
BIOGRAPHICAL SKETCH

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NAME Stephen J. Barenkamp		POSITION TITLE Professor of Pediatrics and Molecular Microbiology	
eRA COMMONS USER NAME (credential, e.g., agency login) barenskj			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Carleton College, Northfield, MN	BA	06/73	Chemistry
University of Chicago, Chicago, IL	MD	06/77	Medicine

A. Personal Statement

The goal of this proposal is to develop and evaluate prototype vaccines for the prevention of otitis media based upon the HMW1/HMW2 and Hia adhesion proteins of nontypeable *Haemophilus influenzae*. My laboratory has more than 25 years experience in the investigation of this bacterial species. In earlier NIH-funded studies, for which I served as the principal investigator, we discovered and characterized the HMW1/HMW2 and Hia proteins, and cloned and sequenced prototype *hmw1/hmw2* and *hia* genes. In complementary studies, we developed a large panel of monoclonal antibodies against the HMW1/HMW2 and Hia proteins and generated a large set of HMW1/HMW2 and Hia recombinant proteins that will be a major focus of the work proposed in the current project. In later NIH-funded work, for which I also served as the principal investigator, we demonstrated the protective ability of parental immunization with HMW1/HMW2 proteins in the chinchilla otitis media model and developed the opsonophagocytic assay for nontypeable *Haemophilus influenzae*. As part of this latter work, we demonstrated that antibodies directed against both the HMW1/HMW2 and Hia proteins were capable of mediating opsonophagocytic activity against homologous and heterologous nontypeable *Haemophilus influenzae*. Finally, in our more recent funded work, we generated a set of prototype recombinant adenovirus vaccines expressing recombinant HMW1/HMW2 and Hia proteins that are a central focus of the current proposal. We have a very large collection of nontypeable *Haemophilus influenzae* isolates collected from patients with acute nontypeable *Haemophilus influenzae* disease and we have extensive experience with all of the experimental methods that will be used in the current proposal. Thus, my laboratory has a track record of successful and productive research in this very important research area that has laid a solid foundation for the studies proposed as part of the current project.

B. Positions and Honors

University and Hospital Appointments

1982-1992 Assistant Professor of Pediatrics, Washington University School of Medicine
1992-1997 Associate Professor of Pediatrics, St. Louis University School of Medicine
1994- Director, Division of Pediatric Infectious Diseases, Cardinal Glennon Children's Medical Center
1997- Professor of Pediatrics, St. Louis University School of Medicine
2000- Professor of Molecular Microbiology and Immunology, St. Louis University School of Medicine

Professional Memberships, Editorial Boards, and Recent NIH Committee Experience

1984- Member, American Society for Microbiology
1987- Member, The Society for Pediatric Research
1987- Fellow, Infectious Diseases Society of America
1998- Member, American Pediatric Society
2006- Editorial Advisory Board, The Journal of Infectious Diseases

Study Section Member, 2000-2005, Auditory System Study Section, NIH

Ad-Hoc Study Section Member, 2005, Microbial Pathogenesis Special Emphasis Panel, NIH

Ad-Hoc Study Section Member, 2005 and 2006, Auditory System Study Section, NIH

Ad-Hoc Member, 2008, Board of Scientific Counselors, Intramural Laboratory Site Visit, NIDCD, NIH

Ad-Hoc Study Section Member, 2008, 2009, 2010, 2011, and 2012, Clinical Research and Field Studies of Infectious Diseases Study Section, NIH

Ad-Hoc Study Section Member, 2012, Vaccines against Microbial Diseases Study Section, NIH

C. Selected peer-reviewed publications (from a total of 62)

1. Barenkamp SJ, Munson RS Jr, Granoff DM. Subtyping isolates of *Haemophilus influenzae* type b by outer membrane protein profiles. *J Infect Dis* 143:668-676, 1981. [PMID:6972422].
2. Barenkamp SJ, Granoff DM, Munson RS Jr. Outer-membrane protein subtypes of *Haemophilus influenzae* type b and spread of disease in day-care centers. *J Infect Dis* 144:210-217, 1981. [PMID:6974205].
3. Edmonson B, Granoff DM, Barenkamp SJ, Chesney JP. Outer membrane protein subtypes and investigation of recurrent *Haemophilus influenzae* type b disease. *J Pediatr* 100:202-208, 1982. [PMID:6977023].
4. Barenkamp SJ, Munson RS Jr, Granoff DM. Outer membrane protein and biotype analysis of pathogenic nontypable *Haemophilus influenzae*. *Infect Immun* 36:535-540, 1982. [PMID:6979511].
5. Barton LL, Granoff DM, Barenkamp SJ. Nosocomial spread of *Haemophilus influenzae* type b infection documented by outer membrane protein subtype analysis. *J Pediatr* 102:820-824, 1983. [PMID:6602214].
6. Munson RS Jr, Shenep JL, Barenkamp SJ, Granoff DM. Purification and comparison of outer membrane protein P2 from *Haemophilus influenzae* type b isolates. *J Clin Invest* 72:677-684, 1983. [PMCID: PMC1129227].
7. Hampton CM, Barenkamp SJ, Granoff DM. Comparison of outer membrane protein subtypes of *Haemophilus influenzae* type b isolates from healthy children in the general population and from diseased patients. *J Clin Microbiol* 18:596-600, 1983. [PMCID: PMC270860].
8. Shenep JL, Munson RS Jr, Barenkamp SJ, Granoff DM. Further studies of the role of noncapsular antibody in protection against experimental *Haemophilus influenzae* type b bacteremia. *Infect Immun* 42:257-263, 1983. [PMCID: PMC264552].
9. Barenkamp SJ, Shurin PA, Marchant CD, Karasic RB, Pelton SI, Howie VM, Granoff DM. Do children with recurrent *Haemophilus influenzae* otitis media become infected with a new organism or reacquire the original strain? *J Pediatr* 105:533-537, 1984. [PMID: 6332891].
10. Glode MP, Halsey NA, Murray M, Ballard TL, Barenkamp SJ. Epiglottitis in adults: Association with *Haemophilus influenzae* type b colonization and disease in children. *Pediatr Infect Dis* 3:548-551, 1984. [PMID: 6393079].
11. Murphy TV, Granoff DM, Chrane DF, Olsen KD, Barenkamp SJ, Dowell SF, McCracken GH Jr. Pharyngeal colonization with *Haemophilus influenzae* type b in children in a day care center without invasive disease. *J Pediatr* 106:712-716, 1985. [PMID: 3873532].
12. Bodor FF, Marchant CD, Shurin PA, Barenkamp SJ. Bacterial etiology of the conjunctivitis-otitis media syndrome. *Pediatrics* 76:26-28, 1985. [PMID: 3874389].
13. Alpert G, Campos JM, Smith DR, Barenkamp SJ, Fleisher GR. Incidence and persistence of *Haemophilus influenzae* type b upper airway colonization in patients with meningitis. *J Pediatr* 107:555-557, 1985. [PMID: 3876417].
14. Musser JM, Barenkamp SJ, Granoff DM, Selander RK. Genetic relationships of serologically nontypable and serotype b strains of *Haemophilus influenzae*. *Infect Immun* 52:183-191, 1986. [PMCID: PMC262217].
15. Barenkamp SJ. Protection by serum antibodies in experimental nontypable *Haemophilus influenzae* otitis media. *Infect Immun* 52:572-578, 1986. [PMCID: PMC261039].
16. Barenkamp SJ, Bodor FF. Development of serum bactericidal activity following nontypable *Haemophilus influenzae* acute otitis media. *Pediatr Infect Dis J* 9:333-339, 1990. [PMID: 2352818].
17. Barenkamp SJ, Leininger E. Cloning, expression and DNA sequence analysis of genes encoding nontypable *Haemophilus influenzae* high molecular weight surface-exposed proteins related to filamentous hemagglutinin of *Bordetella pertussis*. *Infect Immun* 60:1302-1313, 1992. [PMCID: PMC256997].
18. St Geme JW III, Falkow S, Barenkamp SJ. High molecular weight proteins of nontypable *Haemophilus influenzae* mediate attachment to human epithelial cells. *Proc Natl Acad Sci USA* 90:2875-2879, 1993. [PMCID: PMC46199].

19. Barenkamp SJ, St Geme JW III. Genes encoding high molecular weight adhesion proteins of nontypable *Haemophilus influenzae* are part of gene clusters. *Infect Immun* 62:3320-3328, 1994. [PMCID: PMC302962].
20. Noel GJ, Barenkamp SJ, St Geme JW III, Haining WN, Mosser DM. High molecular weight surface-exposed proteins of *Haemophilus influenzae* mediate binding to macrophages. *J Infect Dis* 169:425-429, 1994. [PMID: 8106776].
21. Barenkamp SJ, St Geme JW III. Identification of a second family of high molecular weight adhesion proteins expressed by nontypable *Haemophilus influenzae*. *Mol Microbiol* 19:1215-1223, 1996. [PMID: 8730864].
22. Barenkamp SJ. Immunization with high molecular weight adhesion proteins of nontypable *Haemophilus influenzae* modifies experimental otitis media in chinchillas. *Infect Immun* 64:1246-1251, 1996. [PMCID: PMC173911].
23. Barenkamp SJ, St Geme JW III. Identification of surface-exposed B-cell epitopes on high molecular weight adhesion proteins of nontypable *Haemophilus influenzae*. *Infect Immun* 64:3032-3037, 1996. [PMCID: PMC174184].
24. Gu X-X, Tsai C-M, Ueyama T, Barenkamp SJ, Robbins JB, Lim DJ. Synthesis, characterization, and immunologic properties of detoxified LOS from nontypeable *Haemophilus influenzae* conjugated to proteins. *Infect Immun* 64:4047-4053, 1996. [PMCID: PMC174335].
25. St Geme JW III, Cutter D, Barenkamp SJ. Characterization of the genetic locus encoding *Haemophilus influenzae* type b surface fibrils. *J Bacteriol* 178:6281-6287, 1996. [PMCID: PMC178501].
26. Gu X-X, Sun J, Jin S, Barenkamp SJ, Lim DJ, Robbins JB, Battey J. Detoxified lipooligosaccharide from nontypeable *Haemophilus influenzae* conjugated to proteins confers protection to otitis media in chinchillas. *Infect Immun* 65:4488-4493, 1997. [PMCID: PMC175645].
27. St Geme JW III, Kumar VV, Cutter D, Barenkamp SJ. Prevalence and distribution of the *hmw* and *hia* genes and the HMW and Hia proteins among genetically diverse strains of nontypable *Haemophilus influenzae*. *Infect Immun* 66:364-368, 1998. [PMCID: PMC107903].
28. Gu X-X, Chen J, Barenkamp SJ, Robbins JB, Tsai C-M, Lim D, Battey J. Synthesis and characterization of lipooligosaccharide-based conjugates as vaccine candidates for *Moraxella (Branhamella) catarrhalis*. *Infect Immun* 66:1891-1897, 1998. [PMCID: PMC108140].
29. Dawid S, Barenkamp SJ, St Geme JW III. Variation in expression of the *Haemophilus influenzae* HMW adhesins: A prokaryotic system reminiscent of eukaryotes. *Proc Natl Acad Sci USA* 96:1077-1082, 1999. [PMCID: PMC15353].
30. Lottenbach KR, Mink CM, Barenkamp SJ, Anderson EL, Homan SM, Powers DC. Age-associated differences in IgG1 and IgG2 subclass antibodies to pneumococcal polysaccharides following vaccination. *Infect Immun* 67:4935-4938, 1999. [PMCID: PMC96832].
31. Zhou J, Lottenbach KR, Barenkamp SJ, Lucas AH, Reason DC. Recurrent variable region gene usage and somatic mutation in the human antibody response to the capsular polysaccharide of *Streptococcus pneumoniae* type 23F. *Infect Immun* 70:4083-4091, 2002. [PMCID: PMC128163].
32. Laarmann S, Cutter D, Juehne T, Barenkamp SJ, St Geme JW. The *Haemophilus influenzae* Hia autotransporter harbors two adhesive pockets that reside in the passenger domain and recognize the same host cell receptor. *Mol Microbiol* 46:731-743, 2002. [PMID: 12410830].
33. Winter LE, Barenkamp SJ. Human antibodies specific for the high molecular weight adhesion proteins of nontypable *Haemophilus influenzae* mediate opsonophagocytic activity. *Infect Immun* 71:6884-6891, 2003. [PMCID: PMC308909].
34. Grass S, Buscher AZ, Swords WE, Apicella MA, Barenkamp SJ, Ozchlewski N, St Geme JW III. The *Haemophilus influenzae* HMW1 adhesin is glycosylated in a process that requires HMW1C and phosphoglucomutase, an enzyme involved in lipooligosaccharide biosynthesis. *Mol Microbiol* 48:737-751, 2003. [PMID: 12694618].
35. Surana NK, Cutter D, Barenkamp SJ, St Geme JW III. The *Haemophilus influenzae* Hia autotransporter contains an unusually short, trimeric translocator domain. *J Biol Chem* 279:14679-14685, 2004. [PMID: 14726537].
36. Zhou J, Lottenbach KR, Barenkamp SJ, Reason DC. Somatic hypermutation and diverse immunoglobulin gene usage in the human antibody response to the capsular polysaccharide of *Streptococcus pneumoniae* type 6B. *Infect Immun* 72:3505-3514, 2004. [PMCID: PMC415722].
37. Buscher AZ, Burmeister K, Barenkamp SJ, St Geme JW III. Evolutionary and functional relationships among the nontypeable *Haemophilus influenzae* HMW family of adhesins. *J Bacteriol* 186:4209-4217, 2004. [PMCID: PMC421621].

38. Le T, Cherry JD, Chang S-J, Knoll MD, Lee ML, Barenkamp SJ, Bernstein D, Edelman R, Edwards KM, Greenberg D, Keitel W, Treanor J, Ward JI. Immune responses and antibody decay after immunization of adolescents and adults with an acellular pertussis vaccine: The APERT study. *J Infect Dis* 190:535-544, 2004. [PMID: 15243929].
39. Lottenbach KR, Granoff DM, Barenkamp SJ, Powers DC, Kennedy D, Irby-Moore S, Homan SM, Mink CM. Safety and immunogenicity of *Haemophilus influenzae* type b polysaccharide or conjugate vaccines in an elderly adult population. *J Amer Geriatr Soc* 52:1883-1887, 2004. [PMID: 15507066].
40. Cherry JD, Chang S-J, Klein D, Lee M, Barenkamp SJ, Bernstein D, Edelman R, Decker MD, Greenberg DP, Keitel W, Treanor J, Ward JI. Prevalence of antibody to *Bordetella pertussis* antigens in serum specimens obtained from 1793 adolescents and adults. *Clin Infect Dis* 39:1715-1718, 2004. [PMID: 15578376].
41. Ward JI, Cherry JD, Chang S-J, Partridge S, Lee H, Treanor J, Greenberg D, Keitel W, Barenkamp S, Bernstein D, Edelman R, Edwards K, Rabinovich R, and the APERT Study Group. *Bordetella pertussis* infections in vaccinated and unvaccinated adolescents and adults in a prospective national randomized acellular pertussis vaccine trial (APERT). *N Engl J Med* 353:1555-1563, 2005. [PMID: 16221778].
42. Ward JI, Cherry JD, Chang S-J, Partridge S, Keitel W, Edwards K, Lee H, Treanor J, Greenberg D, Barenkamp S, Bernstein D, Edelman R, and the APERT Study Group. *Bordetella pertussis* infections in vaccinated and unvaccinated adolescents and adults as assessed in a national prospective randomized acellular pertussis vaccine trial (APERT). *Clin Infect Dis* 43:151-157, 2006. [PMID: 16779740].
43. Winter LE, Barenkamp SJ. Antibodies specific for the high molecular weight adhesion proteins of nontypable *Haemophilus influenzae* are opsonophagocytic for both homologous and heterologous strains. *Clin Vaccine Immunol* 13:1333-1342, 2006. [PMCID: PMC1694446].
44. Winter LE, Barenkamp SJ. Antibodies specific for the Hia adhesion proteins of nontypeable *Haemophilus influenzae* mediate opsonophagocytic activity. *Clin Vaccine Immunol* 16:1040-1046, 2009. [PMCID: PMC2708409].
45. Winter LE, Barenkamp SJ. Construction and immunogenicity of recombinant adenovirus vaccines expressing the HMW1/HMW2 or Hia adhesion proteins of nontypeable *Haemophilus influenzae*. *Clin Vaccine Immunol* 17:1567-1575, 2010. [PMCID: PMC2952983].
46. Simon GC, Martin RJ, Smith S, Thaikootathil J, Bowler RP, Barenkamp SJ, Chu HW. Up-regulation of MUC18 in airway epithelial cells by IL-13: Implications in bacterial adherence. *Am J Respir Cell Mol Biol* 44:606-613, 2011. [PMCID: PMC3095981].

D. Current Research Support

1R01 AI081887 Barenkamp (PI) 5/01/11 - 4/30/15
 National Institutes of Health: NIAID
 Title: Development of a vaccine for prevention of *Haemophilus influenzae* otitis media

The overall goals of this project are characterize the contribution of antibodies against the HMW1/HMW2 and Hia proteins to the human protective immune response against nontypeable *Haemophilus influenzae*, to construct recombinant adenovirus vaccines expressing HMW1/HMW2 or Hia proteins, and to assess the protective ability of the vaccines in an animal model of infection.