



Maria Inmaculada Cobos Sillero

Associate Professor of Pathology

CLINICAL OFFICE (PRIMARY)

- **Pathology Department**

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Bio

BIO

Inma Cobos is a physician scientist recently recruited to Stanford in the Department of Pathology. She is a neuropathologist and neuroscientist with expertise in neurodegeneration.

Inma received her medical and doctoral degrees from the University of Murcia in Spain and completed post-doctoral training in Developmental Neurobiology at the University of California, San Francisco. She then pursued a clinical residency and fellowship in Anatomic Pathology and Neuropathology at Massachusetts General Hospital, Harvard Medical School. Before joining Stanford, she was an Assistant Professor in the Department of Pathology and Neuropathology at the UCLA David Geffen School of Medicine.

Her research program combines her background in diagnostic neuropathology, knowledge of developmental neuroscience, and state-of-the-art cellular and molecular technologies to advance the understanding of Alzheimer's disease and related dementias. She is currently applying single-cell methods to human brain to dissect the contributions of distinct cell types to Alzheimer's disease pathogenesis and investigate the mechanisms of tau-mediated neurodegeneration in human brain. Her work is supported by the NIH National Institute of Aging (R01), the Alzheimer's Association, and BrightFocus. She recently received the Ben Barres Early Career Acceleration Award from the Chan Zuckerberg Initiative (CZI).

CLINICAL FOCUS

- Neuropathology
- Anatomic and Clinical Pathology

ACADEMIC APPOINTMENTS

- Associate Professor - University Medical Line, Pathology
- Member, Bio-X
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Ben Barres Early Career Acceleration Award, Chan Zuckerberg Initiative (2018)
- Research Career Development Award, Stop Cancer (2016)
- NAAR Postdoctoral Fellowship, National Alliance for Autism Research/Autism Speaks (2004–2006)
- NARSAD Young Investigator Award, National Alliance for Research on Schizophrenia and Depression (2003–2005)
- Postdoctoral Fellowship, Spanish Ministry of Education and Science (2001-2003)
- Doctoral Extraordinary Prize, University of Murcia, Spain (2001)
- Neuroscience Master's Student Fellowship, International University of Andalusia, Spain (1997)
- Predoctoral Fellowship, Government of Murcia, Spain (1996–2000)

PROFESSIONAL EDUCATION

- Board Certification: Neuropathology, American Board of Pathology (2015)
- Board Certification: Anatomic Pathology, American Board of Pathology (2015)
- Fellowship: Massachusetts General Hospital Dept of Pathology (2015) MA
- Residency: Massachusetts General Hospital Dept of Pathology (2013) MA
- PhD, University of Murcia School of Medicine, Spain (2000)
- Medical Education: University of Murcia School of Medicine (1996) Spain

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our lab uses cellular and molecular methods, single-cell technology, and quantitative histology to study human neurodegenerative diseases. Current projects include:

- Using single-cell RNA-sequencing to understand selective vulnerability and disease progression in human Alzheimer's disease brain
- Investigating mechanisms of tau-related neurodegeneration in human brain
- Studying the neocortical and limbic systems in Diffuse Lewy Body Disease (DLBD) at the single cell level

Teaching

STANFORD ADVISEES

Postdoctoral Faculty Sponsor

Jaume Fores Martos, Jie Pan, Dongkeun Park, Akilaparvathydarshini Sankaraeswaran, Jorge Sanz Ros

Doctoral Dissertation Reader (NonAC)

Tanner Jensen

Publications

PUBLICATIONS

- **Molecular signatures underlying neurofibrillary tangle susceptibility in Alzheimer's disease.** *Neuron*
Otero-Garcia, M., Mahajani, S. U., Wakhloo, D., Tang, W., Xue, Y., Morabito, S., Pan, J., Oberhauser, J., Madira, A. E., Shakouri, T., Deng, Y., Allison, T., He, et al

2022

- **Divergent Cortical Tau Positron Emission Tomography Patterns Among Patients With Preclinical Alzheimer Disease.** *JAMA neurology*
Young, C. B., Winer, J. R., Younes, K., Cody, K. A., Bethausser, T. J., Johnson, S. C., Schultz, A., Sperling, R. A., Greicius, M. D., Cobos, I., Poston, K. L., Mormino, E. C., Alzheimers Disease Neuroimaging Initiative and the Harvard Aging Brain Study, et al
2022
- **Human Astrocytes Exhibit Tumor Microenvironment-, Age-, and Sex-Related Transcriptomic Signatures.** *The Journal of neuroscience : the official journal of the Society for Neuroscience*
Krawczyk, M. C., Haney, J. R., Pan, L., Caneda, C., Khankan, R. R., Reyes, S. D., Chang, J. W., Morselli, M., Vinters, H. V., Wang, A. C., Cobos, I., Gandal, M. J., Bergsneider, et al
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- **Defining the nature of human pluripotent stem cell-derived interneurons via single-cell analysis.** *Stem cell reports*
Allison, T., Langerman, J., Sabri, S., Otero-Garcia, M., Lund, A., Huang, J., Wei, X., Samarasinghe, R. A., Polioudakis, D., Mody, I., Cobos, I., Novitch, B. G., Geschwind, et al
2021
- **Nav1.1-Overexpressing Interneuron Transplants Restore Brain Rhythms and Cognition in a Mouse Model of Alzheimer's Disease.** *Neuron*
Martinez-Losa, M., Tracy, T. E., Ma, K., Verret, L., Clemente-Perez, A., Khan, A. S., Cobos, I., Ho, K., Gan, L., Mucke, L., Alvarez-Dolado, M., Palop, J. J.
2018; 98 (1): 75-89.e5
- **Inhibitory interneuron deficit links altered network activity and cognitive dysfunction in Alzheimer model.** *Cell*
Verret, L., Mann, E. O., Hang, G. B., Barth, A. M., Cobos, I., Ho, K., Devidze, N., Masliah, E., Kreitzer, A. C., Mody, I., Mucke, L., Palop, J. J.
2012; 149 (3): 708-21
- **Dlx transcription factors promote migration through repression of axon and dendrite growth** *NEURON*
Cobos, I., Borello, U., Rubenstein, J. R.
2007; 54 (6): 873-88
- **Mice lacking Dlx1 show subtype-specific loss of interneurons, reduced inhibition and epilepsy.** *Nature neuroscience*
Cobos, I., Calcagnotto, M. E., Vilaythong, A. J., Thwin, M. T., Noebels, J. L., Baraban, S. C., Rubenstein, J. L.
2005; 8 (8): 1059-68
- **Origins of cortical interneuron subtypes.** *The Journal of neuroscience : the official journal of the Society for Neuroscience*
Xu, Q., Cobos, I., De La Cruz, E., Rubenstein, J. L., Anderson, S. A.
2004; 24 (11): 2612-22
- **Enhancing mitosis quantification and detection in meningiomas with computational digital pathology.** *Acta neuropathologica communications*
Gu, H., Yang, C., Al-Kharouf, I., Magaki, S., Lakis, N., Williams, C. K., Alrosan, S. M., Onstott, E. K., Yan, W., Khanlou, N., Cobos, I., Zhang, X. R., Zarrin-Khameh, et al
2024; 12 (1): 7
- **Nuclear RNA catabolism controls endogenous retroviruses, gene expression asymmetry, and dedifferentiation.** *Molecular cell*
Torre, D., Fstkhyan, Y. S., Ho, J. S., Cheon, Y., Patel, R. S., Degrace, E. J., Mzoughi, S., Schwarz, M., Mohammed, K., Seo, J. S., Romero-Bueno, R., Demircioglu, D., Hasson, et al
2023
- **Lifelong restructuring of 3D genome architecture in cerebellar granule cells.** *Science (New York, N.Y.)*
Tan, L., Shi, J., Moghadami, S., Parasar, B., Wright, C. P., Seo, Y., Vallejo, K., Cobos, I., Duncan, L., Chen, R., Deisseroth, K.
2023; 381 (6662): 1112-1119
- **Deregulation of ER-mitochondria contact formation and mitochondrial calcium homeostasis mediated by VDAC in fragile X syndrome.** *Developmental cell*
Geng, J., Khaket, T. P., Pan, J., Li, W., Zhang, Y., Ping, Y., Cobos Sillero, M. I., Lu, B.
2023; 58 (7): 597-615.e10
- **Sex-Specific Oligodendroglia Response in Alzheimer's Disease**
Bharani, K., Dharshini, A., Oberhauser, J., Cobos, I.
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- **Cerebellar Granule Cells Develop Non-neuronal 3D Genome Architecture over the Lifespan.** *bioRxiv : the preprint server for biology*
Tan, L., Shi, J., Moghadami, S., Wright, C. P., Parasar, B., Seo, Y., Vallejo, K., Cobos, I., Duncan, L., Chen, R., Deisseroth, K.
2023
- **Swollen axons impair neuronal circuits** *NATURE*
Cobos, I., Palop, J. J.
2022; 612 (7939): 218-220
- **Swollen axons impair neuronal circuits** *NATURE*
Cobos, I., Palop, J. J.
2022: 218-220
- **Whole-Transcriptome Profiling and circRNA-miRNA-mRNA Regulatory Networks in B-Cell Development.** *Frontiers in immunology*
Pan, J., Hu, S., Ren, X., Hu, H., Deng, X., Yu, B., Cobos, I., Chen, X., Zhang, W.
2022; 13: 812924
- **Dysregulation of brain and choroid plexus cell types in severe COVID-19 (vol 595, pg 565, 2021)** *NATURE*
Yang, A. C., Kern, F., Losada, P. M., Agam, M. R., Maat, C. A., Schmartz, G. P., Fehlmann, T., Stein, J. A., Schaum, N., Lee, D. P., Calcuttawala, K., Vest, R. T., Berdnik, et al
2021
- **Dysregulation of brain and choroid plexus cell types in severe COVID-19.** *Nature*
Yang, A. C., Kern, F., Losada, P. M., Agam, M. R., Maat, C. A., Schmartz, G. P., Fehlmann, T., Stein, J. A., Schaum, N., Lee, D. P., Calcuttawala, K., Vest, R. T., Berdnik, et al
2021
- **Genome-wide association study and functional validation implicates JADE1 in tauopathy.** *Acta neuropathologica*
Farrell, K., Kim, S., Han, N., Iida, M. A., Gonzalez, E. M., Otero-Garcia, M., Walker, J. M., Richardson, T. E., Renton, A. E., Andrews, S. J., Fulton-Howard, B., Humphrey, J., Vialle, et al
2021
- **The CD22-IGF2R interaction is a therapeutic target for microglial lysosome dysfunction in Niemann-Pick type C.** *Science translational medicine*
Pluvinage, J. V., Sun, J., Claes, C., Flynn, R. A., Haney, M. S., Iram, T., Meng, X., Lindemann, R., Riley, N. M., Danhash, E., Chadarevian, J. P., Tapp, E., Gate, et al
2021; 13 (622): eabg2919
- **Hepatic arginase deficiency fosters dysmyelination during postnatal CNS development.** *JCI insight*
Liu, X., Haney, J. R., Cantero, G., Lambert, J. R., Otero-Garcia, M., Truong, B., Gropman, A., Cobos, I., Cederbaum, S. D., Lipshutz, G. S.
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- **Dlx1 and Dlx2 Promote Interneuron GABA Synthesis, Synaptogenesis, and Dendritogenesis.** *Cerebral cortex (New York, N.Y. : 1991)*
Pla, R., Stanco, A., Howard, M. A., Rubin, A. N., Vogt, D., Mortimer, N., Cobos, I., Potter, G. B., Lindtner, S., Price, J. D., Nord, A. S., Visel, A., Schreiner, et al
2018; 28 (11): 3797-3815
- **GABAergic Interneuron Differentiation in the Basal Forebrain Is Mediated through Direct Regulation of Glutamic Acid Decarboxylase Isoforms by Dlx Homeobox Transcription Factors.** *The Journal of neuroscience : the official journal of the Society for Neuroscience*
Le, T. N., Zhou, Q. P., Cobos, I., Zhang, S., Zagozewski, J., Japoni, S., Vriend, J., Parkinson, T., Du, G., Rubenstein, J. L., Eisenstat, D. D.
2017; 37 (36): 8816-8829
- **A 63-Year-Old Man With Progressive Visual Symptoms.** *JAMA neurology*
Mitchell, S. B., Lucente, D., Larvie, M., Cobos, M. I., Frosch, M., Dickerson, B. C.
2017; 74 (1): 114-118
- **CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL. Case 23-2015. A 51-Year-Old Woman with Headache, Cognitive Impairment, and Weakness.** *The New England journal of medicine*
Batchelor, T. T., Chen, Y. B., Rapalino, O., Cobos, I.
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- **Human von Economo neurons express transcription factors associated with Layer V subcerebral projection neurons.** *Cerebral cortex (New York, N.Y. : 1991)*
Cobos, I., Seeley, W. W.

2015; 25 (1): 213-20

- **Influence of a Subtype of Inhibitory Interneuron on Stimulus-Specific Responses in Visual Cortex** *CEREBRAL CORTEX*
Mao, R., Schummers, J., Knoblich, U., Lacey, C. J., Van Wart, A., Cobos, I., Kim, C., Huguenard, J. R., Rubenstein, J. L., Sur, M.
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- **Step-by-step in situ hybridization method for localizing gene expression changes in the brain.** *Methods in molecular biology (Clifton, N.J.)*
Palop, J. J., Roberson, E. D., Cobos, I.
2011; 670: 207-30
- **A mutation in the pericentrin gene causes abnormal interneuron migration to the olfactory bulb in mice.** *Developmental biology*
Endoh-Yamagami, S., Karkar, K. M., May, S. R., Cobos, I., Thwin, M. T., Long, J. E., Ashique, A. M., Zarbalis, K., Rubenstein, J. L., Peterson, A. S.
2010; 340 (1): 41-53
- **Dlx1&2 and Mash1 transcription factors control MGE and CGE patterning and differentiation through parallel and overlapping pathways.** *Cerebral cortex (New York, N.Y. : 1991)*
Long, J. E., Cobos, I., Potter, G. B., Rubenstein, J. L.
2009; 19 Suppl 1: i96-106
- **Dlx1&2 and Mash1 transcription factors control striatal patterning and differentiation through parallel and overlapping pathways.** *The Journal of comparative neurology*
Long, J. E., Swan, C., Liang, W. S., Cobos, I., Potter, G. B., Rubenstein, J. L.
2009; 512 (4): 556-72
- **FGF15 promotes neurogenesis and opposes FGF8 function during neocortical development.** *Neural development*
Borello, U., Cobos, I., Long, J. E., McWhirter, J. R., Murre, C., Rubenstein, J. L.
2008; 3: 17
- **Transcriptional regulation of cortical interneuron development.** *The Journal of neuroscience : the official journal of the Society for Neuroscience*
Butt, S. J., Cobos, I., Golden, J., Kessaris, N., Pachnis, V., Anderson, S.
2007; 27 (44): 11847-50
- **Chicken lateral septal organ and other circumventricular organs form in a striatal subdomain abutting the molecular striatopallidal border.** *The Journal of comparative neurology*
Bardet, S. M., Cobos, I., Puellas, E., Martínez-De-La-Torre, M., Puellas, L.
2006; 499 (5): 745-67
- **Cellular patterns of transcription factor expression in developing cortical interneurons.** *Cerebral cortex (New York, N.Y. : 1991)*
Cobos, I., Long, J. E., Thwin, M. T., Rubenstein, J. L.
2006; 16 Suppl 1: i82-8
- **Severe hearing loss in Dlx1 mutant mice.** *Hearing research*
Polley, D. B., Cobos, I., Merzenich, M. M., Rubenstein, J. L.
2006; 214 (1-2): 84-8
- **The vertebrate ortholog of Aristaless is regulated by Dlx genes in the developing forebrain.** *The Journal of comparative neurology*
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2003; 130 (19): 4539-52
- **Fate map of the avian anterior forebrain at the four-somite stage, based on the analysis of quail-chick chimeras.** *Developmental biology*
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2001; 239 (1): 46-67
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Cobos, I., Puellas, L., Martínez, S.

2001; 239 (1): 30-45

- **Monofocal origin of telencephalic oligodendrocytes in the anterior entopeduncular area of the chick embryo.** *Development (Cambridge, England)*
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- **The early steps of oligodendrogenesis: insights from the study of the plp lineage in the brain of chicks and rodents.** *Developmental neuroscience*
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2001; 23 (4-5): 318-26
- **Spatiotemporal development of oligodendrocytes in the embryonic brain.** *Journal of neuroscience research*
Thomas, J. L., Spassky, N., Perez Villegas, E. M., Olivier, C., Cobos, I., Goujet-Zalc, C., Martínez, S., Zalc, B.
2000; 59 (4): 471-6
- **FGF8 induces formation of an ectopic isthmic organizer and isthmocerebellar development via a repressive effect on Otx2 expression.** *Development (Cambridge, England)*
Martínez, S., Crossley, P. H., Cobos, I., Rubenstein, J. L., Martin, G. R.
1999; 126 (6): 1189-200
- **Calretinin in pretecto- and olivocerebellar projections in the chick: immunohistochemical and experimental study.** *The Journal of comparative neurology*
De Castro, F., Cobos, I., Puellas, L., Martínez, S.
1998; 397 (2): 149-62