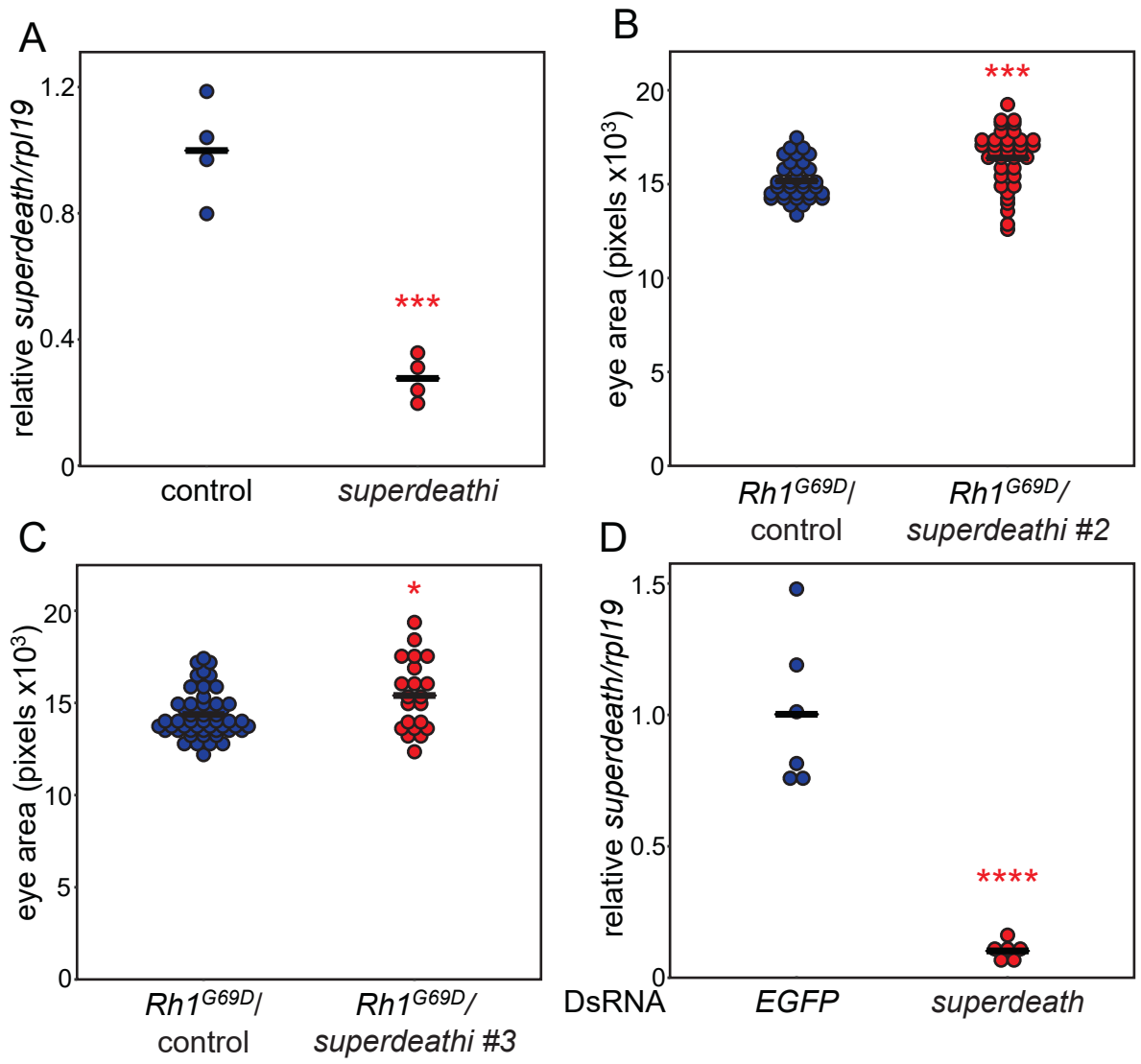
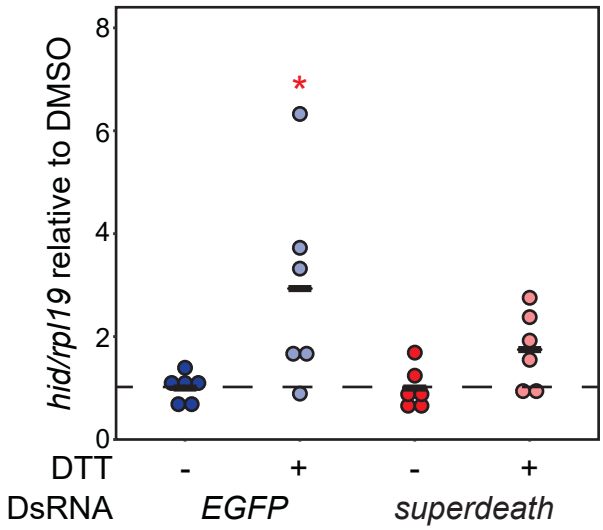
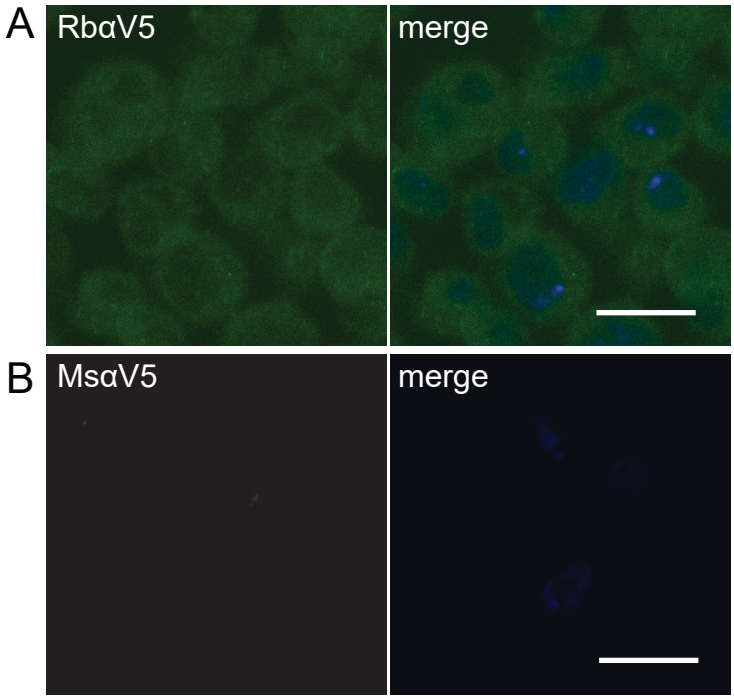


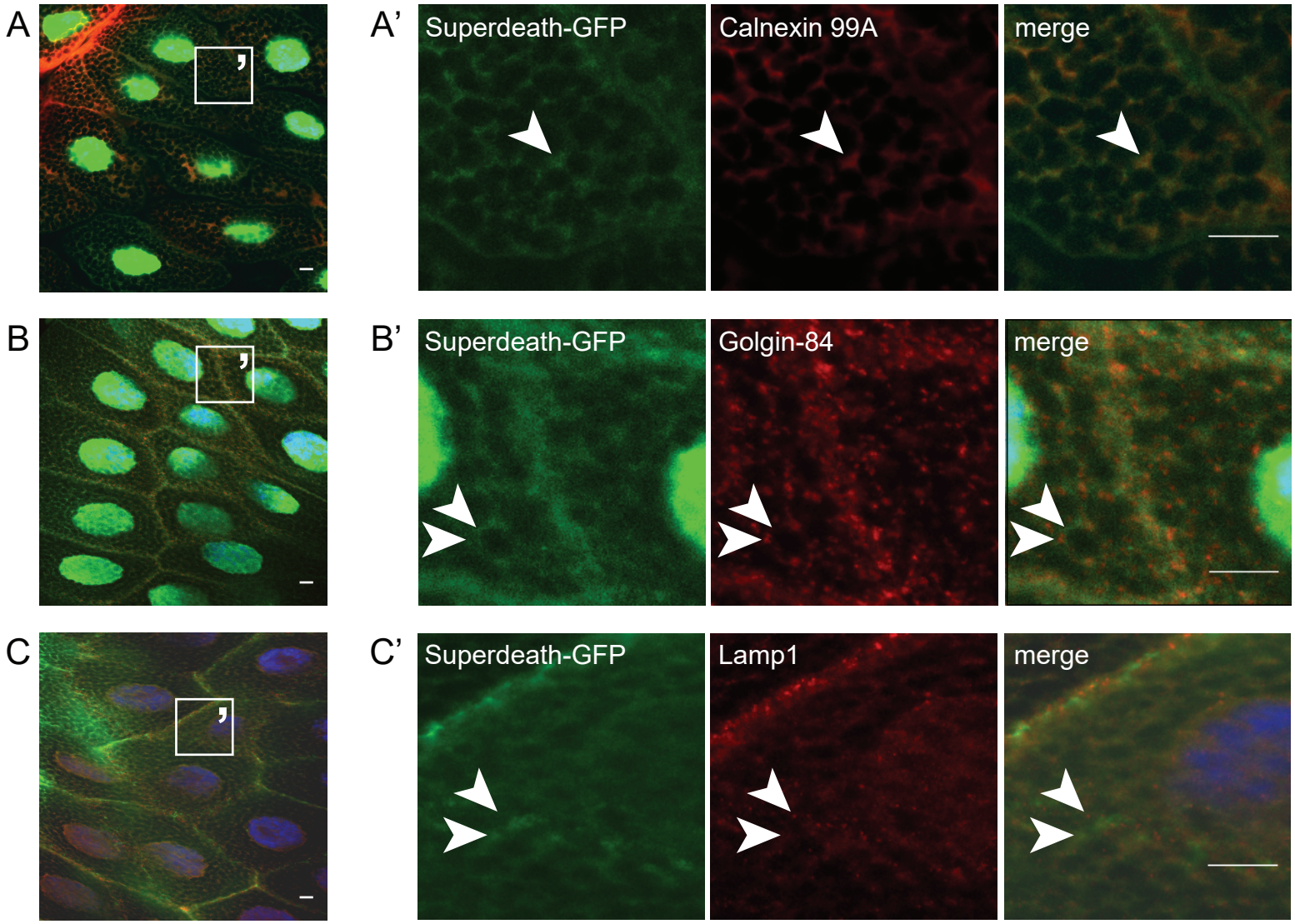
Supplementary Figure 1. *superdeath* expression is efficiently reduced by both RNAi and DsRNA. The RNAi and DsRNA targeting superdeath in our models of ER stress significantly reduce *superdeath* expression. **A.** The Bloomington *Drosophila* Stock Center superdeath RNAi strain (42947) used in this study efficiently reduces expression of *superdeath* (27.8% of controls, N = 4). The RNAi construct was driven ubiquitously by *Tubulin-GAL4*, and expression determined in wandering L3 larvae compared to controls expressing only *Tubulin-GAL4* (N = 4). The control used for this RNAi line throughout the study is the *attP40* strain (Bloomington #36304). **B.** A second RNAi strain for *superdeath* (Bloomington #35802) causes a similar increase in eye size when $Rh1^{G69D}$ is overexpressed. Degeneration caused by overexpression of $Rh1^{G69D}$ is partially rescued by RNAi-mediated knockdown of *superdeath* expression (16391 ± 1603 pixels, N = 36 in $Rh1^{G69D}$/*superdeathi* flies as compared to 15174 ± 1039 pixels, N = 33 in $Rh1^{G69D}$/-controls). Alternate control is the *attP2* strain (Bloomington #36303) **C.** A third RNAi strain for *superdeath* (Vienna #108616) causes a similar increase in eye size when $Rh1^{G69D}$ is overexpressed. Degeneration caused by overexpression of $Rh1^{G69D}$ is partially rescued by RNAi-mediated knockdown of *superdeath* expression (15403 ± 1941 pixels, N = 21 in $Rh1^{G69D}$/*superdeathi* flies as compared to 14371 ± 1225 pixels, N = 52 in $Rh1^{G69D}$/controls). Alternate control is the *attP* strain (VDRC #60100). **D.** S2 Cells treated with DsRNA targeted against *superdeath* also had near complete reduction in *superdeath* transcript levels (10.2%, N = 6) as compared to control cells treated with DsRNA against *EGFP* (N = 6). Values are average ± SD.* P < 0.05, *** P < 0.0005, **** P < 0.00005.



Supplementary Figure 2. Loss of *superdeath* reduces the upregulation of apoptotic transcripts under ER stress.
S2 cells treated with DsRNA against EGFP increased expression of the apoptotic gene *hid* after 7.5 hours of DTT exposure (2.93 ± 1.98, N = 6) as compared to DMSO-treated control cells (1.00 ± 0.284, N = 6). *hid* expression was not significantly increased in S2 cells that were treated with DsRNA against *superdeath* (1.74 ± 0.75, N = 6 in DTT-treated cells compared to 1.00 ± 0.40, N = 6 with DMSO).



Supplementary Figure 3. Specificity of V5 staining.
The signal for Superdeath-V5 in Figure 6 is specific to expression of the V5 tag. A. S2 cells that were not transformed with the pMT-DEST48-Superdeath-V5 vector were stained for rabbit αV5 (green) and counterstained with DAPI. Only background staining and no punctate staining indicative of Superdeath is detectable. B. S2 cells that were not transformed with the pMT-DEST48-Superdeath-V5 vector were stained for mouse αV5 (green) and counterstained with DAPI. No punctate staining indicative of Superdeath is detectable. Scale bars = 0.01 mm.



Supplementary Figure 4. Superdeath is localized to the endoplasmic reticulum *in vivo*.
Superdeath predominantly localizes to the ER membrane in the salivary glands. **A.** Superdeath localizes to the ER. Salivary glands expressing Superdeath-GFP (Bloomington #64447) were stained for GFP (green, Rb antibody Thermo-Fisher #A6455) and Calnexin 99A (red) and counterstained with DAPI. **A'** represents the highlighted panel from **A**. The white arrow highlights select sites of GFP and Calnexin 99A overlap (orange). **B.** Superdeath does not primarily localize to the golgi. Salivary glands expressing Superdeath-GFP were stained for GFP (green, Rb antibody Thermo-Fisher #A6455) and Golgin-84 (red) and counterstained with DAPI. **B'** represents the highlighted panel from **B**. White arrows indicate select sites of independent GFP staining (green) or Golgin-84 staining (red). **C.** Superdeath does not primarily localize to the lysosome. Salivary glands expressing Superdeath-GFP were stained for GFP (green, Ms antibody MBL #M048-3) and Lamp1 (red) and counterstained with DAPI. **C'** represents the highlighted panel from **C**. White arrows indicate select sites of independent GFP staining (green) or Lamp1 staining (red). Non-specific nuclear staining is only seen in cells stained with the rabbit αGFP antibody. Scale bars = 0.01 mm.