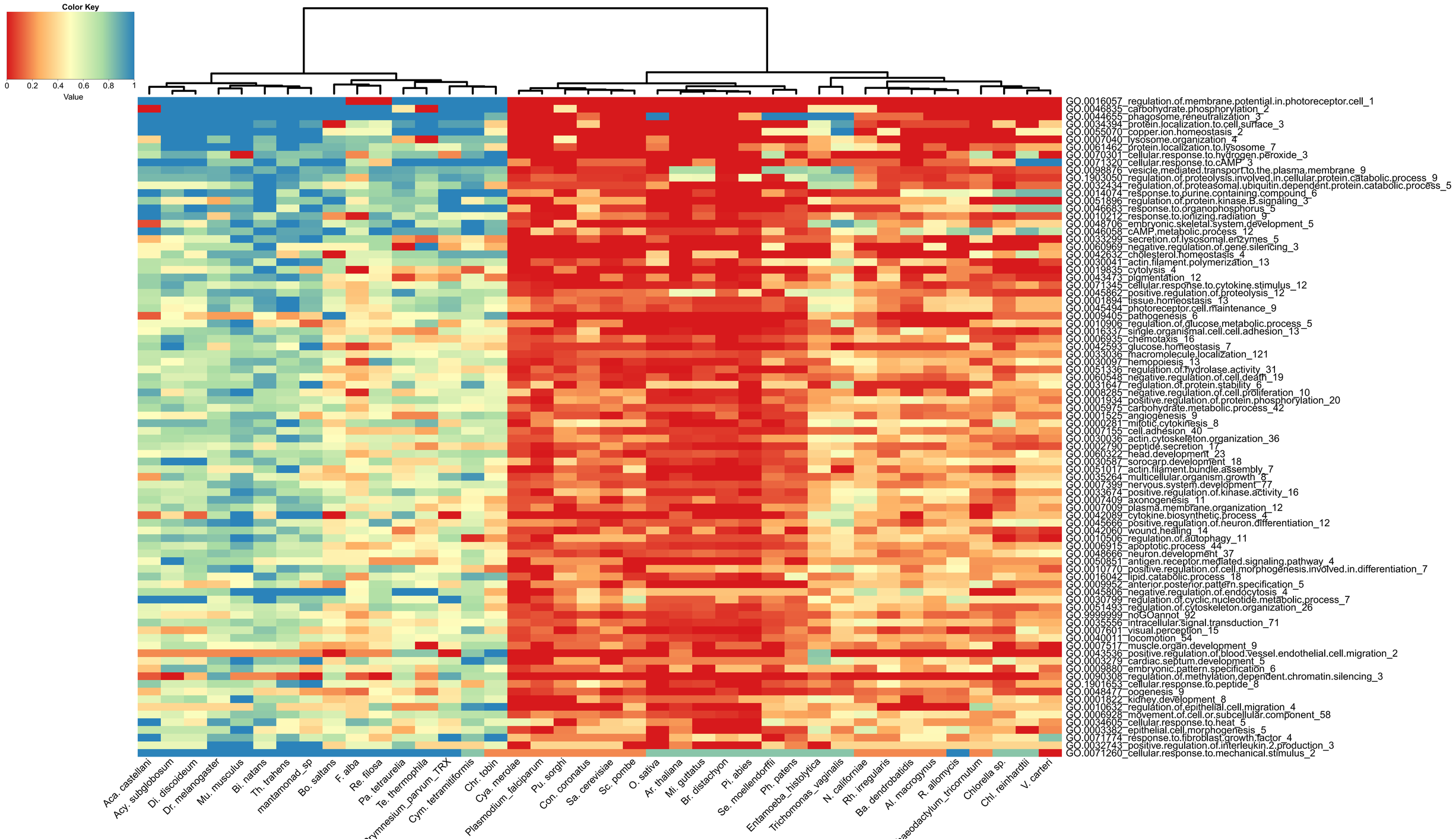Extended Data Figure 1