



## **Ravi Durvasula, MD**

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### **BIOGRAPHY:**

Dr. Ravi Durvasula received his B.Sc. and MD degrees from McGill University in Montreal, Canada. He then completed internship and residency at Baylor College of Medicine in Houston, TX, where he also was appointed as Chief Medical Resident at Methodist Hospital, under Dr. Ed Lynch and Dr. Antonio Gotto. He did his Infectious Diseases fellowship at Yale School of Medicine in New Haven, CT, where he worked under the mentorship of Dr. Frank Richards, Director of The Yale Mac Arthur Center for Molecular Parasitology. Dr. Durvasula was awarded the prestigious Physician Postdoctoral Fellowship of The Howard Hughes Medical Institute and was appointed as Assistant Professor in Yale's Department of Epidemiology and Public Health. In 2005, Dr. Durvasula was appointed as Chief of Medicine at The New Mexico VA Health Care System and Vice-Chairman of Department of Internal Medicine at University of New Mexico School of Medicine. In 2014, he was selected as Chief of Division of Infectious Diseases at UNM and retained his role as Co-Director of The Center for Global Health. For nearly 15 years, the Durvasula Lab has been engaged in the development of paratransgenic strategies for the control of infectious diseases transmission. With RO1 funding from NIH: NIAID and grants from USDA, Burroughs Wellcome Foundation and Bill and Melinda Gates Foundation, the Durvasula Lab has pioneered the development of strategies to manipulate arthropod vectors of disease through a paratransgenic approach. Ongoing projects involving triatomine vectors of Chagas disease, sandfly vectors of leishmaniasis and sharpshooters that transmit plant pathogens involve a collaborative network that spans the US, India, Argentina, Tunisia and Iran. For his scientific achievements, Dr. Durvasula was elected to The American Society of Clinical Investigation in 2009. He also serves on several Study Sections for NIH, Department of Defense and Burroughs Wellcome Foundation. Several patents have arisen from Dr. Durvasula's research and he is the founder of 2 start-up companies based in Santa Fe, NM- Ecopesticides International and Aquaculture Solutions. Dr. Durvasula's seminal contributions to science are summarized:

### **(1) PARATRANSGENIC MANIPULATION OF TRIATOMINE BUG VECTORS OF CHAGAS DISEASE**

Vector-borne diseases remain a leading cause of human morbidity and mortality globally, with few options for vaccines or effective medical cures. Successful manipulation of arthropods via engineered bacterial symbionts- termed paratransgenesis- was first described in a PNAS paper of 1997: **Durvasula RV, Gumbs A, Panackal A, Kruglov A, Aksoy S, Merrifield RB, Richards F & Beard CB. (1997) Prevention of insect-borne disease: an approach using transgenic symbiotic bacteria. *Proc Nat Acad Sci USA*; 94(7):3274-78.** It is summarized in this diagram from *New England Journal of Medicine 1997*:

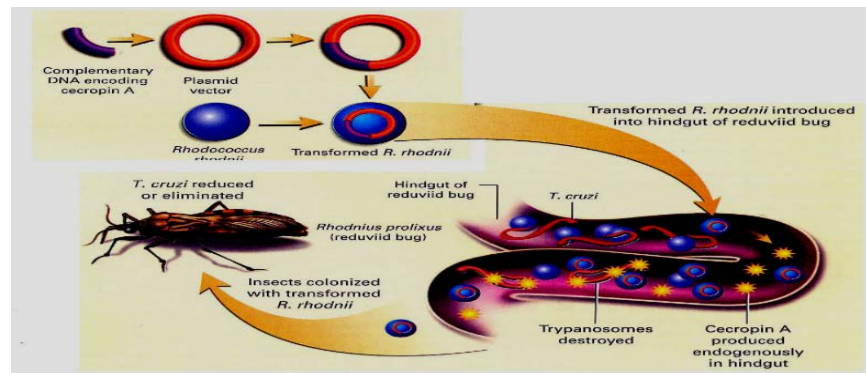
The paratransgenic approach is now being applied by investigators worldwide for control of pathogen transmission by mosquitoes, tsetse flies, ticks, sandflies and agricultural pests. Other relevant publications include: (1)

**Durvasula RV**, Gumbs A, Panackal A, et al (1999)

Expression of a

functional antibody fragment in the gut of *Rhodnius prolixus* via the transgenic bacterial symbiont *Rhodococcus rhodnii*. *Med Vet Entomol*; 13(2):115-9, (2)

**Durvasula RV**, Panackal A, Taneja et al (1999) A strategy for spreading anti-trypanosomal genes in populations of the Chagas disease vector, *Rhodnius prolixus*. *Ann Entomol Soc Am*; 92: 937-943, (3) Beard CB, Cordon-Rosales C & **Durvasula RV** (2002) Bacterial symbionts of the triatominae and their potential use in control of Chagas disease transmission. *Ann Rev Entomol*; 47:123-141, (4) Fieck A, Hurwitz I & **Durvasula RV** (2010) *Trypanosoma cruzi*: synergistic cytotoxicity of multiple amphipathic anti-microbial peptides to *T. cruzi* and potential bacterial hosts. *Exp Parasitol*; 125(4):342-7, (5) Jose C, Klein N, Wyss S, Fieck A, Hurwitz I and **Durvasula RV** (2013). Recombinant *Arthrobacter*  $\beta$ -glucanase as an effector molecule for paratransgenic control of Chagas disease. *Parasit Vectors*. 2013 Mar 14;6:65.



## (2) PARATRANSGENIC MANIPULATION OF SANDFLY VECTORS OF LEISHMANIA PARASITES

Infections caused by parasites of the genus *Leishmania* pose great threats to global health worldwide. Currently, an alarming epidemic of cutaneous leishmaniasis is raging in the Middle East and parts of North Africa. My lab successfully manipulated the sandflies, *P. papatasi* and *P. argentipes*, under laboratory conditions to express GFP via engineered bacteria that were delivered through soil-dwelling larval stages: Hurwitz I, Hillesland H, Fieck A, Das P & **Durvasula R** (2011) The paratransgenic sand fly: A platform for control of Leishmaniasis transmission. *Parasit Vectors* 4:82.

There are currently active collaborations in 3 countries with endemic leishmaniasis- India, Tunisia and Iran- to develop paratransgenic techniques for sandfly manipulation and molecules with anti-leishmania activity for eventual field control of these diseases. Other relevant papers include: (1) Hillesland H, Read A, Subhadra B, Hurwitz I, McKelvey R, Ghosh K, Das P, **Durvasula R** (2008). Identification of aerobic gut bacteria from the kala azar vector, *Phlebotomus argentipes*: a platform for potential paratransgenic manipulation of sand flies. *Am J Trop Med Hyg*. 79(6):881-6, (2) Maleki-Ravasan N, Oshagi M, Davoud A, Mohammad A, Hajikhani S, Amir A, Bagher Y, Mohammad S, Yavar R, Reza J, Koorosh A, Reza F and **Durvasula R** (2015) Aerobic bacterial flora of biotic and abiotic compartments of a hyperendemic Zoonotic Cutaneous Leishmaniasis (ZCL) focus. *Parasit Vectors* 8:63 DOI:10.1186/s1307-014-0517-3 and (3) Satoskar A and **Durvasula RV** (editors). 2014. Pathogenesis of Leishmaniasis: New Developments in Research: 91 pages, Springer, New York

### (3) PARATRANSGENIC MANIPULATION OF SHARPSHOOTER VECTORS OF PIERCE'S DISEASE

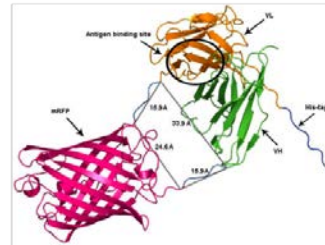
Infections caused by the bacterial pathogen, *Xylella fastidiosa*, that are transmitted by sharpshooters cause billions of dollars of damage annually to US agriculture and are currently decimating Europe's olive industry. As a platform to develop tools that increase global food security through control of agricultural infectious diseases, my lab, together with Dr. Tom Miller at UC Riverside, has developed paratransgenic strategies for manipulation of the Glassy Winged Sharpshooter. We recently identified a strain of *Pantoea* that can be used for delivery of heterologous molecules to the sharpshooter: Arora A, Forshaw A, Miller T, Kang A and **Durvasula RV** (2015) A Novel Microencapsulation Strategy for Field Application of Paratransgenic Control. *BMC Biotechnology* (in press). We have also cloned 2 AMP molecules in the *Pantoea* expression system to generate the first refractory vector of agricultural disease (manuscript in prep for PNAS). See: Arora A, Pesko K, Miller T and **Durvasula R**. Antibody-based Paratransgenics for Pierce's Disease. 2015 Annual Meeting of USDA BRAG Program Directors, Riverdale MD.

### (4) RECOMBINANT ANTIBODIES FOR DIAGNOSTIC AND THERAPEUTIC APPLICATIONS

With Dr. Angray Kang at Queen Mary- University of London, my lab has been developing novel classes of engineered three-domain single chain antibodies that may be used for a variety of applications. The demonstration of paratransgenic expression of rDB3, a murine antibody, in *R. prolixus* was the first report of antibody expression in an arthropod:

**Durvasula RV**, Gumbs A, Panackal A et al.

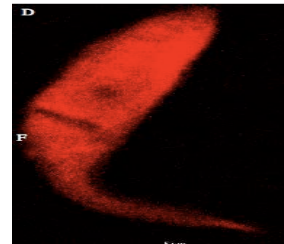
(1999) Expression of a functional antibody fragment in the gut of *Rhodnius prolixus* via the transgenic bacterial symbiont *Rhodococcus rhodnii*. *Med Vet Entomol*; 13(2):115-9. More recently, we have developed novel antibodies with intrinsic fluorescence by cloning mRFP and other fluorophore molecules within the VH-VL apparatus. This has received a US Patent in 2014 (US PTO#8,877,878) and forms the basis for antibody-based attack, possibly with photodynamic components, on *T. cruzi* and *L. donovani*:



Modular assembly of REDantibody with VH and VL regions and an embedded mRFP

Additional references include: (1) Markiv A, Anani B, **Durvasula RV** and Kang AS (2011) Module based antibody engineering: A novel synthetic REDantibody. *J Immunol Methods*; 364(1-2):40-9 and (2) Markiv A, Beatson R, Burchell J,

**Durvasula RV** and Kang AS (2011) Expression of recombinant multi-coloured fluorescent antibodies in *gor -/ trxB- E. coli* cytoplasm. *BMC Biotechnol*; 11(1):117



Confocal image of *T. cruzi*, Y strain, demonstrating diffuse reaction with REDantibody

### (5) NOVEL METHODS OF ENCAPSULATION OF MICRO-ORGANISMS

Since 2012, with the support of USDA and Bill and Melinda Gates Foundation, my lab has been developing new alginate-chitosan materials for encapsulation of biopesticides, with the aim of extending use of these agents in settings of high aridity, temperature and UV radiation. Encapsulation of the EPA-approved agent *P. agglomerans* has been published: Arora A, Forshaw A, Miller T, Kang A and **Durvasula RV** (2015) A Novel Microencapsulation Strategy for Field Application of Paratransgenic Control. *BMC Biotechnology* (in press). This work is also under patent review and forms the basis for a new start-up company, Ecopesticides International, Inc.