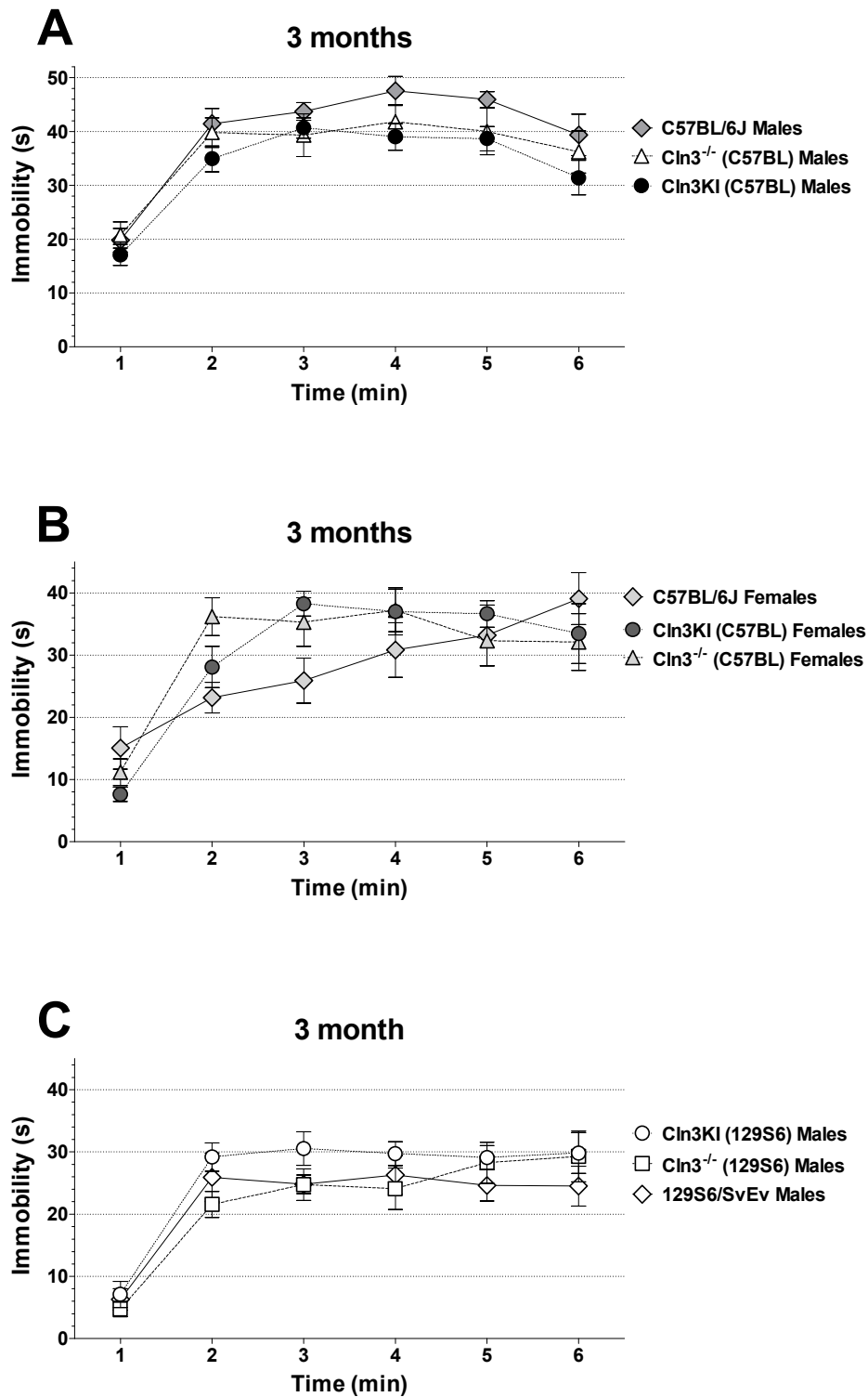


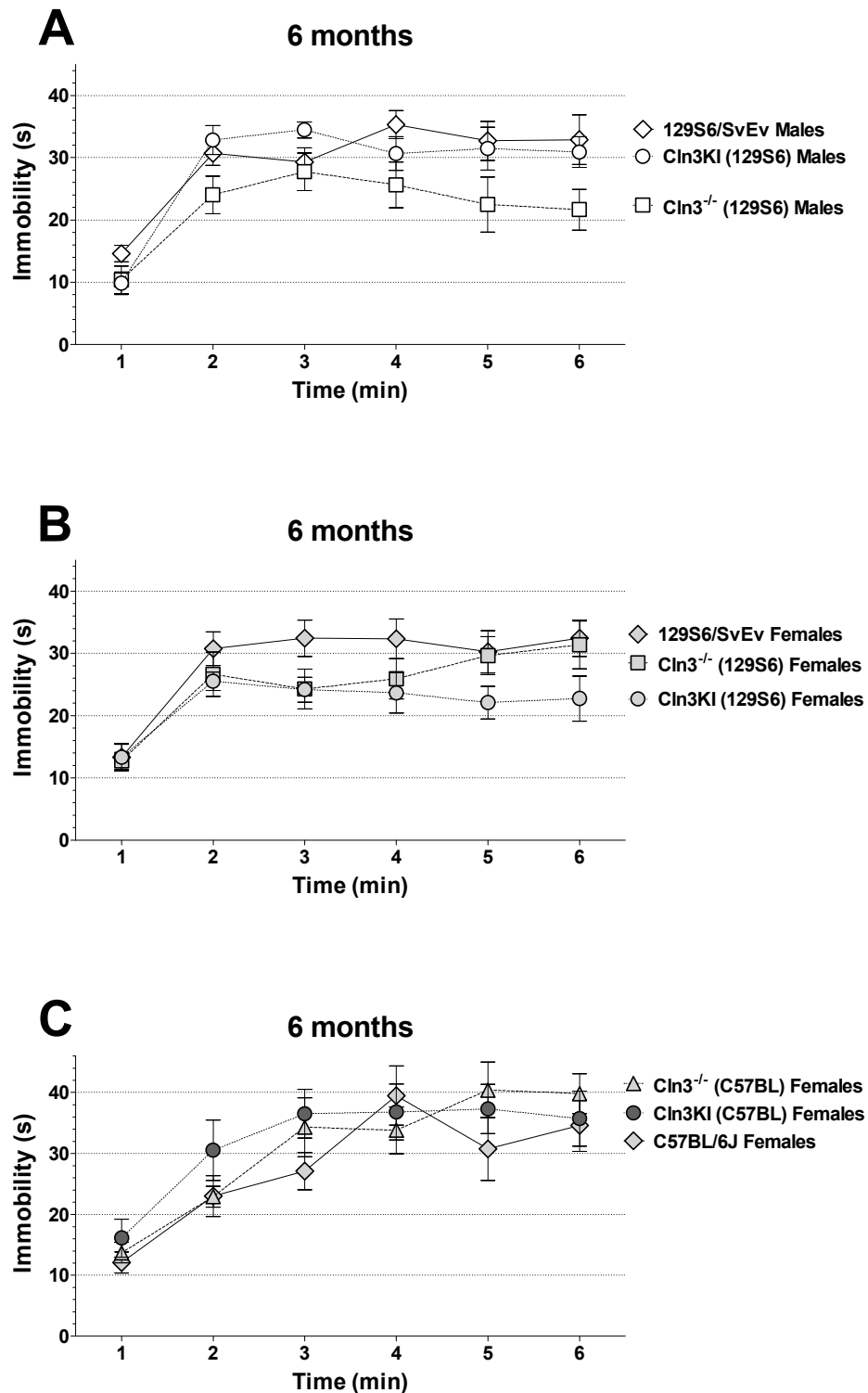
**Supplementary Fig. 1. Similarities in the time course of immobility at 1 month of age.** One-month-old mice were suspended by their tail 45 cm above table level, and the duration of immobility was measured in 1 minute bins for 6 minutes. Symbols and bars represent mean  $\pm$  SEM (n=10-12).

Statistical significance was analyzed by repeated measures 2-way ANOVA with Bonferroni's post-test for pairwise multiple comparisons. **(A)** *Cln3*<sup>-/-</sup> and *Cln3* <sup>$\Delta$ ex7/8</sup>-knock-in (Cln3KI) males on the 129S6/SvEv background, and 129S6/SvEv WT males had very similar time course of immobility. **(B)** *Cln3*<sup>-/-</sup> and *Cln3* <sup>$\Delta$ ex7/8</sup>-knock-in (Cln3KI) males on the C57BL/6J background, and C57BL/6J WT males had similar time course of immobility. The only difference between *Cln3* <sup>$\Delta$ ex7/8</sup>-knock-in (Cln3KI) and C57BL/6J WT males was in the 2<sup>nd</sup> minute of the test (\*p<0.05). **(C)** *Cln3*<sup>-/-</sup> and *Cln3* <sup>$\Delta$ ex7/8</sup>-knock-in (Cln3KI) females on the C57BL/6J background, and C57BL/6J WT females had similar time course of immobility.



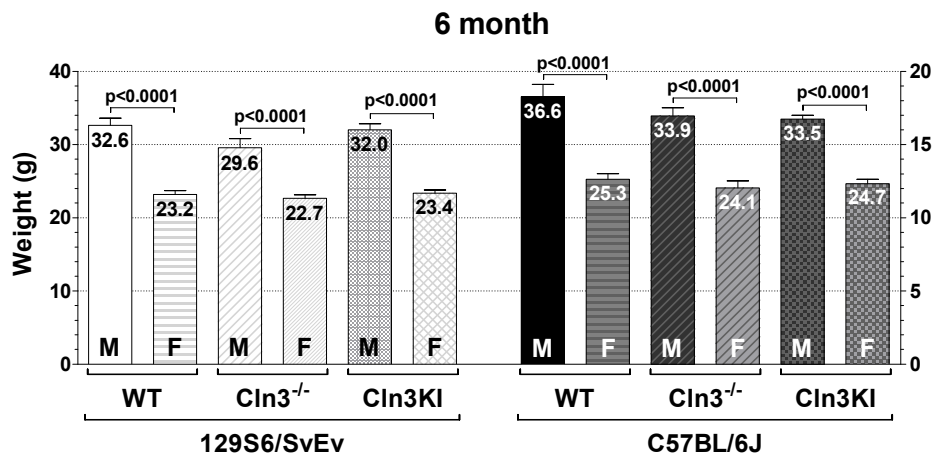
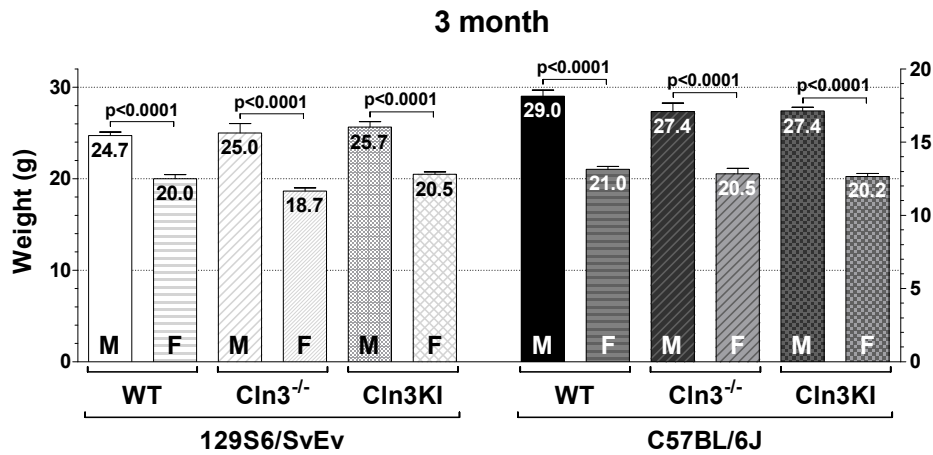
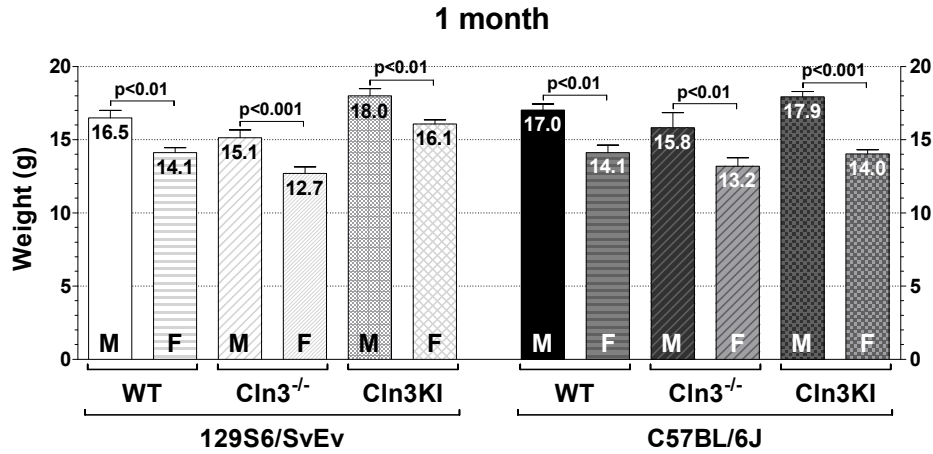
**Supplementary Fig. 2. Similarities in the time course of immobility at 3 months of age.** Three-month-old mice were suspended by their tail 45 cm above table level, and the duration of immobility was measured in 1 minute bins for 6 minutes. Symbols and bars represent mean  $\pm$  SEM (n=10-12).

Statistical significance was analyzed by repeated measures 2-way ANOVA with Bonferroni's post-test for pairwise multiple comparisons. **(A)** *Cln3*<sup>-/-</sup> and *Cln3*<sup>Δex7/8</sup>-knock-in (Cln3KI) males on the C57BL/6J background, and C57BL/6J WT males had very similar time course of immobility **(B)** *Cln3*<sup>-/-</sup> and *Cln3*<sup>Δex7/8</sup>-knock-in (Cln3KI) females on the C57BL/6J background, and C57BL/6J WT females had similar time course of immobility. **(C)** *Cln3*<sup>-/-</sup> and *Cln3*<sup>Δex7/8</sup>-knock-in (Cln3KI) males on the 129S6/SvEv background, and 129S6/SvEv WT males had very similar time course of immobility.



**Supplementary Fig. 3. Similarities in the time course of immobility at 6 months of age.** Six-month-old mice were suspended by their tail 45 cm above table level, and the duration of immobility was measured in 1 minute bins for 6 minutes. Symbols and bars represent mean  $\pm$  SEM (n=10-12).

Statistical significance was analyzed by repeated measures 2-way ANOVA with Bonferroni's post-test for pairwise multiple comparisons. **(A)**  $Cln3^{-/-}$  and  $Cln3^{Aex7/8}$ -knock-in (Cln3KI) males on the 129S6/SvEv background, and 129S6/SvEv WT males had similar time course of immobility. **(B)**  $Cln3^{-/-}$  and  $Cln3^{Aex7/8}$ -knock-in (Cln3KI) females on the 129S6/SvEv background, and 129S6/SvEv WT females had similar time course of immobility. **(C)**  $Cln3^{-/-}$  and  $Cln3^{Aex7/8}$ -knock-in (Cln3KI) females on the C57BL/6J background, and C57BL/6J WT females had very similar time course of immobility.



**Supplementary Fig. 4. Males are always heavier than females independently of the genotype, genetic background and age. The weight of male (M) and female (F) mice used in the behavioral tests was measured. The same mice were weighed at 1, 3 and 6 months of age. Columns and bars**

represent mean  $\pm$  SEM (n=10-12). Statistical significance was determined by 1-way ANOVA with Bonferroni's post-test for multiple comparisons.



Supplementary Table 1. Genome scanning analysis of representative mice.

		% C57BL/6	0.6%	0.6%	0.6%	0.6%	2.5%	2.5%	2.5%	2.2%	99.4%	99.4%	99.4%	99.4%	98.1%	98.1%	98.1%	98.1%
SNP_ID		% 129	99.4%	99.4%	99.4%	99.4%	97.5%	97.5%	97.5%	97.8%	0.6%	0.6%	0.6%	0.6%	1.9%	1.9%	1.9%	1.9%
			Cln3 <sup>-/-</sup> on 129/SvEv				Cln3 <sup>Δex7/8</sup> on 129/SvEv				Cln3 <sup>-/-</sup> on C57BL/6J				Cln3 <sup>Δex7/8</sup> on C57BL/6J			
Chromosome-bp	C57BL/6	129	female 1	female 2	male 1	male 2	male 1	male 2	female 1	female 2	male 1	male 2	female 1	female 2	male 1	male 2	female 1	female 2
01-005230167-M	C	T	T		T	T	T	T	T	T	C	C	C	C	C	C	C	C
01-026072256-M	G	T	T	T	T	T	T	T/G	T/G	T	G	G	G	G	G	G	G	G
01-046003967-M	A	C	C	C	C	C	C	C	C	C	A	A	A	A	A	A	A	A
01-065042402-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
01-086182722-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	G	G/A	G/A	G
01-102073421-M	G	C	C	C	C	C	C	C	C	C	G	G	G	G	G	C/G	C/G	G
01-122978406-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
01-143006008-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
01-162977516-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
01-178701443-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
01-193173300-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
02-003179310-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
02-020551513-M	A	G	G	G	G	G	A	A	A	G/A	A	A	A	A	A	A	A	A
02-041042651-M	C	G	G	G	G	G	G	G	G	G	C	C	C	C	C	C	C	C
02-061161692-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
02-078062303-M	T	G	G	G	G	G	G	G	G	G	T	T	T	T	T	T	T	T
02-101074874-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	
02-119931810-M	A	T	T	T	T	T	T	T	T	T	A	A	A	A	A	A	A	A
02-139603599-M	T	A	A	A	A	A	A	A	A	A	T	T	T	T	T		T	T
02-161858323-M	C	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C		C
02-179086475-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
03-011350737-M	G	C	C	C	C	C	C	C	C	C	G	G	G	G	G		G	G
03-032431792-M	G	A	A	A	A	A	A	A		A	G	G	G	G	G	G	G	G
03-053161686-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
03-073214161-M	A	T	T	T	T	T	T	T	T	T	A	A	A	A	A	A	A	A
03-088155864-N	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
03-110268748-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
03-131286062-N	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
03-151125653-M	A	T	T	T	T	T	T	T	T	T	A	A	A	A	A	A	A	A
03-160287200-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
04-003163167-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
04-022875524-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
04-039199957-M	C	G	G	G	G	G	G	G	G	G	C	C	C	C	C	C	C	C
04-061409675-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
04-084241978-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
04-106314110-M	C	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C	C	C
04-120122875-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
04-141084977-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
04-151168886-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
05-003188964-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
05-023890459-M	C	G	G	G	G	G	G	G	G	G	C	C	C	C	C	C	C	C
05-044010971-M	T	G	G	G	G	G	T	G/T	G/T	T	T	T	T	T	T	T	T	T
05-065734378-N	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
05-082050497-M	C	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C	C	C
05-106058057-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
05-125054661-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
05-139966164-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T

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06-003167392-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
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06-045126062-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
06-062599520-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
06-083216741-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
06-106057600-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
06-122941044-M	T	A	A	A	A	A	A	A	A	A	T	T	T	T	T	T	T	T
06-135955068-M	C	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C	C	C
06-149052281-M	C	G	G	G	G	G	G	G	G	G	C	C	C	C	C	C	C	C
07-004201219-N	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
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07-044964980-M	G	C	C	C	C	C	C	C	C	C	G	G	G	G	G	G	G	G
07-064095712-M	G	T	T		T	T	T	T	T	T	G	G	G	G	G	G	G	G
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07-106153798-M	G	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T
07-135024189-M	C	T	T	T	T	T	C	C	C	C	C	C	C	C	C	C	C	C
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08-025034424-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
08-045080531-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
08-067470102-N	G	C	C	C	C	C	C	C	C	C	G	G	G	G	G	G	G	G
08-086985036-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
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08-123021323-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
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09-016198772-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
09-034961903-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
09-052894456-M	C	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C	C	C
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10-117629082-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
10-129117100-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
11-005661856-N	T	A	A	A	A	A	A	A	A	A	T	T	T	T	T		T	T
11-024515722-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
11-047224208-M	C	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C	C	C
11-070331570-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
11-090199967-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
11-111226923-M	A	C	C	C	C	C	C	C	C	C	A	A	A	A	A	A	A	A
11-122195777-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
12-003567042-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
12-022232159-M	C	G	G	G	G	G	G	G	G	G	C	C	C	C	C	C	C	C
12-041270227-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
12-061271925-M	A	T	T	T	T	T	T	T	T	T	A	A	A	A	A	A	A	A

12-069389027-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
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13-084819885-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
13-101929792-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
13-117094028-M	G	A	A	A	A	A	A	A	A	A	G	G	G	G	G	G	G	G
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14-060626617-N	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
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17-003335010-M	G	C	C	C	C	C	C	C	C	C	G	G	G	G	G	G	G	G
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17-066532305-N	T	G	G	G	G	G	G	G	G	G	T	T	T	T	T	T	T	T
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18-067972780-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
18-078813035-M	A	C	C	C	C	C	C	C	C	C	A	A	A	A	A	A	A	A
18-090060367-M	G	T	T	T	T	T	T	T	T	T	G	G	G	G	G	G	G	G
19-018239318-M	T	G	G	G	G	G	G	G	G	G	T	T	T	T	T	T	T	T
19-021081804-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
19-038092479-M	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
19-048069669-N	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
19-060823449-N	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
X-016114535-G	C	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C	C	C
X-025132696-G	C	G	G	G	G	G	G	G	G	G	C	C	C	C	C	C	C	C
X-054650362-N	T	A	A	A	A	A	A	A	A	A	T	T	T	T	T	T	T	T
X-068494838-M	C	T	T	T	T	T	T	T	T	T	C	C	C	C	C	C	C	C
X-087817653-G	A	T	T	T	T	T	T	T	T	T	A	A	A	A	A	A	A	A

X-100413449-M	T	G	G	G	G	G	G	G	G	G	T	T	T	T	T	T	T	T
X-114340727-M	A	G	G	G	G	G	G	G	G	G	A	A	A	A	A	A	A	A
X-133535206-G	T	C	C	C	C	C	C	C	C	C	T	T	T	T	T	T	T	T
X-143466659-M	A	C	C	C	C	C	C	C	C	C	A	A	A	A	A	A	A	A