
BIOGRAPHICAL SKETCH

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|---|--|-----------|------------------------|
| NAME Rustom Antia | POSITION TITLE Professor, Dept of Biology | | |
| eRA COMMONS USER NAME rantia | | | |
| EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>) | | | |
| INSTITUTION and LOCATION | DEGREE (if applicable) | YEAR(s) | FIELD OF STUDY |
| Indian Institute of Technology, Bombay | M.Sc. | 1978-1983 | Physics |
| University of Massachusetts, Amherst | Ph.D. | 1984-1990 | Mol. and Cell. Biology |
| Imperial College, London | Post-doc | 1990-1994 | Mathematical Biology |

A. Personal statement

I have been modeling the dynamics of immune responses and host-pathogen interactions since my post-doctoral fellowship at Imperial College in 1991. I approach problems in immunology and epidemiology from an ecological and evolutionary viewpoint.

At the within-host level, I view the immune system as a complex web of interconnected species (host cells, immune cells, resources, etc.), which can be perturbed by the introduction of invading pathogens. Studies from my group in the past decade focused on developing a quantitative framework for the understanding of very basic questions in immunology including: (i) Immune diversity: how diverse is the immune system (how many different $\alpha\beta$ T cell receptors are expressed by the T cells in an individual), and how does this affect the number of naïve cells which are specific to a given pathogen? (ii) Generation of immune responses: what are the rules for the expansion and differentiation of T cells following infection and how does it depend on the duration of stimulation by antigen? (iii) How is immunological memory generated, and what dictates the longevity of this memory? (iv) What controls infections, and in particular can we determine the contributions of resource limitation, innate and adaptive immunity in the initial control of infections, and how does this affect the generation of resistance following antimicrobial treatment? (v) Why do pathogens harm their hosts and to what extent can we predict the emergence of novel pathogens and the evolution of their virulence?

More recently we have been extending these studies to consider persistent infections and aging, which are problems of relevance to human health. We are extending our earlier studies in the following directions. (i) What prevents pathogens from being cleared shortly after infection, why do some cause persistent infections? (ii) What are the rules that govern the behavior of immune cells if the pathogen persists, and why do immune cells display an exhausted (dysfunctional) phenotype? (iii) Can we use carefully timed post-exposure treatment shortly after initial infection to generate protective immunity (i.e. treatment as a vaccine)?

I have a rather small but productive group (a graduate student and a couple of post-docs) that works very closely with experimental immunologists (Rafi Ahmed at the Vaccine Center at Emory, and Joseph Blattman at Arizona State University) and statisticians and epidemiologists (Ira Longini's group at the University of Florida). This allows us to rigorously integrate modeling with experimental validation and develop a quantitative understanding of the dynamics of infections.

B. Positions and honors

Positions and Employment

2009 - : Samuel Candler Dobbs Professor of Biology, Emory University
2007 - : Professor, Department of Biology, Emory University
2000 - 2007 : Associate-Professor, Department of Biology, Emory University
1994 - 2000 : Assistant Professor, Department of Biology, Emory University

Other Experience

2004-2007: Regular member of the Modeling and Analysis of Biological Systems (MABS) study section of the NIH.

Ad-hoc reviewer for NSF, NIH, Wellcome Trust, and other agencies.

Editorial Board of Proceedings of the Royal Society Series B, and PLoS Computational Biology.

C. Selected 15 peer-reviewed publications (in chronological order)

Most relevant to the current application

1. Regoes, R.R., Barber, D., Ahmed, R., and **Antia, R.** (2007) Quantifying the rate at which cytotoxic T lymphocytes kill target cells in vivo. *Proceedings of the National Academy of Sciences USA* **104**:1599-1603.
2. Choo, D.K., Murali-Krishna K, **Antia, R.** and Ahmed R. (2010). Homeostatic turnover of virus-specific memory CD8 T cells occurs stochastically and is independent of CD4 T cell help. *Journal of Immunology*. 185:3436-44.
3. Stromberg, S.P., and **Antia, R.** (2011) Vaccination by delayed treatment of infection. *Vaccine*. **29**:9624-9631.
4. Johnson, P.L., Kochin, B.F., McAfee, M.S., Stromnes, I.M., Regoes, R.R., Ahmed, R., Blattman, J.N., and **Antia R.** (2011) Vaccination alters the balance between protective immunity, exhaustion, escape and death in chronic infections. *Journal of Virology*. **85**:5565-5570.
5. Stromberg, S.P. & **Antia, R.** (2012) On the role of CD8 T cells in the control of persistent infections. *Biophysics Journal*. **103**: 1802–1810.

Additional publications of relevance to the field

6. **Antia, R.**, Levin, B.R., and May, R.M. (1994) Within-host parasite dynamics and the evolution and maintenance of parasite virulence. *American Naturalist* **144**: 457-472.
 7. **Antia, R.** Pilyugin, S., and Ahmed, R. (1998) Models of immune memory. *Proceedings of the National Academy of Sciences USA* **95**: 14926-14931.
 8. Blattman, J.N., **Antia, R.**, Sourdive, D.J.D., Kaech, S.M., Krishna, K-M., Altman, J.D., and Ahmed, R. (2002) Estimating the precursor frequency of naïve antigen-specific CD8+ T cells. *Journal of Experimental Medicine*. **195**, 657-664.
 9. **Antia, R.**, Regoes, R.R., Koella, J.C., and Bergstrom, C.T. (2003) The role of evolution in the emergence of infectious diseases. *Nature* **26**:658-661.
 10. **Antia R.**, Ganusov, V.V., and Ahmed, R. (2005) The role of models in understanding CD8+ T cell memory. *Nature Reviews Immunology*. **5**: 101-111.
 11. Ganusov, V.V., Pilyugin, S.S., de Boer, R.J., Murali-Krishna, K., Ahmed, R., and **Antia, R.** (2005) Quantifying cell turnover using CFSE data. *Journal of Immunological Methods*. **298**:183-200.
 12. Vezys, V., Yates, A., Casey, K.A., Lanier, G., Ahmed, R., **Antia, R.**, and Masopust, D. (2009)
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Memory CD8 T-cell compartment grows in size with immunological experience. *Nature*. **457**:196-199.

13. Handel, A., Longini, I.M., and **Antia, R.** (2010) Towards a quantitative understanding of the within-host dynamics of influenza A infections. *Journal of the Royal Society Interface*. 2010. **7**: 35-47.
14. Johnson, P.L., Kochin, B.F., Ahmed, R. and **Antia, R.** (2012) How do antigenically varying pathogens avoid cross-reactive responses to invariant antigens? *Proceedings of the Royal Society Biological Sciences*. **279**: 2777-85.
15. Johnson P.L., Yates A.J., Goronzy J.J., **Antia R.** (2012). Peripheral selection rather than thymic involution explains sudden contraction in naive CD4 T-cell diversity with age. *Proceedings of the National Academy of Sciences USA*. **109**: 21432–21437.

D. Research Support.

Ongoing Research Support:

NIH 1U01 GM70749 Longini/Halloran (PI) 5/01/2009 to 4/31/2014

Project Title: Containing Bioterrorist and Emerging Infectious Diseases

(continuation of MIDAS collaborative grant below.)

PI: Longini, I.M. Role: collaborator

Description: The overall objective of this research is to develop, validate, and implement mathematical and statistical models for the transmission and within-host dynamics of naturally occurring infectious diseases and bioterrorism agents.

My work of this project focuses on modeling the within-host dynamics of infectious diseases such as influenza, and linking the within-host dynamics of infection with the transmission of infections between hosts.

My part of the grant is about \$80,000 direct costs per year.

Completed Research Support

NIH 2R01 AI049334 3/01/2007-2/28/2012 extension thro' 2/2013

Project Title: Quantitative models of CD8+ T-cell memory

Role: PI

NIH 1U01 GM70749 5/01/2004 to 4/31/2009

Project Title: MIDAS collaborative grant on Containing bioterrorist and emerging infectious diseases

PI: Longini, I.M. Role: collaborator

NIH 1RO1 AI 49334

7/01/2001 to 6/01/06 extension thro' 2/07

Project Title: Quantitative models of CD8+ immune memory

PI: Antia, R.

R29 GM54268

7/01/1996 to 6/30/2001 extension thro' 6/02

Project Title: Population Biology and Genetics of Antimicrobial Action

PI: Antia, R.
