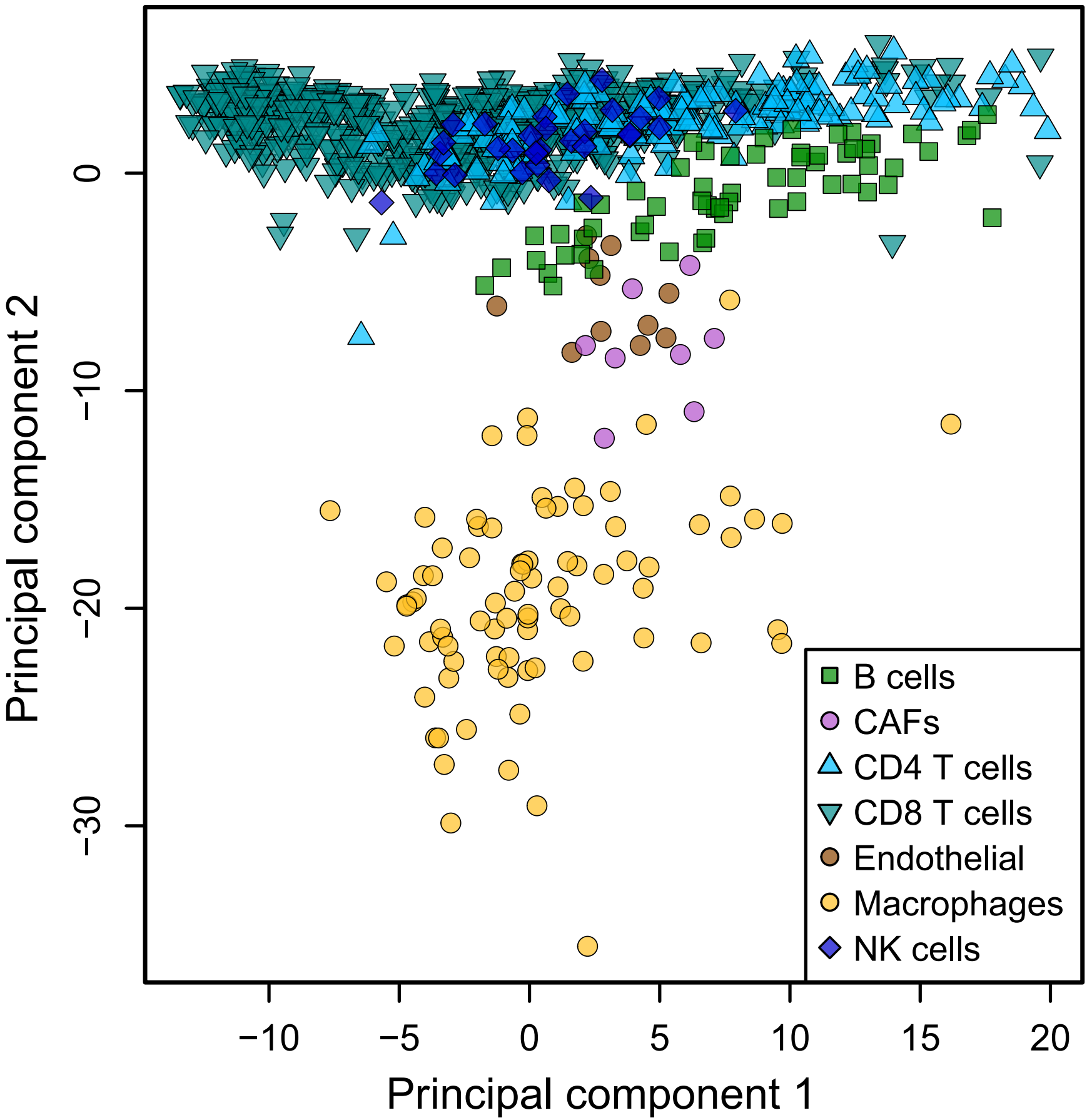Figure 1 - figure supplement 1