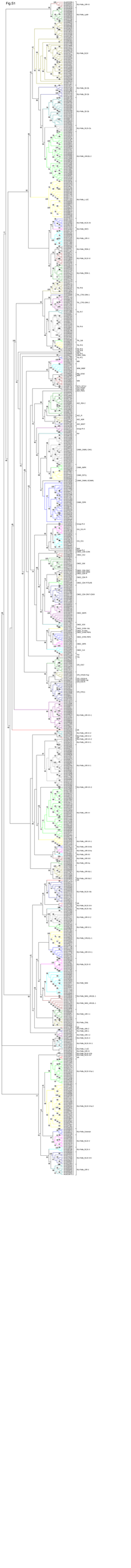Fig.S1