Reviewer's report

Title: Caveolin-2 Associates with Intracellular Chlamydial Inclusions Independently of Caveolin-1

Version: 1 Date: 21 May 2004

Reviewer: Michael Ward

Reviewer's report:

General
The Chlamydiales are successful, widespread and highly adapted obligate intracellular bacterial pathogens of a broad range of eukaryotic cells in hosts ranging from amoebae to humans. Although all members of the clinically important Chlamydiaceae have a broadly similar dimorphic developmental cycle, but there are substantial differences in their interaction with host cells and in the tissue tropisms which they display. Cellular studies of chlamydial infection can therefore be expected, as here, to illuminate basic understanding of host cell biology as well as chlamydial biology. This is an important, novel and well written piece of work which provides convincing evidence that strains of chlamydiae are heterogeneous both with respect to their ability to enter host cells via lipid rafts and to accumulate caveolin 1 or caveolin 2. Furthermore questions the fundamental view that caveolin 2 transport in cells is dependent on co-transportation of caveolin 1. Although essentially a descriptive paper, the study suggest that caveolin 1 and 2 may be very useful markers for understanding how chlamydiae enter cells and interact with intracellular sorting mechanisms. Within C. trachomatis, differences in association with caveolin 1 and 2 may throw insight, together with data from genomic sequencing, on differences in the tropism of this species for ocular, genital or lymphatic tissues.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
None

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Background: The authors imply, perhaps unintentionally, that the genus Chlamydia consists of a single species, C. trachomatis. This is incorrect and should be clarified. The Chlamydia also include Chlamydia muridarum (the mouse pneumonitis agent) and Chlamydia suis. For a diagram of the classification of the Chlamydiales see: http://www.chlamydiae.com/docs/Chlamydiales/diagram/taxondiag.htm. ref 14 is misspelt: the author is Thylefors.

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Discretionary Revisions (which the author can choose to ignore)
The authors refer to the debate in the 1980s as to whether chlamydiae enter by clathrin dependent or independent mechanisms, or both. It would be helpful in the discussion if the authors are able to reinterpret these original findings in the light of their observations. How, if at all, are clathrin and the caveolins functionally related?
The authors experiments are artifactual in that they were performed in the presence of the eukaryotic protein synthesis inhibitor, cycloheximide, in order to achieve reasonable growth of the various chlamydiae. I suggest the authors comment on what role if any cycloheximide might have played. Have the experiments been repeated in the absence of cycloheximide?
What next?: Accept after minor essential revisions

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: None