

## CURRICULUM VITAE

**Carlos López-Otín** is Professor of Biochemistry and Molecular Biology at the University of Oviedo (Spain), where he has undertaken his research and teachings since 1987. His academic training took place at the Universities of Zaragoza and Complutense of Madrid, where he was awarded his PhD in 1984. His scientific work has been developed at the Centro Ramón y Cajal in Madrid, the Severo Ochoa Molecular Biology Center in Madrid, and the Universities of Lund-Sweden, New York and Harvard-USA.

Currently, Carlos López-Otín combines his teaching responsibilities at the University of Oviedo, with his research lines on Cancer and Aging Biology. His research group has identified, cloned and characterized more than 60 novel human genes encoding proteases associated with cancer. López-Otín's work has also delineated essential biological information in regards to the functional role of many of these genes in cancer, as well as in other pathological processes, including the devastating syndromes of accelerated aging. He has also proposed a global approach for the study of proteases in health and disease through novel concepts such as Degradomics and Degradome, together with the development of high-throughput methods that tackle these concepts. In parallel studies, he has been largely involved in the functional annotation of the human genome and other genomes of biomedical and evolutionary relevance, from chimpanzees and other primates to mouse and whales.

Since 2009, Carlos López-Otín has taken the responsibility to coordinate the Spanish contribution to the International Consortium for the study of Cancer Genomes (ICGC-CLL). The scientific work co-directed by him has led to the unveiling of the complete tumor genome sequence of hundreds of patients with chronic lymphocytic leukemia and the identification and functional characterization of recurrent mutations in several genes, which have become preferential targets for therapeutic intervention in this frequent neoplasia. Closely related to the Cancer Genome projects, López-Otín's group has identified the genetic determinants of several hereditary diseases. Foremost amongst these studies is the discovery of a novel kind of hereditary premature aging, the Nestor-Guillermo syndrome, as well as the finding of genes causing hereditary sudden death and familial melanoma. Moreover, the work of López-Otín's group has also contributed to our understanding of the molecular mechanisms associated with physiological aging. He has reported the first integrative analysis of the molecular and cellular hallmarks of aging, and has developed a method to facilitate the cell reprogramming of aged human cells to pluripotent cells with embryonic properties.

The work by Carlos López-Otín is collected in 30 book chapters, 12 patents and more than 350 publications in international journals, including more than 40 manuscripts in *Nature*, *Science* and *Cell* journals. According to the ISI-WOK database, these works have been cited to date more than 32.000 times, with an aggregate Hirsch index of  $h=88$ . Moreover, he has supervised 30 Doctoral Theses related to these projects. Carlos López-Otín is a member of numerous scientific societies, committees and journal editorial boards. He is also a member of the Spanish Royal Academy of Sciences and the European Academy, among others. Throughout his scientific career, he has received different national and international awards and distinctions, such as the Doctorate "Honoris Causa" from the International University Menéndez Pelayo and the University of Zaragoza, the "Carmen y Severo Ochoa" Award in Molecular Biology, the Lilly Award in Pre-clinical Research, the Cobos Award in Biomedicine, the Eladio Viñuela Award in Molecular Biology, the Echevarne Award in Oncology, the Dupont Award in Life Sciences, the "Jaime I" Award in Research, the first Gold Medal from the Spanish Association for Cancer Research, the European "25<sup>th</sup> FEBS Jubilee" Award in Biochemistry, the Mexico Award in Science and Technology and the "Santiago Ramón y Cajal" National Research Award.

## Representative bibliography from Carlos López-Otín's work

- López-Otín C and Overall CM. "Protease degradomics, a new challenge for proteomics" **Nature Rev. Mol. Cell. Biol.** 3: 509-519 (2002)
- Overall CM and López-Otín C. "Strategies for MMP inhibition in cancer: innovations for the post-trial era" **Nature Rev. Cancer** 2: 657-672 (2002)
- Pendás *et al.* "Defective prelamin A processing and muscular and adipocyte alterations in *Zmpste24* metalloproteinase deficient mice" **Nature Genetics** 31: 94-99 (2002)
- Puente XS, Sánchez LM, Overall CM and López-Otín C. "Human and mouse proteases: a comparative genomic approach" **Nature Rev. Genetics** 4: 544-558 (2003)
- Balbín M, Fueyo A, Tester AM, Pendás AM, Pitiot AS, Astudillo A, Overall CM, Shapiro S and López-Otín C. "Loss of collagenase-2 confers increased skin tumor susceptibility to male mice" **Nature Genetics** 35: 252-257 (2003)
- Gibbs *et al.* "Genome sequence of the brown Norway Rat yields insights into mammalian evolution" **Nature** 428: 493-521 (2004)
- The Chimpanzee Sequencing and Analysis Consortium "Initial sequence of the chimpanzee genome and comparison with the human genome" **Nature** 437: 69-87 (2005)
- Liu *et al.* "Genomic instability in laminopathy-based premature aging" **Nature Medicine** 11: 780-785 (2005)
- Varela *et al.* "Accelerated aging in mice deficient in *Zmpste24* protease is linked to p53 signaling activation" **Nature** 437: 564-568 (2005)
- López-Otín C and Matrisian LM. "Emerging roles of proteases in tumour suppression" **Nature Rev. Cancer** 7: 800-808 (2007)
- Warren *et al.* "Genome analysis of the platypus reveals unique signatures of evolution" **Nature** 453: 175-183 (2008)
- Varela *et al.* "Combined treatment with statins and amino-bisphosphonates extends longevity in a mouse model of human premature aging" **Nature Medicine** 14: 767-772 (2008)
- Warren *et al.* "The genome of a songbird" **Nature** 464:757-762 (2010)
- López-Otín C and Hunter T. "The regulatory crosstalk between kinases and proteases in cancer" **Nature Rev. Cancer** 10: 278-292 (2010)
- Hudson *et al.* "International network of cancer genome projects" **Nature** 464: 993-998 (2010)
- Locke *et al.* "Comparative and demographic analysis of orangutan genomes" **Nature** 469: 529-533 (2011)
- Osorio *et al.* "Splicing-directed therapy in a new mouse model of human accelerated aging" **Science Transl. Med.** 3: 106ra107 (2011)
- Puente *et al.* "Whole-genome sequencing identifies recurrent mutations in chronic lymphocytic leukemia" **Nature** 475: 101-105 (2011)
- Quesada *et al.* "Exome sequencing identifies recurrent mutations of the splicing factor *SF3B1* gene in chronic lymphocytic leukemia" **Nature Genetics** 44: 47-52 (2012)
- Senovilla *et al.* "An immunosurveillance mechanism controls cancer cell ploidy" **Science** 337: 1678-1684 (2012)
- Kulis *et al.* "Epigenetic analysis detects widespread gene-body DNA hypomethylation in chronic lymphocytic leukemia" **Nature Genetics** 44: 1236-1242 (2012)
- Quesada V, Ramsay AJ, and López-Otín C. "Chronic lymphocytic leukemia with *SF3B1* mutation" **New Engl. J. Med.** 366(26): 2530 (2012)
- Puente XS and López-Otín C. "The evolutionary biography of chronic lymphocytic leukemia" **Nature Genetics** 44: 1236-1242 (2013)

- Ramsay *et al.* “*POT1 mutations cause telomere dysfunction in chronic lymphocytic leukemia*” **Nature Genetics** 45: 526-530 (2013)
- López-Otín C *et al.* “*The hallmarks of aging*” **Cell** 153: 1194-217 (2013)
- Berndt *et al.* “*Genome-wide association study identifies multiple risk loci for chronic lymphocytic leukemia*” **Nature Genetics** 45: 868-876 (2013)
- De la Rosa *et al.* “*Prelamin A causes progeria through cell-extrinsic mechanisms and prevents cancer invasion*” **Nature Commun.** 4: 2268 (2013)
- Alexandrov *et al.* “*Signatures of mutational processes in human cancer*” **Nature** 500: 415-21 (2013)
- Fanjul-Fernández *et al.* “*Cell-cell adhesion genes CTNNA2 and CTNNA3 are tumour suppressors frequently mutated in laryngeal carcinomas*” **Nature Commun.** 4: 2531 (2013)
- Gordon LB, Rothman FG, López-Otín C, and Misteli T. “*Progeria: a paradigm for translational medicine*” **Cell** 156: 400-407 (2014)
- Robles-Espinoza *et al.* “*POT1 loss-of-function variants predispose to familial melanoma*” **Nature Genet.** 46: 478-481 (2014)
- Quirós PM *et al.* “*ATP-dependent Lon protease controls tumor bioenergetics by reprogramming mitochondrial activity*” **Cell Reports.** 8: 542-556 (2014)
- The Marmoset Genome Sequencing and Analysis Consortium “*The common marmoset genome provides insight into primate biology and evolution*” **Nature Genet.** 46: 850-857 (2014)
- Valdés-Mas *et al.* “*Mutations in filamin C cause a new form of familial hypertrophic cardiomyopathy*” **Nature Commun.** 5: 5326 (2014)
- Quirós PM, Langer T, López-Otín C. “*New roles of mitochondrial proteases in health, ageing and disease*” **Nature Rev. Mol. Cell. Biol.** 16: 345-359 (2015)
- Puente XS *et al.* “*Non-coding recurrent mutations in chronic lymphocytic leukaemia*” **Nature** 526: 519-524 (2015)
- Soria-Valles C *et al.* “*NF-κB activation impairs somatic cell reprogramming in ageing*” **Nature Cell Biol.** 17: 1004-1013 (2015)
- Alioto TS *et al.*, “*A comprehensive assessment of somatic mutation detection in cancer using whole-genome sequencing*” **Nature Commun.** 6: 10001 (2015)
- Osorio FG *et al.* “*Loss of the proteostasis factor AIRAPL causes myeloid transformation by deregulating IGF-1 signaling*” **Nature Med.** 22: 91-96 (2016)