

Review of: "The endoplasmic reticulum adopts two distinct tubule forms"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

The paper is potentially interesting, but it begins with an assumption that must be proven for the rest of the paper to make sense. The authors claim that two parallel lines of Rtn4 staining indicate a wider tubular structure, while one line of Rtn4 staining indicates narrower tubules. They also offer a geometric explanation that Rtn4 stabilizes the two highly curved edges of a somewhat oval R2 tubule giving rise to the parallel staining observed by STORM. Although this is an appealing explanation, I am afraid that it cannot be the premise for subsequent experiments until it is confirmed by other means.

An additional complexity not addressed by the authors is the simple observation that a 90° rotation of the R2 tubule would clearly produce a single line of staining indistinguishable from the putative R1 staining. Thus, the authors seem to assume that all ER tubules have the same orientation in the cell, with the longer axis of the wider, less curved R2 tubules perpendicular to the observational Z axis. Given the complex three-dimensional nature of the ER network, such perfect, univocal orientation of the tubules seems unlikely. Again, these assumptions need to be proven in an independent manner before extending them further. I suggest that the authors attempt to collect new data that confirm or refute their geometric assumptions based on a single interpretation of the Rtn4 staining pattern, even though other interpretations are possible in the absence of experimental evidence.