## BIOGRAPHICAL SKETCH

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NAME: Ribera, Angeles Badell

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

POSITION TITLE: Professor and Chair, Department of Physiology and Biophysics

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 |
|---|---|---|---|
| Harvard-Radcliffe College, Cambridge, MA | A.B. | 06/1976 | Biochemistry |
| Columbia University, New York, NY | M.A. | 05/1978 | |
| | M.Phil. | 05/1979 | |
| | Ph.D. | 05/1982 | |
| Institut Pasteur, Paris, France | Postdoctoral | 03/1985 | Neurobiologie Moléculaire |
| | Postdoctoral | 08/1988 | Developmental Neurobiology |

### A. Personal Statement

I have served as the PD of our P30 award during for the past 13.5 years. My own research benefits from the resources made available by Cores A and B as well as advice from Core C regarding design of behavioral experiments. My research addresses questions that lie at the intersection of ion channel and developmental biology. There are two complementary foci: 1) developmental regulation of ion channel expression and function, and 2) ion channel-dependent regulation of development. Using the *Xenopus* and zebrafish embryo models, my research has revealed unsuspected roles for voltage-gated sodium & potassium channels and neurotransmitter & ion transporters in several key developmental events including neuronal survival, morphological differentiation, development of electrical membrane properties and maintenance of the differentiated state (e.g., Jones and Ribera, 2004; Jones et al., 2005; Nick and Ribera, 200; Svoboda et al., 2001; Pineda et al., 2006; Pineda and Ribera, 2006; 2008; Pineda and Ribera, 2008; Fein et al., 2008; Wright et al., 2010; Wright and Ribera, 2010; McKeown et al., 2011; Doganli et al., 2012; 2013). Several of our findings have received special recognition by the Journals in which they appeared (e.g., Wright et al., 2010; Wright and Ribera, 2010).

I have been on the Faculty at the University of Colorado since 1990. Over the past 25 years, I have collaborated with and trained several post-doctoral fellows, PhD graduate students, MD-PhD students, undergraduate and professional research assistants in the context of accomplishing our research goals. They have developed their individual careers in the context of important contributions to my research program. Five previous trainees currently have Faculty positions (U Minn, U Mich, U Colo), another is the Director of Research at the Colorado Neurological Institute, one previous trainee started a company and another is a leader in the Denver Start-Up community. In addition, I have a history of successful national and international collaborations (e.g., Kukuljan group, U Santiago, Chile; Isom group, U Mich, Ann Arbor; Lykke-Hartmann group, Aarhus University, Denmark). Beyond the science *per se*, the mentoring of junior scientists and collaborations with other PIs have made my career in research and academics especially rewarding. This led me to be involved in teaching or directing summer neuro-related courses at Cold Spring Harbor Laboratories and the Marine Biological Laboratory. At the University of Colorado School of Medicine (UCSOM), I have been an active participant in the Neurosciences Graduate Program, having chaired program committees (Retreat, Curriculum, Seminar) and also served as Director of the program for two years (2010-2012).

**B. Positions and Honors**

**Employment and Leadership**

| | |
|---|---|
| 1983-1985 | Postdoctoral Fellow (MDA Fellowship), Institut Pasteur, Paris, France |
| 1985-1988 | Postdoctoral Fellow (NRSA NIH Fellowship)<br>Department of Biology, University of California San Diego |
| 1988-1990 | Assistant Research Biologist<br>Department of Biology, University of California San Diego |
| 1990-1995 | Assistant Professor<br>Department of Physiology & Biophysics, University of Colorado School of Medicine |
| 1995-2001 | Associate Professor and award of Tenure<br>Department of Physiology & Biophysics, University of Colorado School of Medicine |
| 1997-1998 | Visiting Scientist, Max-Planck Institut für Entwicklungsbiologie, Tübingen, Germany,<br>Abteilung III-Genetik (Dr. Christiane Nüsslein-Volhard, Sponsor) |
| 2001 – present | Full Professor<br>Department of Physiology & Biophysics, University of Colorado School of Medicine |
| 2004 – 2015 | Associate Director<br>Medical Scientist Training Program, University of Colorado School of Medicine |
| 2010 – 2012 | Director Neuroscience Program<br>Graduate School, University of Colorado Denver |
| 2010 – 2012 | Associate Director - Education<br>Center for Neuroscience, University of Colorado School of Medicine |
| 2012 – 2014 | Interim Chair<br>Department of Physiology and Biophysics, University of Colorado School of Medicine |
| 2013-2014 | Leadership in Team Science Program Fellow, University of Colorado School of Medicine |
| 2014 – present | Chair<br>Department of Physiology and Biophysics, University of Colorado School of Medicine |
| 2014 – present | Associate Director - Research Cores<br>Center for Neuroscience, University of Colorado School of Medicine |
| 2016-2017 | Executive Leadership in Academic Medicine Fellow, Drexel University |

**Honors**

| | |
|---|---|
| 1988-1993 | NIH FIRST Award |
| 1991-1993 | Basil O'Connor Scholar, March of Dimes |
| 1991-1994 | Klingenstein Fellow in the Neurosciences |
| 1991-1996 | NIH Research & Career Development Award |
| 1997-1998 | John S. Guggenheim Foundation Fellow |
| 1997-1998 | Fogarty International Fellowship |
| 1997-1998 | Fulbright Kommission Award |
| 1999 and 2000 | Nominator, MacArthur Foundation |
| 2004 and 2005 | Excellence in Teaching Award, University of Colorado School of Medicine |
| 2005 | Kaiser Permanente Award, Best Basic Science Teacher |
| 2009 | Dean's Mentoring Award, University of Colorado Graduate School |
| 2011 | St. Geme Mentoring Award<br>Department of Pediatrics, University of Colorado School of Medicine |

**Editorial/Grant Review**

| | |
|---|---|
| 1989-1992 | Regular Member, NSF Neuronal and Glial Mechanisms Panel |
| 1995 | NSF, Committee of Visitors for Neuroscience |
| 1995 | March of Dimes, Basil O'Connor Awards Review Panel (Ad-Hoc Member) |
| 1995-1997 | Regular Member, NIH Neurology B1 Study Section |
| 1996-2001 | Associate Editor, Journal of Neuroscience (Developmental Neurobiology) |
| 1997 | NSF POWRE Panel Member |
| 1998 | Journal of Neurobiology, Guest Co-Editor (Ion Channels Special Issue, 1998) |
| 1998-1999 | Regular Member, NIH MDCN-3 Study Section |

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| 2000-2004 | Regular Member, NIH NSD-C Study Section |
| 2001 | Ad Hoc Member, Fogarty International Center ICP Study Section |
| 2002-2014 | Editorial Board, Journal of Neurophysiology |
| 2004–2009 | March of Dimes, Review Committee C |
| 2005-2008 | HHMI Medical Fellowship Review Panel |
| 2006–2011 | Regular Member, NIH BPNS Study Section |
| 2012 – present | Ad Hoc Reviewer for several NIH Study Sections |
| 2013 | Member, NIH Director Pioneer Award Study Section |
| 2014 | Member, NSF Integrative Organismal Systems (IOS) Study Section |
| 2015 | External Reviewer, Cell Biology and Neuroscience Department, Montana State |
| 2019-2023 | Regular Member, NIH MNG Study Section |
| 2019 | Special Topics Guest Editor, Frontier in Molecular Neuroscience |

**C. Contributions to Science**

My contributions to science have consistently concerned ion channel function in the context of development. While the model systems used and experimental methods have changed over time, the focus has been on ion channels in the context of development.

1) *Voltage-gated potassium currents are the primary determinant of the action potential waveform of embryonic neurons, and the relevant channel isoforms depend upon the identify of the neuron.* In several systems, embryonic neurons show a dramatic developmental regulation of the waveform of the action potential. Intracellular recording methods had demonstrated that for embryonic Xenopus spinal neurons, action potentials are initially long-duration, calcium-dependent events that subsequently mature to the stereotypic sodium-dependent brief impulses (Baccaglini and Spitzer, 1977). Spurred by the recent advent of patch-clamp recording methods, I used the *Xenopus* embryo spinal neuron culture model to identify the voltage-dependent currents that underlie the generation of the action potential at different stages of development. The results demonstrated that voltage-gated potassium (K) current undergoes dramatic upregulation during development, and it is these changes that underlie those in the action potential waveform. Moreover, the transcriptional requirements for the K current upregulation needed to occur during a limited, critical period.

a) O'Dowd DK, Ribera AB, Spitzer NC. Development of voltage-dependent calcium, sodium, and potassium currents in *Xenopus* spinal neurons. J Neurosci. 1988 Mar;8(3):792-805.

b) Ribera AB, Spitzer NC. A critical period of transcription required for differentiation of the action potential of spinal neurons. Neuron. 1989 Jan;2(1):1055-62.

Incorporating gene cloning and molecular biology approaches subsequently led to the identification of specific K channel genes expressed by *Xenopus* spinal neurons. Given that the heterogeneous population of spinal neurons all showed similar developmental regulation of K current and the action potential, I had initially hypothesized that *a common mechanism governed the electrical differentiation of all spinal neurons.* However, subsequent work provided the unexpected finding that spinal neuron heterogeneity was evident in the repertoire of potassium channel genes expressed by individual neurons, despite their electrophysiological similarities. The mechanisms that coordinate electrical differentiation of neurons remain to be identified.

c) Ribera AB. A potassium channel gene is expressed at neural induction. Neuron. 1990 Nov;5(5):691-701.

d) Ribera AB. Homogeneous development of electrical excitability via heterogeneous ion channel expression. J Neurosci. 1996 Feb 1;16(3):1123-30.

*2) Ion channel activity regulates development of spinal neurons and the somatosensory system.* Studies using either the *Xenopus* spinal neuron system or the zebrafish embryo revealed novel roles for the activity of specific ion channels in spinal neuron survival, morphological differentiation, synapse maturation and maintenance of the differentiated state.

a) Nick TA, Ribera AB. Synaptic activity modulates presynaptic excitability. Nat Neurosci. 2000 Feb;3(2):142-9.

b) Svoboda KR, Linares AE, Ribera AB. Activity regulates programmed cell death of zebrafish Rohon-Beard neurons. Development. 2001 Sep;128(18):3511-20.

c) Pineda RH, Svoboda KR, Wright MA, Taylor AD, Novak AE, Gamse JT, Eisen JS, Ribera AB. Knockdown of Nav1.6a Na+ channels affects zebrafish motoneuron development. Development. 2006 Oct;133(19):3827-36. **(Highlighted in *Research Highlights* in Nature Reviews Neuroscience [7: 759, 2006])**

d) Wright MA, Ribera AB. Brain-derived neurotrophic factor mediates non-cell-autonomous regulation of sensory neuron position and identity. J Neurosci. 2010 Oct 27;30(43):14513-21. PMCID: PMC3319702. **(Highlighted in *This Week in the Journal).***

*3) Novel mechanisms regulate sensory neuron sodium current.* RB sensory neurons mediate the touch response for the zebrafish embryo. Taking advantage of mutations, gene knock-downs or hormones that reduced the embryonic touch response, novel pathways regulating sodium current were identified.

a) Ribera AB, Nüsslein-Volhard C. Zebrafish touch-insensitive mutants reveal an essential role for the developmental regulation of sodium current. J Neurosci. 1998 Nov 15;18(22):9181-91.
b) Yonkers MA, Ribera AB. Sensory neuron sodium current requires nongenomic actions of thyroid hormone during development. J Neurophysiol. 2008 Nov;100(5):2719-25. PMCID: PMC2585397.
c) Moreno RL, Ribera AB. Spinal neurons require Islet1 for subtype-specific differentiation of electrical excitability. Neural Dev. 2014 Aug 22;9:19. doi: 10.1186/1749-8104-9-19. PMCID: PMC4153448.
d) Carmean V, Yonkers MA, Tellez MB, Willer JR, Willer GB, Gregg RG, Geisler R, Neuhauss SC, Ribera AB. *pigk* mutation underlies macho behavior and affects Rohon-Beard cell excitability. J Neurophysiol. 2015 Aug;114(2):1146-57. PMCID: PMC4541141.

*4) Zebrafish sensory neurons undergo cellular reprogramming in vivo, even under control conditions.* The work revealed an unsuspected degree of plasticity in the differentiated state of dorsal root ganglion neurons.

*Wright MA, Mo W, Nicolson T, Ribera AB. I*n vivo* evidence for transdifferentiation of peripheral neurons. Development. 2010 Sep;137(18):3047-56. PMCID: PMC2926955 **(Highlighted in *In this Issue*).**

**Complete Publication List (51 total):**

http://www.ncbi.nlm.nih.gov/sites/myncbi/1h1Wgs7NlXL/bibliography/40691383/public/?sort=date&direction=ascending

## D. Research Support

**Ongoing research support**

National Institutes of Health R01 NS086839 Ribera, A.B. (PI) 02/01/2014 - 01/31/2020
NINDS: Neuronal Transdifferentiation *in vivo*: Mechanism and Potential
The major goals of this project are to identify the mechanisms underlying the process by which dorsal root ganglion neurons undergo transdifferentiation *in vivo*.

National Institutes of Health P30 NS048154 Ribera, A.B. (PI) 09/15/2004 - 12/31/2019
NINDS: Rocky Mountain Neurological Disorders Center Core:
This grant provides funds for four cores (Light Microscopy, Genetic Constructs, Zebrafish Facility, Machine Shop) that support neuroscience research at UCAMC. The award underwent a 1st competitive renewal in 2009. Year 11 started on January 1, 2016 and will supports three new Cores: Optogenetics, Nanoscopy, Animal Behavior.