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Special Topics : Tuberculosis : Stephen Gordon Interview - Special Topic of Tuberculosis

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Stephen Gordon
From the Special Topic of Tuberculosis

According to our Special Topics analysis of tuberculosis (TB) research over the past decade, the scientist whose work ranks at #7 by total cites is Professor Stephen Gordon, with 19 papers cited a total of 3,632 times. His record in Essential Science Indicators SM from Thomson Reuters includes 40 papers, largely classified in the field of Microbiology, cited a total of 4,325 times between January 1, 1998 and October 31, 2008.

Professor Gordon has been an Associate Professor in the Veterinary Sciences Centre at University College Dublin's School of Agriculture, Food Science, & Veterinary Medicine since January 2008. Previously, he was affiliated with the TB Research Group of the Veterinary Laboratories Agency in Weybridge, UK.

In the interview below, ScienceWatch.com *talks with Professor Gordon about his TB research.*

SW: Would you tell us a bit about your educational background and research experiences?

I did my B.Sc. degree at University College Galway, Ireland, followed by a Ph.D. with Peter Andrew at the University of Leicester, UK, on mycobacterial molecular genetics. After struggling to sequence a few kilobases of mycobacterial DNA during my Ph.D., I realized it was time to get into genomics. Stewart Cole's lab at the Institut Pasteur, France, was leading the way in mycobacterial genomics, so in 1995 I went to do a post-doc with Stewart.

After three and a half years at the Institut Pasteur working on the human tubercule bacillus, *Mycobacterium tuberculosis*, I then went to the Veterinary Laboratories Agency in the UK to work with Glyn Hewinson on the genomics of the animal pathogen, *Mycobacterium bovis*, and to investigate how genetic differences between the human and animal pathogens translates into their distinct host preferences. This is one of the research angles that I am now continuing in Dublin.

SW: What made you decide to focus on tuberculosis?

I became interested in tuberculosis during my undergraduate degree, mainly in the social impact that the disease had had on Irish society in the past and the work of Dr. Noel Browne in introducing free health screening for tuberculosis. However, I also realized that while tuberculosis was seen as a disease of the past in many quarters, it still exacted an enormous toll in terms of morbidity and mortality in the developing

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world.

From a research point of view, I was attracted to the idea of applying the new tools of molecular biology to understand both the fundamental biology of the causative agent, *Mycobacterium tuberculosis*, and how this basic knowledge could then be translated to novel disease-control tools.

SW: **Your most-cited paper is the 1998 *Nature* paper you coauthored with Stewart Cole and Roland Brosch, among others ("Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence," 393[6685]: 537, 11 June 1998). Would you talk a little about this paper, its findings, and its importance to the field?**

The *Mycobacterium tuberculosis* sequence was one of the first genomes to be completed, and as such drew a lot of attention. In the decade since its publication, the genome has underpinned advances across a range of areas such as identification of diagnostic antigens, evolution of the tubercle bacilli, discovery of virulence factors, and elucidation of novel drug targets. There's no doubt that the access to genome data accelerated many advances across the field, and the citations for the paper reflect this.

SW: **You were principle author on another paper with this team, "Identification of variable regions in the genomes of tubercle bacilli using bacterial artificial chromosome arrays." What is it about this paper that continues to attract citations?**

This paper described a range of gene-deletion events from the pathogens that cause tuberculosis, a.k.a. the *Mycobacterium tuberculosis* complex. The work gave us our first insight into how this complex of bacteria has evolved over time, uncovered molecular markers for the tubercle bacilli, and identified regions that may explain why the members of the complex show such distinct host preference.

The fact that the work generated leads across these disparate areas probably explains why the paper has been well cited. Parenthetically, the genesis of this work was in a local bar that we frequented during my time at Pasteur and where many good ideas were born; I often think all labs should be within walking distance of a good bar.

SW: **A great deal of your work focuses on the tuberculosis genome. What would you say are the most important things that have been discovered about this genome over the years? Do we know all there is to know about this genome yet (or are we not even close)?**

"…I also realized that while tuberculosis was seen as a disease of the past in many quarters, it still exacted an enormous toll in terms of morbidity and mortality in the developing world"

It's difficult to single out one particular area where the genome has had its greatest impact; as I've said earlier, the genome has underpinned advances across many areas. From an entirely personal point of view, it has been fascinating to see how access to genome data has altered our understanding of the evolution of *M. tuberculosis*.

Prior to the availability of mycobacterial genome sequences, the conventional wisdom was that *M. tuberculosis* was derived from *Mycobacterium bovis*, the agent of tuberculosis in cattle. So the idea was that when man domesticated cattle, *M. bovis* jumped the species barrier to become *M. tuberculosis*. However, our initial comparative genomics experiments showed that this couldn't be the case; *M. tuberculosis* was not derived from *M. bovis*. If anything, the data suggested that the common ancestor of tuberculosis in animals was more closely related to a human-adapted strain. I like these serendipitous discoveries that change the way we think about things.

SW: **What would you like the "take-away lesson" about your research to be?**

I suppose one of the key things that anyone takes away from genome analysis of the *Mycobacterium tuberculosis* complex is just how similar these organisms are, with greater than 99.9% identity at the nucleotide level. However, the variation in their genomes, slight as it may seem to be, has given us a range of very successful host-adapted pathogens.

Linking these host-adaptation phenotypes back to their genetic basis is a tall order, but the information is there, encoded in the genome and staring us in the face; we just don't know how to read and translate this information into function yet. So the take-home message is that while decoding the wealth of information in genome sequences will take a long time, it's going to be a fascinating adventure. ◾

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Stephen Gordon's current most-cited paper in *Essential Science Indicators*, with 2,752 cites:

Cole ST, *et al.*, "Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence," *Nature* 393(6685): 537-+, 11 June 1998. Source: *Essential Science Indicators* from Thomson Reuters.

Keywords: tuberculosis, Mycobacterium tuberculosis, Mycobacterium bovis, complete genome sequence, mycobacterial genomics, diagnostic antigens, evolution, virulence factors, drug targets, host-adapted pathogens.

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