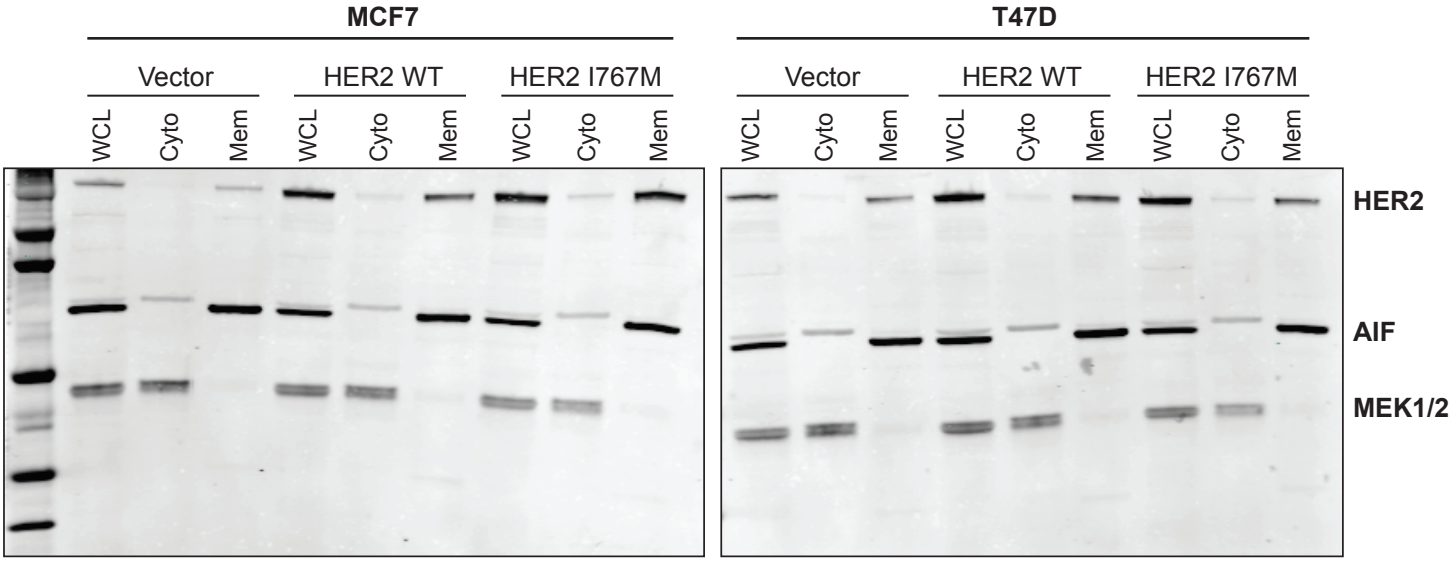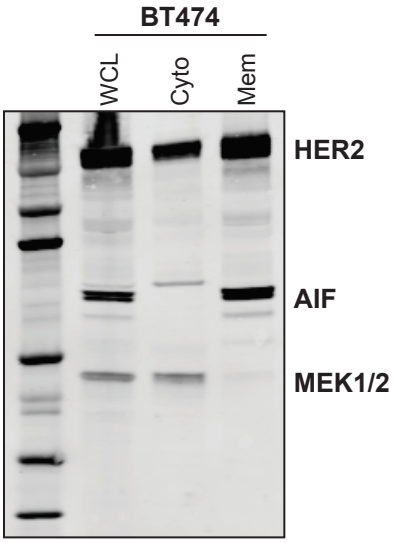Additional file 14