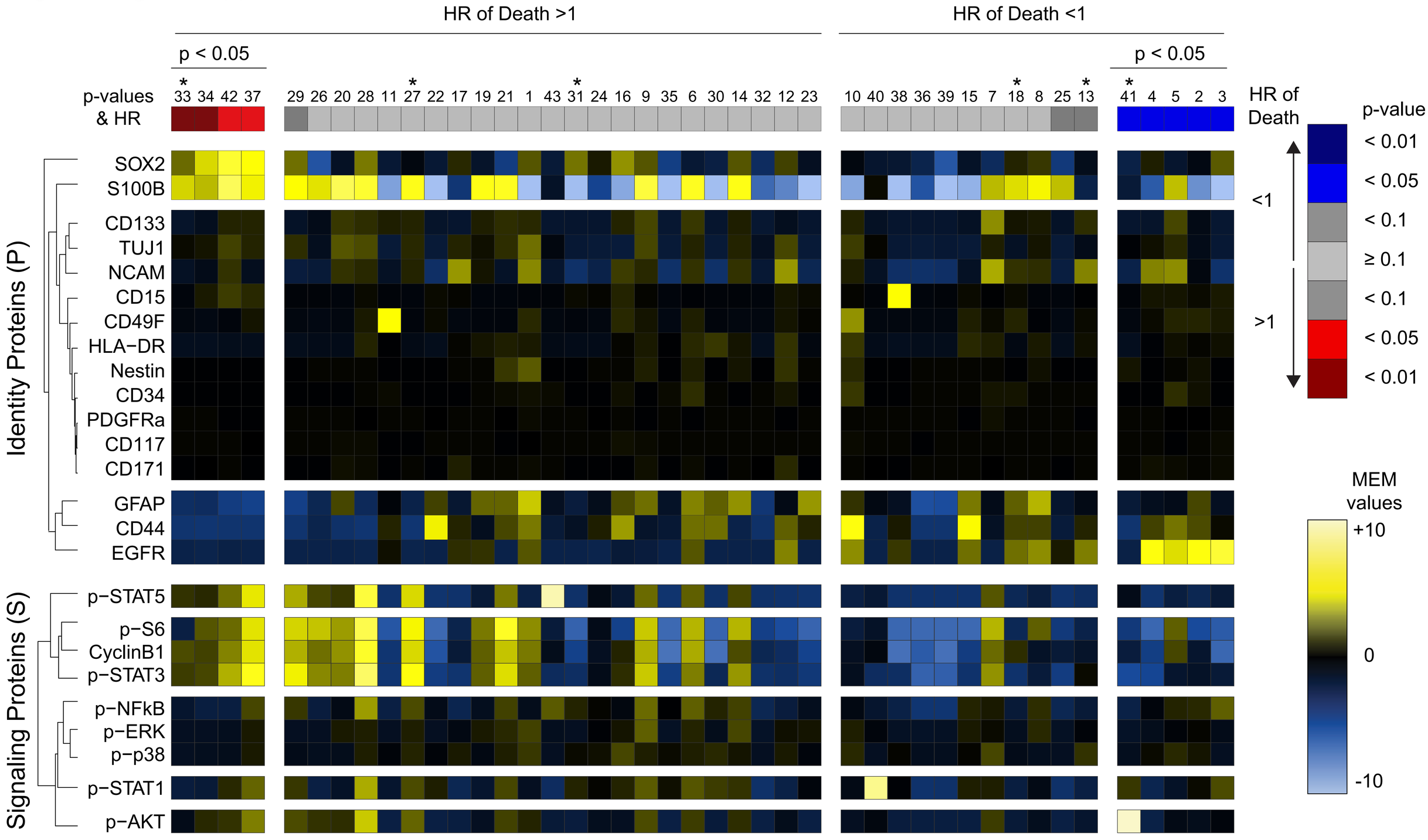Figure 1-figure supplement 3