Loss of doublecortin (DCX) domain containing protein causes structural defects in tubulin-based organelle of Toxoplamsa gondii and impairs host cell invastion

Cassi Johnson[1] and Sandipto Sarkar[1]

[1]Affiliation not available

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Abstract

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CASSI JOHNSON SANDIPTO SARKAR

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CORRESPONDENCE:
cjohnson14@kumc.edu

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In the manuscript 'Loss of doublecortin (DCX) domain containing protein causes structural defects in a tubulin-based organelle of *Toxoplasma gondii* and impairs host cell invasion' the authors look to elucidate why tubulin dimers in the conoid region arrange in a different manner than those same tubulin dimers found elsewhere within the same cell. The authors speculated that a non-tubulin protein is responsible for the structural differences. Through an unbiased proteomics study of the apical complex, Hu *et. al.* discovered that the protein doublecortin (DCX) was highly enriched in the apical complex of *T. gondii*. Interestingly, the DCX protein contains domains (P25 and DCX) that have been found in proteins that interact with microtubules in other systems.

Evidence provided by this study does support the claims that 1) DCX is expressed in the conoid region of both adult and daughter parasites, 2) DCX maintains the structure of the conoid fibers, and 3) loss of DCX impairs the invasion abilities of these parasites. The points below would aid in further convincing readers of these claims.

· In Figure 3, the authors concluded that DCX expression is observed early in daughter parasite development. It would be helpful to provide images of daughter parasite and DCX expression at various time points of development.

· With the antibody produced for this study, a co-immunoprecipitation experiment to pull down tubulin-dimers using DCX as bait would strengthen the theory that DCX may be physically interacting with tubulin dimers (as it is known to do in other systems) to maintain the structure of the conoid region.

· In regards to the structural defects observed in the DCX-knockout parasites (Figures 10-12), it would be helpful if the authors were to at the very least, more clearly describe the defects observed in the images provided throughout the manuscript. If possible, quantification of structural defects would be ideal. Whether it would be the number of conoid fibers, periodicity of the fibers, or the dimensions of the conoid region.

· While the authors provided quantification of the host cell invasion (Table I), it is important to provide representative images of each experimental group to allow the reader a visual of the assay.

Additionally, reading this section of the paper, I was left wondering whether there was a difference between the number of parasites that bound to the cells in culture in addition to those that invaded into the cells.

Upon reading this manuscript, I was left with a few questions that may or may not be able to be speculated with results obtain from experiments already done, or may warrant further investigation in future manuscripts.

- Why was there such variance in phenotype observed in the knockout parasites?
- Does the P25 or DCX domain play a bigger role in maintaining the conoid fiber structure?
- Did parasite phenotype correlate with invasion capabilities?
- What was the mechanism of diminished host cell invasion?