COMMENTARY

A Potentially New Treatment for Tuberculosis; Will a Diarylquinoline Work for Leprosy?

The recent publication by Koen Andries, *et al*. ([1]) (see *Current Literature* of this issue, p. 43), describing the extraordinary anti-tuberculosis activity of the new diarylquinoline "R207910" from Johnson and Johnson, may bode well for several of the mycobacterioses including leprosy. Basic studies had revealed mutations in resistant isolates of *Mycobacterium tuberculosis* and *M. smegmatis* that mapped to an ATPase that is involved with ion transport. Interestingly, this protein had not previously been proposed as a drug target although it is apparently essential for *in vitro* growth and has little sequence homology with its human counterpart.

Might this compound or compound class be of value in the treatment of leprosy? The broad spectrum activity of R207910 against a range of mycobacteria (but not of non-mycobacterial species) suggests that it will likely be active against the leprosy bacillus as well. In addition, the *M. tuberculosis* and *M. leprae* ATPase proteins share 92.6% identity, again suggesting that the latter may well be highly susceptible. The long half-life and ability to shorten the treatment duration required for organ sterilization in *M. tuberculosis*-infected mice suggests that, should the spectrum of activity extend to *M. leprae*, this compound (or compound class) may help shorten the duration of leprosy treatment as well. Combinations containing R207910, a rifamycin and a fluoroquinolone—all of which appear to be both bactericidal and to have the ability to eliminate some percentage of persistent mycobacteria—may dramatically shorten treatment duration in both tuberculosis and leprosy, even in patients with a relatively high bacterial loads.

Of course much of this speculation regarding leprosy can be put to rest by a few well designed *in vitro* and *in vivo* experiments with *M. leprae*. While a phase I clinical trial has looked promising, the ultimate clinical utility in tuberculosis and in leprosy and other mycobacterioses can only be determined following phase II/III studies in these diseases.

—Scott Franzblau, Ph.D., Professor

Institute of Tuberculosis Research
University of Illinois Abraham Lincoln School of Medicine
Chicago, Ill. USA

REFERENCES

1. Andries, K., P. Verhasselt, J. Guillemont, H. W. Gohlmann, J. M. Neefs, H. Winkler, J. Van Gestel, P. Timmerman, M. Zhu, E. Lee, P. Williams, D. de Chaffoy, E. Huitric, S. Hoffner, E. Cambau, C. Truffot-Pernot, N. Lounis, and V. Jarlier. A diarylquinoline drug active on the ATP synthase of *Mycobacterium tuberculosis*. Sciencexpress **10** (2004) 1126/science.1106753.