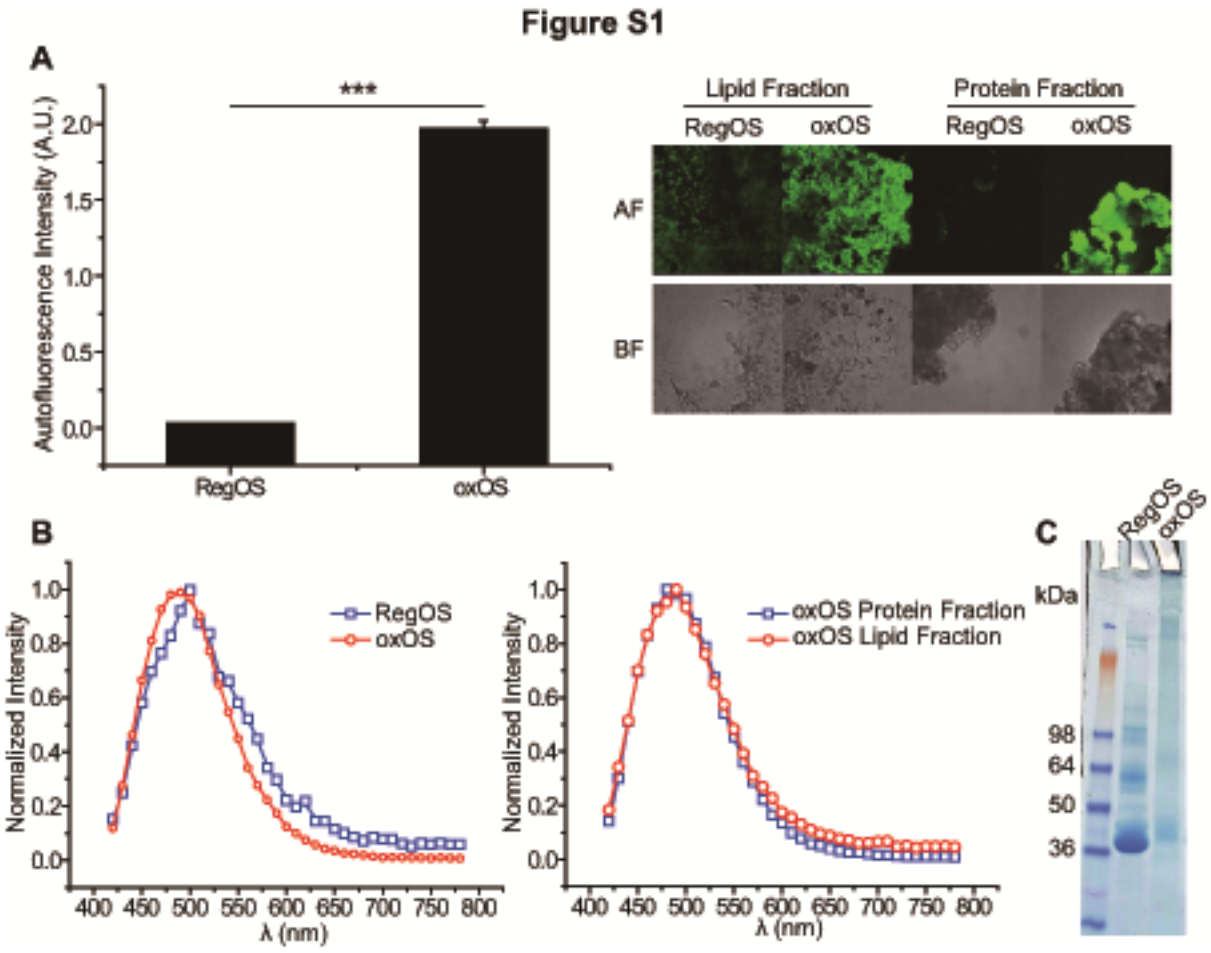

Figure S1. Characterization of oxOS. A) oxOS are significantly more autofluorescent than RegOS, as assessed by flow cytometry (n=3), and this autofluorescence is distributed across both the lipid and protein fraction of the oxOS. Lipid and protein precipitates from RegOS vs. oxOS viewed by brightfield (BF) and autofluorescence (AF). **B)** Autofluorescence emission spectrum of oxOS is blue-shifted compared to RegOS. Emission spectra of lipid vs. protein fraction of oxOS are identical. 405 nm excitation. **C)** oxOS contains significantly more cross-linked protein compared to RegOS, as assessed by Coomassie staining. Each well was loaded with 20 µg of protein. Left column is ladder. *** $p<0.001$.

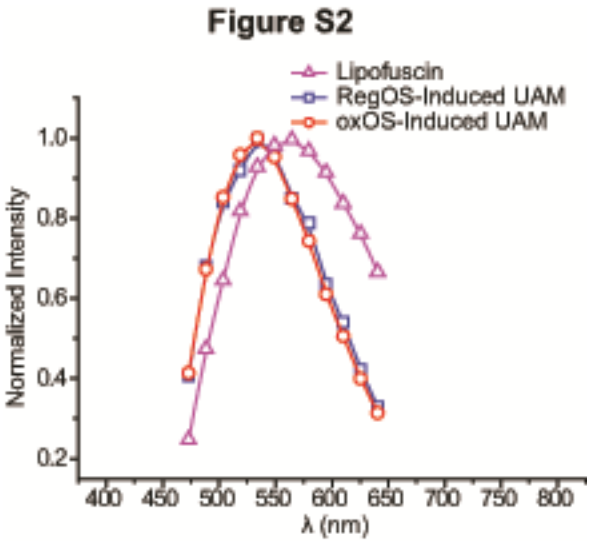

Figure S2. Emission spectrum of UAM formed from oxOS vs. RegOS. UAM granules formed in ahRPE from RegOS vs. oxOS had the same emission spectrum (458 nm excitation). This suggests a similar UAM composition despite differences in the chemical constituents of RegOS vs. oxOS. Lipofuscin curve derived from "carry-over" lipofuscin granules in unfed ahRPE cultures.

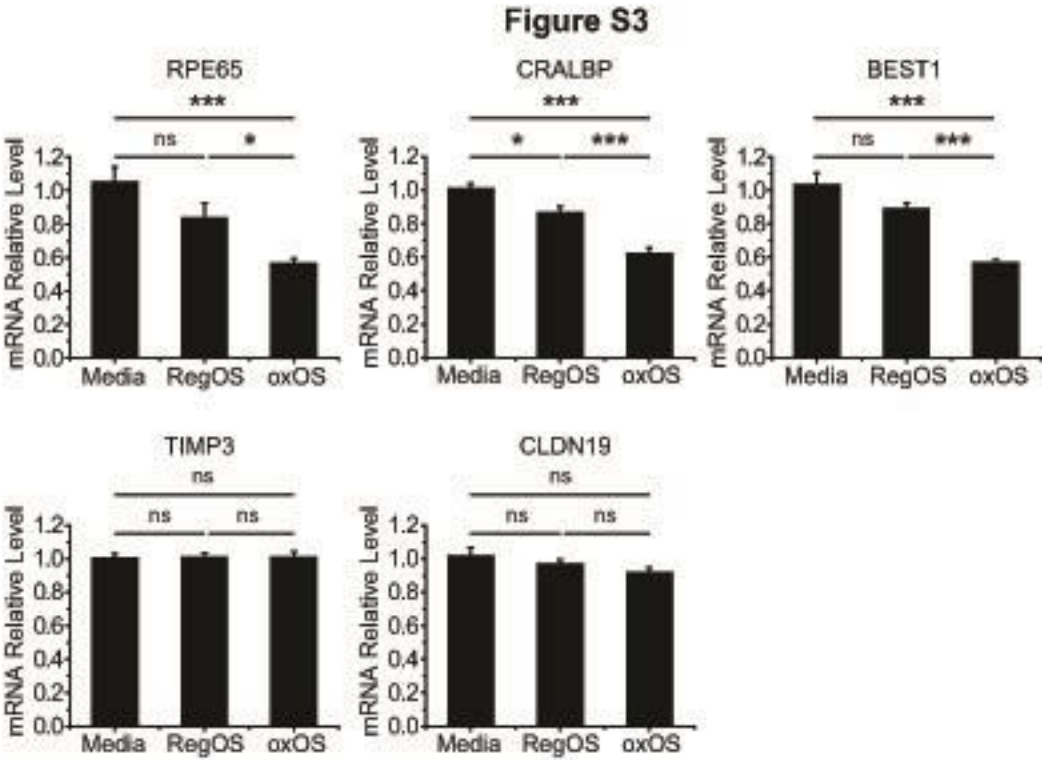

Figure S3. RPE-enriched gene expression is partly altered in UAM-laden cultures. Two months after last OS feeding, hfRPE cultures fed oxOS and consequently loaded with UAM demonstrated reduced expression of visual cycle proteins RPE65 and CRALBP as well as the RPE-specific membrane channel BEST1. Expression of the RPE-specific tight-junction protein CLDN19 and the ECM protein TIMP3, however, are unchanged. Controls include cultures fed RegOS or Media only. ns=non-significant, * $p<0.05$, *** $p<0.001$.