Review of: "Plasma membrane protrusions mediate host cell-cell fusion induced by Burkholderia thailandensis"

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Plasma membrane protrusions mediate host cell-cell fusion induced by *Burkholderia thailandensis*

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Burkholderia thailandensis is a species of the pseudomallei group of *Burkholderia* bacteria that includes the much more virulent species, *B.pseudomallei*, the causative agent of the serious tropical disease melioidosis and *B.mallei*, the causative agent of glanders. Uniquely, this group of bacteria is able to mediate host cell fusion, which facilitates cell-cell spread and contributes to pathogenesis in vivo, but is also observed in cultured cells in vitro. Whilst bacterial motility is important for cell-cell fusion, it has previously been shown that components of the bacterial type VI secretion system (TSS6), that form a needle-like structure, are vital. In particular, the needle tip component of the TSS6-5 system, VgrG5, is essential for fusion mediated by *B.thailandensis*, since other workers have shown that bacteria with mutations in the gene encoding this protein are fusion defective.

The paper by Kostow and Welch expands on this previous research by using elegant live cell fluorescent imaging techniques. They investigate fusion of the human lung epithelial cell line, A549, induced by *B.thailandensis* and bacteria with mutations of the *vgrg5* gene and that of another TSS6-5 component, TagD5. The authors demonstrate that fusion occurs in membrane protrusions, which appear to be formed by the bacteria pushing against the host cell membrane. Interestingly, cell-cell fusion occurred at the protrusion tip (60% of cases), but could also occur elsewhere in the protrusion (40% of cases). However, these membrane protrusions in themselves do not mediate cell-cell fusion; rather, the VgrG5 protein and the TagD5 PAAR protein, which is likely to interact with VgrG5, are required. The authors report that *B.thailandensis* with mutations in these genes are able to induce the formation of membrane protrusions similar to non-mutant bacteria, but do not cause cell-cell fusion. In my view, this makes the title of the article slightly misleading. However, the authors demonstrate that VgrG5 must be secreted within membrane protrusions for fusion to occur, since the *vgrg5* mutation could not be rescued by wild type VgrG5 secreted elsewhere in the infected cells.

In summary, this is a well-executed piece of research that makes good use of live cell imaging techniques to improve our understanding of cell-cell fusion induced by *B.thailandensis*, and by analogy, the more virulent *B.pseudomallei* and *B.mallei* species. It is interesting that membrane protrusion are similarly observed in other types of cell-cell fusion e.g. macrophage fusion and myoblast formation. The paper is very well written and clear. In describing TagD5 (first sentence, last section of Results), the paper first proposing this nomenclature (Shalom et al 2007, Microbiology **153** 2689 – 2699) should really have been cited.