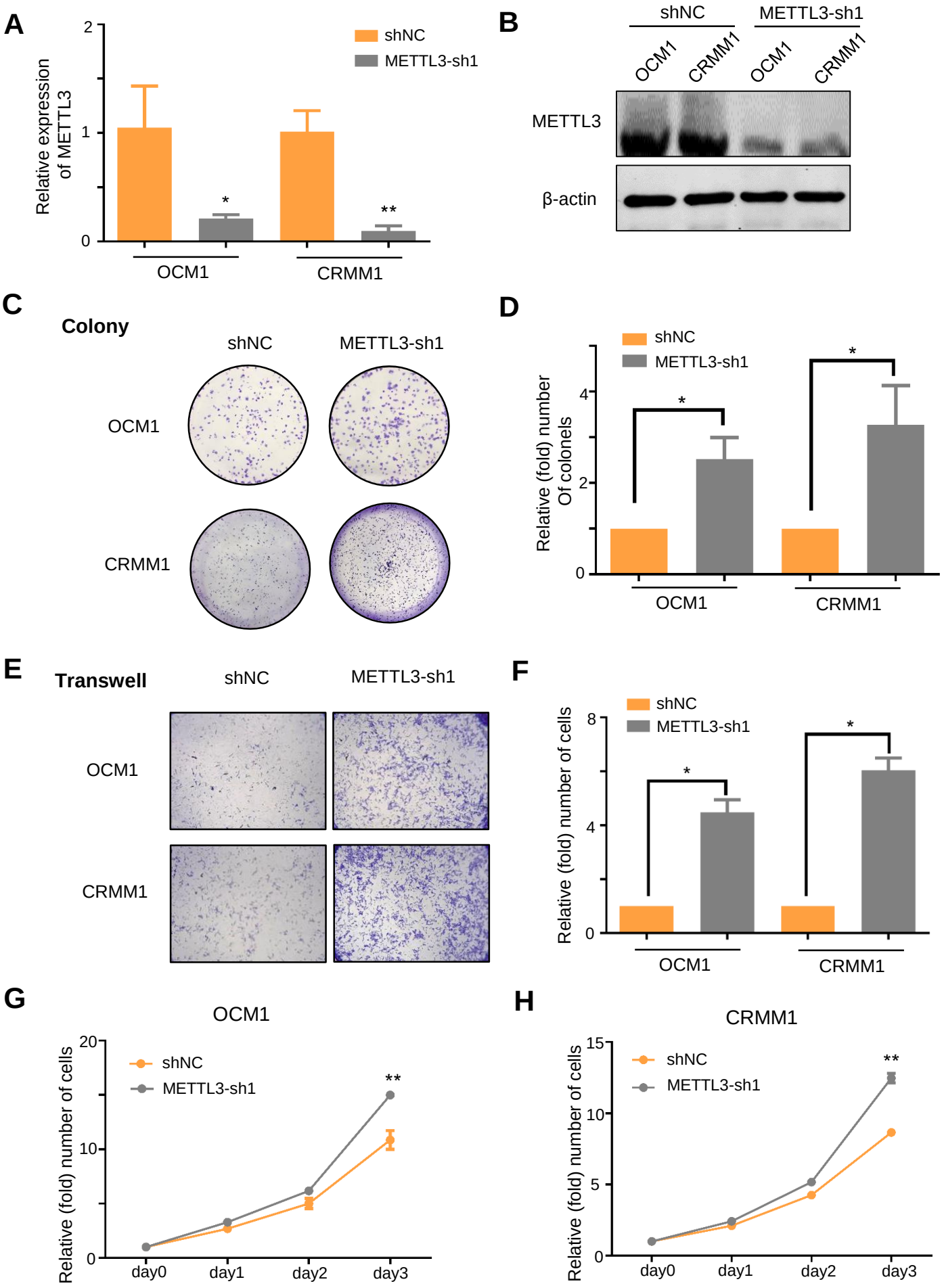Additional file 5：**Figure S2**