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Ultrastructural evaluation to understand *Mycobacterium brumae* and BCG interaction with bladder tumor cells

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Intravesical bacillus Calmette-Guérin (BCG) is routinely used as immunotherapy agent in non-invasive human bladder tumors. Despite of well known BCG beneficial effects in retarding tumor progression and recurrence, there are adverse side-effects due to the use of a live strain from the *M. tuberculosis* complex, e.g. infections due to BCG. Therefore, there is a growing interest in the use of less deleterious agents. In this line, the efficacy of the non pathogenic *Mycobacterium brumae* as antitumor agent has been recently demonstrated in our laboratory. Although *M. brumae* inhibits tumor growth similarly to BCG in vitro, nothing is known about their interaction with bladder tumor epithelial cells.

A qualitative and quantitative evaluation of *M. brumae* and BCG-infected human bladder tumor cells (T24 cell line) was carried out. T24 cell line was infected with mycobacteria (MOI 10:1) during 48 hours and ultrastructural changes, with respect to non-infected cells, were analyzed using SEM and TEM. In parallel, colony-forming units (cfu) from mycobacteria-T24 infected cells were counted.

Although preliminary, we obtained two main results. Firstly, BCG appears to be more invasive than *M. brumae*. While 17% of T24 cells contain BCG bacilli, only 8% were infected with *M. brumae*. Secondly, a high number of well structured BCG in medium and phagocyted by T24, often in megasomes, was observed. In marked contrast, *M. brumae* cells were mainly found inside little phagosomes with one or two degraded bacilli. This last result is in agreement with cfu counts. Whereas BCG remains viable in T24 cells after 48 hours of infection, *M. brumae* does no persist inside T24 cells. Our results suggest that *M. brumae* is both less invasive and less persistent than BCG on tumor bladder cells.