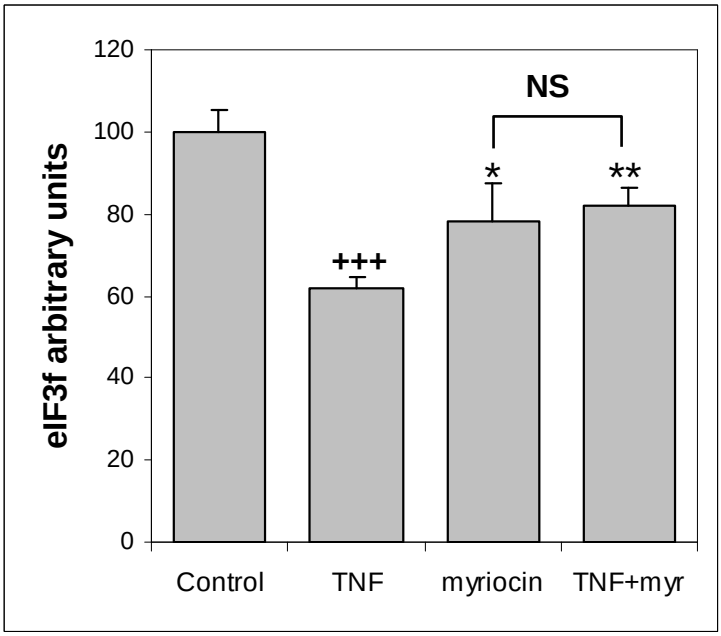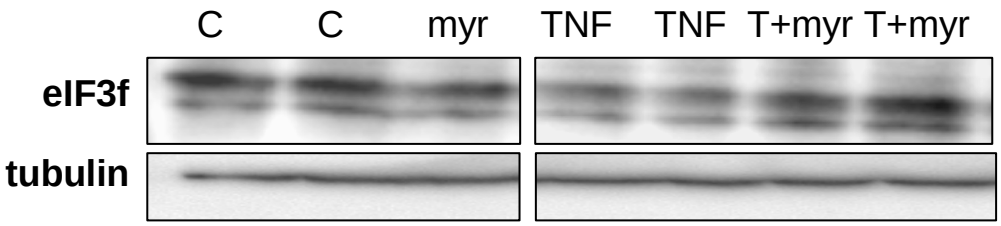Additional file 3.