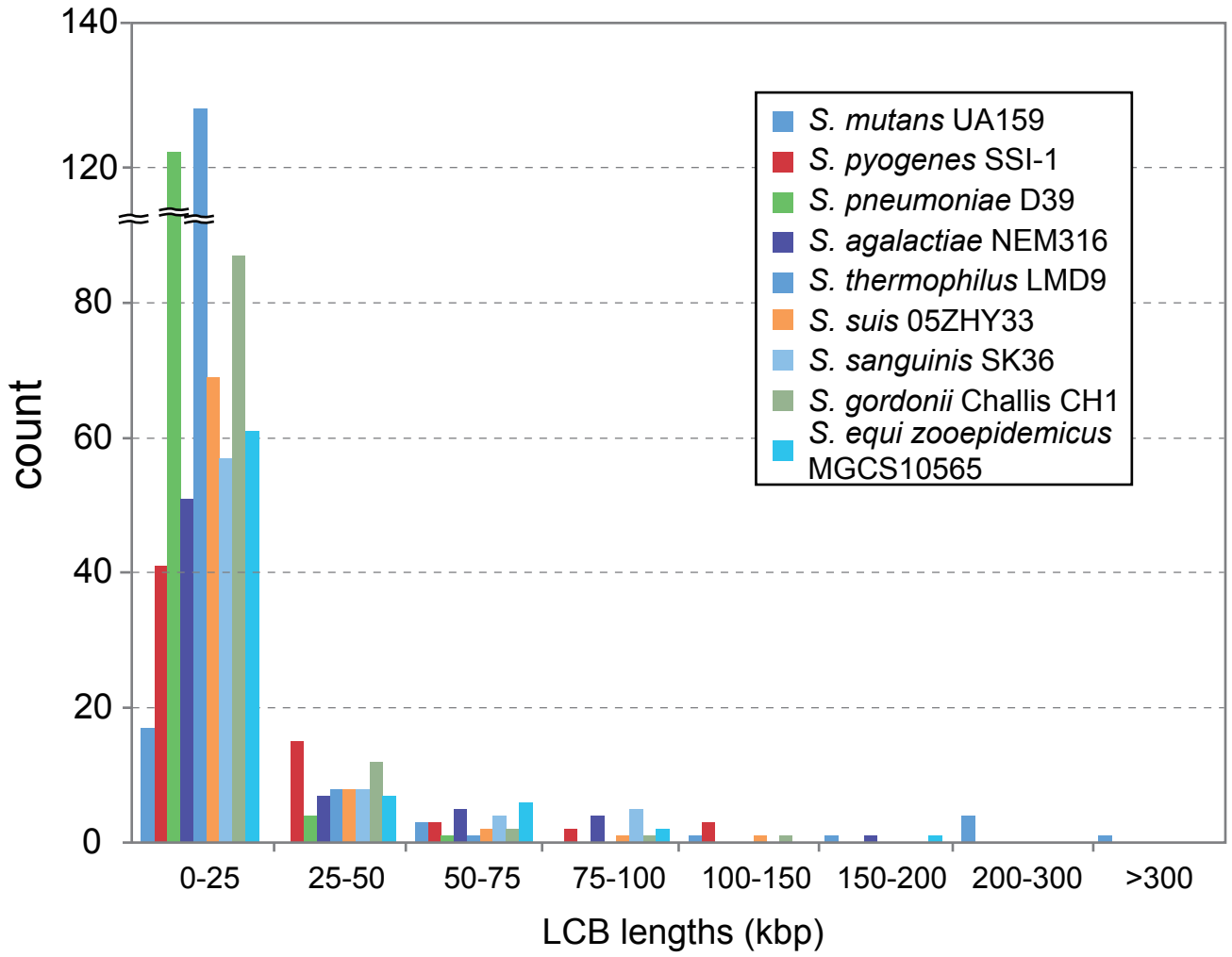Additional file 19