

BIOGRAPHICAL SKETCH

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NAME Bonny Lynn Dickinson	POSITION TITLE Assistant Professor The Research Institute for Children and the Louisiana State University Health Sciences Center		
eRA COMMONS USER NAME BDICKINSON			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Santa Clara University, Santa Clara, CA	BS	1987-1991	Biology
Tulane University, New Orleans, LA	PhD	1991-1995	Microbiology & Immunology
National Heart, Lung, and Blood Institute, NIH, Bethesda, MD	Postdoctoral fellow	1996-1997	Biochemistry
Children's Hospital and Harvard Medical School, Boston, MA	Postdoctoral fellow	1997-2000	Gastrointestinal Cell Biology
Children's Hospital and Harvard Medical School, Boston, MA	Instructor in Pediatrics	2000-2004	Gastrointestinal Cell Biology

A. Positions and Honors

Positions and Employment

- 2004 - present Assistant Professor of Pediatrics at the Louisiana State University Health Sciences Center School of Medicine and The Research Institute for Children, New Orleans, LA
- 2004 - present Assistant Professor of Microbiology, Immunology and Parasitology at the Louisiana State University Health Sciences Center School of Medicine
- 2004 - present Adjunct Assistant Professor in the Department of Microbiology and Immunology at Tulane University, New Orleans, LA
- 2004 - present Distinguished faculty member at the Center of Excellence in Oral and Craniofacial Biology. Louisiana State University Health Sciences Center School of Medicine

Other Experience and Professional Memberships

- 2004 - present Institutional Animal Care and Use Committee, The Research Institute for Children, Children's Hospital, New Orleans, LA
- 2004 Search Committee to nominate an incumbent for the T.G. and Doris Solomon Family Endowed Chair for the Study of Crohn's Disease and Related Disorders
- 1992 - present American Society for Microbiology
- 1997 - present American Association for the Advancement of Sciences
- 2003 - present American Society for Cell Biology
- 2006 - present Crohn's and Colitis Foundation of America
- 2006 - present North American Society for Pediatric Gastroenterology, Hepatology and Nutrition
- 2006 - present Graduate committee member, LSUHSC Department of Genetics
- 2007 - present Reviewer, The Journal of Pediatric Gastroenterology and Nutrition

Honors

- 1991 Class honors, Magna Cum Laude, Santa Clara University
- 1995 Leah Seidman Shaffer Award, Tulane University, New Orleans, LA
- 2002 Laura and Arthur Colwin Fellowship Award for summer research at the Marine Biological Laboratory, Woods Hole, MA
- 2003 Excellence in Teaching Award for Integrated Human Physiology on behalf of the Class of 2006 at Harvard Medical School and Harvard School of Dental Medicine
- 2005 Junior faculty award for best poster presentation. LSUHSC Pediatrics Research Day
- 2007 Participant in the 1st NASPGHAN Junior Faculty Academic Skills Workshop
- 2007 Elected member of the LSUHSC Faculty Assembly

Patents

"Construction and characterization of a non-toxic mutant of the *Escherichia coli* heat-labile enterotoxin effective as an oral adjuvant" US patent number: TX 4-346-544, issued 10/10/96

B. Peer-reviewed publications

1. **Dickinson BL** and JD Clements. 1995. Dissociation of *Escherichia coli* Heat-Labile Enterotoxin Adjuvanticity from ADP-Ribosyltransferase Activity. Infection and Immunity. 63: 1617-1623
2. Rufo PA, Merlin D, Riegler M, Ferguson-Maltzman MH, **Dickinson BL**, Brugnara C, Alper SL, and WI Lencer. 1997. The Antifungal Antibiotic, Clotrimazole, Inhibits Chloride Secretion by Human Intestinal T84 Cells via Blockade of Distinct Basolateral K⁺ Conductances: Demonstration of Efficacy in Intact Rabbit Colon and in an *In Vivo* Mouse Model of Cholera. Journal of Clinical Investigation. 100: 3111-3120
3. **Dickinson BL**, Badizadegan K, Wu Z, Ahouse JC, Zhu X, Simister NE, Blumberg RS, and WI Lencer. 1999. Bidirectional FcRn-Dependent IgG Transport in a Polarized Human Intestinal Epithelial Cell Line. Journal of Clinical Investigation. 104: 903-911
4. Badizadegan K, **Dickinson BL**, Wheeler HE, Blumberg RS, Holmes RK, and WI Lencer. 2000. Heterogeneity of Detergent-Insoluble Membranes from Human Intestine Containing Caveolin-1 and Ganglioside G_{M1}. American Journal of Physiology, Gastrointestinal & Live Physiology. 278:G895
5. Blumberg RS, van de Wal Y, Claypool S, Corazza N, **Dickinson B**, Nieuwenhuis E, Pitman R, Spiekermann G, Zhu X, Colgan S, Lencer WI. 2001. The multiple roles of major histocompatibility complex class-I-like molecules in mucosal immune function. Acta Odontol Scand. 59(3):139
6. Zhu X, Meng G, **Dickinson BL**, Li X, Mizoguchi E, Miao L, Wang Y, Robert C, Wu B, Smith PD, Lencer WI, and RS Blumberg. 2001. MHC Class I- Related Neonatal Fc Receptor for IgG is Functionally Expressed in Monocytes, Macrophages, and Dendritic Cells. J. Immunol. 166(5):3266
7. Claypool SM, **Dickinson BL**, Yoshida M, Lencer WI, and RS Blumberg. 2002. Functional Reconstitution of Human FcRn in MDCK Cells Requires Co-Expressed Human β_2m . J. Biol. Chem. 277(31):28038
8. Spiekermann, GM, Finn PW, Ward ES, Dumont J, **Dickinson BL**, Blumberg RS, and WI Lencer. 2002. Receptor-mediated IgG Transport Across Mucosal Barriers in Adult Life: Functional Expression of FcRn in the Mammalian Lung. J. Exp. Med. 196(3):303
9. Shah U, **Dickinson BL**, Blumberg RS, Simister NE, Lencer WI, and WA Walker. 2003. Distribution of the IgG Fc Receptor, FcRn in the Human Fetal Intestine. Pediatr. Res. 53(2):295
10. Claypool SM, **Dickinson BL**, Wagner JS, Johansen F-E, Venu N, Borawski JA, Lencer WI, and RS Blumberg. 2004. Bi-directional Transepithelial IgG Transport by a Strongly Polarized Basolateral Membrane Fc gamma-Receptor. Molecular Biology of the Cell. 15(4):1746
11. **Dickinson BL**, Claypool SM, D'Angelo JA, Aiken MA, Venu N, Yen EH, Wagner JS, Borawski JA, Pierce AT, Hershberg R, Blumberg RS, and WI Lencer. 2008. Ca²⁺-dependent Calmodulin-binding to FcRn Affects IgG Transport in the Transcytotic Pathway. Molecular Biology of the Cell. 19:414
12. Anosova, NG, Chabot S, Shreedhar V, Borawski JA, **Dickinson BL**, and MR Neutra. 2008. Cholera toxin, *E. coli* heat-labile toxin, and non-toxic derivatives induce dendritic cell migration into the follicle-associated epithelium of Peyer's patches. Mucosal Immunology. 1:59

Book Chapters

1. **Dickinson BL** and JD Clements. 1996. Use of *Escherichia coli* Heat-Labile Enterotoxin as an Oral adjuvant, in MUCOSAL VACCINES: New Trends In Immunization. H Kiyono, PL Ogra, and JR McGhee, Eds. Academic Press. 73-85
2. **Dickinson BL** and WI Lencer. 2003. Transcytosis of Bacterial Toxins Across Mucosal Barriers, in Bacterial Protein Toxins. D Burns, J Barbieri, B Iglewski, and R Rappuoli. ASM Press 173-186
3. F-E Johansen, E Yen, **BL Dickinson**, M Yoshida, S Claypool, RS Blumberg, WI Lencer. 2006. Biology of Gut Immunoglobulins. L. Johnson Ed. Physiology of the Gastrointestinal Tract, 4eC. Research Support

Manuscripts Under Preparation

1. The Cyclic AMP-Protein Kinase A Pathway Regulates Dendritic Cell Random Migration and Chemotaxis. Jone Garai, June A. D'Angelo, YongKeun Park, Martha L. Aiken, Eric Morales, Kamran Badizadegan, Michael S. Feld, and **Bonny L. Dickinson**.
2. Dendritic Cells Express a Functional Cystine/Glutamate Antiporter. June A. D'Angelo, Jone Garai, Eric Morales, and **Bonny L. Dickinson**.

Current Support

1. Title: Cholera toxin increases dendritic cell expression of CXCR4 and CXCR7 and drives SDF-1-dependent chemotaxis by activating PKA, Epac1, or both molecules

Funding agency: Louisiana Board of Regents PFund Award; Total award \$10,000

Dates 5/1/08 – 4/30/09

Role: PI

Overlap: 100%

Specific Aim 1: Determine whether cholera toxin activation of protein kinase A, the Epac1-Rap1 pathway, or both regulates dendritic cell CXCR4 expression and SDF-1-dependent chemotaxis.

- Verify that the mechanism by which cholera toxin increases dendritic cell expression of CXCR4 and SDF-1-dependent chemotaxis depends upon toxin activation of adenylate cyclase and the generation of cAMP.
- Verify that cholera toxin modulation of dendritic cell CXCR4 expression and SDF-1-dependent chemotaxis is dependent upon activation of protein kinase A.
- Determine whether cholera toxin modulation of dendritic cell CXCR4 expression and SDF-1-dependent chemotaxis is dependent upon activation of the Epac1-Rap1 pathway.

Specific Aim 2: Define the molecular mechanism(s) by which cholera toxin regulates dendritic cell CXCR4 expression and SDF-1-dependent chemotaxis.

- Determine whether the mechanism involves regulation at the transcriptional, translational, or post-translational level (i.e. increased expression of CXCR4 on the plasma membrane or decreased internalization of membrane-associated CXCR4).

2. Title: Cholera Toxin Regulates Dendritic Cell Chemotaxis

Funding agency: Louisiana State University Health Sciences Center; Total award \$50,000

Role: PI

Anticipated start date: January 1, 2009

Overlap: 50%

Specific Aim 1: Measure the rate and directionality of DC spontaneous migration and CXCL12- and CCL19-directed chemotaxis following activation with CT or LPS.

A major limitation of the Transwell system for measuring cell locomotion is that it does not distinguish chemotaxis (*direction* of cell locomotion determined by a chemical substance) from chemokinesis (*speed* of cell locomotion determined by a chemical substance), and it does not provide information on spontaneous migration. In this aim we will use time-lapse video microscopy to better understand how CT regulates DC chemotaxis, chemokinesis, and spontaneous migration.

- A. Measure the rate of DC spontaneous migration and CXCL12- and CCL19-directed chemotaxis using phase-contrast time-lapse video microscopy.
- B. Quantify the effect of highly selective PKA and Epac agonists on DC spontaneous migration and CXCL12- and CCL19-directed chemotaxis with time-lapse video microscopy.
- C. Quantify the effect of specific small molecule CXCR4 and CXCR7 agonists and antagonists on DC spontaneous migration and CXCL12- and CCL19-directed chemotaxis with time-lapse video microscopy.

Specific Aim 2: Determine whether oxygen levels regulate the DC chemotaxis.

Currently, DC chemotaxis is studied under non-physiologic atmospheric oxygen levels (20% O₂/ 5% CO₂/75% N₂). However, DCs migrate through inflamed peripheral tissues and within lymph nodes, microenvironments that exhibit 2-4-fold lower oxygen levels. In this aim we will study DC chemotaxis under both atmospheric oxygen levels and physiological oxygen levels (5% O₂/ 5% CO₂/ 90% N₂) using hypoxia chambers.

- A. Examine the effect of physiological oxygen levels on DC spontaneous migration and CXCL12- and CCL19-directed chemotaxis using a Transwell chamber system.
- B. Determine whether oxygen levels regulate DC expression of the CXCL12 chemokine receptors CXCR4 and CXCR7, and the CCL19 chemokine receptor CCR7 using flow cytometry.

3. Title: Human carcinoid tumor dysregulation of dendritic cell function

Funding agency: Louisiana State University Health Sciences Center; Total award \$60,000

Role: Co-PI

Anticipated start date: January 1, 2009

Overlap: None

Specific Aim 1: Elucidate the mechanisms by which carcinoid tumors induce DC apoptosis.

- A. Verify and extend the observation that carcinoid tumors induce DC apoptosis. Tumor-conditioned medium will be tested for apoptotic activity against DCs. In all studies, colon carcinomas will be examined to determine whether carcinoid-induced DC apoptosis is unique to carcinoid, or a mechanism shared by other cancers.
- B. Determine whether oxygen tension and pH influence carcinoid-induced DC apoptosis. Conditioned medium collected from tumors grown under atmospheric oxygen tension at neutral pH, or under hypoxic and acidic conditions will be tested for the ability to induce DC apoptosis.
- C. Determine whether angiogenesis is required for carcinoid tumor induced DC apoptosis. We will examine tumor-conditioned medium collected from tumors at various stages of angiogenesis for apoptotic activity against DCs.

Specific Aim 2: Determine whether carcinoid tumor-derived factors inhibit DC chemotaxis.

- A. Determine whether carcinoid tumors release factors that impair DC chemotaxis. We will determine whether the absence of DCs in carcinoid tumors reflects tumor-mediated dysregulation of DC chemotaxis. DCs will be cultured with tumor-conditioned medium (6-12h) and examined for a defect in chemotaxis towards inflammatory chemokines associated with tumors and lymph node-directing chemokines using Transwell chamber assays, phase contrast time-lapse video microscopy, and quantitative phase microscopy.
- B. Determine whether hypoxia and acidic pH, conditions that characterize the tumor microenvironment, are essential to regulate DC chemotaxis. DCs will be cultured under atmospheric oxygen tension at neutral pH, or under hypoxic and acidic conditions and chemotaxis will be assessed as described in Aim 2A.
- C. Determine whether angiogenesis is required for carcinoid tumor dysregulation of DC chemotaxis using the approach described in Aim 2A.

Specific Aim 3: Identify the carcinoid tumor-derived factors that regulate DC apoptosis and/or chemotaxis.

- A. We will use a series of chromatographic separations in combination with mass spectrometry and proteomics to identify factors elaborated by tumors that regulate DC apoptosis and chemotaxis. If oxygen tension and pH regulate carcinoid tumor secretion of factors that induce DC apoptosis and/or chemotaxis, we will also analyze medium collected from tumors cultured under hypoxic and acidic conditions.

Pending Support

None.

Completed Funding

2000-2002	NIH NIDDK Individual National Research Service Award (NRSA)
2000, 2002	American Gastroenterology Association student fellowship awards to train high school summer students in the laboratory
2000-2001	Harvard Digestive Diseases Center Pilot/Feasibility Grant (PI)
2001-2004	NIH NIDDK Mentored Research Scientist Development Award (K01)
2004-2006	Crohn's and Colitis Foundation of America Senior Scientist Award (PI)