BIOGRAPHICAL SKETCH

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NAME: Eva Nogales

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Universidad Autónoma de Madrid, Spain	Physics	1988	Physics
Keele University, UK	Biophysics	1993	Biophysics
Life Science Division, Lawrence Berkeley National Laboratory (LBNL)		1995	Biophysics

A. Personal Statement

My lab is dedicated to gaining mechanistic insight into two important areas of eukaryotic biology: central dogma machinery in the control of gene expression, and cytoskeleton interactions and dynamics in cell division. We study macromolecular assemblies as whole units of molecular function by direct visualization of their architecture, functional states, and regulatory interactions using state-of-the-art cryo-electron microscopy (cryo-EM) and image analysis, as well as biochemical and biophysical assays. Our motto is "Visualizing Macromolecular Function." Over the years my lab has made key contributions to the understanding of tubulin and microtubules structure and interactions with microtubule associated factors, in order to gain insight into the mechanism of dynamic instability and its regulation and utilization by the cell. Through all our studies, and while guided by important biological questions, we have pushed the limits of the use of cryo-EM and contributed to the excitement that this methodology is now bringing to structural biology.

B. Positions and Honors

Positions

1995-1998 Scientist, Lawrence Berkeley National Laboratory, Life Sciences Division
1998-2003 Assistant Professor of Biochemistry and Molecular Biology, University of California, Berkeley
1998-2008 Faculty Scientist, Lawrence Berkeley National Laboratory, Life Sciences Division
2000-present **Investigator**, Howard Hughes Medical Institute
2003-2006 Associate Professor of Biochemistry and Molecular Biology, University of California, Berkeley
2006-present **Professor** of Biochemistry, Biophysics and Structural Biology, University of California, Berkeley
2008-2015 Senior Faculty Scientist, Lawrence Berkeley National Laboratory, Life Sciences Division
2010-2015 Chair, Berkeley Biophysics Graduate Program.
2010-2013 Deputy Director of the Bioenergy/GTL & Structural Biology Department at the Life Sciences Division, LBNL
2013-2015 Member of the Scientific Advisory Committee for the Life Sciences Division, LBNL
2015-present **Senior Faculty Scientist**, Lawrence Berkeley National Laboratory, MBIB Division
2015-present **Head**, Biochemistry, Biophysics and Structural Biology Division, MCB, UC Berkeley
2016-present **Head**, Bay Area Cryo-EM Facility (BACEM), Berkeley Site

Awards

1998 Outstanding Performance Award by Lawrence Berkeley National Laboratory
2000 Burton Award by the Microscopy Society of America

2005 Chabot Science Award for Excellence
2005 American Society for Cell Biology Early Career Award
2015 Distinguished Role Model in the Life Sciences, Northwestern University
2015 Dorothy Crowfoot Hodgkin Award by the Protein Society
2016 Mildred Cohn Award by the American Society for Biochemistry and Molecular Biology
2016 Keith Porter Lecture Award, ASCB
2016 LBNL Director's Award for Exceptional Science Achievement
2018 Sandra K. Masur Senior Leadership Award by the American Society for Cell Biology
2019 Grimwade Medal by the University of Melbourne

Honors

1984-1988 Undergraduate fellowship by the Spanish Ministry of Education
1989-1992 Doctoral fellowship by the Spanish Ministry of Education and the MRC (U.K.)
2007-2008 Fundación BBVA Chair in Biomedicine, Spain.
2009 Member of the Search Committee for the LBNL Director
2009 Distinguished Lecture at EMBL, Heidelberg
2009 Max Birnstiel Lecture at IMP, Vienna
2011 Keynote speaker, IUCr Annual Meeting, Madrid
2011 Keynote speaker, Gordon Research Conference on "Motile and Contractile systems"
2012 Fitzgerald Lecture, Duke University.
2013 NIH WALS Lecture
2013 Keynote speaker, Gordon Research Conference on "Proteins"
2014 Lamport Lecture, Dept. of Biophysics and Physiology, University of Washington
2014 University of Colorado Medical School Dean's Distinguished Lecture
2014-2015 Visiting Scholar of the Fundación Jesús Serra (at CNIO, Madrid)
2015 Dr. Smith Freeman Endowed Lecture, Chicago Cytoskeleton Meeting
2015 Elected **Member of the National Academy of Sciences**
2016 Elected **Member of the American Academy of Arts and Sciences**
2016 Harvey Lecture, New York
2016 NCI Distinguished Scientist lecture series speaker
2016 James P. Holland Memorial Lecture, Indiana University
2017 Katherine D. McCormick Distinguished Lecture at Stanford University
2017 Ernest C. Pollard Lecture in Biophysics at Penn State University
2017 Russell Marker Lectures, University of Maryland
2017 Elected **Fellow of the American Society for Cell Biology**
2018 Gruber Science Fellowship Lecture, Yale University
2018 Rosalind Franklin Lecture, Institute of Structural and Molecular Biology Symposium, UCL/Birbeck, London
2018 Horowitz Lecture, UT Health San Antonio
2018 Hans Neurath Lecture, University of Washington

Participation in Scientific Societies, Advisory Boards, Editorial Boards, and Conference Organizing

1999 Member of the Program Committee for the American Society for Cell Biology.
2000-2015 Member of the Editorial Board of Journal of Structural Biology
2001-2005 Elected member of the Biophysical Society Council
2002-present **Chair** - Advisory Board for the National Resource for Automated Molecular Microscopy
2002 Co-organizer of the Biophysical Discussions on "Frontiers in structural cell biology"
2003 Organizer of the first QB3 Annual Symposium: "Challenges in Biological Imaging: from cells to molecules".
2003-2005 Elected member of the Biophysical Society Executive Board
2003-2006 Elected Member of the Program Committee for the Biophysical Society
2003 Organizer of the QB3 Symposium: "Challenges in Biological Imaging: from cells to molecules".
2004 Co-organizer of HHMI-MPI joint Workshop on Molecular and Cellular Imaging
2005 Co-organizer of "Imaging" Mini-symposium at the Annual Meeting of the ASCB
2007 Co-organizer of the "Imaging Techniques" workshop of the GTL-DOE Annual Conference
2008 Organizer CNIO Cancer Conference: "Structure of essential complexes for cell survival"

2008 Co-organizer of Workshop "Frontiers in Cryo-EM" at Janelia Farm, HHMI.
2009 Chair of the Early Career Selection Committee of the ASCB
2010 Co-organizer, Structural Biology Workshop at Janelia Farm
2011-present **Member** (**co-Chair** since 2016) of the National Advisory Committee of the Pew Latin American Fellows Program
2012-present **Member** of the Editorial Board of Journal of Molecular Biology
2015-present **Associate Editor** of the Journal of Structural Biology
2015 Elected Chair of the Gordon Research Conference on "Three-dimensional Electron Microscopy"
2012-present **Member** of the Editorial Board of Journal of Cell Biology
2015-present **Member,** Advisory Council for Princeton's Molecular Biology Department
2015-present **Member**, Krios Oversight Committee, OHSU
2016-present **Member**, External Advisory Board for CUNY ASRC-SBI
2016 Ad hoc scientific advisor for the Beckmann Foundation
2016-present **Member**, External Advisory Board for the NSF-CREST Center for Cellular and Biomolecular Machines at UC Merced.
2016-present **Member**, International Academic Advisory Committee for the Beijing Innovation Center for Structural Biology at Tsinghua University.
2018-present **Member**, Life Sciences Institute Scientific Advisory Board, University of Michigan
2019 **President elect of the ASCB**

Service on Federal Government and International Advisory Committees

2005-2009 Macromolecular Structure and Function C Study Section Member
2012 MSFC study section, ad hoc member
2013 CMP study section, ad hoc member
2013 NCSD study section, ad hoc member
2015 NIH special study section panel
2017 Reviewer for the Villum Fonden, Denmark

C. Contributions to Science

I – Structural Basis of Microtubule Dynamics – We are studying the conformational landscape of tubulin as defined by its nucleotide and assembly states. As a postdoc, I used electron crystallography to produce the first atomic model of tubulin, and established the structural basis of nucleotide exchange, polymerization-coupled hydrolysis, and taxol binding. Later my lab obtained two structures proposed to mimic intermediates in the assembly and disassembly of microtubules (**MTs**) that illustrated the conformational consequences of the nucleotide state and how they relate to longitudinal and lateral assembly. We later produced structures at ~5 Å resolution for three MT states: stable MTs bound to GMPCPP, dynamic MT (where GTP has been hydrolyzed to GDP), and MTs stabilized by taxol. These structures showed that GTP hydrolysis results in a compaction at the interdimer longitudinal interface (by the E-site nucleotide) and a conformational change in α-tubulin that generates strain in the MT lattice. Taxol appears to allosterically inhibit these changes. More recently we have been able to produced atomic structures of MT (~3.5 Å) that illustrate the details of lateral interaction between protofilaments, the mode of binding of the +TIP EB3 and how this protein promote GTP hydrolysis in tubulin.

1. **Nogales**, E., Wolf, S. G., & Downing, K. H. (1998) Structure of the $\alpha\beta$ tubulin dimer by electron crystallography. Nature 391, 199-203.
2. Wang, H-W. and **Nogales**, E. (2005) The nucleotide-dependent bending flexibility of tubulin regulates microtubule assembly, Nature 435, 911-915.
3. Alushin, G.M., Lander, G.C., Kellogg, E.H., Zhang, R., Baker, D. and **Nogales**, E. (2014) High-resolution microtubule structures reveal the structural transitions in $\alpha\beta$-tubulin upon GTP hydrolysis. Cell 157, 1117-1129.
4. Zhang, R., Alushin, G.M., Brown, A. and **Nogales** e. (2015) Mechanistic origin of microtubule dynamic instability and its regulation by EB proteins. Cell 162, 849-859.

II – Interactions of Microtubules with Kinetochore and other Mitotic Proteins. MT dynamics are coupled to the accurate segregation of chromosomes during mitosis via interaction with kinetochores. Our studies of the yeast *Dam1 kinetochore complex* showed that it assembles into rings around MTs that move processively with MT ends. We produced the only existing structures of the Dam1 complex and ring around MTs, defining its subunit organization. We visualized the full-length yeast **Ndc80 complex** and found a dramatic kink at a

conserved break in the coiled-coil and proposed its importance in kinetochore geometry and likely in tension sensing. Using a bonsai human Ndc80 complex, we obtained a subnanometer structure of Ndc80 bound to the MT. The binding is coupled to a self-interaction of Ndc80 complexes and allows to "probe" the conformational state of the MT. Our studies led to a model of how Ndc80's interaction with MT is tuned by Aurora B phosphorylation of the unstructured N-terminus of Ndc80. Our work, in the context of additional in vivo studies, has led us to propose models for the organization of both the yeast and the metazoan kinetochore. In addition to our kinetochore studies we are also interested in the interaction of MTs with partners important in mitosis. We have recently obtained the structure of the **PRC1** bound to the MT. This protein forms antiparallel MT arrays important for setting the spindle. We determined the residues in PRC1 contacting the MT and found that PRC1 promotes MT assembly. The binding mode observed suggests that the MT–PRC1 spectrin domain interface determines the geometry of the MT arrays cross-linked by PRC1.

1. Wang,H-W., Ramey, V.H., Westermann, S., Leschziner, A., Welburn, J.P.I., Nakajima, Y., Drubin, D.G., Barnes, G. and **Nogales**, E. (2007) Architecture of the Dam1 kinetochore ring complex: implications for microtubule-driven assembly and force-coupling mechanisms. NSMB 14, 721-726.
2. Alushin, G., Ramey, V.H., Pasqualato, S., Ball, D., Grigorieff, N., Musacchio, A. and **Nogales**, E. (2010). The NDC80 complex forms oligomeric arrays along microtubules. Nature 467, 805-810.
3. Alushin, G. M., Musinipally, V., Matson, D., Tooley, J., Stukenberg P.T. and **Nogales**, E. (2012) Multimodal microtubule binding by the Ndc80 kinetochore complex. NSMB 19, 1161-1167.
4. Kellogg, E., Howes, S., Ti, S-C., Ramirez-Aportela, E., Kapoor, T., Chacon, P. and **Nogales**, E. (2016) Near-atomic resolution cryo-EM structure of PRC1 bound to the microtubule. PNAS 113, 9430-9439.

III – Transcriptional Regulation of Gene Expression. The accurate initiation of transcription requires the assembly of a pre-initiation complex (PIC) that include TFIID, TFIIA, TFIIB, TFIIE, TFIIF, TFIIH and RNA pol II. Binding of TFIID to the core promoter is the first step. We visualized the stepwise assembly of a human **PIC** in which TBP substituted for TFIID, and thus defined the relative positions of all the protein components and the DNA. More recently we determined near-atomic resolution structures of the human PIC in a closed state (engaged with duplex DNA), an open state (engaged with a transcription bubble), and an initially transcribing complex (containing six base pairs of DNA-RNA hybrid). Comparison of the different structures has revealed the sequential conformational changes that accompany the transitions from one state to the other throughout the transcription initiation process. We also defined the structure of human **TFIIH** by cryo-EM at 4.4 Å resolution. This structure revealed the molecular architecture of the TFIIH core complex, the detailed structures of its constituent XPB and XPD ATPases, and how the core and kinase subcomplexes of TFIIH are connected. Finally, as a most challenging project, we obtained the first 3-D model of **TFIID** and showed the existence of significant flexibility within the complex. A novel conformation of TFIID, the rearranged state, interacts with promoter DNA in a TFIIA-dependent manner. This has led us to propose that the dynamic conformational landscape of TFIID may have regulatory consequences. We obtained the structure of human TFIID in complex with TFIIA and core promoter DNA at sub-nanometer resolution. We showed that TAF1 and TAF2 mediate major interactions with the downstream promoter and that TFIIA bridges the TBP-TATA complex with lobe B. More recently, we have used cryo-electron microscopy (cryo-EM), chemical crosslinking-mass spectrometry (CX-MS) and biochemical reconstitution to determine the complete molecular architecture of TFIID and define the conformational landscape of TFIID in the process of TATA-box binding protein (TBP) loading onto promoter DNA.

1. Louder, R.K., He, Y. Lopez-Blanco, J.R. Fang, J., Chacon, P., and **Nogales**, E. (2016) Structure of promoter-bound TFIID and insight into human PIC assembly. Nature 531, 604-609.
2. He, Y., Yan, C., Inouye, C., Tjian, R., Ivanov, I. and **Nogales**, E. (2016) Near-atomic resolution visualization of human transcription promoter opening. Nature 533, 359-365.
3. Greber, B.J., Nguyen, T.H.D., Fang, J., Afonine, P.V., Adams, P.D. and **Nogales, E.** (2017) The cryo-EM structure of human TFIIH. Nature **549**, 414-417.
4. Patel, A. Louder, R.K., Greber, B.J., Grünberg, S., Luo, J., Fang, J., Liu, Y., Ranish, J., Hahn, S. and **Nogales, E.** (2018) Structure of human TFIID and mechanism of TBP loading onto promoter DNA. Science 362, eaau8872.

Full list of publications can be found at:
https://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/40450390/

D. Research Support

R35 GM127018 (Nogales, Eva) 05/01/18-04/30/23

Structural Studies of Function and Regulation of Microtubules and Transcriptional Gene Expression Machinery
Characterization of the architecture and the interactions that regulate the microtubule cytoskeleton and the process of transcription initiation in eukaryotes using cryo-EM

P01 GM051487 (Nogales, Eva) 06/01/16-05/31/19

Electron Microscopy of Biological Macromolecules
Structural studies of microtubule dynamics and interaction with kinetochore complexes.

101525—004 (Niyogi, Kris) 10/01/17-09/30/20
DOE
The regulation of photosynthetic light harvesting
This research program aims to investigate the fundamental principles underlying the regulation of photosynthetic light harvesting in algae, mosses, and plants using an integrating approach that takes full advantage of the outstanding resources and highly complementary combination of expertise in the study of photosynthesis.
Role: Co-Investigator

HHMI 003073 (Nogales, Eva) 09/01/00-present
Structural Characterization of Macromolecular Assemblies
Gaining mechanistic insight into crucial molecular processes in the life of the eukaryotic cell.

BIOGRAPHICAL SKETCH

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NAME: Avinash Patel

eRA COMMONS USER NAME (credential, e.g., agency login): PATELAB

POSITION TITLE: Graduate students

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Irvine	BS	2013	Molecular Biology and Biochemistry
University of California, Berkeley	PhD	In progress	Biophysics

A. Personal Statement

My PhD thesis focus has been to determine mechanism of transcription initiation. I have used cryo-EM to determine the structures of several transcription complexes involved in the eukaryotic transcription initiation. Cryo-EM is the best means to determine these structures as they are relatively large and flexible.

B. Positions and Honors

C. Contributions to Science

I have used cryo-EM to determine the structure of the general transcription factor IID (TFIID). From my findings I have determine the mechanism for how TFIID load TBP onto promoter DNA. From further analysis of the data the mechanism by which the transcription preinitiation complex assembly further assembles has also been determined.

D. Additional Information: Research Support and/or Scholastic Performance