the transient induction of senescence favors tissue regeneration.

In cancer, we showed that inflammation can contribute to pancreatic cancer development by inhibiting oncogene-induced senescence and identified the Cardiac glycosides as a new family of broad spectrum senolytic compounds. This discovery provides a new set of senolytics, reveals vulnerabilities of senescent cells, and proves the “one-two punch” strategy against cancer based on the combination of pro-senogenic chemotherapy and senolytics.

We have also worked on cellular reprogramming and used it to deepen our knowledge of the plasticity associated with oncogenic transformation. In this sense, we identified a previously unrecognized tumor suppression activity for cell cycle regulators p27Kip1 and the retinoblastoma family related with the transcriptional repression of pluripotency gene Sox2. We also observed how the activation of oncogenic Ras results in signaling promoting dedifferentiation, measured as enhanced reprogramming to pluripotency. This might be one of the key elements in the transforming activity of this oncogene. Finally, we demonstrated how the exhaustion of adult stem cell populations leads to cellular senescence and premature aging as demonstrated by using a mouse model of conditional depletion of Sox2+ cells.

We have also contributed review articles by invitation to recapitulate our current knowledge of senescence in development, repair and regeneration, and senolytics, as well as a key review in the field setting the standards of definition, description, markers, function, etc, of cellular senescence (published in Cell).

We have published 75 articles, receiving close to 120 citations per item on average, h-index 32.

I am part of the International Cell Senescence Association (ICSA) steering committee and organized their second conference in Santiago de Compostela in July 2015. I created the Cellular senescence coordinated group of the SEBBM. I am part of the Spanish Network in Cellular Senescence and organized our latest meeting in Santiago in November 2021. I am frequently invited to review articles for top journals (Nature Communications, Nature Aging, Nature Cancer, Nature Metabolism, Nature Cell Biology, Cancer Cell, Aging Cell, PNAS, etc), and grants and contracts from international funding agencies from Israel, France, UK, The Netherlands, Belgium, Czech Rep, Switzerland, etc.

Impact on society: The results obtained in our laboratory from our previous grant are poised to advance innovative approaches into first-in-human clinical trials thanks to the support of the Cancer Innova Program, which is funding research to accelerate the

translation of laboratory results to patients with the support of Xunta de Galicia, Kaertor Foundation, Janssen, Lilly and AECC. We recently received support from this initiative to further develop these findings into clinical application. We are very active in science outreach activities and have helped organize different activities (some of them funded by FECYT). We also frequently give talks in local, regional, national, and international events. We keep a lab webpage (www.colladolab.com) and Twitter profiles (@mcollado_CHUS and @ColladoLab).

Formative activities: I have supervised the work of 2 lab technicians and 1 postdoc, and 5 PhD students defended their thesis. I have also supervised 5 lab technicians, 15 TFM, 13 TFG, and 11 summer students. Currently, I am supervising 2 postdocs, 5 PhDs within the lab and 2 more co-directed, and 2 TFGs. PhD students obtained fellowships from FPU, Xunta de Galicia or internal fellowships from our institute. Postdoc was funded by CONACYT and the current ones through Xunta de Galicia. Fellowships from AECC and Becas de Colaboración were used to fund short stays of students. I am also involved in teaching activities, coordinating a subject within the Genomics & Genetics Master from USC, and I have co-organized several summer courses of the USC.

Part C. RELEVANT MERITS

C.1. Publications in the last 5 years

Estévez-Souto V, Da Silva-Álvarez S, Collado M. The role of extracellular vesicles in cellular senescence. FEBS J. 2023 Mar;290(5):1203-1211. doi: 10.1111/febs.16585. Epub 2022 Aug 18. PMID: 35904466.

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Benítez S, Cordero A, Santamaría PG, Redondo-Pedraza J, Rocha AS, Collado-Solé A, Jimenez M, Sanz-Moreno A, Yoldi G, Santos JC, De Benedictis I, Gómez-Aleza C, Da Silva-Álvarez S, Troulé K, Gómez-López G, Alcazar N, Palmero I, Collado M, Serrano M, Gonzalez-Suarez E. RANK links senescence to stemness in the mammary epithelia, delaying tumor onset but increasing tumor aggressiveness. Dev Cell. 2021 Jun 21;56(12):1727-1741.e7. doi: 10.1016/j.devcel.2021.04.022. Epub 2021 May 17. PMID: 34004159; PMCID: PMC8221814.

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Da Silva-Álvarez S, Collado M. The Jekyll and Hyde of Senescence in Cancer: TIMP1 Controls the Switch from Tumor-Controlling to Tumor-Promoting Senescence. Cancer Cell. 2021 Jan 11;39(1):13-15. doi: 10.1016/j.ccell.2020.12.013. Epub 2020 Dec 24. PMID: 33357453.

Da Silva-Álvarez S, Guerra-Varela J, Sobrido-Cameán D, Quelle A, Barreiro-Iglesias A, Sánchez L, Collado M. Developmentally-programmed cellular senescence is conserved and widespread in zebrafish. Aging (Albany NY). 2020 Sep 29;12(18):17895-17901. doi: 10.18632/aging.103968. Epub 2020 Sep 29. PMID: 32991320; PMCID: PMC7585104.

García-Caballero L, Caneiro J, Gándara M, González-Ortega N, Cepeda-Emiliani A, Gude F, Collado M, Beiras A, Gallego R. Merkel cells of human oral mucosa express the pluripotent stem cell transcription factor Sox2. Histol Histopathol. 2020 Sep;35(9):1007-1012. doi: 10.14670/HH-18-231. Epub 2020 May 4. PMID: 32495847.

Gorgoulis V, Adams PD, Alimonti A, Bennett DC, Bischof O, Bishop C, Campisi J, Collado M, Evangelou K, Ferbeyre G, Gil J, Hara E, Krizhanovsky V, Jurk D, Maier AB, Narita M, Niedernhofer L, Passos JF, Robbins PD, Schmitt CA, Sedivy J, Vougas K, von Zglinicki T, Zhou D, Serrano M, Demaria M. Cellular Senescence: Defining a Path Forward. Cell. 2019 Oct 31;179(4):813-827. doi: 10.1016/j.cell.2019.10.005. PMID: 31675495.

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