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MICROBIOLOGY IN SCHOOLS ADVISORY COMMITTEE
50th Anniversary Articles

New drugs from an old desert

Mike Goodfellow

When Alexander Fleming accepted his part of the Nobel Prize for the discovery of penicillin just over seventy years ago, he warned that the misuse of antibiotics would lead to the emergence of drug-resistant pathogens. As this and subsequent warnings fell on deaf ears the misuse of antibiotics in agriculture and medicine has led to the evolution and spread of drug-resistant pathogens, as exemplified by drug-resistant *Neisseria gonorrhoeae,* the causative agent of the sexually transmitted disease gonorrhoea, the second most frequently reported disease in the USA. Increasingly dire directives from the World Health Organisation warn of a return to pre-antibiotic days of medicine. It is difficult to be sanguine about such warnings though there are glimmers of hope. Thus, advances in our understanding of microbial diversity coupled with the application of new technologies based on whole genome sequencing are providing new routes to the discovery of novel antibiotics of clinical value.

Historically, filamentous bacteria, now known as actinobacteria (formerly as actinomycetes) have been the major source of clinically used antibiotics. However, the costly rediscovery of known antibiotics from common actino-bacteria isolated from well-studied habitats, such as temperate and tropical soils, contributed to the marked decline in the discovery of novel microbial antibiotics of clinical value. However, the discovery that the genomes of filamentous actinobacteria are rich in biosynthetic gene clusters (BGCs) that have the potential to make many more bioactive compounds than previously thought rekindled interest in these organisms as a source of novel antibiotics. Especially gifted actinobacteria with large genomes (>8Mb) that contain species/group specific BGCs are now at a premium in the search for novel natural products using state-of-the-art technologies, such as genome mining, that is, the detection and expression of novel BGCs in whole genome sequences.

Gifted actinobacteria are now being sought from extreme ecosystems on the premise that the conditions therein will give rise to populations of new actinobacteria which will be the source of novel antibiotics with new modes of action. Novel actinobacteria from deep-sea sediments are proving to be a particularly good source of new antibiotics, as witnessed by the discovery of a new family of polyketides known as the abyssomicins, from *Verrucosispora maris*, the anticancer drug salinosporamide from *Salinispora tropica* and the dermacozines from strains of *Dermacoccus abysii* isolated from the Challenger Deep of the Mariana Trench in the Pacific Ocean. Extensive studies of *Salinispora* strains show clear evidence of coupling between taxonomic and chemical diversity thereby supporting the working hypothesis that previously unknown filamentous actinobacteria isolated from extreme habitats are likely to be a source of new antibiotics.

Another underexplored ecosystem that has only recently attracted the attention of microbiologists is the Atacama Desert of northern Chile (**Figure 1**).

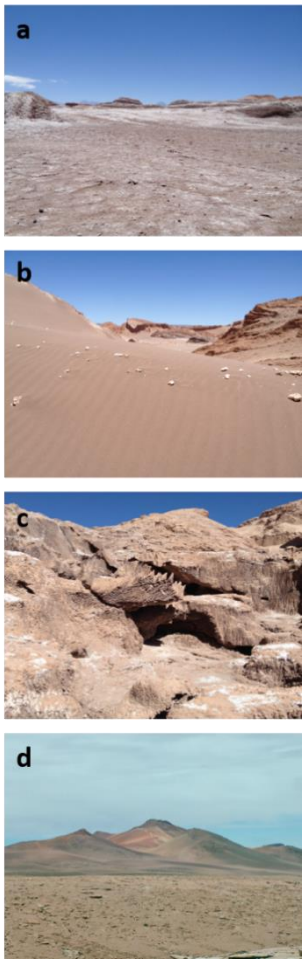

Figure 1. Atacama Desert sampling sites yielding novel, antibiotic-producing filamentous actinobacteria : (a) and (b), extreme hyper-arid soils; (c) rocks – all from the Valle de la Luna and (d) arid, high altitude soil at 15,000 feet on the Chajnantor Plateau with the peak of Cerro Chajnantor in the background.

This, the oldest and continuously most arid non-polar temperate desert on the planet is a source of interest to astrobiologists as the harsh environmental conditions are considered to provide an accurate analogue of those prevailing in Martian soils. However, until recently, the harsh conditions found in the Atacama, notably extreme aridity, low levels of organic carbon, high oxidising capacity and remarkable levels of ultra-violet irradiance were seen to be so severe that no form of life could be supported. Nothing could be further from the truth as it is now clear that Atacama habitats support a rich microbiota, including small, but taxonomically diverse filamentous actinobacteria.

Collaborative research involving the Universities of Aberdeen, Kent and Newcastle together with the University of Chile in Santiago has shown that filamentous actinobacteria isolated from diverse Atacama habitats are not only markedly bioactive but belong to new species. To date, 46 natural products representing different chemical classes have been detected from novel actinobacterial strains. Pride of place goes to gifted members of the novel species, *Streptomyces leeuwenhoekii*, which synthesises new anticancer (chaxapeptin) and antibacterial (chaxamycin) antibiotics. Indeed, it can be concluded from our pioneering studies that actinobacterial communities in the Atacama Desert represent an enormous untapped resource for biotechnological discovery programmes at a time when resistance to existing antibiotics is rapidly becoming an immense threat to global health.

AUTHOR PROFILE

Professor Michael Goodfellow MBE graduated from the University of Liverpool and held postdoctoral positions at Penn State and Leicester Universities prior to moving to Newcastle University. He is best known for his extensive contributions to prokaryotic systematics and has been the recipient of several international prizes. He served as chairman of Bergey's Manual Trust and was senior editor of the latest volume of the Manual devoted to The *Actinobacteria*. He was awarded an MBE in 2010 in recognition of his contributions to secondary education.

This article is one of a number invited as part of the MiSAC 50th anniversary celebrations. The articles are written by experts and are both up to date and relevant to microbiology in schools. MiSAC is grateful to all contributing authors.