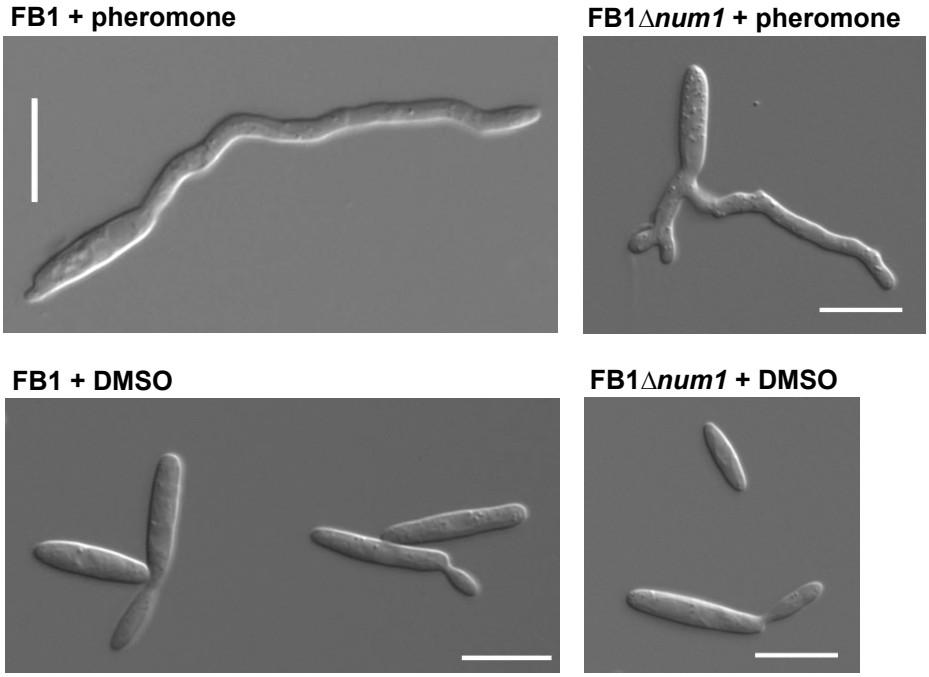Figure_S4