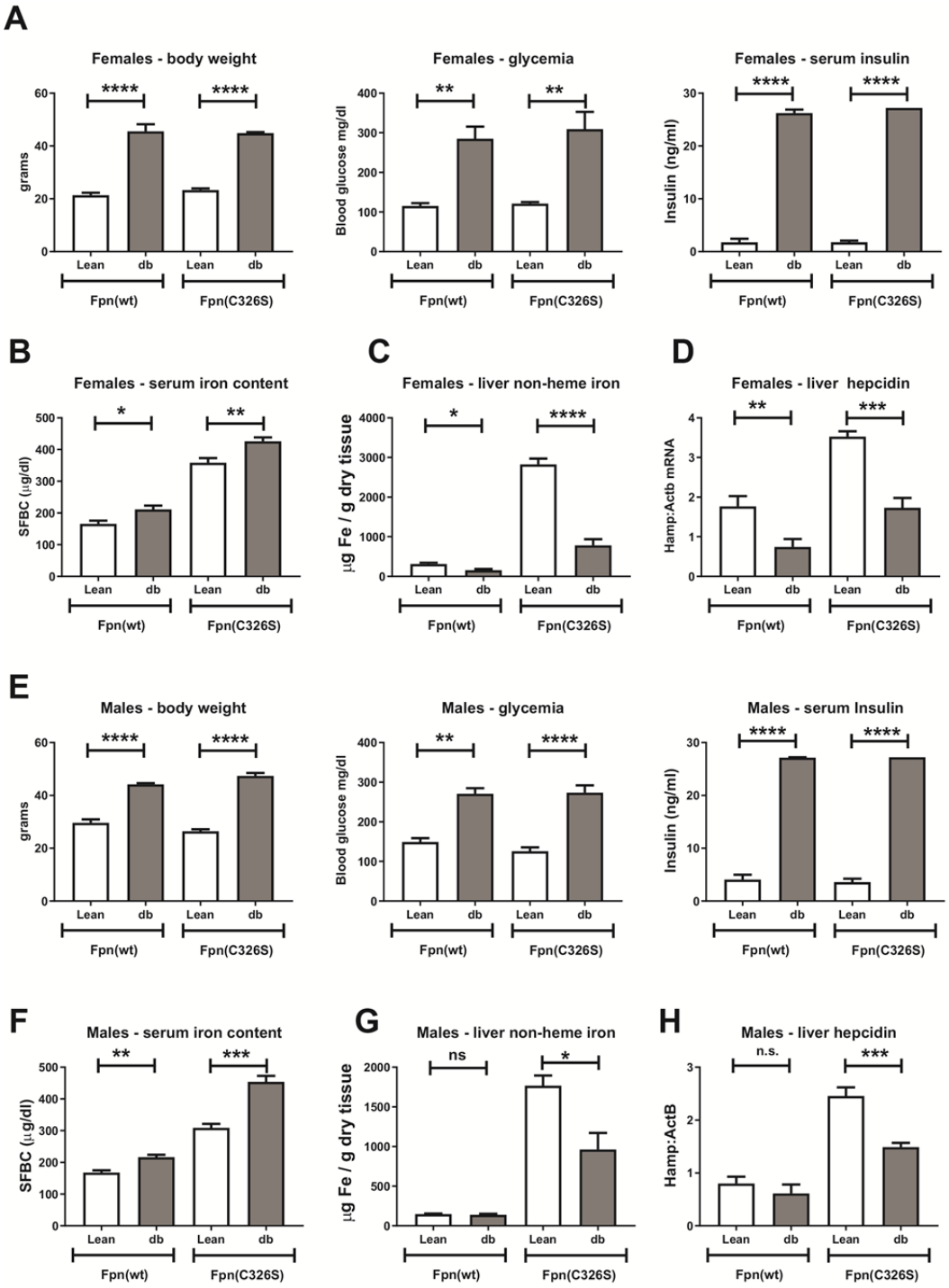

Figure S1

Figure S1: Diabetic and iron parameters in young Lepr$^{db/db}$; Fpn$^{wt/C326S}$ mice. Biomarkers that hallmark type 2 diabetes and iron-related parameters were measured in 15-week-old animals with the gender and genotype indicated. (A,E) Body weight (in grams), blood glycemia (mg/dl) and serum insulin (ng/ml) were measured in 15-week old female (A) or male (B) mice. (B-D, F-H) Measurement of serum iron content (µg/dl) (B,F), hepatic non-heme iron levels (C,G) and hepatic hepcidin mRNA expression in female and male mice, as indicated. Gene expression values were normalized to the housekeeping gene β-actin (ACTB). Data are reported as mean ± SEM. Six or more mice per group were analyzed. Student's t-test p-value: * $p<0.05$; ** $p<0.01$; *** $p<0.001$; **** $p<0.0001$.

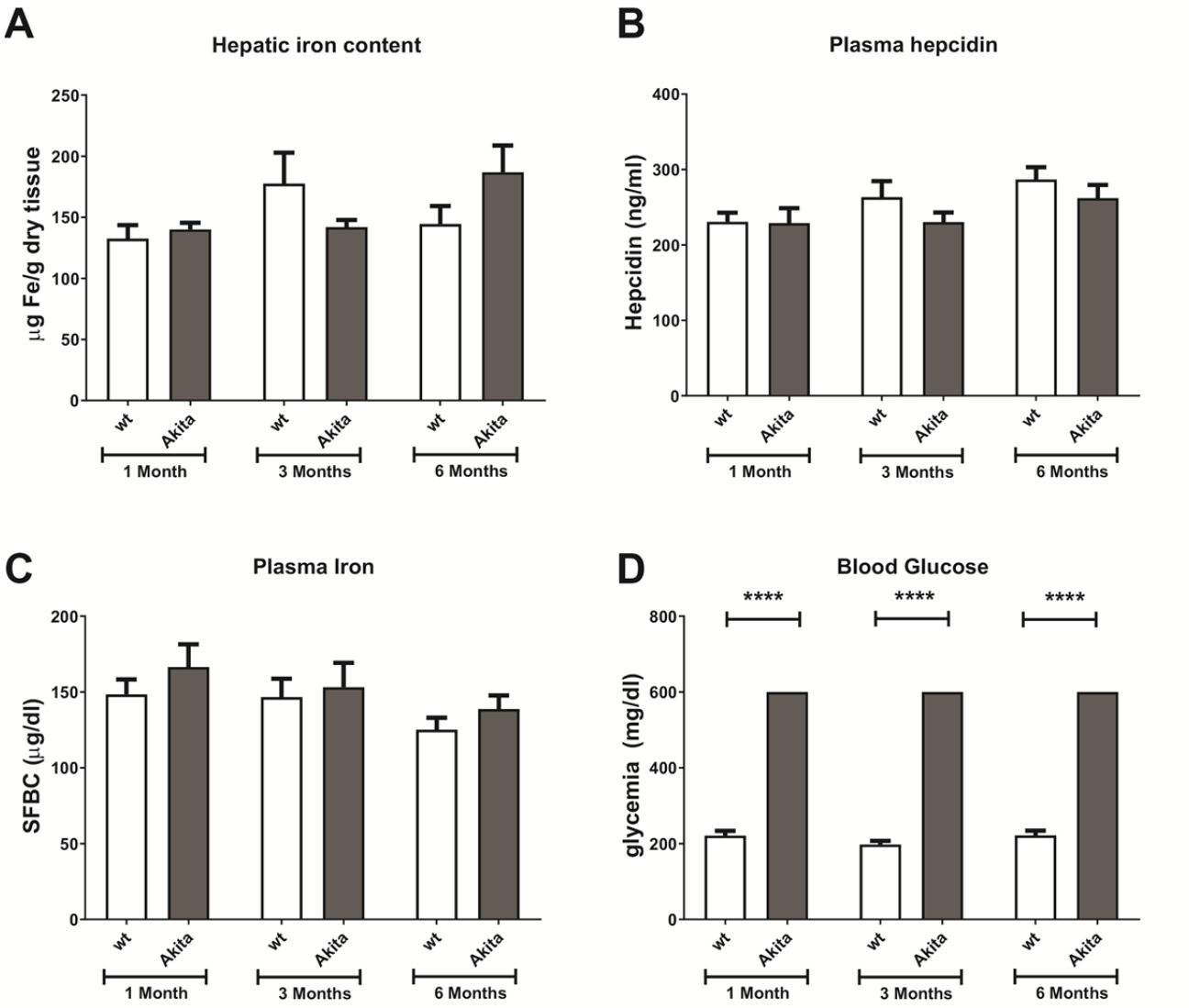

Figure S2

Figure S2: Iron-related parameters remain unaltered in Ins2^{Akita} mice. A-D) Ins2^{Akita} male mice and age and gender-matched controls have been analyzed at the times indicated for (A) hepatic non-heme iron content, (B) plasma hepcidin levels (ng/ml), (C) blood glucose (mg/dl) and (D) plasma iron content (µg/dl). Six or more mice per group were analyzed. Data are reported as mean ± SEM. Student's t-test p-value: * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001.

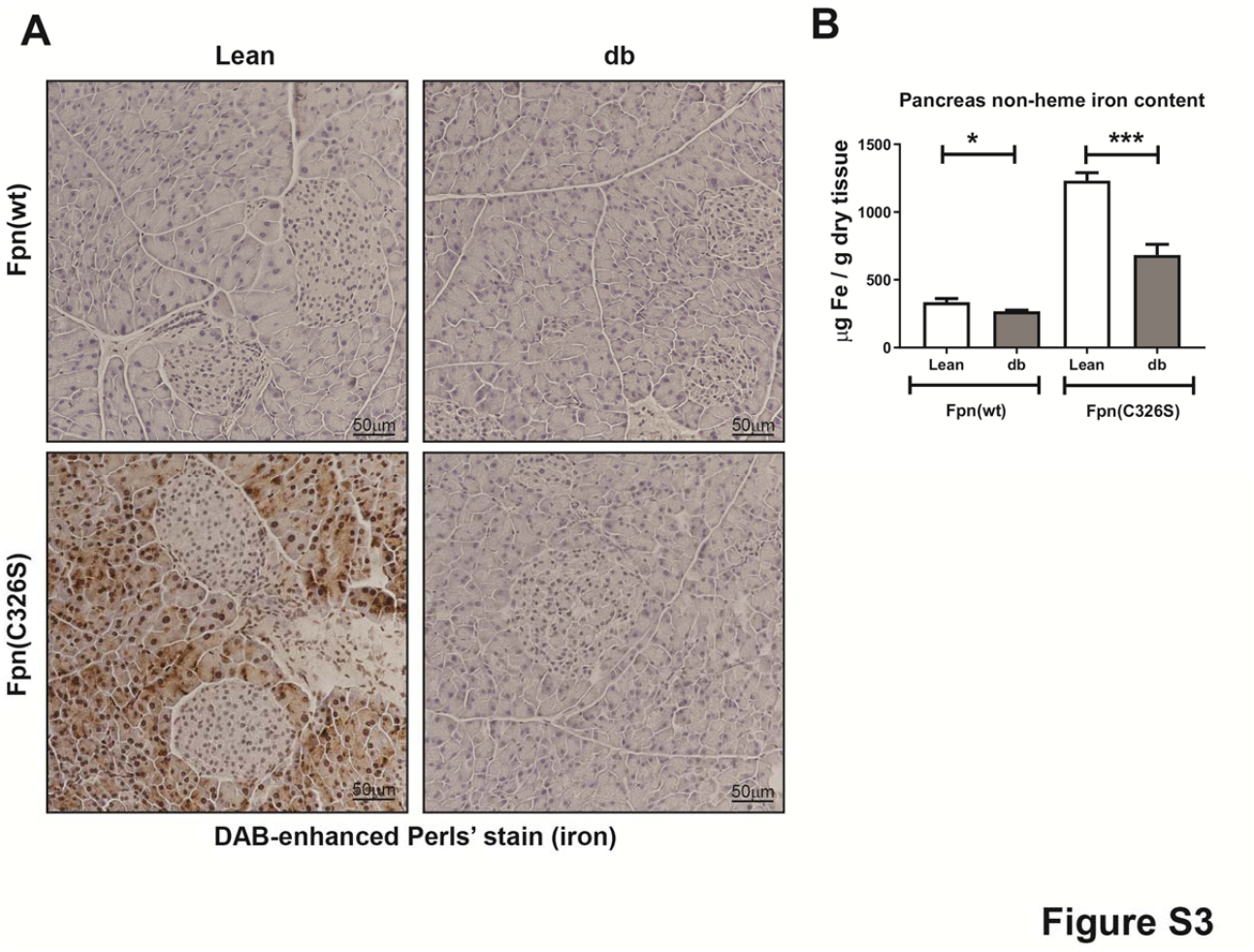

Figure S3: Characterization of the pancreatic iron content and distribution. A) DAB-enhanced Perls' iron staining of pancreata of female mice with the genotype indicated. B) Quantification of the pancreatic non-heme iron content normalized against dry tissue weight. Data are reported as mean ± SEM. Six or more mice per group were analyzed. Student's t-test p-value: * $p<0.05$; ** $p<0.01$; *** $p<0.001$; **** $p<0.0001$.

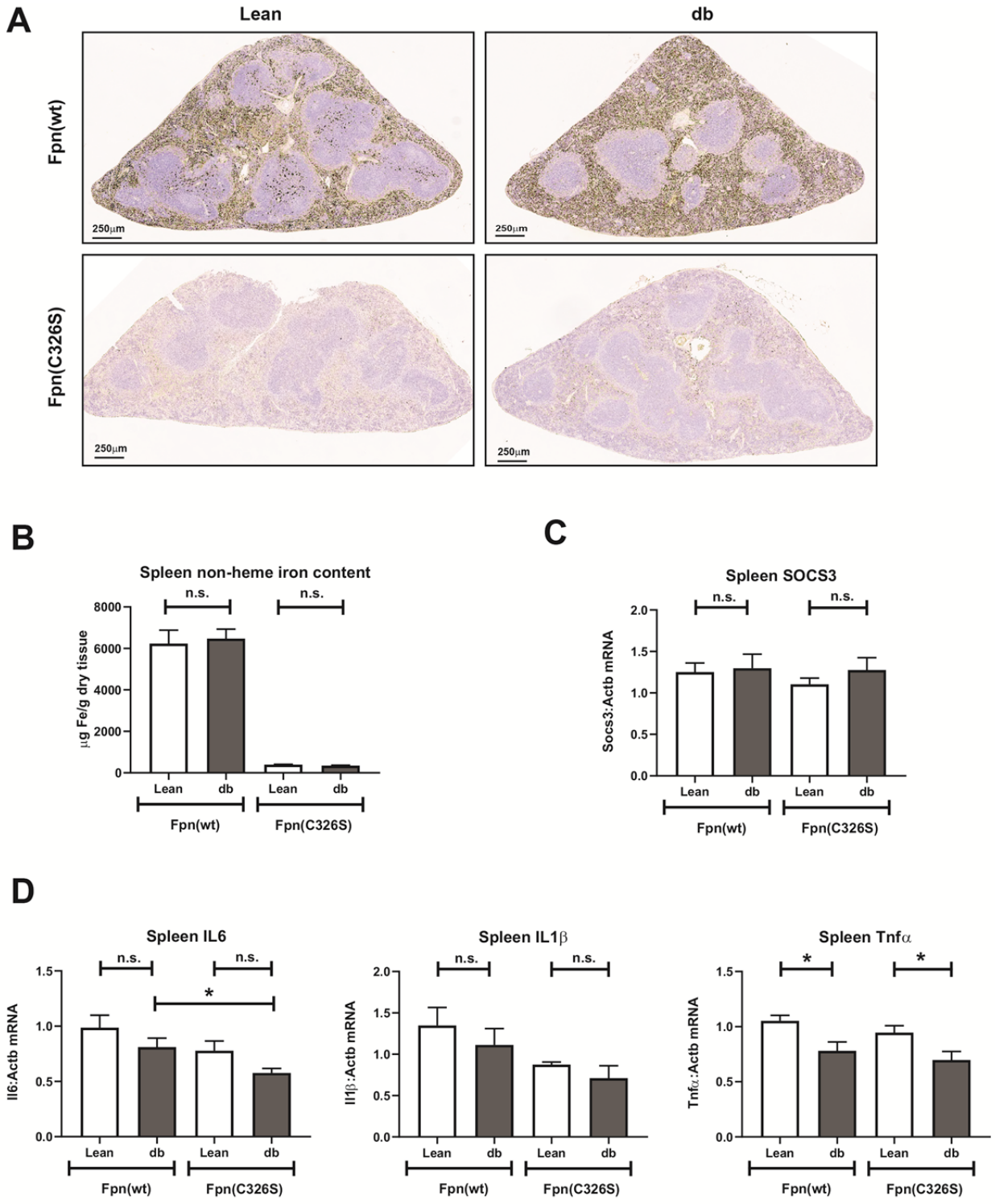

Figure S4

Figure S4: Characterization of the splenic iron and inflammatory status. A) DAB-enhanced Perls' iron staining of spleen of female mice with the genotype indicated. B) Quantification of the splenic non-heme iron content normalized against dry tissue weight. C-D) Gene expression analysis of the JAK/STAT3 target gene SOCS3 (D) and of the pro-inflammatory cytokines IL6 (D), IL1β (E) and TNFα (F). Gene expression values were normalized to the housekeeping gene β-actin (ACTB). Data are reported as mean ± SEM. Six or more mice per group were analyzed. Student's t-test p-value: * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001.

Table S1. SYBR green qPCR primers

Gene	Forward	Reverse	Gene	Forward	Reverse
Hamp	ATACCAATGCAGAAGAGAAGG	AACAGATACCACACTGGGAA	**Pepck**	CCGTAGACCTGAAGGTGT	GGCAAAGGGGTCGTGCAT
TfR1	CCCATGACGTTGAATTGAACCT	GTAGTCTCCACGAGCGGAATA	**Fbp**	GTTCCCTCCGGATGGTTCA	CAGCAGCCGCAGCTTTCCA
Fpn	TGTCAGCCTGCTGTTTGCAGGA	TCTTGCAGCAACTGTGTCACCG	**Nqo1**	AGCGTTCGGTATTACGATCC	AGTACAATCAGGGCTCTTCTCG
Bmp6	ATGGCAGGACTGGATCATTGC	CCATCACAGTAGTTGGCAGCG	**Socs3**	CCTTTGACAAGCGGACTCTC	GCCAGCATAAAAACCCTTCA
Id1	ACCCTGAACGGCGAGATCA	TCGTCGGCTGGAACACATG	**Acc1**	GCAGATCCGCAGCTTGGT	CGTGGAAGGGGAATCCAT
Smad6	GTTGCAACCCCTACCACTTC	GGAGGAGACAGCCGAGAATA	**Lpin**	GTCCAGTGTTTGACAGAC	GGGTTCACAGTGAAGATCCTAT
Atoh8	TCAGCTTCTCCGAGTGTGTG	TAGCCTGTGGCAGGTCACT	**Fasn**	CGTGTTGGCCTACACCCAGAGCT	GGCAGCAGGGCCTCCAGCACCTT
ACTB	GCTTCTTTGCAGCTCCTTCGT	ACCAGCGCAGCGATATCG	**Gpx4**	CGCTCCATGCACGAATTCTC	GCACACGAAACCCCTGTACT
Glut2	GTCGCCTCATTCTTTGGTG	CTGATACACTTCGTCCAGC	**Glut4**	GACGGACACTCCATCTGTTG	GCCACGATGGAGACATAGC
Srebp1c	CGGAGCCATGGATTGGACATTTGA	GGAGAGTTGGCACCTGGGCT	**Scd1**	GGTGATGTTCCAGAGGAGGTACT	GGTGCTAACGAACAGGCT
Gpat	GCCTACAGCTCTGCTGCCAT	GTATGTGGCACTCTCAGCGT	**Acl**	GTGGACATGCTCAGGAACT	CTGGTCAAGGTAGTGCCCA
Adipoq	GGAGAGAAAGGAGATGCAGGT	CTTTCCTGCCAGGGGTTC			

Table S2: Western blot antibodies and dilutions

Antibody	Dilution	Cat nr	Company
AKT	1:1000	9272S	Cell signaling
phospho-AKT	1:1000	4060s	Cell signaling
Fpn	1:500	MTP1A	Alphadiagnostics
IRS-1	1:2000	2382S	Cell signaling
Phospho-IRS-1	1:250	2381S	Cell signaling
Vinculin	1:1000	SAB4503069	Sigma Aldrich