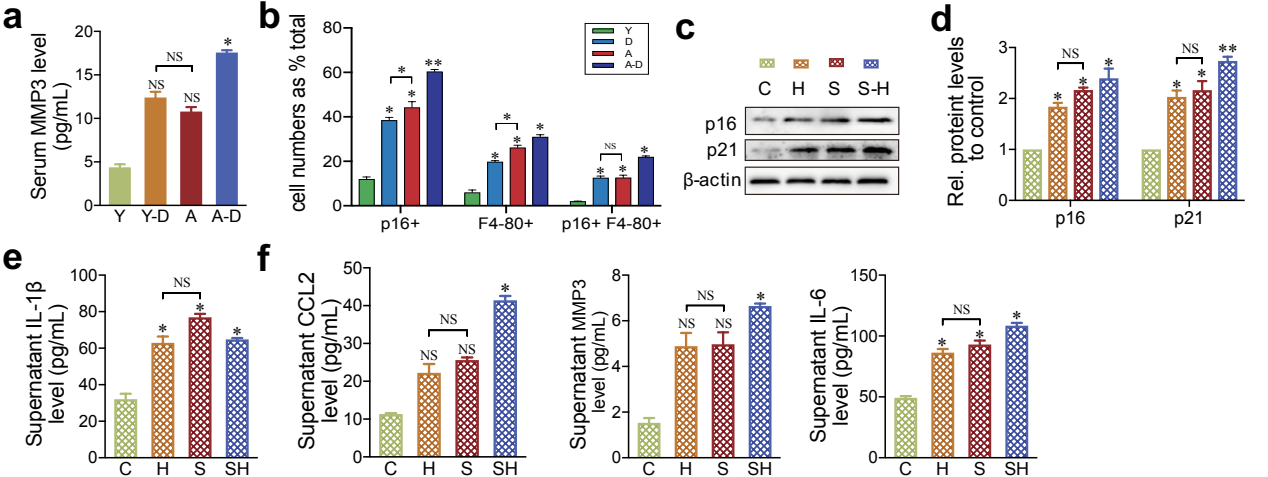Extended Data Fig. 1