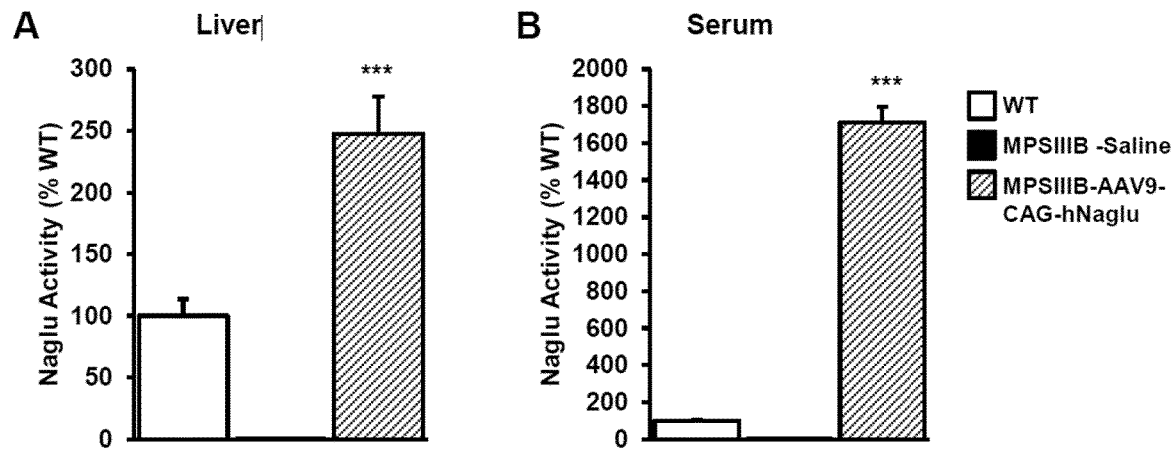


Figure 1

HDTV – Human NAGLU



A Liver

Naglu Activity (% WT)

Group	Naglu Activity (% WT)	Significance
WT	100	nd
MPSIII B	~710	***
MPSIII B-AAV9-CAG-hNaglu	~710	***

B Serum

Naglu Activity (% WT)

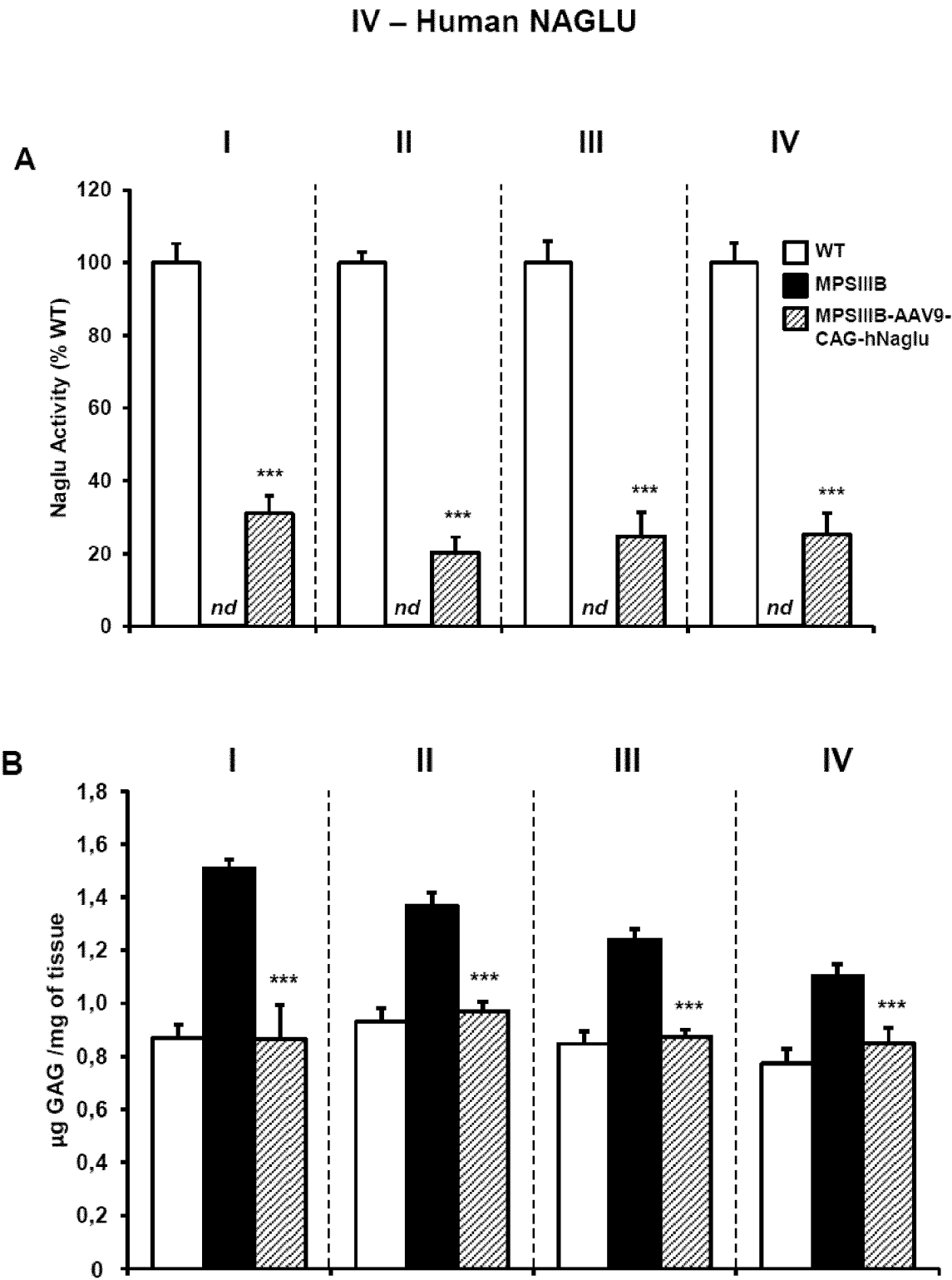
Group	Naglu Activity (% WT)	Significance
WT	100	
MPSIII B	~1	nd
MPSIII B-AAV9-CAG-hNaglu	~32	**

C

µg GAG/mg of tissue

Tissue	WT	MPSIII B	MPSIII B-AAV9-CAG-hNaglu	Significance
Liver	~1.0	~9.5	~1.5	***
Spleen	~0.32	~1.02	~0.28	***
Heart	~0.40	~0.78	~0.40	***
Lung	~0.35	~0.70	~0.22	**
Kidney	~0.7	~4.4	~1.6	***, \$\$\$
Testis	~0.32	~0.75	~0.45	***
U. bladder	~0.7	~1.45	~0.75	***

Figure 3



IV – Codon-optimized human NAGLU

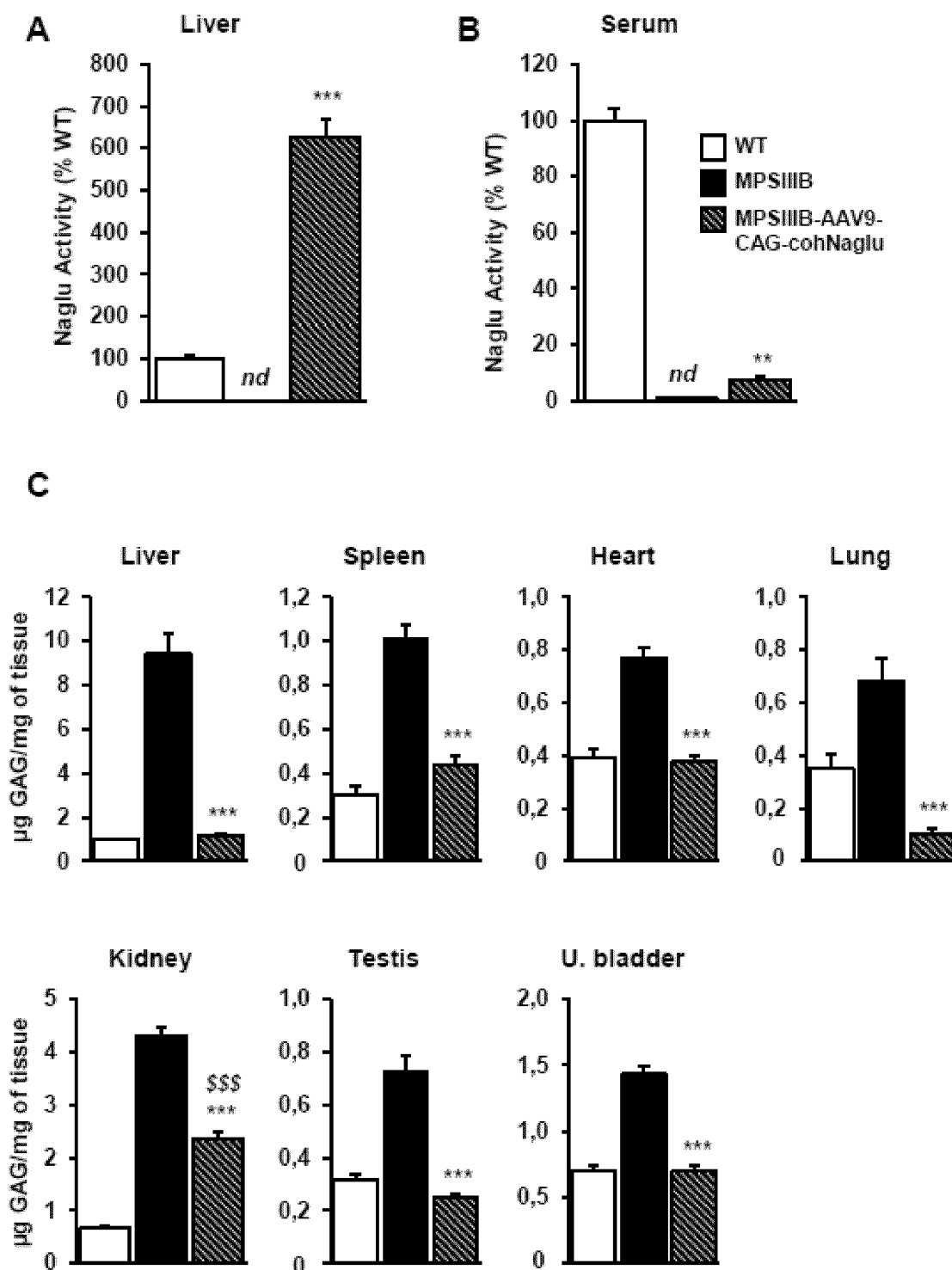


Figure 5

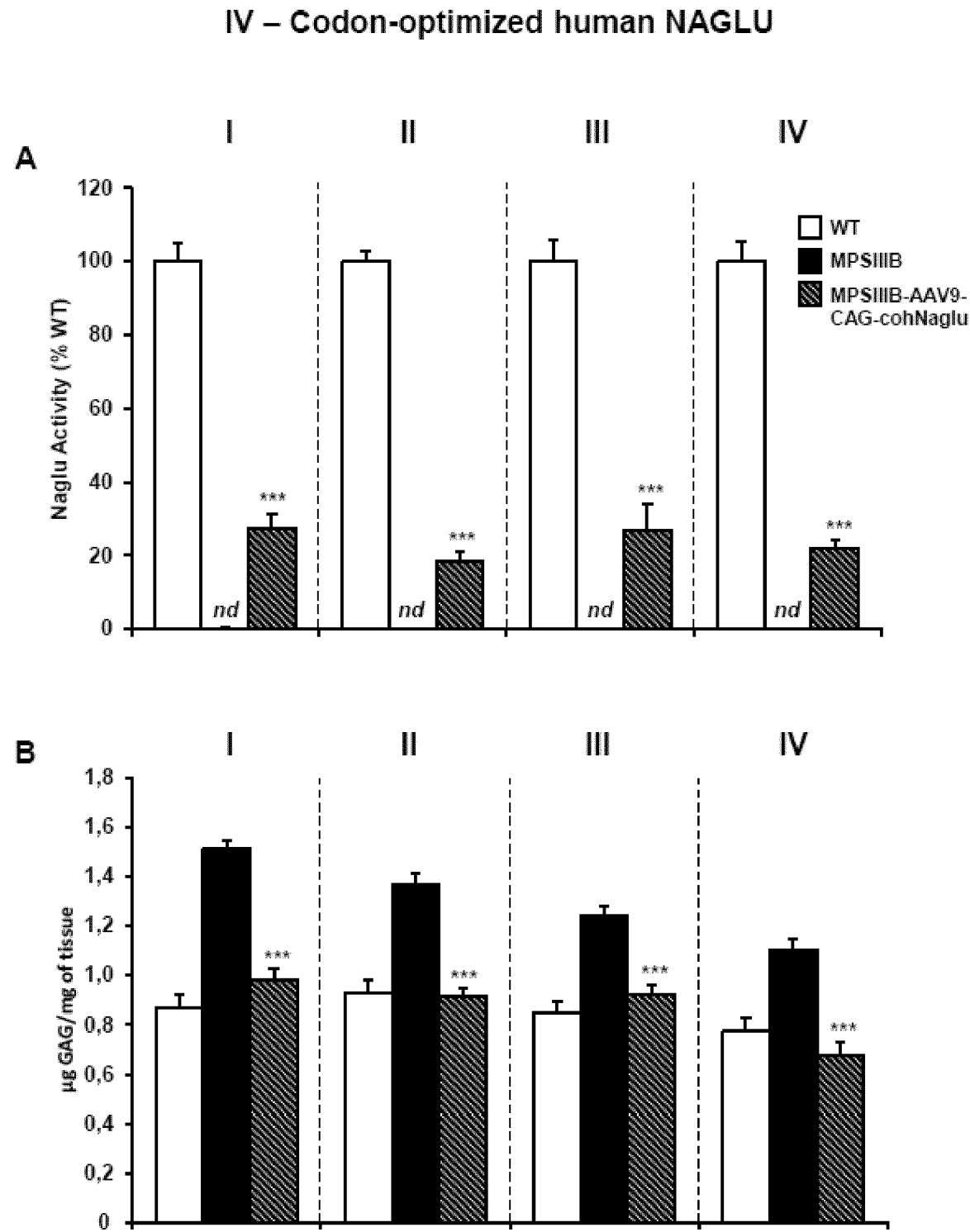


Figure 6

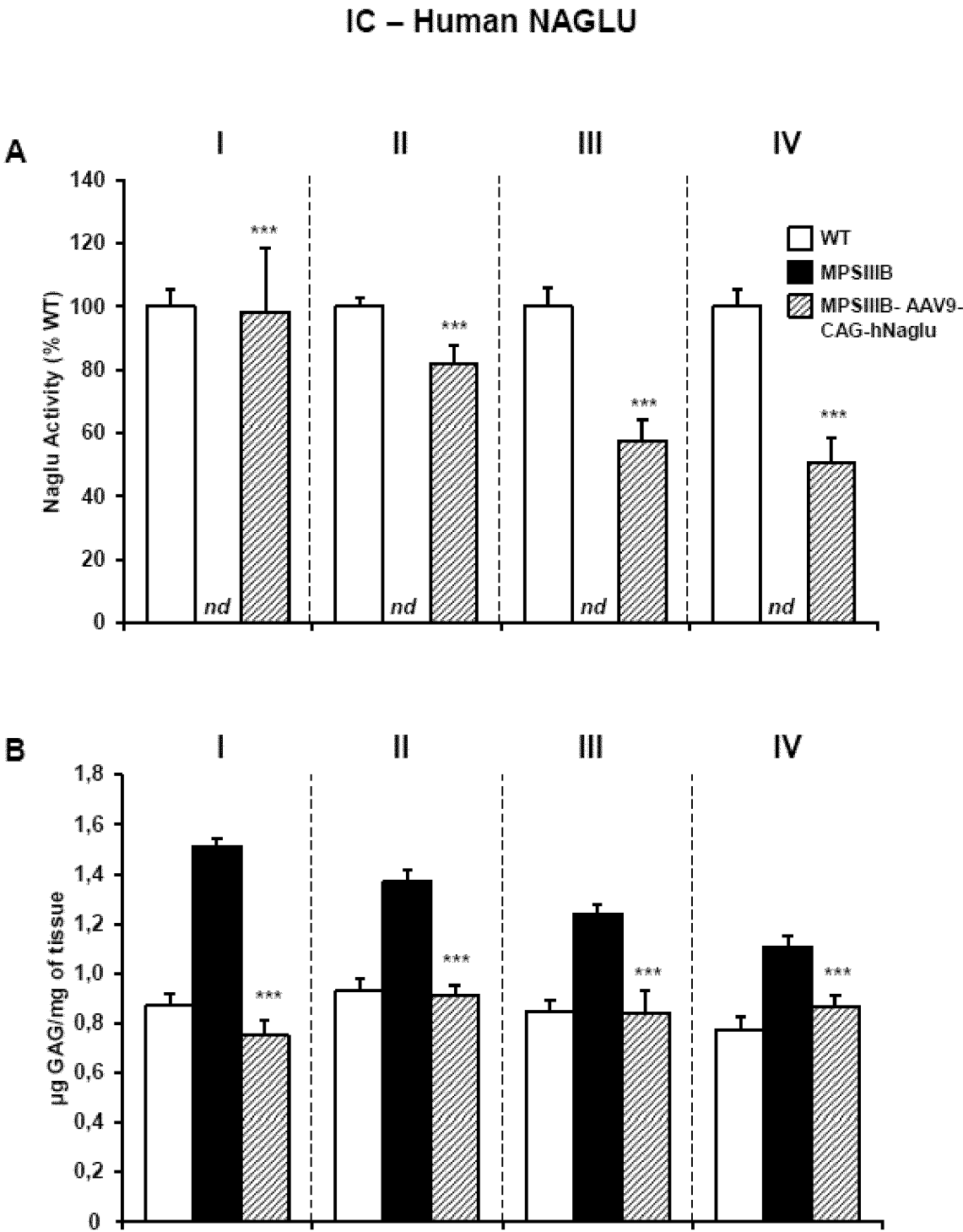


Figure 7

IC – Human NAGLU

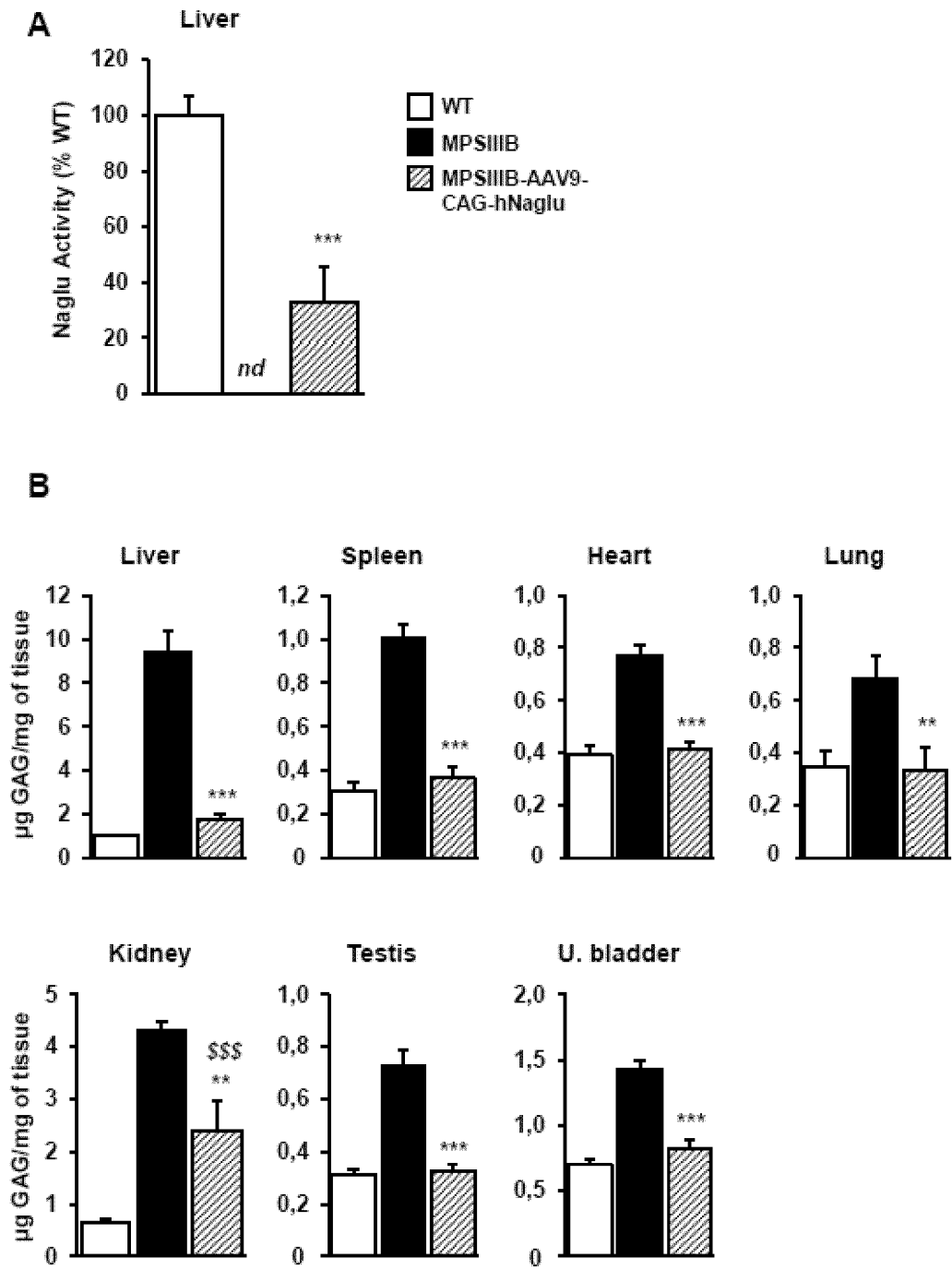


Figure 8

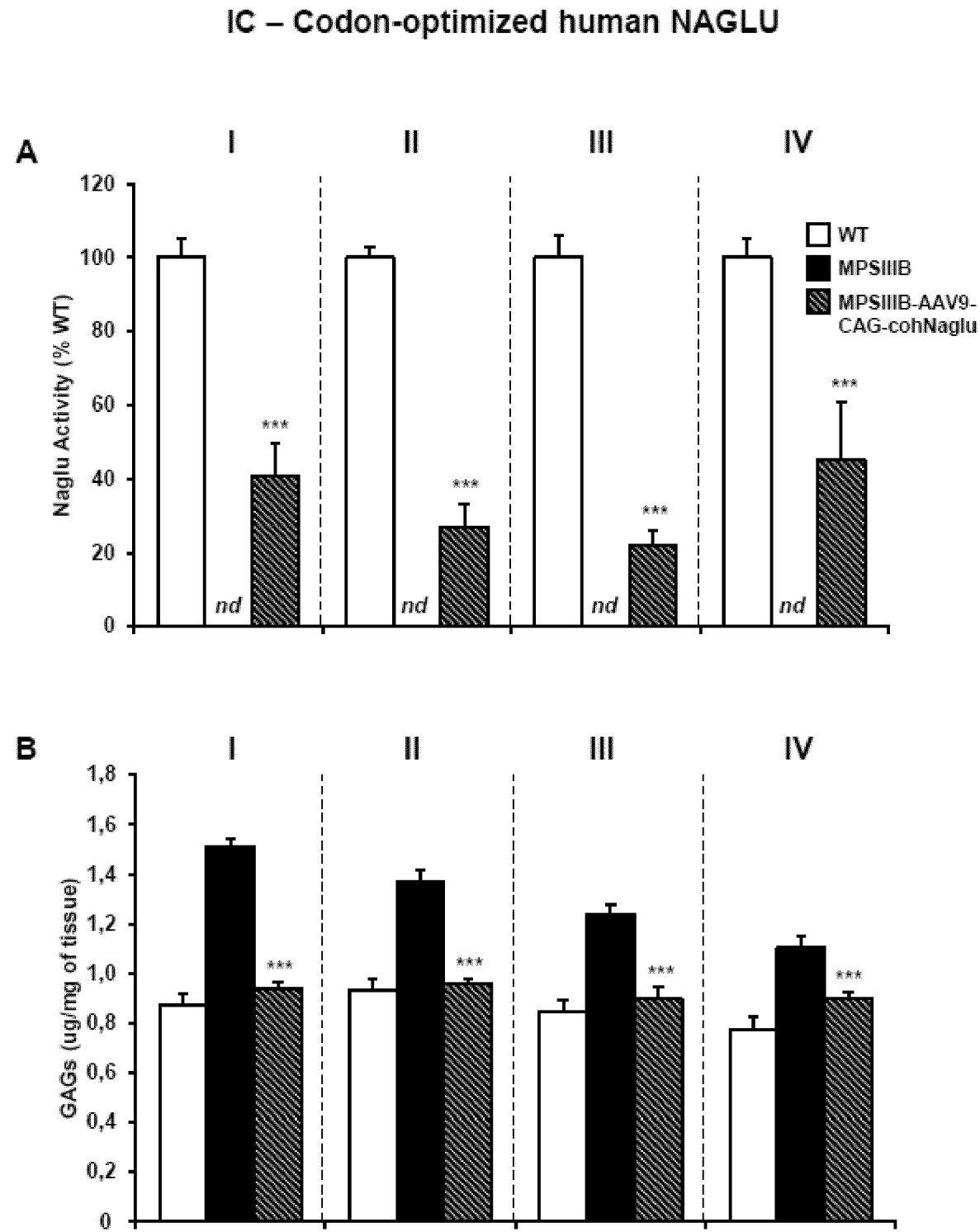


Figure 9

IC – Codon-optimized human NAGLU

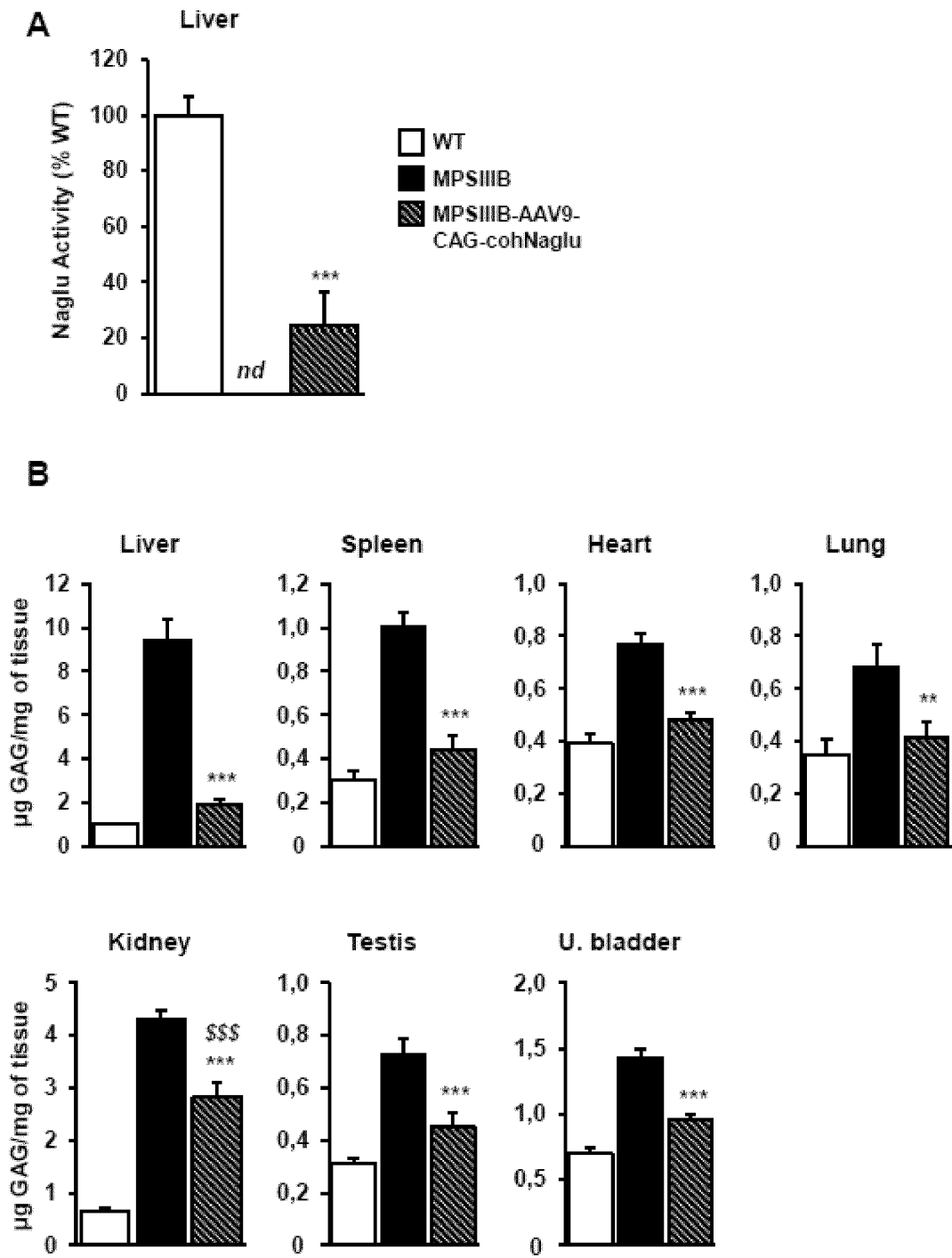


Figure 10

HDTV – Codon-optimized human NAGLU version2

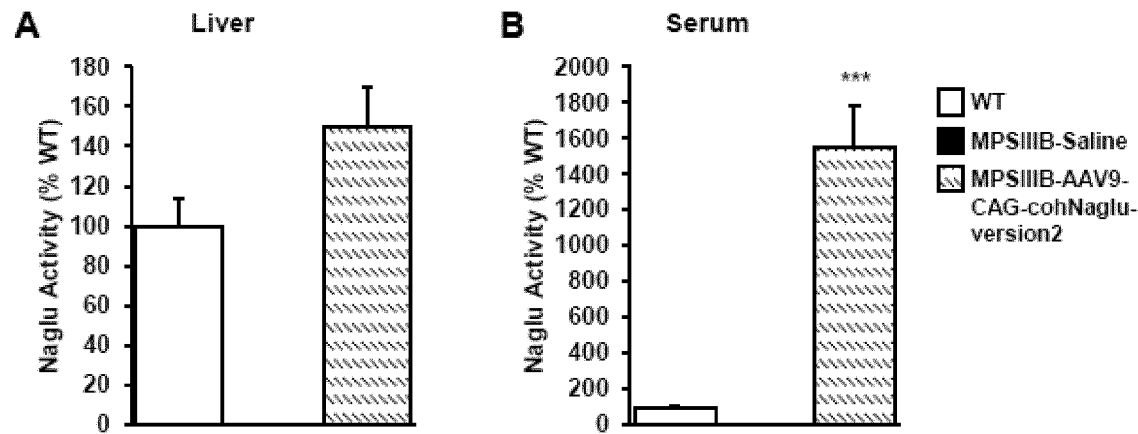


Figure 11

HDTV – Codon-optimized human NAGLU version3

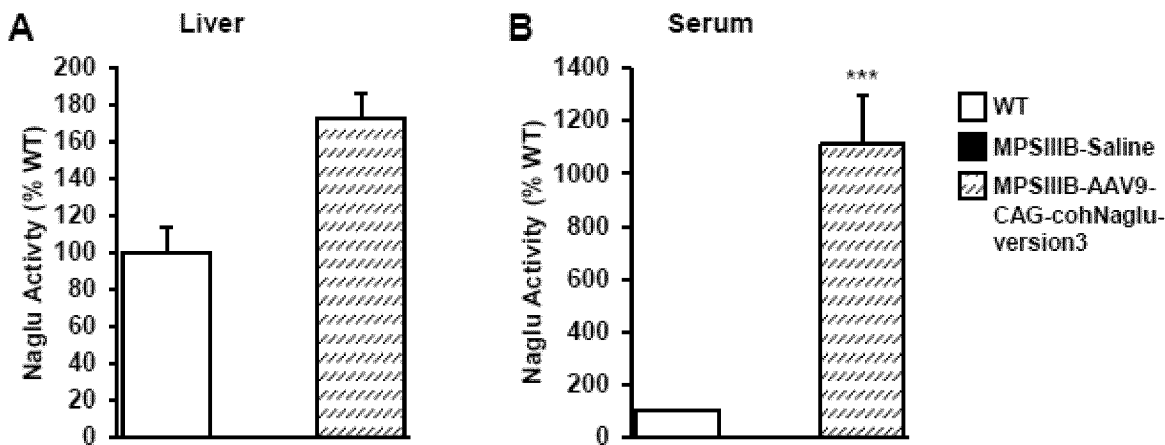
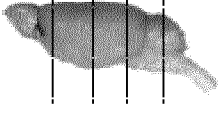


Figure 12

IC – Codon-optimized murine NAGLU**A**

Brain Section 	Vector genomes /diploid genome	
	<i>Males</i>	<i>Females</i>
I	0.14 ± 0.04	0.13 ± 0.03
II	0.09 ± 0.01	0.12 ± 0.04
III	0.13 ± 0.04	0.19 ± 0.10
IV	1.61 ± 0.73	0.80 ± 0.55
V	0.94 ± 0.15	1.35 ± 0.74
Spinal cord	0.14 ± 0.07	0.07 ± 0.02

B

Tissue	Vector genomes /diploid genome	
	<i>Males</i>	<i>Females</i>
Liver	0.78 ± 0.33	0.72 ± 0.33
Spleen	0.03 ± 0.02	0.02 ± 0.01
Heart	0.01 ± 0.00	0.01 ± 0.01
Kidney	0.01 ± 0.00	0.01 ± 0.00
Lung	0.01 ± 0.00	0.01 ± 0.00
Adrenal gland	0.04 ± 0.01	0.10 ± 0.01
Mandibular lymph node	0.12 ± 0.02	0.12 ± 0.02
Inguinal lymph node	0.01 ± 0.00	0.02 ± 0.01
White adipose tissue	0.02 ± 0.00	0.03 ± 0.01
Bone marrow	ND	ND
Skin	0.01 ± 0.00	ND
Thymus	ND	ND
Skeletal muscle	ND	ND
Intestine	ND	ND
Pancreas	ND	ND
Urinary bladder	ND	ND
Epididymus	ND	ND
Testicle	ND	ND
Oviduct	ND	ND

Figure 13

IC – Codon-optimized murine NAGLU

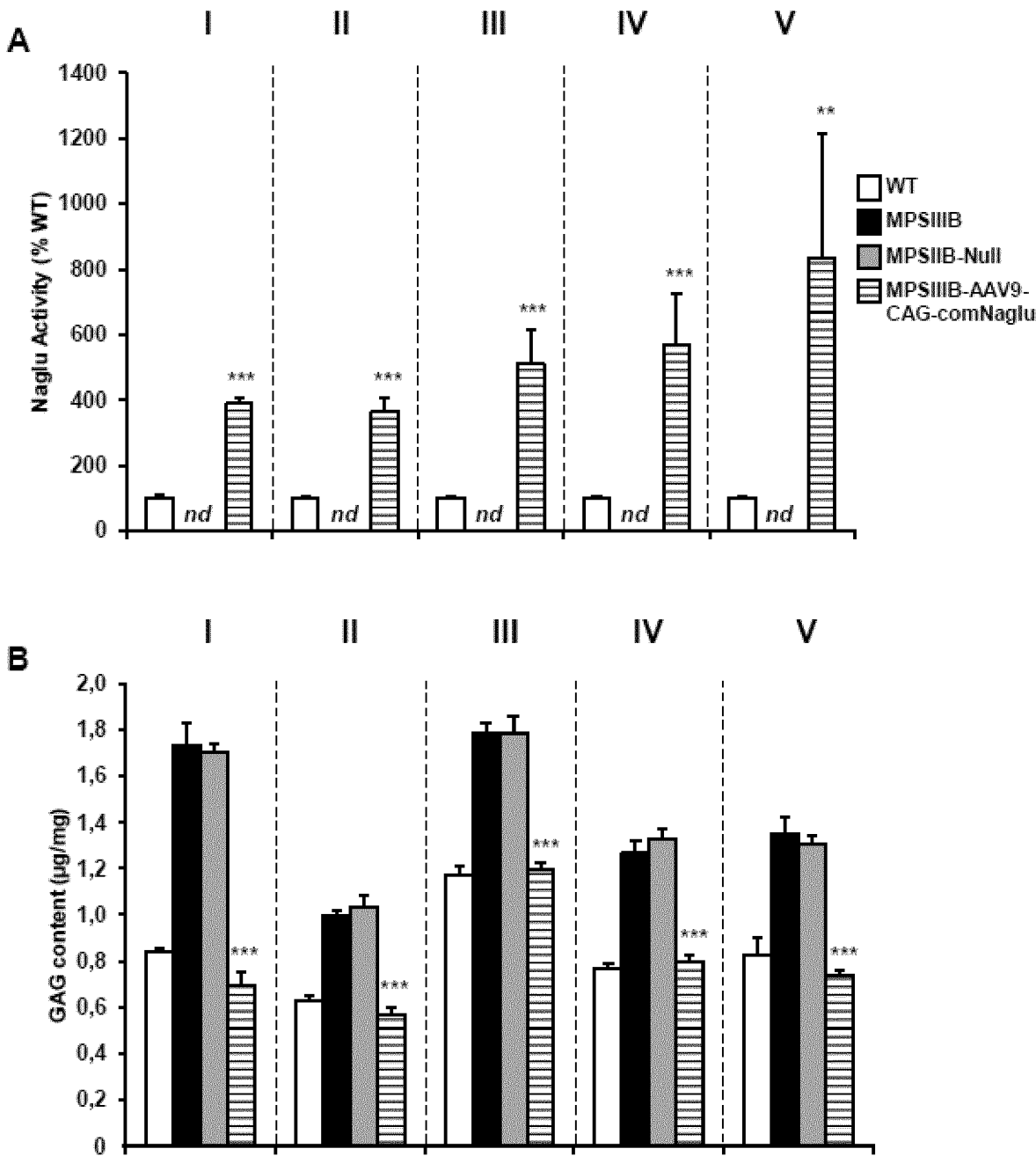
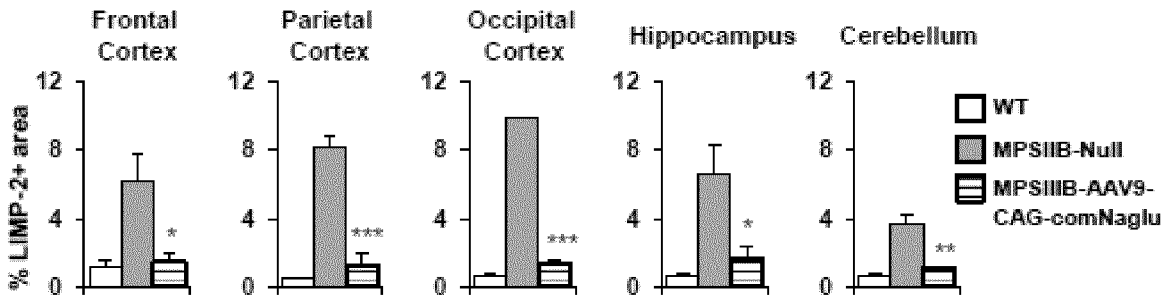


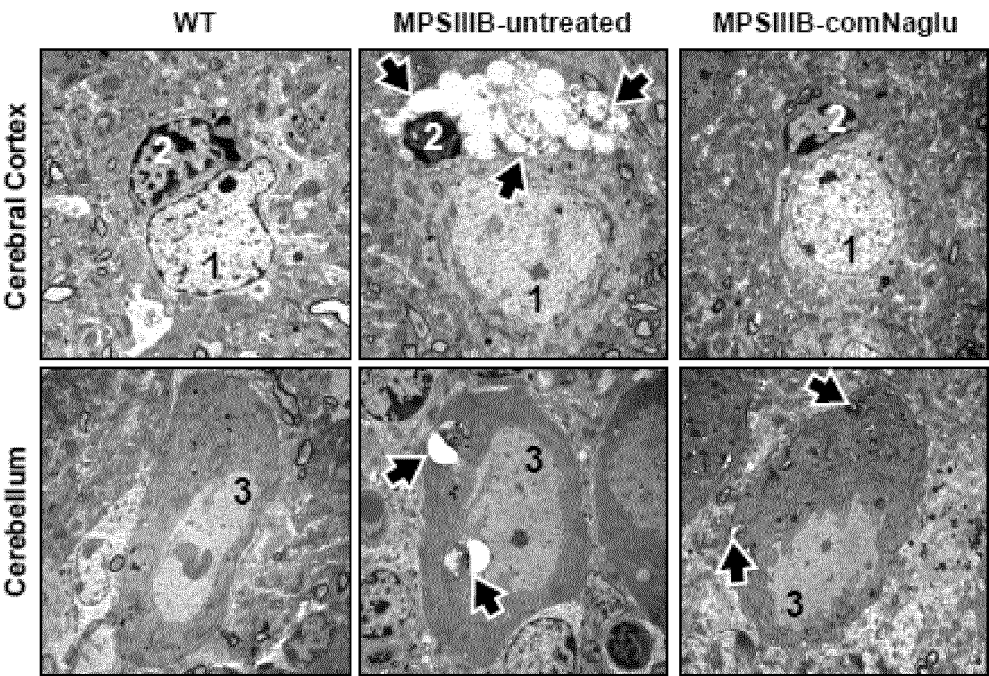
Figure 14

IC – Codon-optimized murine NAGLU

A



B



C

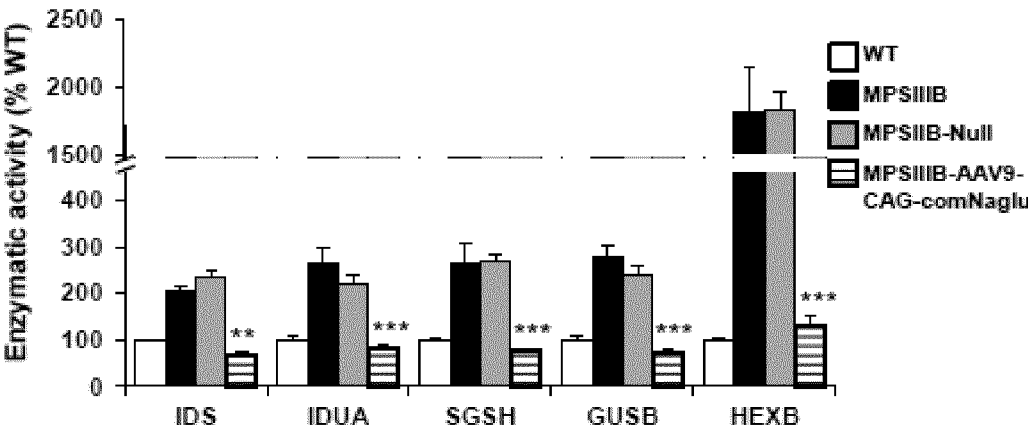


Figure 15 IC – Codon-optimized murine NAGLU

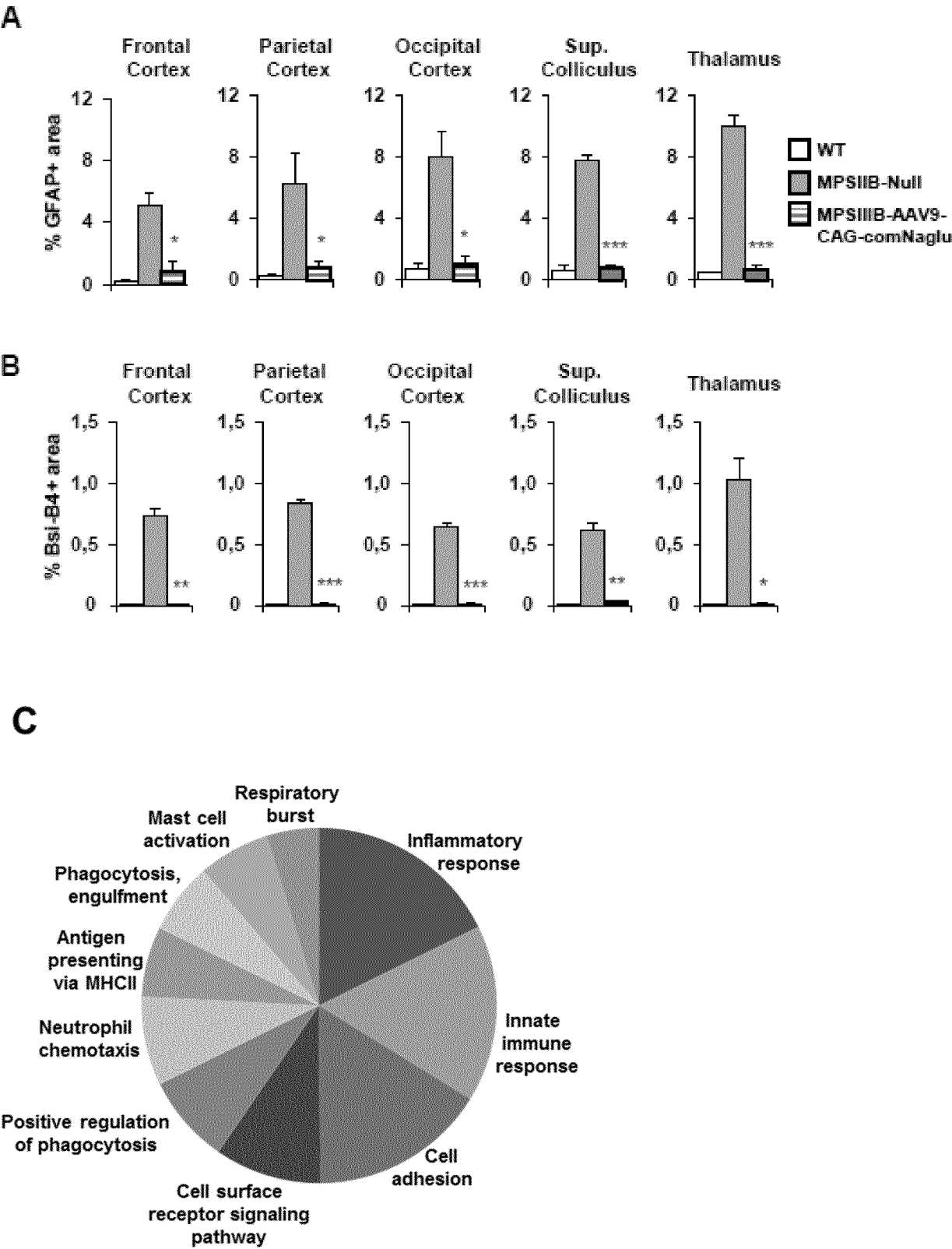


Figure 15

D

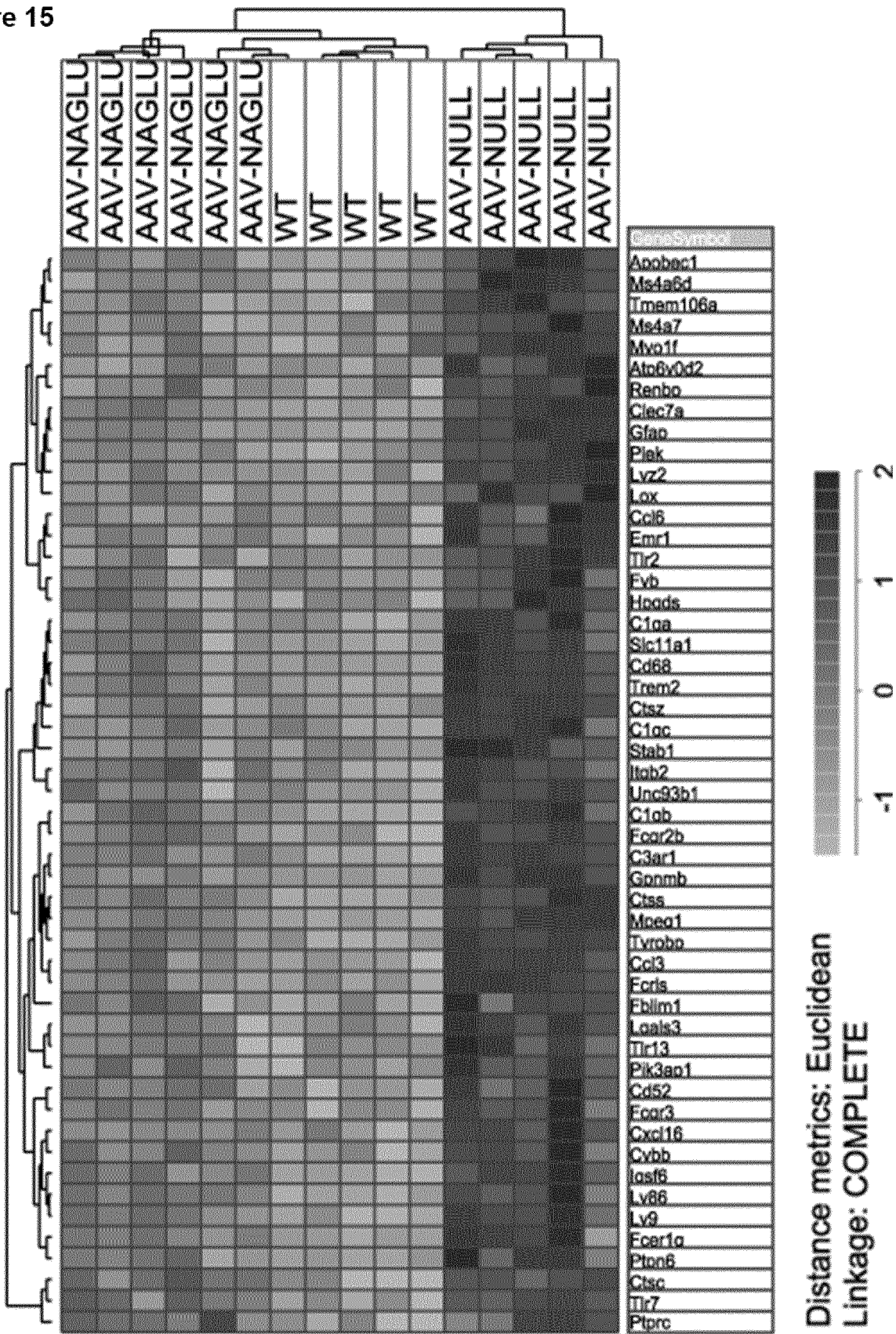


Figure 16
IC – Codon-optimized murine NAGLU

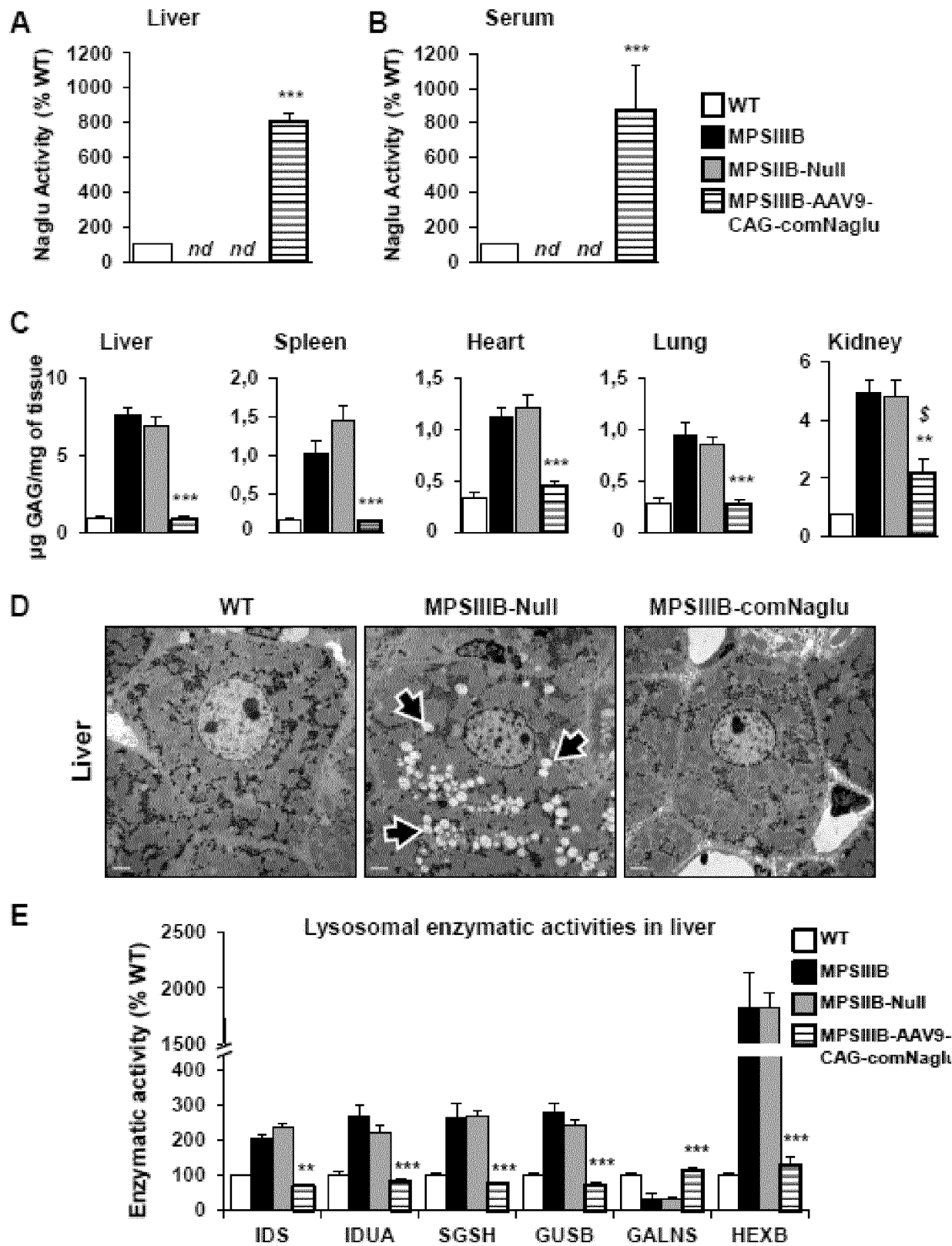


Figure 17

IC – Codon-optimized murine NAGLU

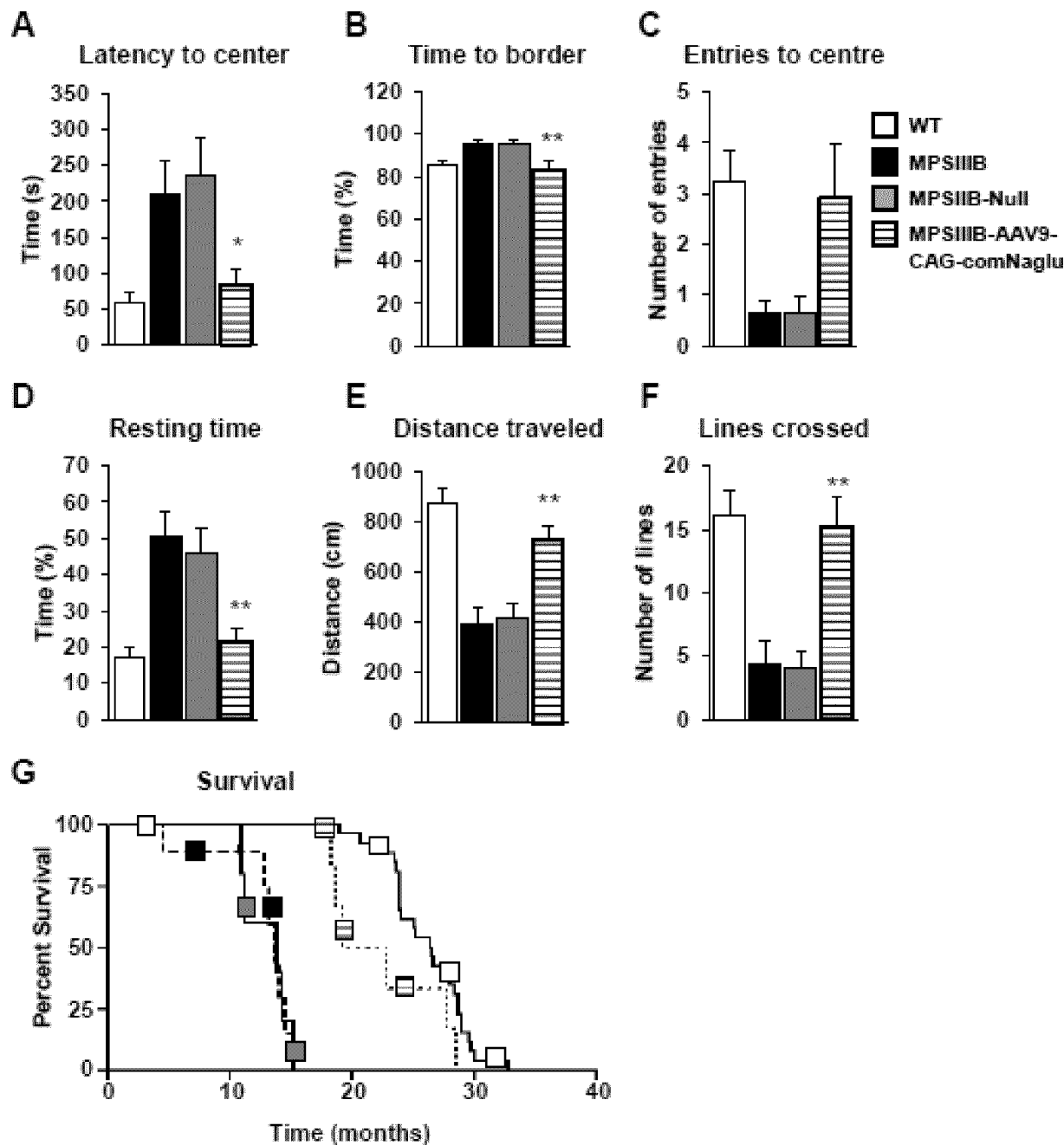


Figure 18

IC – Codon-optimized canine NAGLU

A

Anti-AAV9 Neutralizing antibodies								
Week	Non-immunized dogs				Immunized dogs			
	Dog 1		Dog 2		Dog 3		Dog 4	
	Serum	CSF	Serum	CSF	Serum	CSF	Serum	CSF
W -6	-	-	-	-	1:1	-	1:1	-
W -5	-	-	-	-	>1:316	-	>1:316	-
W -1	-	-	-	-	1:100	-	1:100	-
W 0	<1:1	1:1	<1:1	1:1	1:100	1:1	1:1000	1:1
W 1	>1:31,6	1:1	>1:31,6	1:1	1:10000	1:1	1:1000	1:1

B

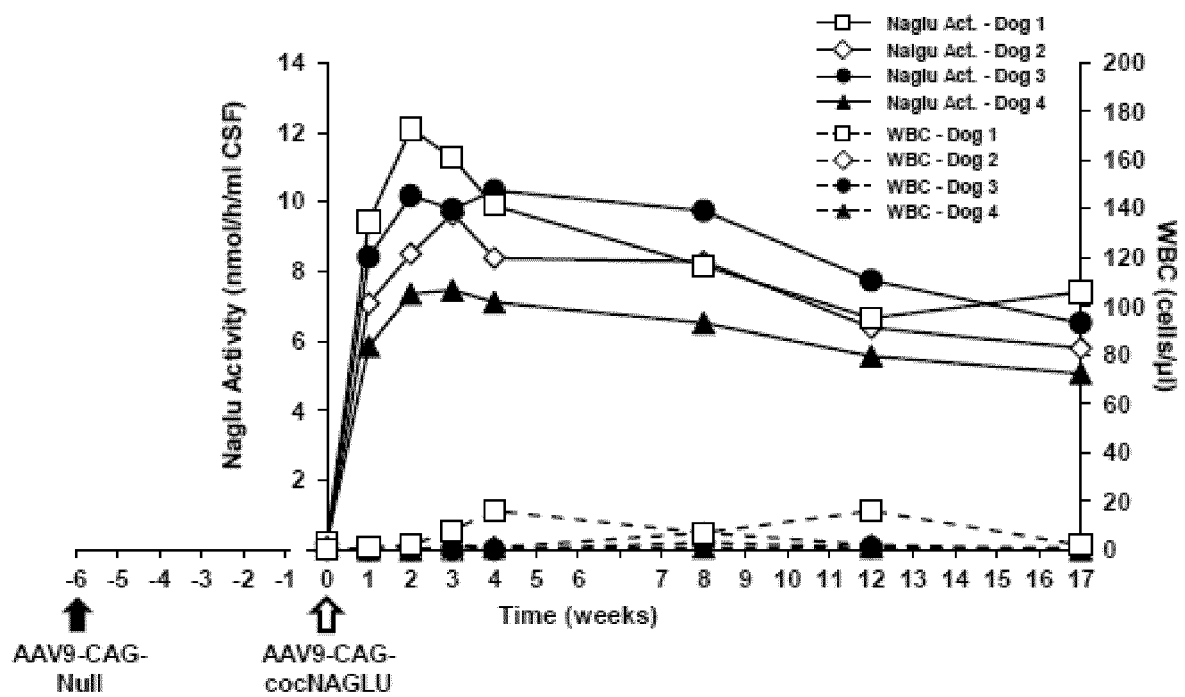
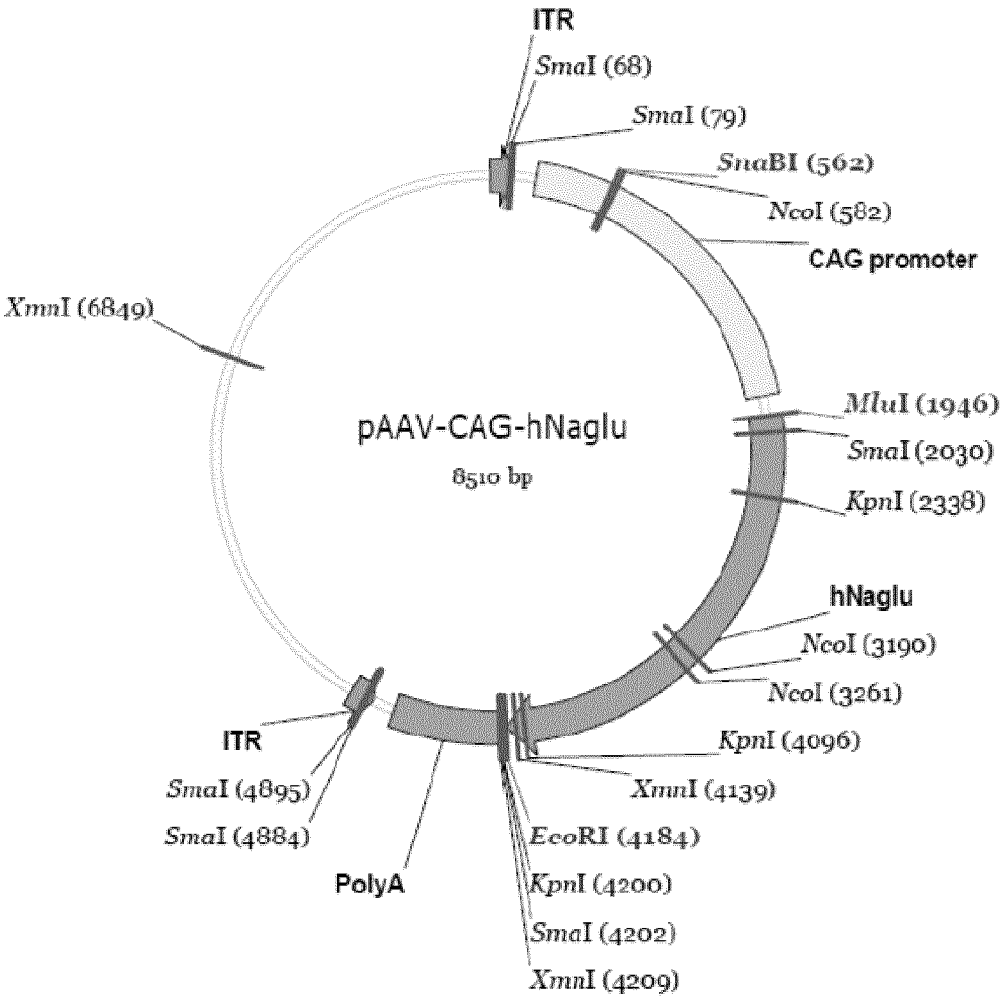


Figure 19

Human Naglu

A



B



Figure 20

Codon-optimized human Naglu

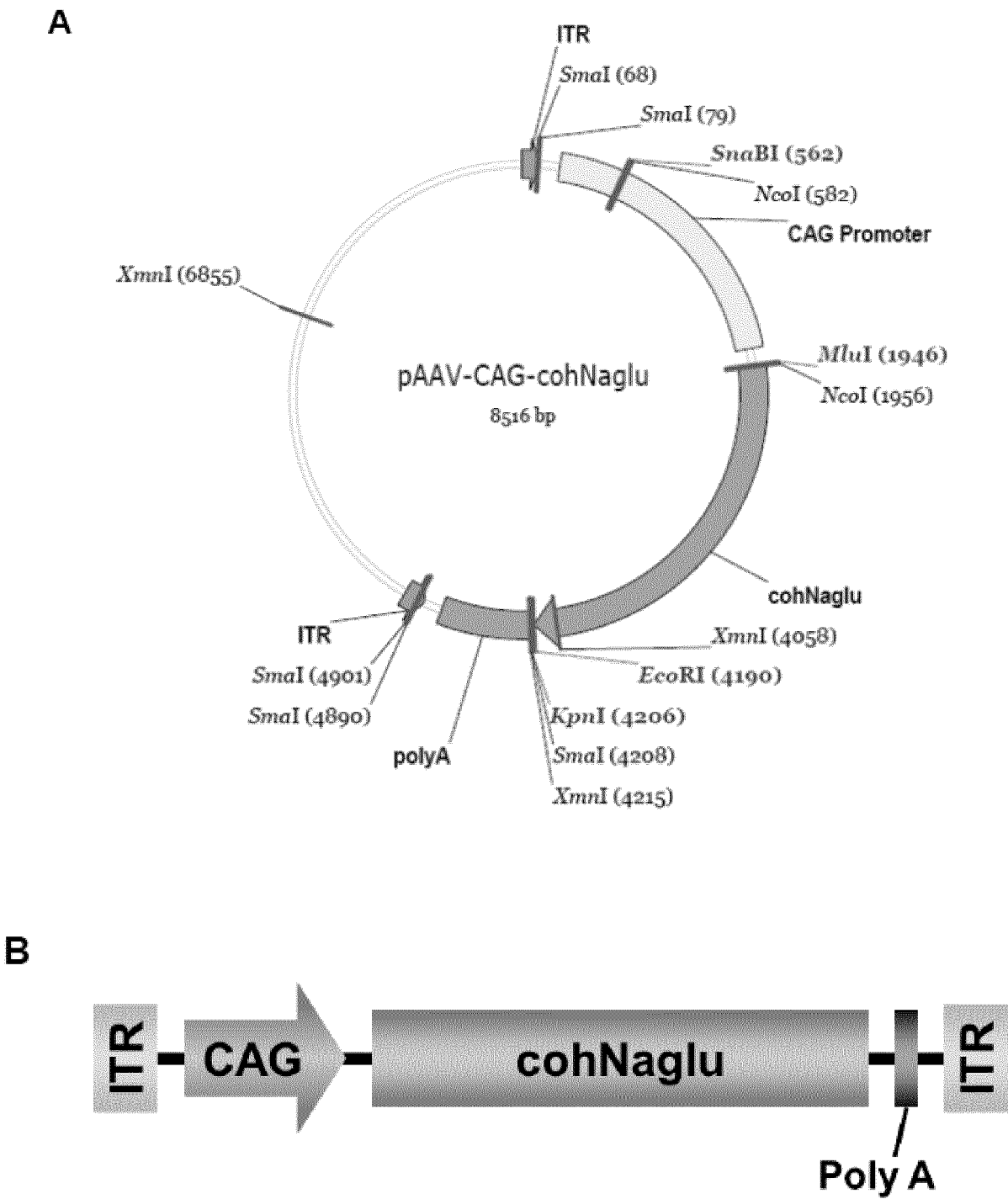


Figure 21

Codon-optimized human Naglu version2

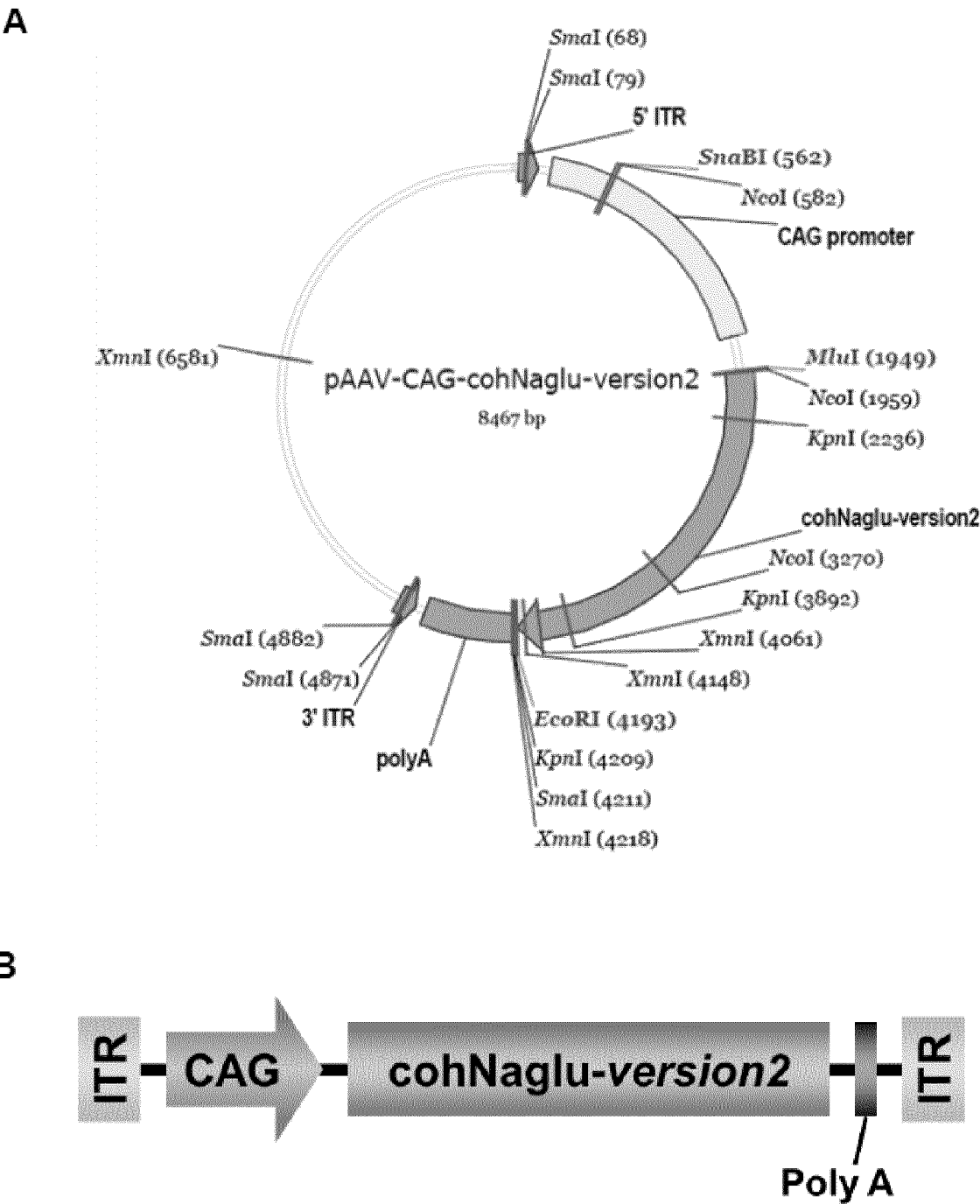
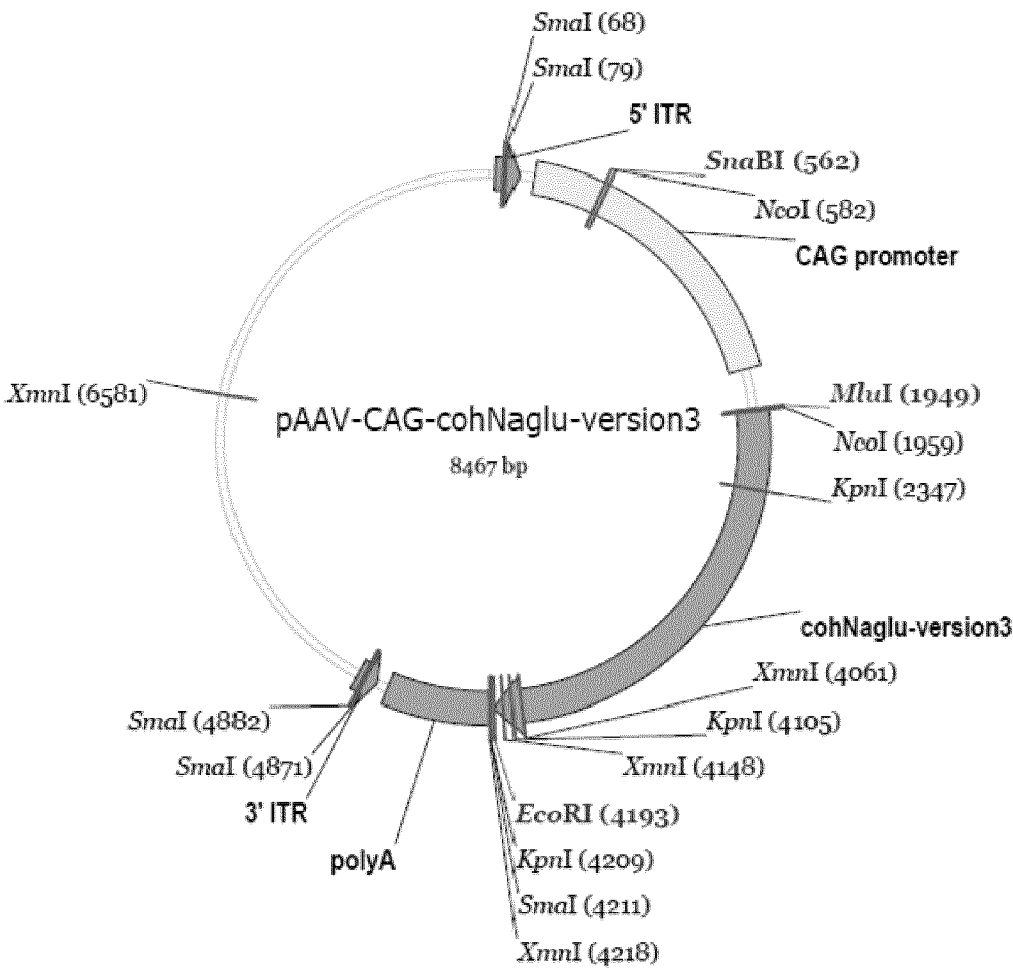


Figure 22

Codon-optimized human Naglu version3

A



B

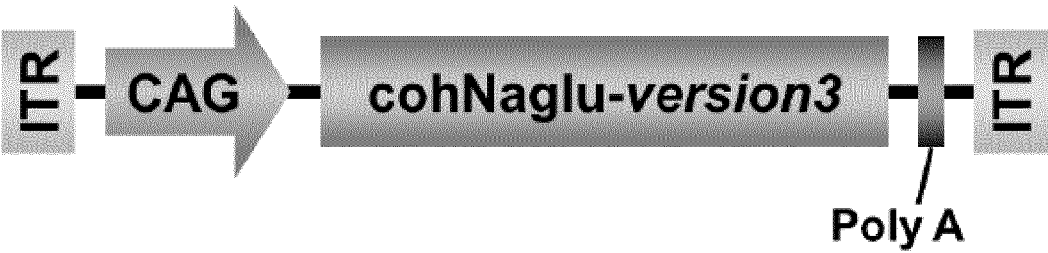


Figure 23

Codon-optimized murine Naglu

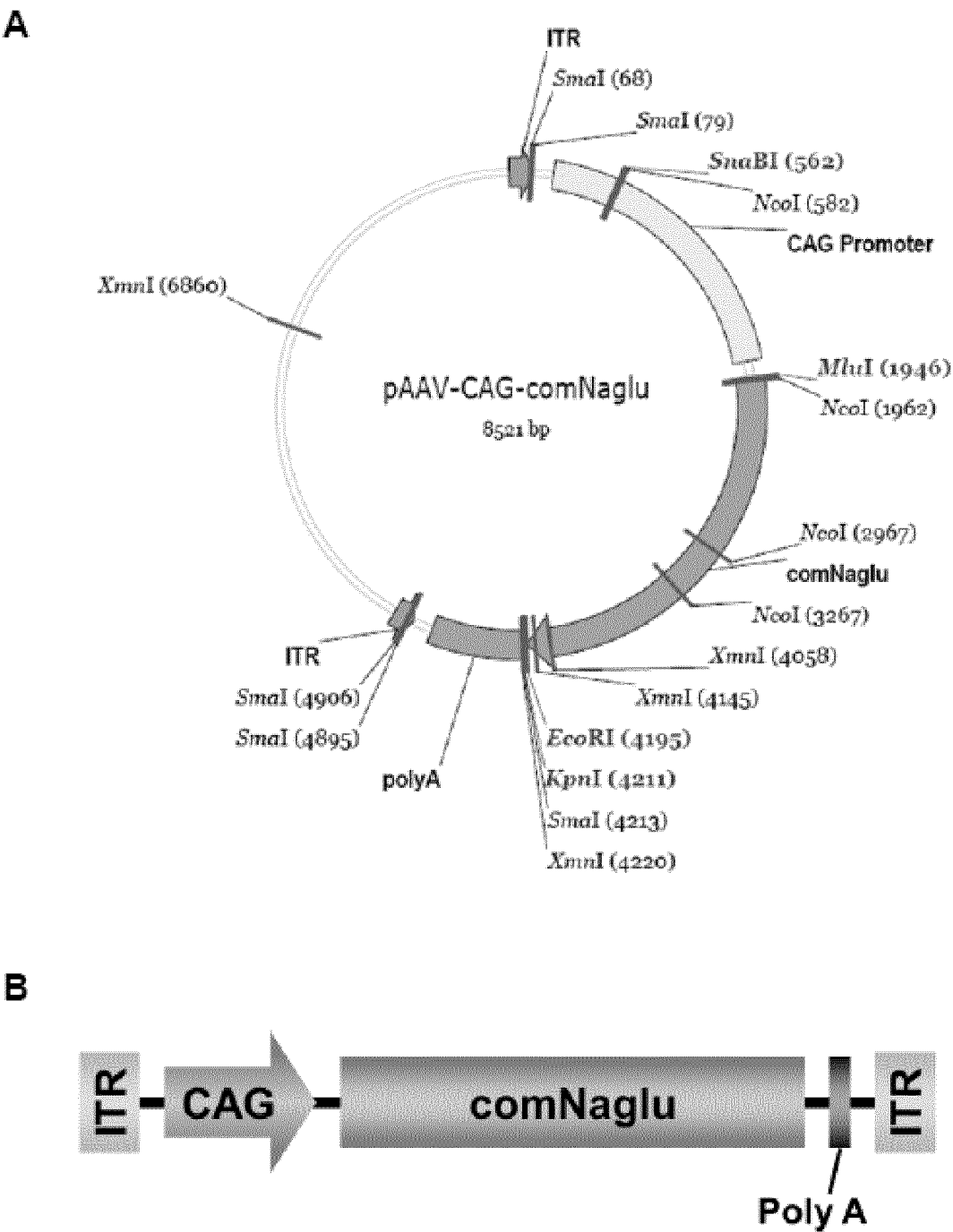


Figure 24

Codon-optimized canine Naglu

