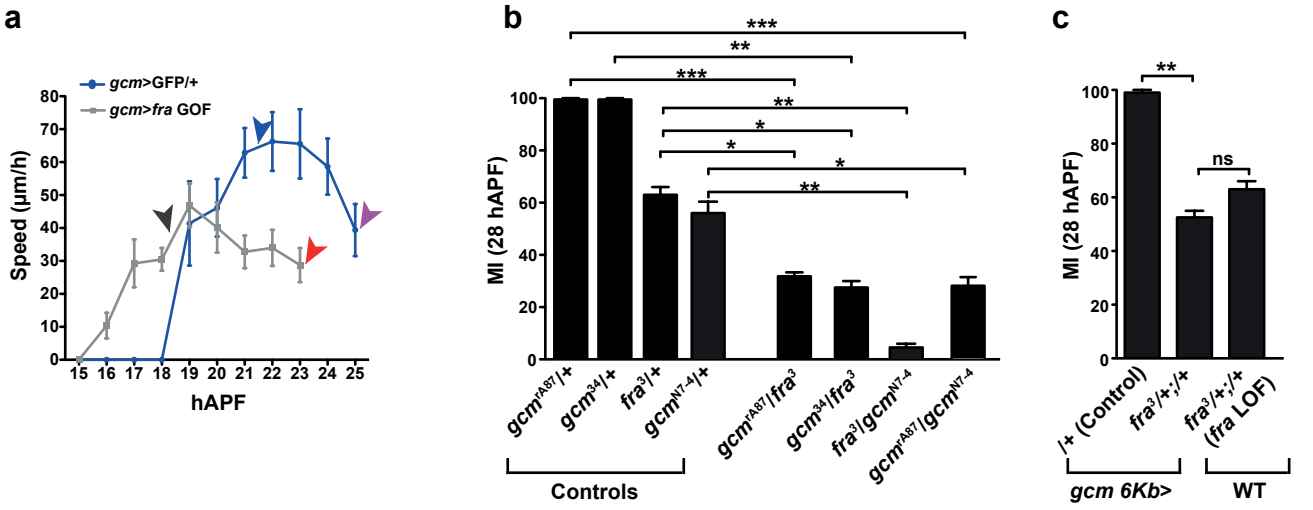Figure 3- figure supplement 2