Identification of protective immune responses and development of vaccines against ETEC and H. pylori

Research group: Ann-Mari Svennerholm, Professor, MD, PhD; Anna Lundgren, PhD; Joshua Tobias, PhD; Marianne Jertborn, Professor, MD, PhD; Susanna Leach, MD, PhD student; Jennie Adamsson, M. Lic.; Joanna Kaim, M.Sc.; Gudrun Wiklund, Research engineer/BMA; Biljana Aleksic, M.Sc., Lisbeth Eklund, Research nurse

Projects: Enterotoxigenic *Escherichia coli* (ETEC) is the most common cause of diarrhea in children in developing countries and in travelers to these areas. We are studying the prevalence of such bacteria and their expression of various virulence factors in different countries and populations using phenotypic and genotypic methods. We are also conducting studies on identification of protective immune mechanisms against ETEC in animal and human birth cohort studies in ETEC endemic countries as a basis for development of an effective ETEC vaccine. Such a candidate oral ETEC vaccine consisting of recombinant *E. coli* bacteria over-expressing the main protective ETEC antigens and a new toxoid component has been produced under GMP conditions and will be tested by us for safety and immunogenicity in an initial Phase I clinical during 2010. This study will be followed by evaluation of a more complete ETEC vaccine together with a new mucosal adjuvant in Phase I and II trials, initially in Swedish adults and subsequently in children in an ETEC endemic area. As a basis for the vaccine trials work is in progress to establish optimal methods to determine mucosal immune responses and immunological memory to oral vaccines in humans. We are also, in collaboration with international scientists, exploring different possibilities for the decreased immunogenicity of oral vaccines in children in developing countries. This is done by evaluating the influence of different nutritional factors, breastfeeding, parasitic infections, tropical enteropathy and various environmental factors, for vaccine immunogenicity.

Since *H. pylori* is one of the most common gastrointestinal infections that primarily infect young children, in particular in developing countries, we are also studying infection with these bacteria and development of immune responses in children during the first years of life in a high endemic area, i.e. Bangladesh. This includes studies to evaluate a possible protective role of maternal antibodies, both transferred via placenta and breast milk antibodies, and if protective immunity can develop in infants that may explain spontaneous eradication. We are also comparing mucosal and systemic immune responses in Swedish and Bangladeshi asymptomatic carriers and duodenal ulcer patients as a background for development of an *H. pylori* vaccine that
can be used worldwide. Studies are also in progress to try to identify immunological markers or down-regulated immune responses that may be related to development of gastric cancer in *H. pylori* infected individuals.

**Collaborations:** Main collaborations with researchers at ICDDR,B in Dhaka, Bangladesh, Johns Hopkins in Baltimore, IVI in Seoul, Korea, and Harvard, Boston, USA. We are also part of a large EU consortium (STOPENTERICS) for development of vaccines against ETEC and Shigella. We have also ongoing, active collaborations with institutes/universities in several developing countries in Africa and Latin America.

**References in the field of total ca 400 (A-MS):**

**Original articles:**


**Reviews:**


Short Curriculum Vitae, Ann-Mari Svennerholm, 471213-1442

Civil status:
Married (to professor Jan Holmgren)
Two children, born 1978 and 1984

Education:
PhD, University of Gothenburg (UG) 1975
Associate Professor “Docent” in Medical Microbiology at UG, 1975
Medical Licentiate (M.D.), 1977

Current positions:
Professor of Infection & Immunity, UG, 1994 -
Head, Department of Microbiology and Immunology, 2006 –

Previous positions and periods of appointment:
1975-78 Assistant Professor in Tropical Medicine, Swedish Medical Research Council
1978-88 Associate professor, the Department of Medical Microbiology, UG
1988-94 Professor of Infections and Immunity, Swedish Medical Research Council
1999-2003, Vicerector, University of Gothenburg

Research training:
- PhD students: main supervisor 16, co-supervisor ca 15; 4 PhD students at present
- postdocs ca 25; 5 at present

National and international assignments of importance; University of Gothenburg:
- Committee for Recruitment of Professors to the Faculty, 1994-2001.
- Committees for Appointing Professors to Medical Faculty (Tjänsteförslags-nämnderna) 1994-99
- Responsible for Equality between sexes (“Jämställdhetsansvarig”), Med. Faculty, 1994- 2003
- The Board of the Medical Faculty (“Fakultetsnämnden”), 1997- 2003.
- The Medical Faculty Committee for Research (“Forskningsnämnden”), 1997-2003
- Vice rector, UG, with special responsibility for gender equality and equity, 1999-2003
- Chairperson of the Election Committee at the Sahlgrenska Academy, UG, 2005- 2008
- Head Department of Microbiology and Immunology , 2006 -

National and International, member of the:
- Board of the National Bacteriol. Laboratory in Sweden (SBL), 1992-93.
- Board of the Swedish Institute for Infectious Disease Control (SMI), 1993-97.
- Medical Working Groups, Board of Strategic Funds Sweden (SSF) 1995-96 & 2003-04
- Board of the Swedish Research Council (MFR&VR, medicine), 1995-98 & 2004-06
- Swedish SAREC expert group for Health 1999-04.

Present Committees and Missions:
- Steering Committee on Diarrheal Disease Vaccines WHO, 2003-; Chairperson 2006-
- Board Global Health and Vaccine (GLOBVAC) program, Norwegian Research Council 05-, Chairperson 2006-
- Board of Institute for One World Health, Seattle 2006-
- Board of the International Vaccine Institute (IVI), Korea 2007-
- Board of the Centre for Global health, KI, Stockholm, 2007-
- Director, WHO reference lab for research on ETEC, 2007-
- Director, Center for Global Health, SA, UG, 2009-
- Swedish Research Links committee, the Swedish Research Council, 2008-
- The committee for Future research leaders, SSF, 2010

Major research areas:
Basic studies on mechanisms of disease and immunity in enterotoxin-induced diarrhoeal diseases; development of diagnostic methods for detection and epidemiologic studies of enteropathogens; development of oral cholera and E. coli (ETEC) vaccines including phase I-III clinical trials; development of methods and basic studies of mucosal immune response to vaccines and infections in human; studies of pathogenic and immune mechanisms in Helicobacter pylori infections including identification of prognostic markers for gastric cancer and work on the development of a therapeutic vaccine against such infections.

Main collaborations:
With research groups in the USA: Johns Hopkins &University of Maryland, Baltimore; NIH, Washington; WRAIR, Washington; CDC, Atlanta etc., in Europe: Pasteur Institute, Paris; Institute of International Health, Bergen, Norway; several research institutes in Holland and Belgium; in Asia: ICDDR,B, Dhaka, Bangladesh; IVI, Seoul, Korea; AFRIMS, Bangkok, Thailand; National Institute of Hygiene, Hanoi, Vietnam; Namru II, Indonesia, Aga Khan university, Karachi, Pakistan and in Latin America: UMSA, La Paz, Bolivia; Laboratorio Diagnóstico Molecular, Guatemala City, Guatemala; Mexico university, Mexico City; Instituto Nacional de Microbiologia, Buenos Aires; Universidad Peruana, Lima, Peru etc, Africa: Namru III, Cairo, Egypt; different laboratories in Mozambique, Gambia, Djibouti, Kenya, Mali, etc

Main Funding: the Swedish Research Council, Swedish SIDA, the Cancer Foundation, WHO, Gates Foundation, Marianne &Marcus Wallenberg Foundation, PATH Foundation (EVI-program), EU (STOPENTERICS), LUA-ALF etc

Distinctions:
- Eric Fernström Prize for young researchers for vaccine studies 1991.
- The Swedish Medical Society Prize (Torsten and Ragnar Söderberg’s Prize) for development of vaccines against cholera and enterotoxigenic E. coli, 1994.
- Elect member The Royal Swedish Academy of Science (KVA), 2008

Publications:
Ca 400 scientific papers (published and accepted papers and review articles) in microbiology, immunology, infectious diseases, vaccinology and biotechnology