Effect of Rifampin Treatment on Armadillo Nerves Infected with *M. leprae*

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M. leprae infect peripheral nerves
Most problems in HD are results of nerve injury
Background

- Anti-mycobacterial treatment kills *M. leprae*
- Nerve injury occurs even after completion of treatment
- Steroid treatment has limited benefit

- What is the effect of anti-mycobacterial treatment on *M. leprae* load in nerves?
Experimental Design: Armadillo Model

5 Animals per group:
A: Wild infected, treated for 12 mos
B: Experimentally infected, Not treated

A: Wild infected
B: Exp. infected

Rifampin monthly for Group B

Anti-PGL-1 antibody levels

Treated  Non Treated

Months
Experimental Protocol (2)

- At sacrifice, Posterior Tibial nerves removed
- Divided into 1 CM segments
  - Sections for histology
  - Isolation of DNA & RNA
- Enumeration of *M. leprae* by PCR
- Assessment of *M. leprae* viability by RNA assay
- Profile of host gene expression in nerves
  - Inflammation (IFN-γ, TNF-α)
  - Neuroproteins (PGP9.5, β-tubulin, Neurofilament)
  - Growth factors (DLK-1, NGF-β, MAG)
Total *M. leprae* load in the nerves from infected armadillos:
* treated with Rifampin for one year (Treated), or
* allowed to progress without treatment (Untreated)
Enumeration of Viable *M. leprae* in Nerves from Treated and Untreated Armadillos
Total vs Viable *M. leprae* in Nerves from Infected Armadillos Treated with Rifampin (Treated) or Allowed to Progress Without Treatment (Untreated).
Differential Expression of Neural and SC Markers in Armadillos
Conclusions

- Rifampin treatment kills *M. leprae* in nerves
- Abundant dead bacilli remain in nerves
- Killing of *M. leprae* → changes in host gene expression

- Unknown:
  - Mechanism of removing dead bacilli
  - Rate of decline of dead *M. leprae* in nerves

- In skin, bacterial burden declines VERY slowly after killing of *M. leprae*
Is the decline of *M. leprae* similarly slow in nerves? . . . even slower in nerves than in skin? Strategies to treat leprosy neuritis must recognize that a high antigenic load is present in nerves for many years after successful MDT.
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