CURRICULUM VITAE

Personal Details:

Name: Nirmala Jagadish

Date of Birth: 25th Feb'1973

Nationality: Indian

Corresponding Address c/o Dr. Anil Suri,

Genes and Protein Laboratory

Aruna Asaf Ali Marg

JNU Campus, New Delhi-67

INDIA

E-mail <u>nirmalanishi@hotmail.com</u>

nirmala@nii.res.in

Permanent Address: K G Villa, Konchady,

Yayyadi, Mangalore,

Karnataka, India.

Positions Held

Post-doctoral Project Associate, Genes and Proteins Lab, National Institute of Immunology, New Delhi, India. March 2003 - till date.

Post-doctoral Project Associate, Genes and Proteins Lab, National Institute of Immunology, New Delhi, India, from Nov'1999 to Sep'2000.

Senior research fellow in the project "Sero diagnosis of child-hood

tuberculosis" at the department of Pediatrics, King George Medical College,

Lucknow, INDIA, from July 1997 to June 1998

Education

Ph.D. (Zoology): Research work done at Dept. of Pathology, King George's Medical College, Lucknow, 2003, INDIA.

Title of the Thesis: "Histopathology of spleen and pathogenesis of anemia in malaria. Degree from Dr RML University, Faizabad, UP INDIA

M.Sc. (Zoology, Specialization Parasitology) Lucknow University, Lucknow, India. 1993 (First div).

B.Sc. Lucknow University, Lucknow, India, 1991 (First div).

Technical Experience

Cloning Isolation of plasmid and genomic DNA, cloning of various constructs for prokaryotic and eukaryotic expression studies and for gene silencing (Si RNA cloning).

Protein - Protein expression in prokaryotic system. Protein purification using affinity column chromatography, characterization by Native and SDS-PAGE, Western blotting, Immunoblotting, Protein-protein interaction.

Mammalian cell culture – Experience in culture of mammalian cells CHO, COS-1 and cancer cell lines. B16, MCF, PA cells, A549 and Hela cells, Transfection, detection of protein by immuno- fluorescence, western blotting and ECL developing.

Culture –*Plasmodium falciparum*, *M.tuberculosis* culture and drug sensitivity.

Immunology Immunoprecipitation, ELISA, IFA, Protein detection by Immunohistochemistry of various cancer tissues.

Pathology Hematology, biochemical assays, histopathology, enzyme assays.

PUBLICATIONS

- Jagadish N, Rana R, Selvi R, Mishra D, Garg M, Yadav S, Herr JC, Okumura K, Hasegawa A, Koyama K, Suri A Characterization of a novel human sperm associated antigen 9 (SPAG9) having structural homology with c-Jun NH₂-terminal Kinase interacting protein. *Biochemical Journal* 389: 73-82 2005.
- 2. **Jagadish N**, Rana R, Mishra D, Garg M, Selvi R, Suri A Characterization of immune response in mice to plasmid DNA encoding human Sperm associated antigen 9 (SPAG9). *Vaccine* Jul 29; [Epub ahead of print] 2005.
- 3. **N. Jagadish**, S. Shankar, B. Mohapatra, R. Selvi, and A. Suri. Molecular Cloning and Characterization of a Haploid Germ Cell Specific Sperm Associated Antigen 9 (*SPAG9*) from the Macaque. *Molecular and Reproduction Development* .71:58-66 2005.
- 4. Rana R, **Jagadish N**, Garg M, Mishra D, Dahiya N, Chaurasiya D, Suri A. Small interference RNA-mediated knockdown of sperm associated antigen 9 having structural homology with c-Jun N-terminal kinase-interacting protein. *Biochem Biophys Res Commun.* 2006 Feb 3; 340(1):158-64.
- **5.** R. Rana, **N. Jagadish**, M. Garg, D. Mishra, N. Dahiya, D. Chaurasiya, A. Suri. (2006) Immunogenicity study of recombinant human sperm associated antigen 9 (SPAG9) in a bonnet macaque (*Macaca radiata*): assessment of contraceptive effect of sperm based recombinant protein. Hum. Reprod. (*in press*).

- 6. **Jagadish N**, Rana R, Mishra D, Kumar M, Ramasamy S, Suri A. Sperm Associated Antigen 9 (SPAG9): a new member of c-Jun NH₂-terminal Kinase (JNK) interacting protein exclusively expressed in testis. *Keio Journal of Medicine* 54: 266-71 2005.
- 7. **Jagadish N,** Rana R, Mishra D, Garg M, Hasegawa A, Koyama K, Suri A Evaluation of humoral response of recombinant human sperm associated antigen 9 (SPAG9) in rat model. *J Reprod Immunol.* 2005 Oct; 67(1-2):69-76. Epub 2005 Sep 6.
- 8. S. Shankar, B. Mohapatra, S. Verma, R. Selvi, **N. Jagadish** and A. Suri Isolation and Characterization of a Haploid Germ Cell Specific Sperm Associated Antigen 9 (*SPAG9*) from the Baboon. *Molecular and Reproduction Development* 69:2:186-93 2004.
- 9. S Verma, B Mohapatra, **N Jagadish,** R Selvi, P Roy, A Suri. Cloning, Characterization and Expression of Testicular Transcript Abundant in Germ Cells: Human Sperm Surface Protein. *American Journal of Reproductive Immunology* 52:2:164-73, 2004.
- 10. **Nirmala**, A. Kumar, AK Kapoor, B Lal, GP Dutta and A Swaroop. *Plasmdium falciparum* Drug resistant malaria complicating leukemia and lymphomas in children. *Experimental Parasitology* 91:33-37 (1999).
- 11. A K Kapoor, **Nirmala**, B Lal, and GP Dutta. Detection of raised serum ferritin levels in patients with faciparum malaria. JNGMC 1: 21-23(2001).

Paper presented in conferences

- N. Jagadish, R. Rana, M. Garg, D. Mishra, N. Dahiya, D. Chaurasiya, A. Hasegawa, K. Koyama, A. Suri. Characterization of a haploid germ cell specific Sperm Associated Antigen 9 (SPAG9) in non-human primate. International Congress on Gamete Biology: Emerging Frontiers in Fertility and Contraceptive Development. Feb 22-25, 2006, New Delhi, India.
- R. Rana, N. Jagadish, M.Garg, D. Mishra, N. Dahiya, D. Chaurasiya, A. Suri. Small interference RNA (siRNA) mediated knockdown of Sperm Associated Antigen 9 (SPAG9) having structural homology with c-Jun-terminal kinase interacting protein. International Congress on Gamete Biology: Emerging Frontiers in Fertility and Contraceptive Development. Feb 22-25, 2006, New Delhi, India.
- 3. **N Jagadish**, Ritu Rana, Manoj Garg, Deepshikha Mishra, Neetu Dahiya, Dipak Chaurasiya, Anil Suri. Molecular cloning and Characterization of a Testis Specific Sperm Associated Antigen 9 (*SPAG9*) presented at "BIOTECH 2005", Dec 22-25, 2005, at Manesar, Gurgaon, India.

- 4. **N Jagadish**, Ritu Rana, Manoj Garg, Deepshikha Mishra, Neetu Dahiya, Dipak Chaurasiya, Akiko Hasegawa, Koji Koyama, Anil Suri. Characterization of a Haploid Germ Cell Specific Sperm Associated Antigen 9 (*SPAG9*) in non-human primate to be presented at International conference on male reproduction and infertility, Sep16-18, 2005, at IISc, Bangalore, India.
- 5. R Rana, **N Jagadish,** D Mishra, M Garg, A, Suri. An orthologue of human Sperm associated antigen 9 (SPAG9) from macaque; identification of animal model for sperm based vaccine, Presented at Advances and Challenges in Reproductive Health Research in the Post genomic era, 9-12 Jan, 2005, Mumbai, India.
- 6. **N Jagadish**, D, Mishra, M Garg, R Rana, P.Roy, A Suri. A proteomic homologue of sperm associated in sperm-egg interaction, Presented at Advances and Challenges in Reproductive Health Research in the Post genomic era, 9-12 Jan, 2005, Mumbai, India.
- 7. **N Jagadish,** S Yadav, R. Selvi, R Rana, A Hasegava, K Koyama, A Suri. Characterization of a novel human sperm associated antigen, A protein required for human sperm egg interaction, Presented at IX international congress on reproductive immunology, held at Hakone, Japan, from 11th Oct'2004 -15th Oct' 2004.
- 8. **Nirmala Jagadish,** Shikha Yadav, R. Selvi, Anil Suri. An evolutionary and molecular analysis of germ cell specific SPAG 9 gene. Presented in symposia Deep roots open sky, new biology in India, at National Institute of Immunology, on 25th Feb' 2004.
- 9. Balan, S. Vaishnava, **N. Jagadish** and A. Suri. "Cloning and Characterization of a Novel Human Sperm Specific Gene *hss*: A potential Sperm Protein for Development of Sperm Based Vaccine". Presented in International Congress on Fertilization, Embryo, Development and Implantation, National Institute of Immunology, New Delhi, India, 6-9 November 2000.
- 10. **Nirmala,** A. Kumar, AK Kapoor, B Lal, GP Dutta and A Swaroop. Drug resistant malaria complicating leukemia and lymphomas in children." presented at 2nd global meet on parasitic diseases held at Hyderabad from 18th to 22nd Aug'1997.
- 11. **Nirmala,** A. Kumar, AK Kapoor, B Lal, GP Dutta and A Swaroop. Serum iron status of patients with faciparum malaria." presented at 45th annual congress of Indian association of Pathologist and Microbiologist held at IISc, Bangalore from 18th to 22nd Dec'1996.

- 12. **Nirmala,** A. Kumar, AK Kapoor, B Lal, GP Dutta and A Swaroop. Recurrent episodes of drug resistant malaria in children with hematologic malignancies" presented at *National conference on Oncology* at KGMC, Lucknow from 1st to 3rd March 1996.
- 13. **Nirmala,** A. Kumar, AK Kapoor, B Lal, GP Dutta and A Swaroop. Possible role of antibody-dependent complement mediated immune mechanism in pathogenesis of anemia in malaria presented at 12th congress of Parasitology from 22nd to 25th Jan'1995 held at Panjim, Goa.

Workshop Attended

- 1. Satellite Symposium on Cancer Research" held at National Institute of Immunology, New Delhi, India in collaboration with Queen's University Belfast (U.K.) from 10-11 April 2006.
- 2. Indo-US joint workshop on Adjuvants, Delivery systems and combination vaccines, held at National Institute of Immunology, New Delhi, from September 20-21, 2004.
- **3.** Indo US workshop on male contraception research and the role of men in reproductive health, Held at National Institute of Immunology, New Delhi, INDIA from 20-21, October 2003.
- **4.** Cultivation of parasites of biomedical importance held at Central Drug research institute, Lucknow, INDIA from 1-10, December 1995.

FELLOWSHIP/AWARD

- **1.** Travel grant award from International society of reproductive immunology, to attend congress at Hakone Japan.
- **2.** Travel grant award from International society of Parasitology and Wellcom trust, UK, to attend 2^{nd} global meet on parasitic diseases.
- 3. Senior research fellowship from Council of science and Technology, UP, India.

Computer skill

Basic computer application in general and biological sciences as MS word, Power Point, excel, window 98, window 2000, window XP, Photo Shop, Scanning, Internet Explorer, e-mail.

Basic knowledge of Bioinformatics: - sequencing Analysis, Designing of gene specific primers from database sequences, nucleotide Blast, and lalign.

Referees:

Dr. Anil Suri

Chief, Genes and Proteins Lab. National Institute of Immunology, New Delhi 110067 Ph; 26703700, 26703720, 26717165

E.Mail-anil@nii.res.in

Dr. Lalit Garg

Chief, Gene Regulation Laboratory. National Institute of Immunology, New Delhi-110067 Ph; 26703652, 26717169 E.Mail- lalit@nii.res.in

Present research projects

We are working upon molecular characterization and expression of sperm antigen 9 (SPAG9) gene. The aims and objectives of our study are:

- 1. Characterization and expression of SPAG9 gene and its role in signaling pathway in sperm egg interaction.
- 2. To study the humoral response and SPAG9 gene expression in various cancer tissues by Immunohistochemistry.
- 3. Gene silencing of SPAG9, fused with reporter gene by using Si RNA technology in various cell lines.

Sperm antigen 9 (SPAG9) is a novel gene, isolated from testis cDNA library, is mapped to chromosome 17q21 (a chromosomal region involved in gene amplification in various cancers), and is exclusively expressed in haploid round spermatid cells during spermatogenesis. A few of the signaling molecules including G proteins, tyrosine kinases, the IP3 receptor, MAP kinases, scaffolding protein JIP1 have been found in the sperm and oocyte; however, the biochemical networks that connect these molecules and their functions are poorly understood. Studies on IB1/JIP1 in the unfertilized oocyte and the sperm indicated that it might play a role during fertilization and may possibly be linked to the JNK pathways. Recently, in human sperm, ERK a member of MAPK family was shown to be associated with human spermatozoa with direct or indirect function in sperm capacitation. Based on structural homology with JIP3, SPAG9 was earlier defined as JIP3 γ scaffolding protein and has been recently classified as JIP4 protein. It was found that SPAG9 is structurally distinct from the previously described JIP1 and JIP2 proteins. The purpose of the study was to extensively characterize SPAG9 protein and to investigate a possible role of SPAG9 molecule in human sperm-egg interaction.

Genes expressed both in normal testis and in malignancies (Cancer/ Testis antigens-CT) have become the most extensively studied antigen group in the field of tumour immunology. Forty five CT antigen genes or gene families have been identified to date, but coordinated humoral and cellular immune responses have been reported for only a few CT antigens, including MAGE-A1, MAGE-A3, and

NY-ESO-1. In this regard, *SPAG9* may be of particular interest attributed to its role in signal transduction pathways involved in reproductive processes. Recent advances in tumor immunology suggest that many tumor cells are immunogenic in the autologous setting. The immunogenicity of these cells originates from either neo-protein expressed by the tumor cells as a result of gene mutation and chromosomal translocation or aberrantly expressed normal proteins. They are normal testicular antigens expressed aberrantly in tumor cells. Their restricted normal tissue expression makes them ideal molecules for immune targeting. The identification of a panel of antigenic markers that are tumor specific and that elicit immunoreactivity early in tumor development and at high frequency would provide an effective strategy for cancer screening. We have successfully cloned testis specific gene *SPAG9*. Sequence analysis using NCBI Blast searches revealed that SPAG9 gene had nucleotide sequence similarities (hits) with ESTs from various cancerous tissues and cancer cell lines (based on exons homology with EST of human tumors). So we are investigating humoral response against SPAG9 protein by detection of circulating anti-SPAG9 antibodies in serum of various cancer patients using ELISA and Western Blotting and SPAG9 protein expression by immuno-histochemistry in various cancer tissues.

Another aim of our study is gene silencing or to knock down the expression of target SPAG9 protein by RNA interference. The RNA interference (RNAi) gene-silencing mechanism is induced by double-stranded RNA (dsRNA) and is highly sequence-specific. Small interfering RNAs (siRNAs), which are small double-stranded RNA (dsRNA) oligonucleotides with or without overhangs, are substrates for the RNA-induced silencing complex. Synthetic siRNAs strongly inhibit expression of the target protein in mammalian cells when they are transfected into the cells. So we are also exploring the potential of siRNAs by co-transfecting siRNAs with target SPAG9 gene fused with reporter gene in *in vitro* and *in vivo*.

.