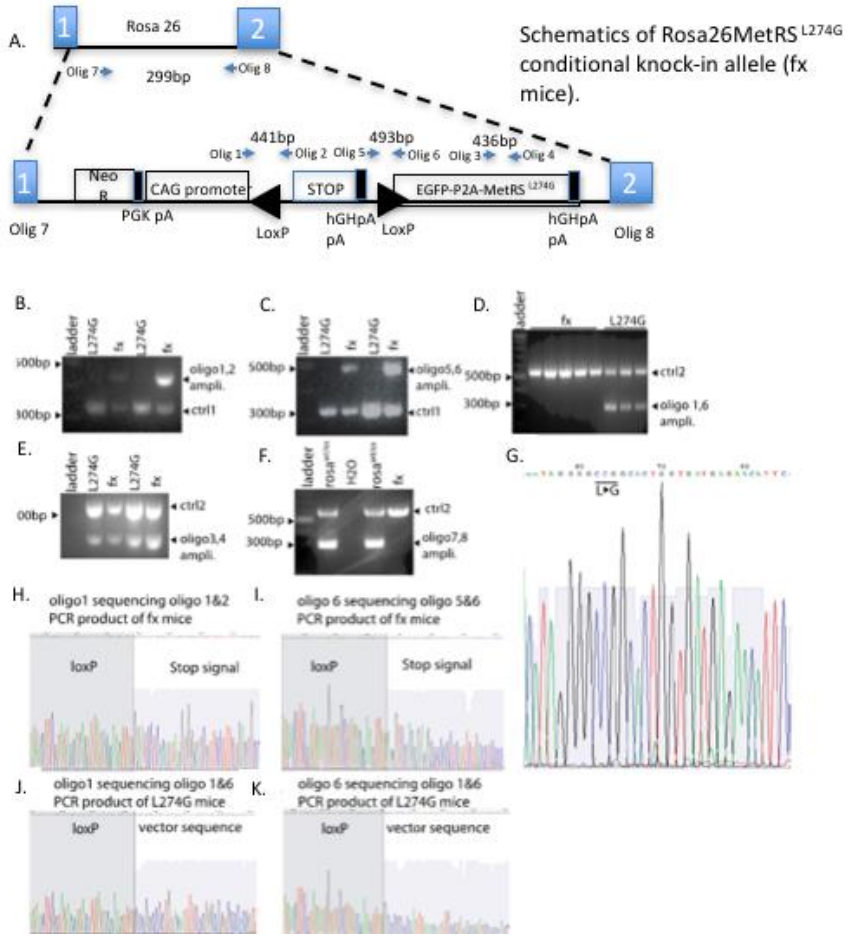
**Description of Supplementary Files**

File Name: Supplementary Information
Description: Supplementary Figures, Supplementary Tables.

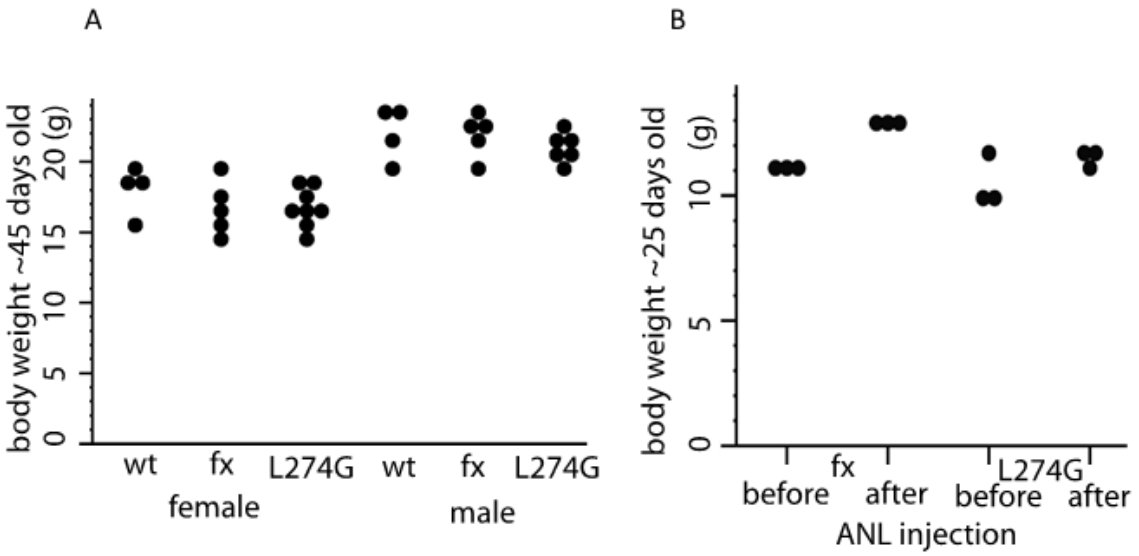



Supplementary Figure 1.

**Supplementary Figure 1. The generation of MetRS$^{L274G}$ mice**

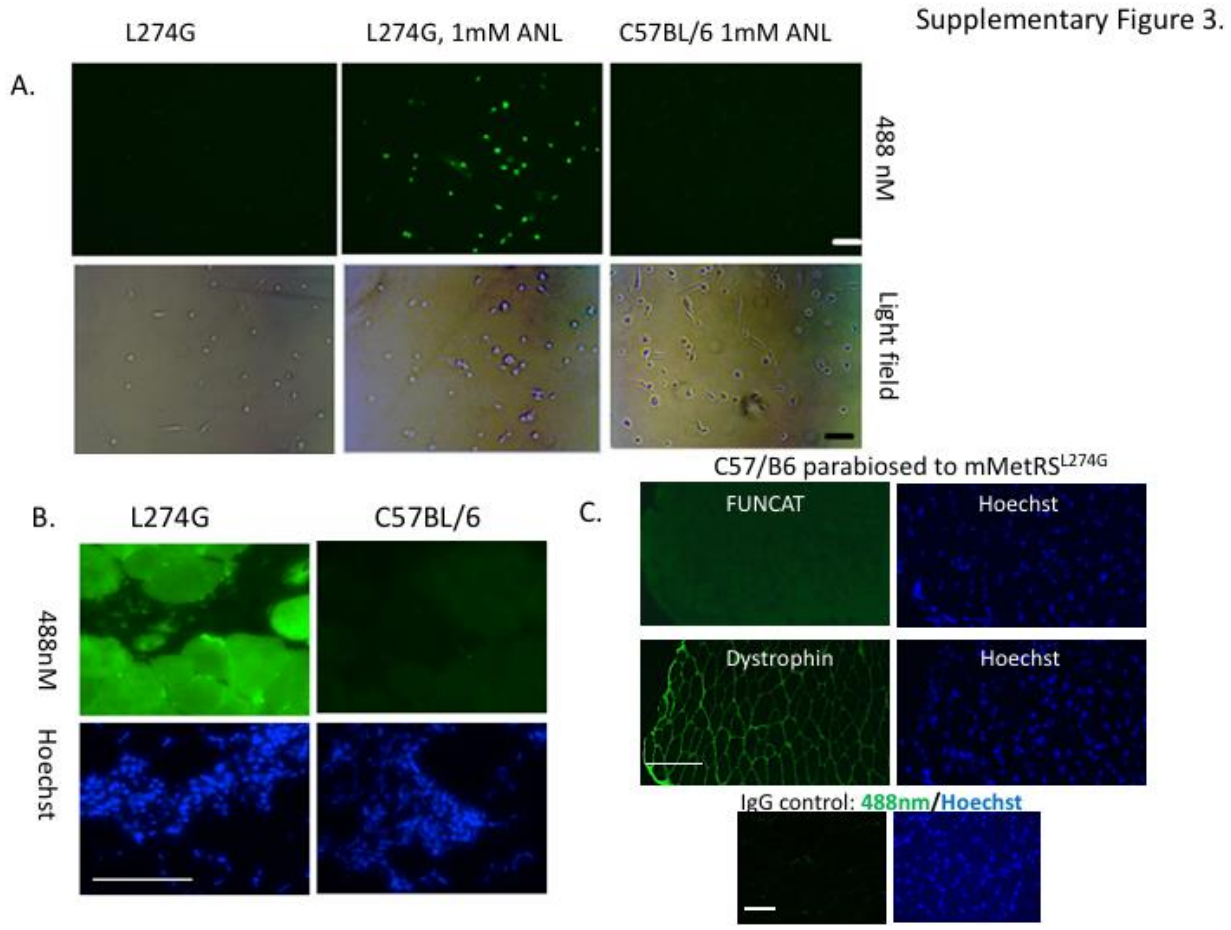
**A.** Schematic map of Gt(Rosa26) mMetRS$^{L274G}$ conditional Knock-In allele (fx mice). B-F**:** PCR images showing genotyping. PCR reactions were performed on each studied MetRS$^{L274G}$ animal (>30) and at least on 10 fx mice for genotyping. **G.** Sequencing confirmation of the L274G mutation in MetRS$^{L274G}$ mice. **H-K:** sequencing confirmation of the “stop signal” excision by Cre recombinase. ex, cre recombinase excised allele. fx, conditional knock-in allele. Sequencing confirmation of restriction analysis was done on two MetRS$^{L274G}$ mice and two fx mice.

Supplementary Figure 2.




**Supplementary Figure 2. Body weight of fx and MetRS$^{L274G}$ mice with and without ANL treatment.**

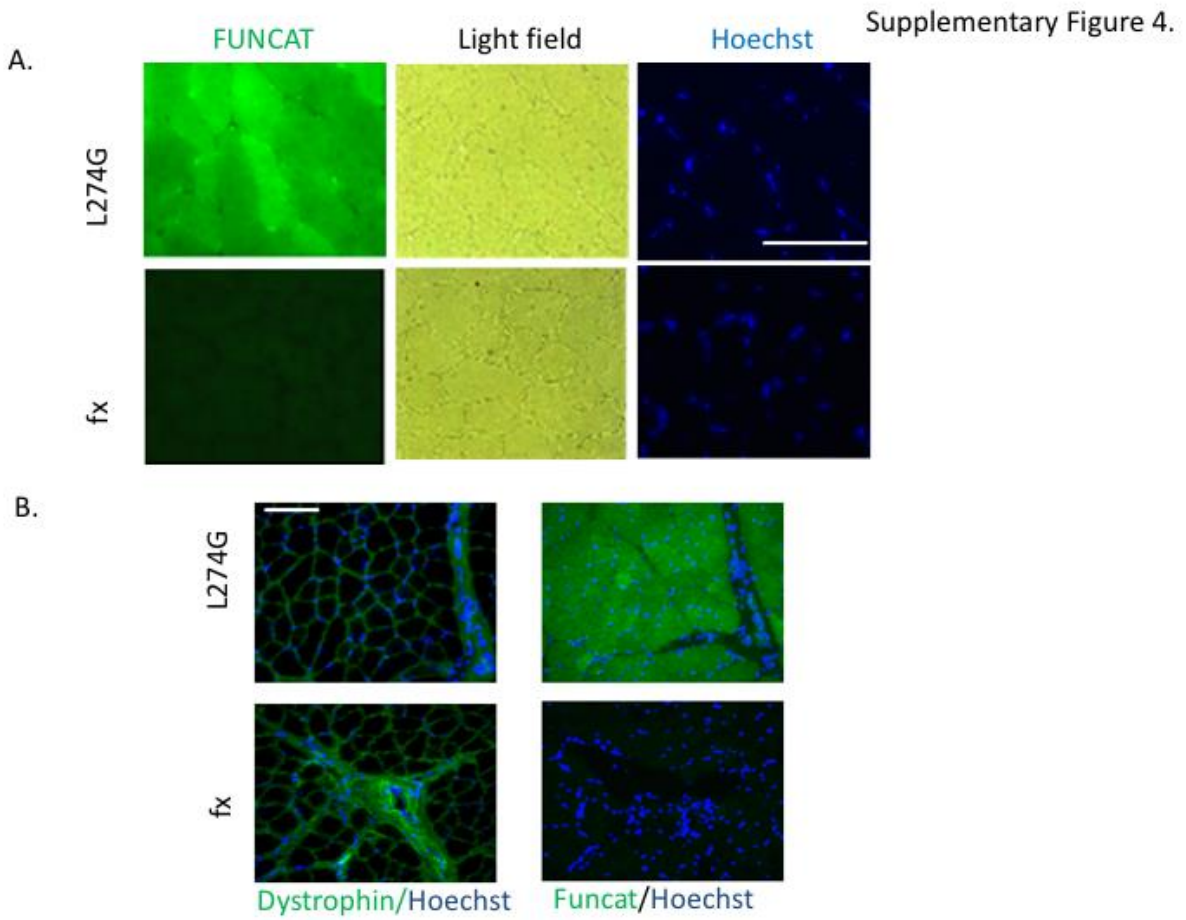
ANL (0.2 mmol/kg) was administered to 25-day-old MetRS$^{L274G}$ mice and fx mice by daily I.P. injections for 6 consecutive days, body weights increased after treatment in both cohorts, consistent with normal growth of mice at this age. By daily observations, fx and *MetRS$^{L274G}$* mice looked equally healthy and active. A. Body weight of wild type, fx and MetRS$^{L274G}$ mice at the age of ~45 days. B. Body weight of MetRS$^{L274G}$ and fx mice before and after ANL injection that started at the age of ~25 days. Each dot represents an individual animal. No significant differences were detected between MetRS$^{L274G}$ and fx mice (N=3-6**,** P>0.05, Wilcoxon Rank Sum test). These data were also confirmed by the daily observation of MetRS$^{L274G}$ parabionts.




**Supplementary Figure 3. Additional FUNCAT studies.**

**A.** FUNCAT on ANL labeled proteins in MetRS$^{L274G}$ cells, as compared to the cells from C57BL/6 mice, treated or not with ANL. Similar results were obtained with at least three independently derived primary cell preparations from three of each: MetRS$^{L274G}$ mice and C57BL/6 mice. **B.** FUNCAT on ANL labeled proteins in muscle cryosections from parabiotic MetRS$^{L274G}$ or C57BL/6 mice that were administered with ANL *in vivo* (as in Figure 4A). **C.** FUCNAT assay and dystrophin immunofluorescence were performed on ~10-micron adjacent sections of C57BL/6 muscle that was derived from parabiotic partners of MetRS$^{L274G}$ animals (with ANL administration *in vivo* as described schematically in Figure 4A). Isotype matched IgG controls for dystrophin immuno-detection are also shown. Hoechst (blue) labels all nuclei. Scale

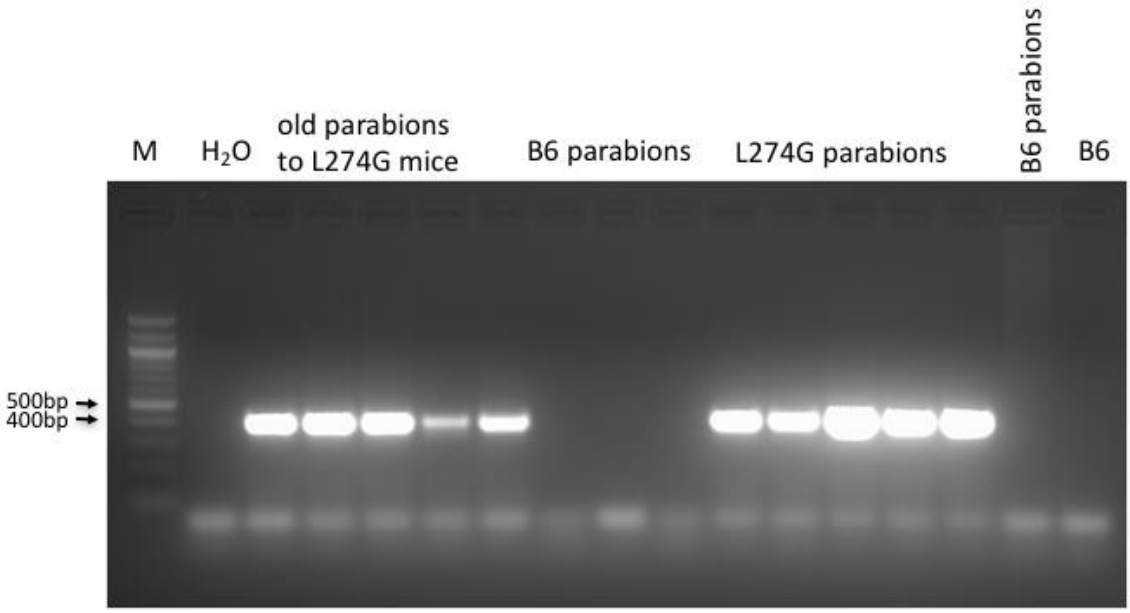
bar, 100μm. Similar results were obtained from at least three C57BL/6 parabiosed to MetRS$^{L274G}$ mice and three MetRS$^{L274G}$ parabiosed to C57BL/6 mice.




**Supplementary Figure 4. FUNCAT comparison between** MetRS$^{L274G}$ and fx muscle tissue and **co-detection with dystrophin immunofluorescence.**

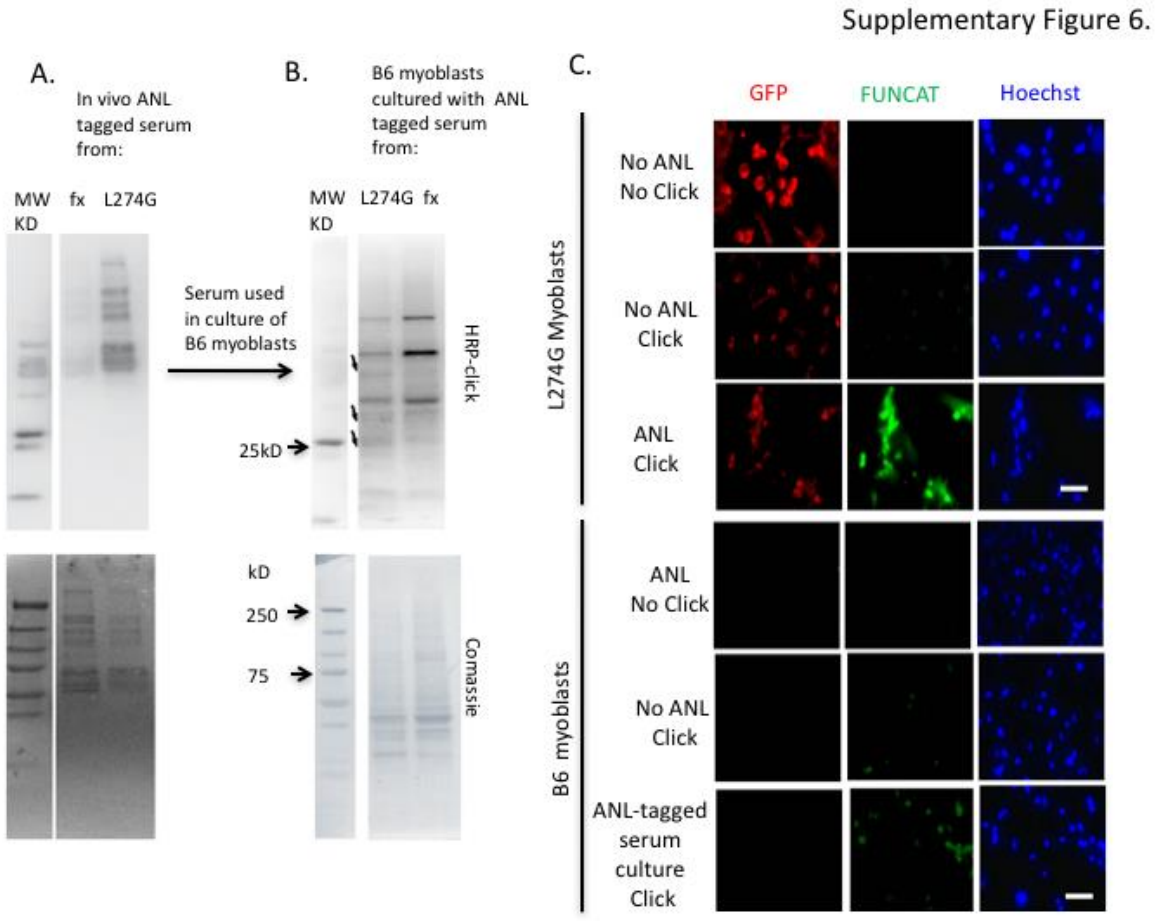
Representative images of 10-micron muscle cryosections that were derived from MetRS$^{L274G}$ or fx mice administered with ANL *in vivo*, and assayed by **(A).** FUNCAT or **B.** FUNCAT with dystrophin immunostaining on adjacent sections. Hoechst (blue) labels all nuclei. Scale bar, 100μm. Similar results were obtained with at least 3 MetRS$^{L274G}$ and fx mice.

Supplementary Figure 5.




**Supplementary Figure 5. Blood chimerism.**

Gel electrophoresis on PCR wiith Cre-specific primers that was performed on genomic DNA isolated from heart-bleed derived blood cells of parabionts and control C57BL/6 mice, as indicated. Cre-specific primers (OL2642 and OL 2647) were used to amplify the 450bp Cre DNA fragment. I kb ladder (M). Similar results were obtained from 7 pairs of old C57BL/6 to young $MetRS^{L274G}$ parabionts and 6 pairs of old C57BL/6 to young C57BL/6 parabionts.




**Supplementary Figure 6. Detection of ANL-tagged proteins from primary myoblasts incubated with *in vivo* ANL labeled serum.**

MetRS$^{L274G}$ mice and the negative control fx mice were labeled with ANL for 5 days *in vivo*, as in Methods. Their blood serum was collected. A. Click-Chemistry Western Blotting was used to assay for effective ANL tagging of serum proteome in MetRS$^{L274G}$ but not fx mice. B. Primary C57BL/6 myoblasts were cultured with serum from MetRS$^{L274G}$ and fx mice (as illustrated in the schematic) and Click-Chemistry Western Blotting was used to assay for the association of the *in vivo* ANL tagged serum proteins with the C57BL/6 myoblasts in culture. A few above-background (of the fx negative control) bands were detected (arrow heads) C. FUNCAT assay has also detected the above background ANL labeled proteins in C57BL/6 myoblasts that were cultured with MetRS$^{L274G}$ ANL-tagged serum, which rendered these cells visible by the Click-

fluorescence. At least 6 individual serum samples from each: 3 MetRS$^{L274G}$ mice and 3 fx mice produced similar results after incubation with primary myoblasts and subsequent analysis by Click-Western.

Supplementary Table 1: Primers that were used in these studies.

| | |
|---|---|
| Oligo1 | TGGCAGGCTTGAGATCTGG |
| Oligo2 | TTATTGATCCGCGCCTGG |
| Oligo3 | GACCACTACCAGCAGAACACC |
| Oligo4 | AGAAGAGGTAGTTGCCACTATCC |
| Oligo5 | ACGTCCAGACACAGCATAGG |
| Oligo6 | GGACACGCTGAACTTGTGG |
| Oligo7 | CTCTTCCCTCGTGATCTGCAACTCC |
| Oligo8 | CATGTCTTTAATCTACCTCGATGG |
| Ctrl1forward | GTGGCACGGAACTTCTAGTC |
| Ctrl1reverse | CTTGTCAAGTAGCAGGAAGA |
| Ctrl2forward | GAGACTCTGGCTACTCATCC |
| Ctrl2reverse | CCTTCAGCAAGAGCTGGGGAC |
| OL2642 | tgcctgcattaccggtcgatgc |
| OL2643 | ccatgagtgaacgaacctggtcg |
| 2839reverse | GCTTGGTCACCTCATCCGTC |
| 1169reverse | ACTGGCGAAGGCGACAATAC |
| 162 reverse | CATGCCGAGAGTGATCCCG |
| GAPDH-F | CCACTTGAAGGGTGGAGCCA |
| GAPDH-R | TCATGGATGACCTTGGCCAG |

Supplementary Table 2: Genes that have been found by the BONCAT focused Antibody array studies. N=3 independent array experiments for each parabiotic cohort. $P<0.05$ (Wilcoxon rank sum test), 2-fold increase over negative control.

| Name | Unigene ID |
|---|---|
| 1. B7-1/CD80 | Mm.89474 |
| 2. BCMA / TNFRSF17 | Mm.12935 |
| 3. BLC | Mm.10116 |
| 4. CCR6 | Mm.8007 |
| 5. Cerberus 1 | Mm.6780 |
| 6. Coagulation Factor III / Tissue Factor | Mm.273188 |
| 7. Cripto | Mm.5090 |
| 8. DKK-1 | Mm.214717 |
| 9. Dtk | Mm.424496 |
| 10. EGF R | Mm.420648 |
| 11. Endostatin | Mm.4352 |
| 12. FGF R4 | Mm.276715 |
| 13. FLRG (Follistatin) | Mm.251710 |
| 14. Follistatin-like 1 | Mm.182434 |
| 15. Fractalkine | Mm.103711 |
| 16. Galectin-3 | Mm.248615 |
| 17. GDF-5 | Mm.4744 |
| 18. GFR alpha-4 / GDNF R alpha-4 | Mm.198399 |
| 19. Granzyme B | Mm.14874 |
| 20. ICAM-2 / CD102 | Mm.394 |
| 21. IFN-alpha / beta R2 | Mm.6834 |
| 22. IGFBP-1 | Mm.21300 |
| 23. IGFBP-3 | Mm.29254 |
| 24. IGF-I | Mm.268521 |
| 25. IL-10 | Mm.874 |
| 26. IL-10 R alpha | Mm.379327 |
| 27. IL-15 R alpha | Mm.200196 |
| 28. IL-17BR | Mm.269363 |
| 29. IL-17R | Mm.4481 |
| 30. IL-21 R | Mm.155643 |
| 31. IL-22 | Mm.103585 |
| 32. IL-22BP | Mm.331979 |
| 33. IL-27 | Mm.222632 |
| 34. IL-31 RA | Mm.380801 |
| 35. IL-9 R | Mm.384 |

| | |
|---|---|
| 36. KC | Mm.21013 |
| 37. LEPTIN(OB) | Mm.277072 |
| 38. LIF | Mm.4964 |
| 39. MIG | Mm.766 |
| 40. MIP-3 alpha | Mm.116739 |
| 41. MIP-3 beta | Mm.426373. |
| 42. MMP-24 / MT5-MMP | Mm.389325 |
| 43. MMP-3 | Mm.4993. |
| 44. MMP-9 | Mm.4406 |
| 45. PDGF R beta | Mm.4146 |
| 46. Progranulin | Mm.1568. |
| 47. Resistin | Mm.1181 |
| 48. Serum Amyloid A1 | Mm.148800 |
| 49. SLPI | Mm.371583 |
| 50. SPARC | Mm.291442 |
| 51. TARC | Mm.41988 |
| 52. TCA-3 | Mm.1283 |
| 53. TFPI | Mm.124316 |
| 54. TGF-beta 1 | Mm.248380 |
| 55. TGF-beta RI / ALK-5 | Mm.197552 |
| 56. TGF-beta RII | Mm.172346 |
| 57. Thymus Chemokine-1 | Mm.293614 |
| 58. TIMP-1 | Mm.8245 |
| 59. TIMP-4 | Mm.255607 |
| 60. TL1A / TNFSF15 | Mm.208152 |
| 61. TLR1 | Mm.273024 |
| 62. TLR3 | Mm.33874 |
| 63. TMEFF1 / Tomoregulin-1 | Mm.422686 |
| 64. TNF RII | Mm.235328 |
| 65. TNF-beta / TNFSF1B | Mm.87787 |
| 66. TRAIL R2 / TNFRSF10B | Mm.193430 |
| 67. TRANCE / TNFSF11 | Mm.249221 |
| 68. TREM-1 | Mm.248352 |
| 69. VE-Cadherin | Mm.21767 |
| 70. VEGF R3 | Mm.3291 |