The emergence and spread of drug resistant pathogens and our inability to develop new antimicrobials to combat resistance (phenotypic and genetic) has motivated scientists to consider non-traditional targets where human homologs clearly exist. Cellular bioenergetics is an area showing promise for the development of new antimicrobials, but the success of this area will only emerge by understanding the role of these energetic processes (e.g. respiration and oxidative phosphorylation) under conditions that prevail in host tissues. In this seminar, I will discuss the recent developments in the field suggesting cellular energetics as a target space for the development of new antimicrobials.