

## Description of Additional Supplementary Files

### **Supplementary Movie 1**

Super-resolution time-lapse images of iPSDM incubated with the cathepsin activity-based probe iABP (magenta) and MitoTracker Green (green). Video shows the sequence corresponding to the montages observed in Fig. 4a. The ROIs showing the respective M-L contacts are indicated. Frame interval = 20 s. Scale bar = 5  $\mu$ m.

### **Supplementary Movie 2**

Super-resolution time-lapse images of iPSDM incubated with the cathepsin activity-based probe iABP (magenta) and MitoTracker Green (green). Video shows the sequence corresponding to the montages observed in Fig. 4b. The ROIs showing the respective M-L contacts are indicated. Frame interval = 20 s. Scale bar = 5  $\mu$ m.

### **Supplementary Movie 3**

Super-resolution time-lapse images of iPSDM expressing Lamp1-mNeonGreen (magenta), incubated with MitoTracker Deep Red (RGB rainbow scale) and stimulated with LLOMe (0.5 mM). Frame interval = 30 s. Video shows the full sequence corresponding to the cell displayed in Fig. 4n. Scale bar = 10  $\mu$ m.

### **Supplementary Movie 4**

Super-resolution time-lapse images of iPSDM expressing Lamp1-mNeonGreen (magenta), incubated with MitoTracker Deep Red (RGB rainbow scale) and stimulated with LLOMe (0.5 mM). Frame interval = 30 s. Video shows the sequence corresponding to the montages displayed in Fig. 4k. Scale bar = 5  $\mu$ m.

### **Supplementary Movie 5**

Super-resolution time-lapse images of iPSDM expressing Lamp1-mNeonGreen (magenta), incubated with MitoTracker Deep Red (RGB rainbow scale) and stimulated with LLOMe (0.5 mM). Frame interval = 30 s. Video shows the sequence corresponding to the montages displayed in Fig. 4l. Scale bar = 5  $\mu$ m.

### **Supplementary Data 1.**

Mitochondrial proteomics data related to Figure 2 and Supplementary Figure 2.

### **Supplementary Data 2.**

Metabolomics data related to Figure 5 and Supplementary Figure 7.

### **Supplementary Data 3.**

Table shows differentially expressed genes for each population identified in the BAL scRNA-seq dataset, related to Figure 7 and Supplementary Table 2.

### **Supplementary Data 4.**

Table shows Reactome pathway scores for each population identified in the BAL scRNA-seq dataset, related to Figure 7 and Supplementary Figure 8.