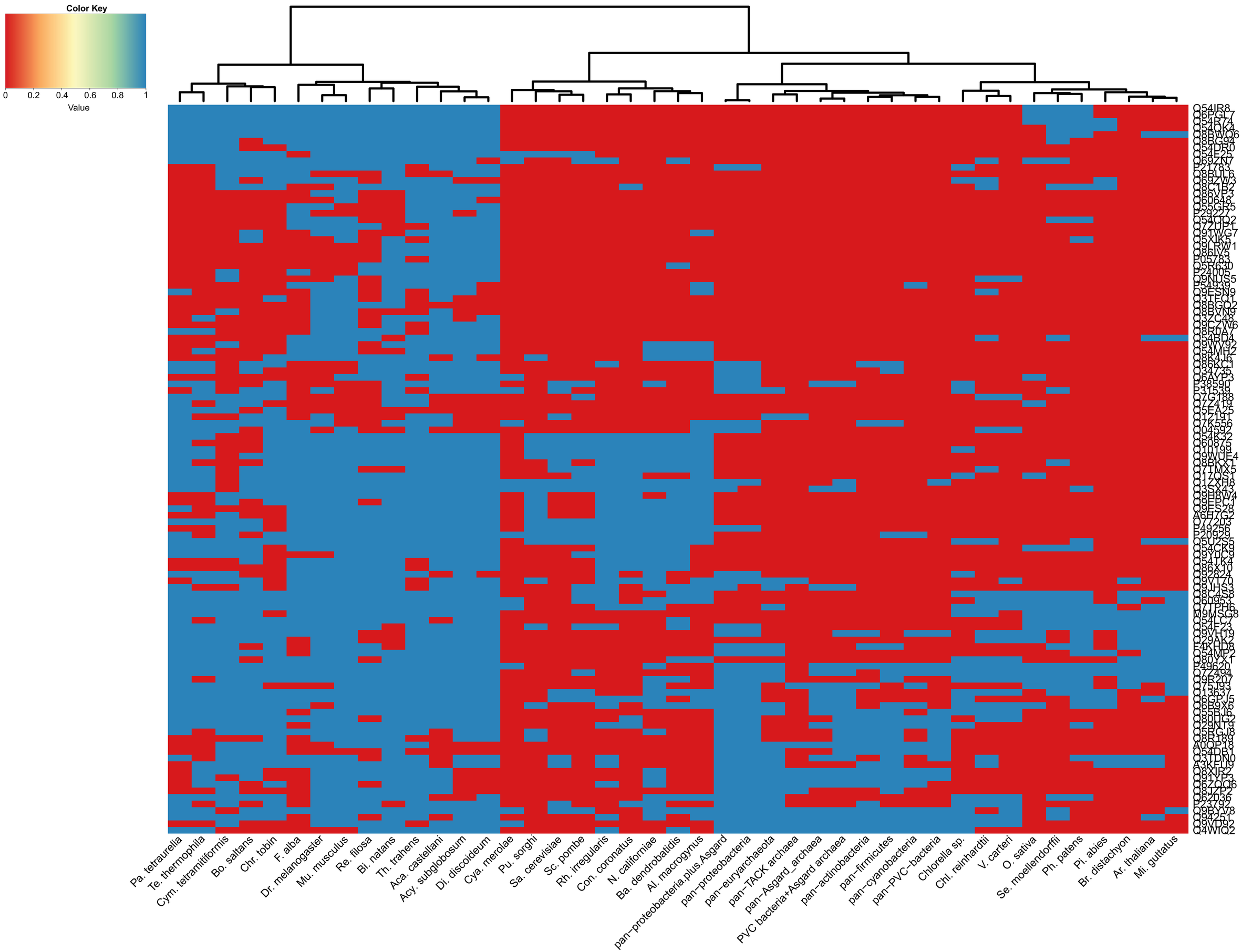Extended Data Figure 18