

Reply to Cosgrove: Non-enzymatic action of expansins

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In our computational study, we use molecular simulations to substantiate a hypothetical mechanism for glycosidic bond cleavage in the presence of a single catalytic acid at the active site of the mutant D10N *HiCel45A*. In addition to discussing this plausible mechanism from the context of structurally related MltA lytic transglycosylase and subfamily C GH45s, we also suggest the implications of the plausible mechanism for our current understanding of the action of expansins and lytic transglycosylases. As correctly pointed out by Professor Cosgrove (1), there is large body of evidence, a significant portion of which was regrettably not discussed in our paper, that suggests that expansins are incapable of lytic action on polysaccharide substrates. Whereas these insights do not change the results or the conclusions of our article, we would like to thank Professor Cosgrove for these additional insights. In particular, our main

point with respect to expansins is that our results suggest the possibility that expansins are capable of nonhydrolytic lytic activity. Our intention was not to suggest this was the mechanism of expansins, but that it should be considered based on our results and the similarity of the active sites.

The molecular mechanisms of how expansins enable cell wall expansion remains to be fully understood. Whereas our proposed mechanism resulting in the formation of the 1,6-anhydro product might be found in expansins and might contribute to the mode of action of expansins, we would like to emphasize that the intent of this study was only to suggest this as a possibility that requires thorough experimental verification and validation. Our intent in relating the mechanistic predictions to expansins was only to stimulate discussion that could lead to alternative directions for future experimental investigations, which may improve our molecular-level understanding of expansin action.

The authors declare that they have no conflicts of interest with the contents of this article.

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Reference

1. Cosgrove, D. J. (2020) Non-enzymatic action of expansins. *J. Biol. Chem.* **295**, 6782–6782