

# The role of resuscitation promoting factors in the control of bacterial dormancy

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Many bacteria seem able to persist in a low growth state after exposure to stress. The adoption of a reversible dormant state in pathogenic bacteria has significant health implications due both to the difficulty in detection of low levels of dormant bacteria and the prolonged treatment periods required to kill such bacteria. In some cases, the exit from this growth state requires specific stimuli; the resuscitation promoting factors (RPF) are secreted proteins first found expressed by the gram-positive bacterium *M. luteus*. Dormant *M. luteus* cells could be induced to grow upon treatment with purified native or recombinantly produced RPF. Proteins homologous to RPF have been found in many pathogenic bacteria including five in *M. tuberculosis*. One member of the five, RPF B, was shown first to have sequence similarity to lysozyme and then structural homology when the NMR structure of the RPF domain of this protein was determined. A functional role of cell wall remodelling through a lysozyme like digestion of peptidoglycan seemed likely, however, we were unable to detect a corresponding lysozyme activity. We now report an HPLC assay that shows for the first time Rpf activity for RpfB and *M.luteus* Rpf. However, the activities were found to be orders of magnitude less than lysozyme. Given that the RPF proteins were capable of resuscitating dormant bacteria at picomolar levels, a simple non-specific cell wall remodelling function seems unlikely. Alternate functional mechanisms are discussed.