Dr. A. Selvapandiyan, Ph.D.

Research Activities:

Development of Live Attenuated Vaccines for Intracellular Pathogenic Diseases: Protozoan parasites like *Plasmodium* and *Leishmania* are some of the intracellular pathogens causing a variety of diseases (including fatal manifestations) in mammals worldwide. Until now there is no licensed vaccine against any of the parasitic infections. Attempts to develop vaccines for such parasitic agents did not result in a successful vaccine candidate, which could be tested in humans. However, there is an increasing consensus among vaccine researchers that parasite persistence may be important for effective protective response and can be achieved by live attenuated parasite immunization. Many successful bacterial and viral vaccines are live attenuated pathogens that do not cause disease but retain replication and immunogenic properties and protect host from reinfection. Hence, the current research focus of the team of Dr. Angamuthu Selvapandiyan (Selva) is to develop live attenuated vaccine candidates against intracellular parasites.

Selva's work on developing live vaccines against parasitic infections, started at the Center for Biologics Evaluation and Research, FDA, Maryland, USA (1999-2009), where he was involved in developing an attenuated vaccine candidate against the fatal Visceral Leishmaniasis (VL) which is endemic in sevaral tropical countries including India. He has developed a centrin gene deleted *L. donovani* (*LdCen1-/-*) that has a defect in amastigote (mammal macrophage intracellular stage) replication both *in vitro* and *ex vivo* in human macrophages (Selvapandiyan et al 2004). Mice, hamsters and dogs immunized with *LdCen1-/-* as *in vitro* cultured promastigotes (extracellular form in the vector sandfly) showed attenuated parasite does not survive beyond few weeks in the host and induces a protective immune response against virulent challenge. The protection was long lasting signifying a sustained immunity (Selvapandiyan et al 2009; Fiuza et al 2013). These studies indicate that *LdCen1-/-* can be a safe and effective live attenuated vaccine candidate against VL. Efforts to initiate clinical trial to confirm safety and efficacy of this live attenuated vaccine candidate are also underway. Since 2009 Selva is working at IMM as Team Lead. His continued focus is to generate more such attenuated vaccine lines for the *Leishmania* infection and extend similar conceptual strategies to diseases due to other intracellular pathogens.

Predictive Immunity in vaccination: A major shortcoming in the vaccine development is the inadequate predictive power of the early immune responses mounted in the host against the vaccines. Also, for the live attenuated parasite vaccines, the primary barrier against widespread use remains the safety in terms of avirulence of the parasites in host. Therefore, understanding of the pathogenesis of live attenuated parasites in human PBMC in different clinical groups will provide valuable information regarding avirulence of parasite and efficacy prior to the evaluation in human trials. Obtaining such information via 'systems biology', proteomic and metabolomic approaches will enable us to understand how vaccine-induced immune responses are coordinately regulated in normal, infected and individuals recovered from infection. This will provide information regarding correlates of protection as well as biomarkers of safety. Finally, this research at Selva's laboratory will enable identification of immune predictors to *Leishmania* live attenuated vaccine candidate in the human cells that have not been previously identified and might be useful in shaping the final vaccine formulation in the clinical trials.

Patents

1. LIVE ATTENUATED LEISHMANIA VACCINES. **US patent number: WO 2005/021030.**
2. LIVE ATTENUATED LEISHMANIA VACCINES. **India patent number: 243725**

Selected Publications:

K. Avishek, S. Gannavaram, R. Dey, A. Selvapandiyan, HL. Nakhasi & P. Salotra et al. 2016. Gene deleted live attenuated *Leishmania* vaccine candidates against visceral leishmaniasis elicit pro-inflammatory cytokines response in human PBMCs. **Scientific Reports** 6:33059.

Selvapandiyan, A*., Ahuja, K., Krishnan, A., 2015. *Leptomonas* and *Leishmania* co-infection in leishmaniasis in India. **Parasitology,** 142(14):1657-62. *Corresponding author.

Bhattacharya P, Dey R, M, Debrabant A, Takeda K, Selvapandiyan A, McCoy JP Jr, Nakhasi HL. et al. 2015. Genetically modified live attenuated L.donovani parasites induce innate immunity through classical activation of macrophages that direct Th1 response in mice. **Infect Immun**. 83(10):3800-15.

Kavita, A., Arora, G., Khade, P., Selvapandiyan A*, 2015. Selective elimination of *Leptomonas* from the *in vitro* co-culture with *Leishmania.* **Parasitol. Intl. 64(4):1-5 *Corresponding author**.

Fiuza JA., Gannavaram S., Santiago, HC., Selvapandiyan A., et al 2015. Vaccination using live attenuated Leishmania donovani centrin deleted parasites induces protection in dogs against L. infantum. **Vaccine** 33(2):280-8.

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Sreenivas, G., Dey, R., Kumar, A., Selvapandiyan, A., Poonam S. and Nakhasi, H.L. 2014. Biomarkers of safety and immune protection for genetically modified live attenuated Leishmania vaccines against visceral leishmaniasis – discovery and implications. **Frontiers Immunol**. 23;5:241 pages 1-9.

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Fiuza JA, Santiago, H, Selvapandiyan, A., Gannavaram, S.,, R., Nakhasi, H. Fujiwara, R. 2013. Induction of immunogenicity by live attenuated *Leishmania donovani* Centrin deleted parasites in dogs. **Vaccine** 14:1785-92.

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Selvapandiyan*, A., Kumar, P., Salisbury, J., Wang, C.C. and Nakhasi, H.L. 2012. Centrins 2 and 3 involved in organelle segregation and cytokinesis in *Trypanosoma brucei*. **PLOS one** 7(9) e45288. (*Corresponding author).

Selvapandiyan, A., R. Dey, S. Nylen, R. Duncan, D. Sacks and H. L. Nakhasi 2009. Intracellular replication deficient *Leishmania donovani* induces long lasting protective immunity against visceral leishmaniasis. **J Immunol** *183:1813-1820*.

Selvapandiyan, A*., R. Duncan, P. Salotra, H. L, Nakhasi. 2008. A *Leishmania* minicircle DNA footprint assay for sensitive detection and sepciation of clinical isolates: **Transfusion** *48:1787-1798.* (*Corresponding author)

Mahajan B., A. Selvapandiyan, N. Kumar, H. L. Nakhasi and S. Kumar. et al. 2008. Centrins, Cell Cycle Regulation Proteins in Human Malaria Parasite *Plasmodium falciparum.* **J Biol Chem** *283:31871-31883.*

Kanswal S., N. Katsenelson, A. Selvapandiyan, R. J. Bram and M. Akkoyunlu. 2008. Deficient TACI expression on B lymphocytes of newborn mice leads to defective immunoglobulin secretion in response to BAFF or APRIL **J Immunol** *181:976-990.*

Lee, N., G. Sreenivas, A. Selvapandiyan and A. Debrabant. 2007. Characterization of metacaspases with trypsin-like activity and their role in programmed cell death in the protozoan parasite *Leishmania*. **Eukaryotic Cell** *6:1745-1757.*

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Selvapandiyan, A*, P. Salotra, R. Duncan, H. L. Nakhasi. 2005. Fluorescence-based multiplex PCR assay for rapid simultaneous detection of bacterial and parasitic pathogens. **J Mol Diagn** *7(2):268-275.* (*Corresponding author)

Selvapandiyan A. A. Debrabant, R. Duncan, J. Muller, P. Salotra, G. Sreenivas, J. L. Salisbury, H. L. Nakhasi. 2004. Centrin gene disruption impairs stage-specific basal body duplication and cell cycle progression in *Leishmania.* **J Biol Chem** *2004 279(24):25703-10*.

Selvapandiyan, A., R. Duncan, A. Debrabant, S. Bertholet, G. Sreenivas, N. Negi, P. Salotra and H. L. Nakhasi. 2001. Expression of a mutant centrin of *Leishmania donovani* reduces the growth of the parasite. **J Biol Chem** *276 (16): 43253-43261*.

Selvapandiyan, A., N. Arora, R. Rajagopal. S. K. Jalali. T. Venkatesan. S. P. Singh and R.K. Bhatnagar. 2001. Toxicity analysis of N- and C-terminal deleted vagetative insecticidal protein from *Bacillus thuringiensis*. **Appl Environ Microbiol** *2001 67(12): 5855-8.*

Majumder K., Fattah F.A., Selvapandiyan A., Bhatnagar R.K., 1995. Background minimized Cassette Mutagenesis by PCR using cassette-specific Selection Markers: A Useful General Approach for Studying Structure-Function Relationships of Multi-substrate Enzymes. **Genome Research**. 4:212-218.

Graduations and Important Positions: PhD from MS University, Baroda, Gujarat (1988); As Support/Senior Research Scientist at Intl' Cen' for Genetic Eng' Biotech' (ICGEB), New Delhi (1988-1999); As Visiting Scientist at Center for Biologics Evaluation and Research, FDA, Maryland, USA as (1999-2009) and as Team Lead at IMM, New Delhi (2009…..)

Specific Awards: *US-NIH Fellows Award for Research Excellence (2002); US-FDA Scientific Achievement Award (2010).*

Current Team Members in the Laboratory: **Dr. Rati Tandon** PhD, Post doctoral Fellow (DST: SERB); **Ms. Kavita Ahuja**, PhD student (Fellowship: DST INSPIRE); **Ms. Inam Riaz**, PhD student (Fellowship: M. Azad); **Ms. Rosanara**, PhD student (Fellowship: DST: SERB); **Mr. Adil Beig**, PhD student (Fellowship: ICMR).