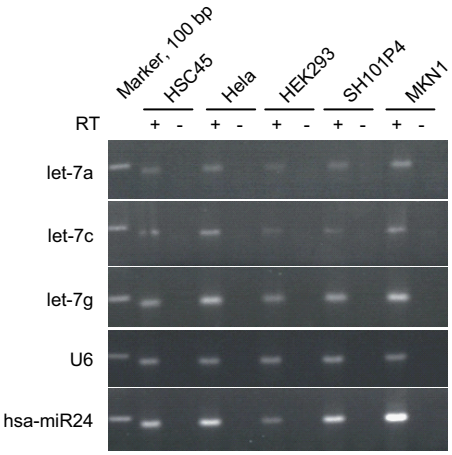Additional file 12.