

Table S1. **Ensembl accession number, classification and name of DNase1L2 proteins included in the multiple alignment.**

Organism	Classification	Name ^a	Accession n°
<i>H. sapiens</i>	Mammalia	DNase1L2-L	ENSP00000316938.5
<i>H. sapiens</i>	Mammalia	DNase1L2-S	ENSP00000371874.4
<i>P. troglodytes</i>	Mammalia	DNase1L2-L	ENSPTRP000000013061
<i>G. gorilla</i>	Mammalia	DNase1L2-S	ENSGGOP000000013907
<i>M. mulatta</i>	Mammalia	DNase1L2-S	ENSMMPUP000000053522
<i>A. nancyanae</i>	Mammalia	DNase1L2-L	ENSANAP000000013147
<i>O. cuniculus</i>	Mammalia	DNase1L2-S	ENSOCUP000000016098
<i>T. truncatus</i>	Mammalia	DNase1L2-L	ENSTTRP000000007777
<i>B. taurus</i>	Mammalia	DNase1L2-S	ENSBTAP000000013142
<i>P. vampyrus</i>	Mammalia	DNase1L2-L	ENSPVAP000000004824
<i>E. telfairi</i>	Mammalia	DNase1L2-L	ENSETEP000000007838
<i>R. norvegicus</i>	Mammalia	DNase1L2-S	ENSRNOP000000012203
<i>M. musculus</i>	Mammalia	DNase1L2-S	ENSMUSP000000085862
<i>L. africana</i>	Mammalia	DNase1L2-S	ENSLAFP000000027192
<i>M. monoceros</i>	Mammalia	DNase1L2-S	ENSMMPNP000015009148
<i>M. domestica</i>	Mammalia	DNase1L2-S	ENSMODP000000019845
<i>G. gallus</i>	Sauropsida	DNase1L2-S	ENSGALP000000064712
<i>A. carolinensis</i>	Sauropsida	DNase1L2-S	ENSACAP000000000576
<i>C. pictabellii</i>	Sauropsida	DNase1L2-S	ENSCBPB000000015855
<i>P. major</i>	Sauropsida	DNase1L2-S	ENSPMJP000000013429

^aName in accordance with the presence (DNase1L2-L) or absence (DNase1L2-S) of the P-rich region (see Figure 1A)

Table S2. Viscosity measurements of CF artificial mucus after incubation with DNase1L2 or rhDNase in the presence or absence of actin (0.2 mg/ml).

	Viscosity mPa·s (mean ± SD)		
	90 s	300 s	600 s
no enzyme	9783 ± 1656	9667 ± 1457	ND
no enzyme + Actin	8141 ± 689	8171 ± 932	ND
DNase1L2	1847 ± 263	603 ± 155	236 ± 40
DNase1L2 + Actin	4649 ± 960	2570 ± 865	1292 ± 446
rhDNase	410 ± 58	18 ± 16	ND
rhDNase + Actin	9330 ± 1537	8469 ± 2068	6666 ± 2747
rhDNase* + Actin	8606 ± 1377	4925 ± 2663	1432 ± 1410

Enzyme concentration was: DNase1L2, 20 ng/μl - 5 U; rhDNase, 2 ng/μl - 5 U; rhDNase*, 20 ng/μl - 50 U