



Biochemistry
UNIVERSITY OF WISCONSIN-MADISON

July 28, 2021

Benjamin Werth
Senior Science Editor
Medicine/Chemistry/Biochemistry
Journal of Visualized Experiments (JoVE)
1 Alewife Center Suite 200
Cambridge MA 02140

Re: “Micropatterning TEM grids to direct cell positioning within whole-cell cryo-electron tomography workflows”

Dear Mr. Werth:

Thank you very much for your consideration of our manuscript (JoVE62992), “Micropatterning TEM grids to direct cell positioning within whole-cell cryo-electron tomography workflows” by Sibert *et al.*

We hereby submit a revised word version of the manuscript, figures, and tables, and a point-to-point response to the editor’s reviewers’ comments. For convenience, the original cover letter follows.

Thank you for your consideration.

Yours sincerely,

Elizabeth R. Wright, PhD
Professor, Department of Biochemistry, UW-Madison
Director, Cryo-EM Research Center, UW-Madison
Affiliate Investigator, Morgridge Institute for Research

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June 4, 2021

Benjamin Werth
Senior Science Editor
Medicine/Chemistry/Biochemistry
Journal of Visualized Experiments (JoVE)
1 Alewife Center Suite 200
Cambridge MA 02140

Re: "Micropatterning TEM grids to direct cell positioning within whole-cell cryo-electron tomography workflows"

Dear Mr. Werth:

We submit for your consideration a manuscript that describes workflows for using the Alvéole PRIMO system to micropattern electron microscopy (EM) grids for directed cell adherence and growth. The protocol defines the major and minor steps associated with selecting EM substrates, micropatterning the substrate, culturing cells on the substrates through the basic processes of imaging and data processing. Within the protocol, we provide significant experimental detail in steps in which our protocol is unique or is modified from procedures previously published by others or us. We think the addition of micropatterning to cryo-EM/cryo-ET workflows will improve experimental reproducibility, data throughput and enable new experiments that will benefit from a seamless correlative imaging workflow.

In summary, we think that our protocol detailing the micropatterning workflow and its successful application to cryo-ET studies of immortalized and primary cells will be well received by and a valuable resource for investigators in the fields of microscopy, cell biology, virology, microbiology, and structural biology. Thank you for your consideration of our manuscript for publication in the *Journal of Visualized Experiments*.

Yours sincerely,



Elizabeth R. Wright, PhD
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Director, Cryo-EM Research Center, UW-Madison
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