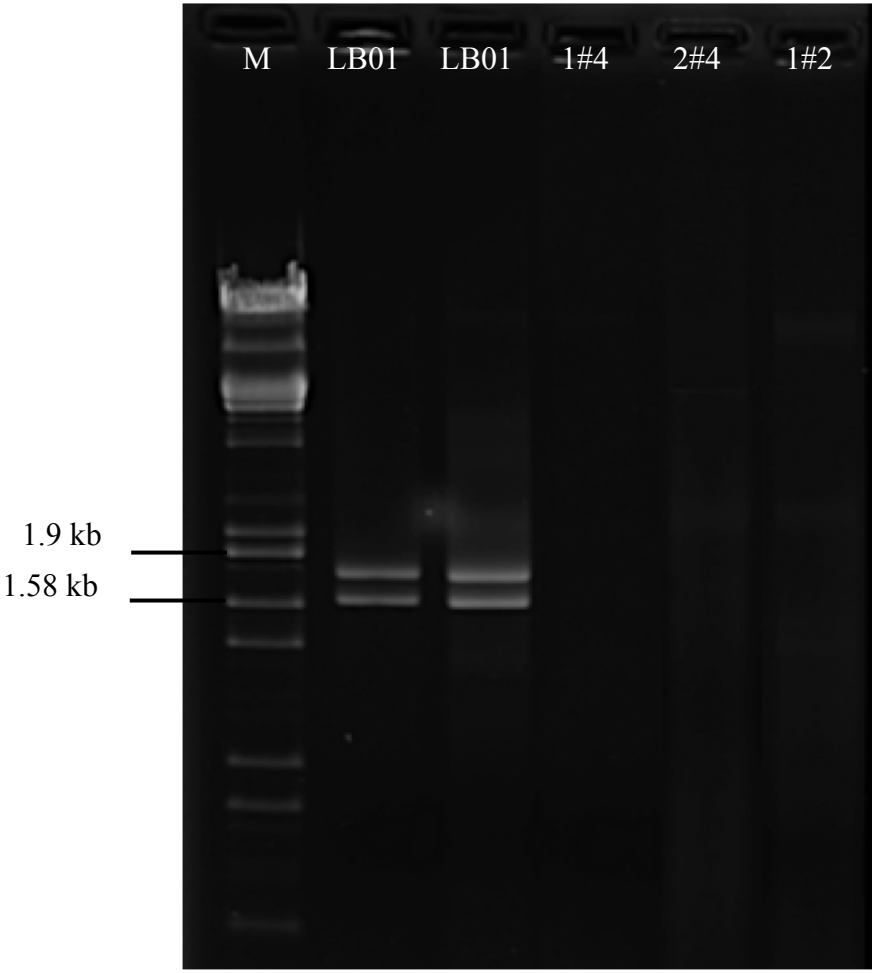Fig S1