BIOGRAPHICAL SKETCH

NAME: Katherine L. Knight

eRA COMMONS USER NAME: kknight

POSITION TITLE: Professor and Chair

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	FIELD OF STUDY
Elmira College	BA	Chemistry
Indiana University, Bloomington, Indiana	PhD	Biochemistry
University Illinois Chicago, Chicago, Illinois	Post-doctoral	Immunogenetics

Personal Statement

I am a molecular immunologist, having spent most of my career studying B lymphocyte development and antibody structure and genetics. We discovered that the intestinal microbiota is required for development of gut-associated lymphoid tissues and for the generation of the primary antibody repertoire. This work led us to search for other functions the microbiota play in host defense. We discovered that a molecule, EPS, of the biofilm made by the harmless commensal organism *Bacillus subtilis* protects mice from enteric disease caused by infection. We discovered that EPS functions by generating anti-inflammatory monocytic cells which protect mice from enteric disease caused by bacterial infection, sepsis from *Staphyloccus aureus*, allergic responses, and graft vs host disease after allogeneic stem cell transplantation. Our goal is to develop EPS into a prophylactic to prevent GVHD and other inflammatory diseases.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

1989-Present Professor and Chair, Department of Microbiology & Immunology, Stritch School of Med. Loyola University Chicago
2007-2015 Co-Founder and Co-Director, Infectious Disease and Immunology Institute, Loyola University Chicago
1980 Visiting Associate, California Inst. Technology, Pasadena, CA
1975-1976 Scientist, Basel Institute of Immunology, Basel, Switzerland.
1968-1989 Assistant Professor, Associate Professor, Professor, Dept. of Microbiology and Immunology, University of Illinois Medical School, Chicago, Illinois.

Honors

2019 Recipient, Distinguished Fellow of the American Association of Immunologists
2015 Recipient, Marion Spencer Fay Award, Drexel University
2014 Master Teacher Award, Loyola University Stritch School of Medicine
2013 Lifetime Achievement Award: American Association of Immunologists
1996-1997 President, American Association of Immunologists
1992-1996 Elected, Council Member of American Association of Immunologists

1986 AAAS Elected Fellow

C. Contributions to Science

1. **Probiotic EPS protection from inflammatory diseases.** After discovering the requirement of intestinal bacteria for generation of the primary antibody repertoire, we began to examine intestinal bacteria protection from enteric pathogens. We found that a single dose of the commensal bacteria *Bacillus subtilis* can protect mice from disease caused by the enteric pathogen, *Citrobacter rodentium*. We identified the protective molecule as bacterial exopolysaccharide (EPS). While numerous probiotic bacteria have been identified, EPS was only the 2nd molecule (in addition to PSA from *B. fragilis*) to be identified with probiotic-like properties. The mechanism of action for EPS is however, significantly different from that of PSA because protection is mediated through anti-inflammatory M2 macrophages. We also found that EPS protects from allergic sensitization, sepsis due to *Staphylococcus aureus* infection, and graft vs host disease. Recent data demonstrate that EPS-treated DC inhibit GvHD in a humanized mouse model.

   a. Paynich, M.L., Jones- Burrage, S.E., and Knight, K.L., (2017) Exopolysaccharide from Bacillus subtilis induces anti-inflammatory M2 macrophages that inhibit T cell mediated diseases. *J. Immunology*, **198**:2689-98. PMID: 28202619

   b. Paik, W., Alonzo, F. III, Knight, K.L. (2019) Probiotic exopolysaccharide protects against systemic *Staphylococcus aureus* infection, inducing dual-functioning macrophages that restrict bacterial growth and limit inflammation. *Infection and Immunity* **87**: e00791-18. PMID:30396894

   c. Kalinina, O, Talley, S., Zamora-Pineda, J., Paik, W., Campbell, E., and Knight, K. L., (2021) Amelioration of graft-versus-host disease by exopolysaccharide from a commensal bacterium. *J. Immunology* **206**:2101-2108 PMID: 33846225

   d. Kalinina, O., Minter, L.M., Sperling, A.I., Hollinger, M.K., Le, P., Osborne, B.A., Zhang, S., Stiff, P., and Knight, K.L., (2023) Exopolysaccharide-treated dendritic cells effectively ameliorate acute graft vs host disease. *Transplantation and Cellular Therapy*. doi.org/10.1016/j.jtct.2023.10.023

2. **Genetics of rabbit allotypes and generation of a rabbit hybridoma fusion partner.** We studied rabbit allotypes for several decades and mapped the IgH chain locus, showing that the genome contains a single Cγ gene and 13 Cα genes. We also generated transgenic rabbits, and developed a plasmacytoma. From this, we generated a hybridoma fusion partner, 240E. All currently available commercial and non-commercial hybridoma-derived rabbit monoclonal antibodies are derived from this cell line.

   a. Burnett, R. C. Hanly, W. C., Zhai, S. and Knight, K. L. (1989) The IgA Heavy Chain Gene Family in Rabbit: Cloning and Sequence Analysis of 13 Cα genes. EMBO J., 8, 4041-4047.PMID 2512120
   b. Knight, K.L., Burnett, R.C. and McNicholas, J.M. (1985). Organization of rabbit immuno-globulin heavy chain genes, J. Immunol., 134: 1245-1250.PMID 25185680
   c. Spieker-Polet, H., Setupathi, P., Yam, P.C. and Knight, K.L. (1995) Rabbit Monoclonal Antibodies: Generating a Fusion Partner to Produce Rabbit-Rabbit Hybridomas. Proc. Natl. Acad. Sci. 92:9348-9352.PMID 7568130

   We also solved the "antibody enigma" which was: If multiple V_H genes are present in the germline, how could essentially all rabbit IgH chains carry the same allelically-inherited allotypic marker? We solved this problem by showing that although the rabbit VH locus contains multiple functional VH gene segments, only one of them is used in almost all VDJ gene rearrangements.

a. Knight, K. L. and Becker, R. S. (1990) Molecular basis of the allelic inheritance of rabbit immunoglobulin VH allotypes: Implications for the generation of antibody diversity. Cell 60, 963-970. PMID 2317867

3. **Generation of the Primary Antibody Repertoire.** After showing that rabbits utilize only one VH gene segment in most VDJ gene rearrangements, we then asked how a diverse antibody repertoire was generated. We showed that, like chickens, rabbits diversify the Ig genes by somatic gene conversion. We also showed that the VDJ genes diversify by somatic hypermutaion.

   a. Becker, R. S. and Knight, K. L., (1990) Somatic Diversification of Immunoglobulin Heavy Chain VDJ Genes: Evidence for Somatic Gene Conversion in Rabbits, Cell, 63, 987-997.PMID2124176

   b. Lanning, D. and Knight, K.L., (1997). Somatic Hypermutation: Mutations 3' of Rabbit VDJ H-Chain Genes, J. Immunology, 159:4403-4407.

   c. Winstead, C. R., Zhai, S.-K., Sethupathi, P. And Knight, K. L., (1999) Antigen-induced somatic diversification of rabbit IgH genes: Genes conversion and hyperpointmutation. *J. Immunology*, 162:6602-6612. PMID10352277

4. **B cell development and aging.** After showing that Ig of all B cells was somatically diversified by a few weeks after birth, we found that essentially all rabbit B cells are made by ~ 2 months of age. After 6 months of age, B lymphopoiesis is almost undetectable, meaning that rabbit B cells must be long-lived and/or self-renewing. A similar decline of B lymphopoiesis is not observed in mice or humans, but is likely similar to other species such as chickens and sheep where the sites of generation of the Ab repertoire (bursa and ileal Peyer's patch, respectively) involute early in life. We have recently made the novel finding that adipocytes inhibit B lymphopoiesis and that this process is mediated by MDSCs and IL-1.

   a. Jasper, P., Zhai, S.-K., Kalis, S.L., Kingzette, M. and Knight, K.L. (2003) B Lymphocyte Development in Rabbit: Progenitor B cells and Waning of B Lymphopoiesis, *J. Immunology*, 171: 6372-6380. PMID:14662835

   b. Bilwani, F. and Knight, K.L., (2012) Adipocyte-derived factor(s) inhibits early stages of B-lymphopoiesis in rabbits and humans, *J. Immunology*, **189**:4379-4386. PMID 23002443

   c. Kennedy, D.E. and Knight, K.L. (2015) Inhibition of B lymphopoiesis by adipocytes and IL-1-producing myeloid-derived suppressor cells. *J. Immunology*, **195**:2666-2674 doi:10.4049/jimmunol.1500957

   d. Kennedy, D.E. and Knight, K.L. (2017) Inflammatory changes in bone marrow microenvironment associated with declining B lymphopoiesis. J. Immunology **198**:3471-3479 DOI: https://doi.org/10.4049/jimmunol.1601643 Highlighted "In this issue"

5. **Importance of GALT and intestinal microbiota for B cell development.** After discovering that Ig genes of all B cells were somatically diversified, we asked where the diversification occurred. We found that somatic diversification of Ig genes occurs in GALT and that it requires bacteria. We showed that some, but not all bacteria can promote B cell expansion and somatic diversification in GALT.

   a. Vajdy, M., Setupathi, P., and Knight, K.L., (1998). Dependence of antibody somatic diversification on gut-associated lymphoid tissue in rabbits. *J. Immunology*, 160:2725-2729.

   b. Rhee, K.-J., Sethupathi, P., Driks, A., Lanning, D.K., Knight, K.L.. (2004) Development of Gut-Associated lymphoid tissues and preimmune antibody repertoire by select commensal microflora. *J. Immunology*, 172:1118. PMID:14707086

c. Rhee, K.-J., Jasper, P.J., Sethupathi, P., Shanmugam, M., Lanning, D and Knight, K.L., (2005) Positive selection of the peripheral B cell repertoire in gut-associated lymphoid tissue. *J. Exptl. Med.*, 201:55-62. PMID: 15623575

d. Bukhari, A., Kalinina, O., and Knight, K.L. Death of Tonsillar B Cells by NETosis. (2023) Cell Death Discovery, **9**:108 PMID 36997529

URL for My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1ZEqnZZJjwcQx/bibliography/47956439/public/?sort=date&direction=ascending