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Experimental phage therapy against *Mycobacterium ulcerans* in mice model

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Buruli Ulcer (BU), caused by *Mycobacterium ulcerans*, is a difficult-to-treat, neglected necrotizing disease of the skin. Currently, an antibiotic regimen is recommended by WHO, but in advanced stages of the disease surgery remains the only effective recourse. In alternative or in association to antibiotherapy, the use of phages has been considered for the control of bacterial infections. In this study, we investigated the efficacy of lytic D29 phage in controlling *M. ulcerans* infection, using the mouse footpad model. A single dose of 10^6 D29 phage was administrated s.c., in *M. ulcerans* infected footpads, at a advanced stage of experimental BU. Control mice were injected with bacteria, phage or phage buffer only. In order to evaluate the efficacy of phage administration, *M. ulcerans* growth in footpad tissues was evaluated. As an index of lesion development, footpad swelling was also measured over time. Our results show that mice treated s.c. in infected footpads with D29 phage had a significant reduction in bacterial numbers as compared with untreated infected mice, at day 40 after treatment, and that phage administration prevented the ulceration of footpads induced by *M. ulcerans* infection. In order to monitor the bacteriophage persistence in footpads of mice, a 24 h assay was performed. Numbers of phages significantly decreased in footpads of treated mice from 2 to 24 h. More detailed studies will be needed to determine if the reduction of phage titres is a consequence of the phage property of replicating only when the bacterial density is above a threshold or due to recirculation to other organs like drain lymph nodes and spleen.Overall, our results suggest that a single dose of D29 phage seems to be an effective approach for reducing *M. ulcerans* colonization and the severity of BU disease.