BIOGRAPHICAL SKETCH

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NAME: Morgan, Deri

POSITION TITLE: Assistant Professor

eRA COMMONS USER NAME (credential, e.g., agency login): dmorgan1

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
Queen Elizabeth Comprehensive, Carmarthen, UK		07/1992	
University of Wales, Swansea, UK	B.Sc.	07/1997	Biochemistry
University of Hertfordshire, Hatfield, UK	Ph.D	12/2002	Pharmacology
Rush University Medical Center, Chicago, IL		02/2001 to present	Voltage gated proton channels

A. Personal Statement

I have worked on voltage gated proton channels for over 14 years, most of my professional life. The wide variety of projects I have been involved with over that time has given me experience in a range of techniques including patch clamp, confocal microscopy, cellular assays, biochemistry, molecular biology and gene targeting. These techniques and the experience of having investigated the role of voltage gated proton channels in a variety of different systems makes me uniquely suited to the project at hand. I am invested in the physiological roles of the channel and understanding the structure and function of these channels is imperative to elucidating the channel's role in various systems. I am excited to work on this project and continuing to contribute to the understanding of the form and function of this channel in nature.

B. Positions and Honors

Positions and Employment

2001-2010. Instructor, Department of Physiology, Rush Presbyterian St. Luke's Medical Center, Chicago, Illinois

2010-present. Assistant Professor, Department of Physiology, Rush University Medical Center, Chicago, Illinois

Professional Memberships

Biophysical Society (2001-present)

University Committees, Administrative Work (selected)

2010-present Department Advisory Committee

Honors

2003 Sigma Xi – RUSH excellence in research

C. Contributions to Science

1. Beginning in 2001, I learned and perfected the perforated patch clamp technique in the DeCoursey lab. Using this technique we confirmed that the role of voltage gated proton channels in human phagocytes was to prevent the self inhibition of NADPH oxidase during the respiratory burst. We showed that the NADPH oxidase ceased to function at voltages >200 mV and that electron current from the oxidase was exquisitely sensitive to changes in pH. Both high membrane potentials and low intracellular pH occur during the respiratory burst and we showed the voltage gated proton channel alleviates both of these stressors. We also showed, using the perforated patch technique, that the channel enters an "enhanced gating mode" due to phosphorylation at Thr^{29} that improves the channel's ability to perform both the voltage and pH compensation roles.
    a. DeCoursey, T.E., D. Morgan, and V.V. Cherny. (2003). The voltage dependence of NADPH oxidase reveals why phagocytes need proton channels. ***Nature***. 422:531-534.
    b. Morgan, D., V.V. Cherny, R. Murphy, B.Z. Katz, and T.E. DeCoursey. (2005). The pH dependence of NADPH oxidase in human eosinophils. ***Journal of Physiology***. 569:419-431.
    c. Morgan, D., V.V. Cherny, A. Finnegan, J. Bollinger, M.H. Gelb, and T.E. DeCoursey. (2007). Sustained activation of proton channels and NADPH oxidase in human eosinophils and murine granulocytes requires PKC but not $cPLA_2\alpha$ activity. ***Journal of Physiology***. 579:327-344.
    d. Musset, B., M. Capasso, V.V. Cherny, D. Morgan, M. Bhamrah, M.J.S. Dyer, and T.E. DeCoursey. (2010). Identification of Thr^{29} as a critical phosphorylation site that activates the human proton channel *Hvcn1* in leukocytes. ***Journal of Biological Chemistry***. 285:5117-5121.

2. My first project in the DeCoursey lab was to demonstrate, unequivocally, that the voltage gated proton channel and the NADPH oxidase were separate entities. Several labs reported that a component of NADPH oxidase was the voltage gated proton channel. We showed in 2002 that cells expressing NADPH oxidase components did not have proton currents. Even though our data was strong, it was not until the channel was cloned in 2006 that the debate was settled and our work proved correct. I also contributed to disproving the claims that phagocytes contain BK channels. This claim created a large controversy in the phagocyte field until the original paper Ahluwalia et al., 2004 was retracted in 2010.
    a. DeCoursey, T.E., V.V. Cherny, D. Morgan, B.Z. Katz, M.C. Dinauer. (2001). The $gp91^{phox}$ component of NADPH oxidase is not the voltage-gated proton channel in phagocytes, but it helps. ***Journal of Biological Chemistry***. 276:36063-36066.
    b. Morgan, D., V.V. Cherny, M.O. Price, M.C. Dinauer, and T.E. DeCoursey. (2002). Absence of proton channels in COS-7 cells expressing functional NADPH oxidase components. ***Journal of General Physiology***. 119:571-580.
    c. DeCoursey, T.E., D. Morgan, and V.V. Cherny. (2002). The $gp91^{phox}$ component of NADPH oxidase is not a voltage-gated proton channel. ***Journal of General Physiology***. 120:773-779.
    d. Femling, J.K., V.V. Cherny, D. Morgan, B. Rada, A.P. Davis, G. Czirják, P. Enyedi, S.K. England, J.G. Moreland, E. Ligeti, W.M. Nauseef, and T.E. DeCoursey. (2006). The antibacterial activity of human neutrophils and eosinophils requires proton channels but not BK channels. ***Journal of General Physiology***. 127:659-672.

3. In 2008 I became the first person to modify the SEER technique (Launikonis et al., 2005) for use with pH dyes. Previously, the SEER technique had only been used for Ca^{2+} imaging and my adaptation of this technique allowed sensitive pH measurements in individual living cells. Using this technique we showed that, contrary to established dogma, phagocytosing neutrophils undergo a rapid acidification upon the initiation of phagocytosis. The drop in pH recovers over time due to the pH compensating mechanisms of the cell. We showed that voltage gated proton channels were essential for the recovery of this pH spike. We showed that basophils also show a drop in intracellular pH when stimulated to release histamine and this drop is exacerbated by the block of voltage gated proton channels.

a. Morgan, D., M. Capasso, B. Musset, V.V. Cherny, E. Ríos, M.J.S. Dyer, T.E. DeCoursey. (2009). Voltage-gated proton channels maintain pH in human neutrophils during phagocytosis. ***Proceedings of the National Academy of Sciences, U.S.A.*** 106:18022-18027.
b. Musset, B., D. Morgan, V.V. Cherny, D.W. MacGlashan Jr, L.L. Thomas, E. Ríos, T.E. DeCoursey. (2008) A pH-stabilizing role of voltage-gated proton channels in IgE-mediated activation of human basophils. ***Proceedings of the National Academy of Sciences, U.S.A.*** 105(31):11020-5.

4. I have been involved in structure function studies of the voltage gated proton channel since it was cloned in 2006. These structure function studies have contributed several significant advances in the proton channel field. We demonstrated that an aspartate residue was crucial for proton selectivity and permeation (Musset et al, 2011) and that this aspartate must reside within two turns of the helix in the middle of S1 (Morgan et al., 2013). Recent collaborations involving quantum mechanical calculations have modelled the mechanism by which the aspartate, along with arginines on S4 mediates proton permeation and selectivity.

a. Musset, B., S.M.E. Smith, S. Rajan, D. Morgan, V.V. Cherny, and T.E. DeCoursey. (2011). Aspartate 112 is the selectivity filter of the human voltage gated proton channel. ***Nature***. 480:273-277.
b. Kulleperuma, K., S.M.E. Smith, D. Morgan, B. Musset, J. Holyoake, N. Chakrabarti, V.V. Cherny, T.E. DeCoursey, and Régis Pomès. (2013). Construction and validation of a homology model of the human voltage-gated proton channel hH_V1. ***Journal of General Physiology***. 141:445-465.
c. Morgan, D., B. Musset, K. Kulleperuma, S.M.E. Smith, S. Rajan, V.V. Cherny, R. Pomès, T.E. DeCoursey. (2013). Peregrination of the selectivity filter delineates the pore of the human voltage gated proton channel hH_V1. ***Journal of General Physiology.*** 142:625-640.
d. Dudev, T., B. Musset, D. Morgan, V.V. Cherny, S.M.E. Smith, K. Mazmanian, T.E. DeCoursey, and C. Lim. (2015). Selectivity mechanism of the voltage-gated proton channel, H_V1. ***Scientific Reports***. 5:10320.

D. Research Support

Ongoing Research Support

R01 GM102336 DeCoursey (PI) Smith (co-PI) 09/01/2013-04/30/2017
"Selectivity and Permeation in the Human Voltage-gated Proton Channel, hH_V1"
The goals include identifying the molecular components of the permeation pathway and determining the mechanisms that produce proton selective conduction.
Role : Co-investigator

MCB-1242985 DeCoursey (PI) S.M.E. Smith (co-PI) 09/01/2013-08/31/2017.
"Collaborative Research: Voltage-gated Proton Channels in Dinoflagellates." National Science Foundation.
The goals include identifying proton channel genes in bioluminescent dinoflagellates, expressing them and determining their properties and functions.
Role:Co-investigator
My role included maintaining dinoflagellates, isolating scintillons (intracellular organelles), measuring luminescence, and patch-clamp.

Bears Care Morgan PI 1/31/2014-1/31/2016
RTSC: The Role of Voltage-Gated Proton Channels in pH Regulation and Reactive Oxygen Species in Metastatic Breast Cancer Cells.
The goal of this project is to establish a link between the expression of voltage gated proton channels and cellular metabolism in metastasizing breast cancer cells
Role - PI

Gavers Community Cancer Fund Morgan PI 1/31/2014-1/31/2016
The Relationship Between Voltage Gated Proton Channels and NADPH Oxidase in Metastatic Breast Cancer
The goal of this project is to demonstrate a relationship between voltage gated proton channels and NADPH oxidase activity in a breast cancer cell line.
Role - PI

Completed Research Support

NSF EAGER Proposal No: 0943362. 09/01/2009 to 08/31/2011.
“Bioluminescence in Dinoflagellates Triggered by Voltage-gated Proton Channels.”
The goal was to identify proton channels in dinoflagellates and determine if they activate bioluminescence.
Role – Co-investigator

NIH R01 R01-GM087507 DeCoursey (PI) 05/01/2010 to 4/30/2014.
“Structure-Function Relationships of Voltage-Gated Proton Channels.”
The goal was to identify structural components of the proton channel molecule that play key roles in function.
Role – Co-investigator