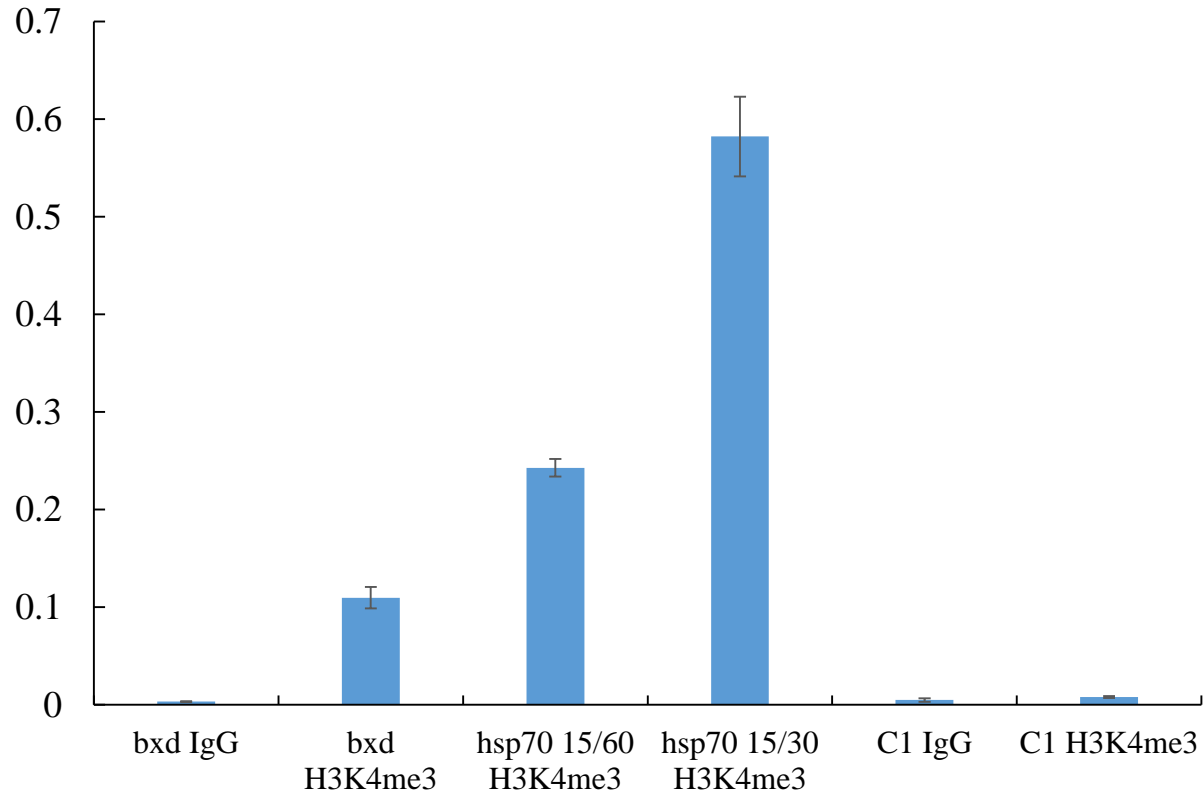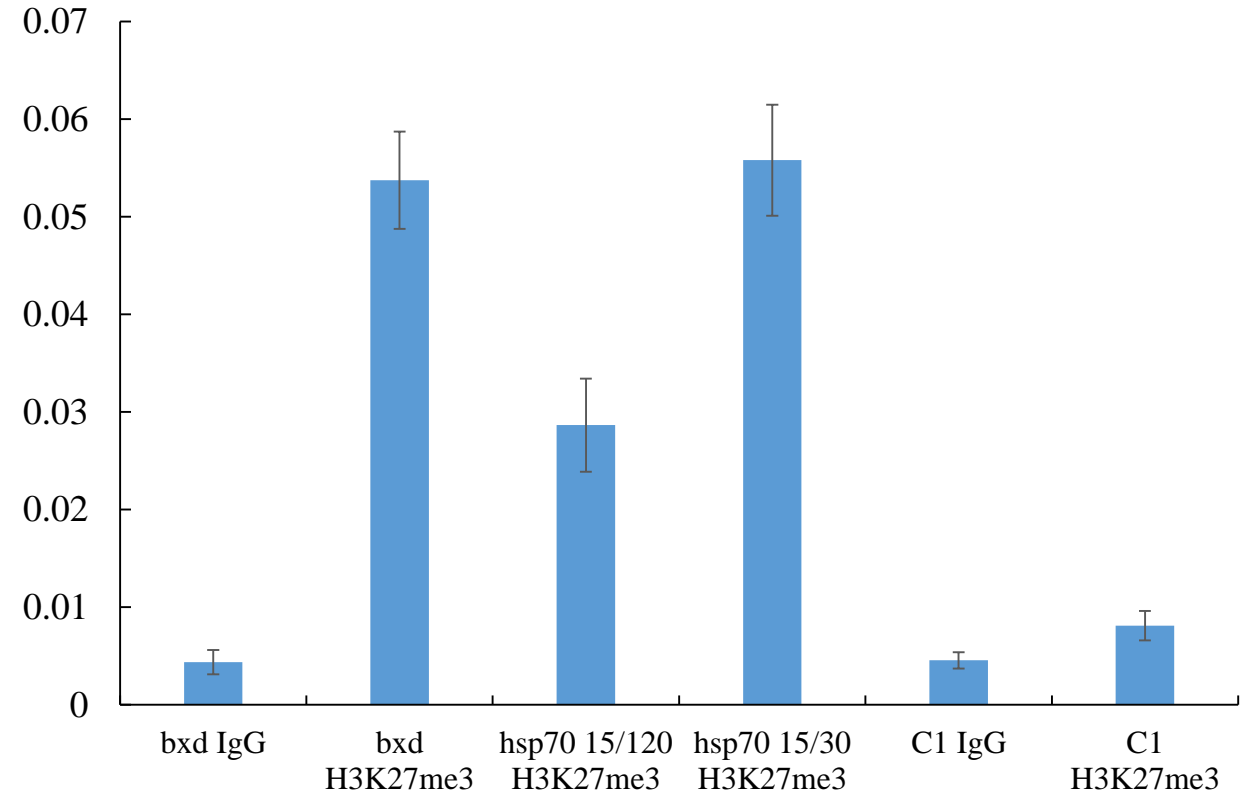**Figure S4**