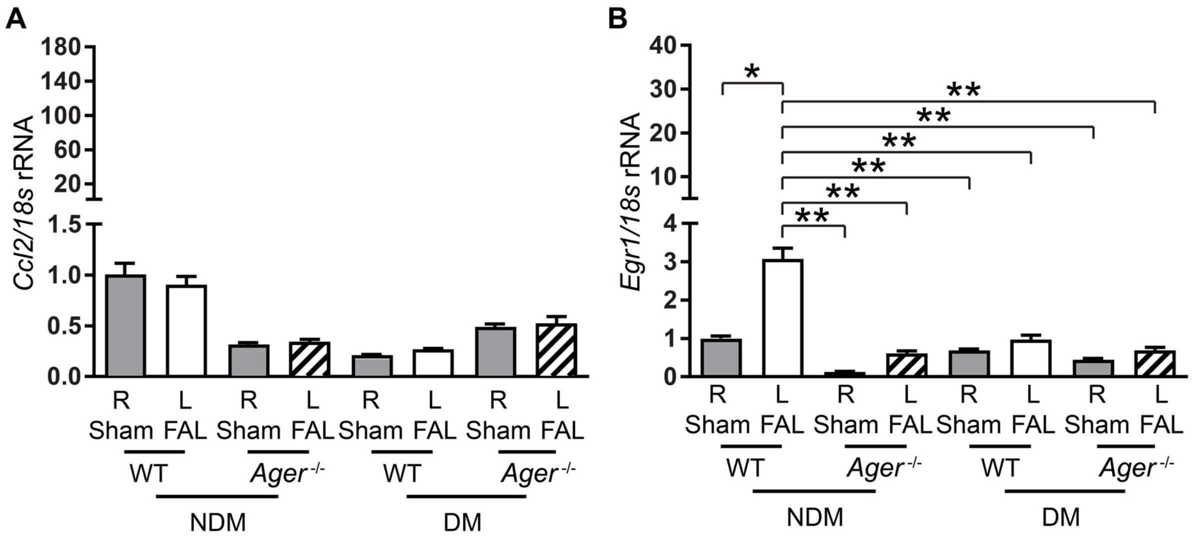
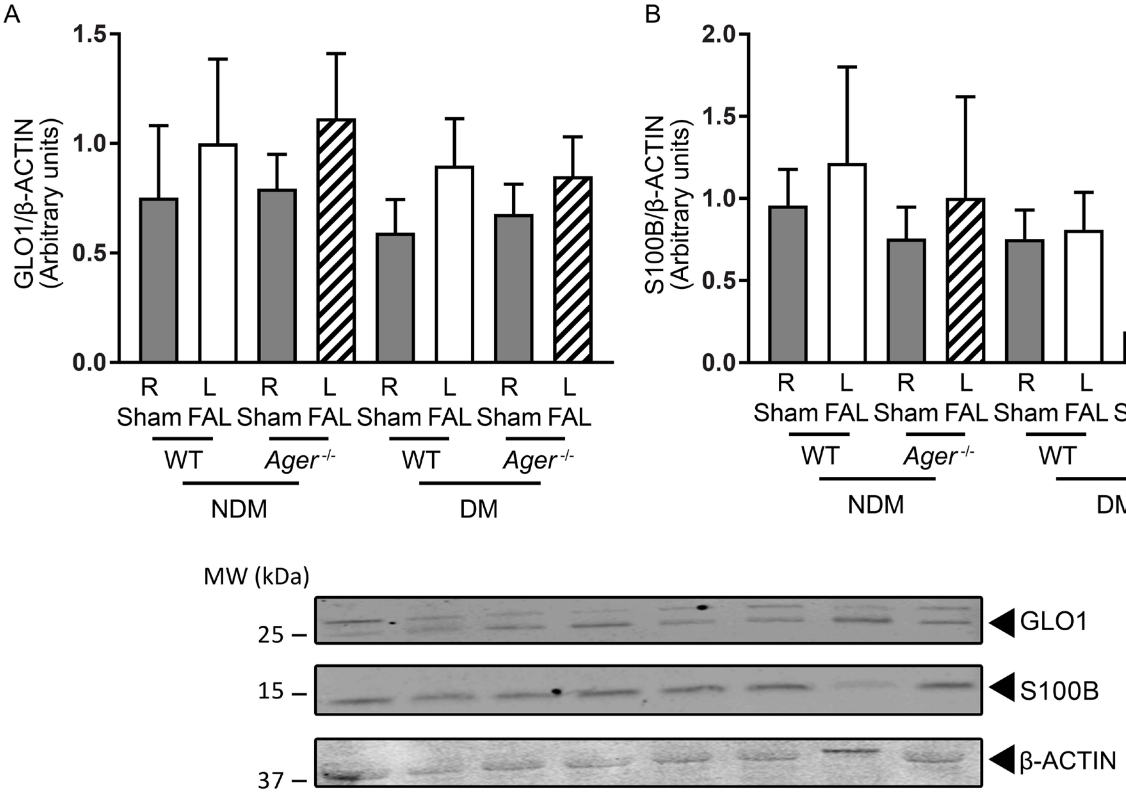
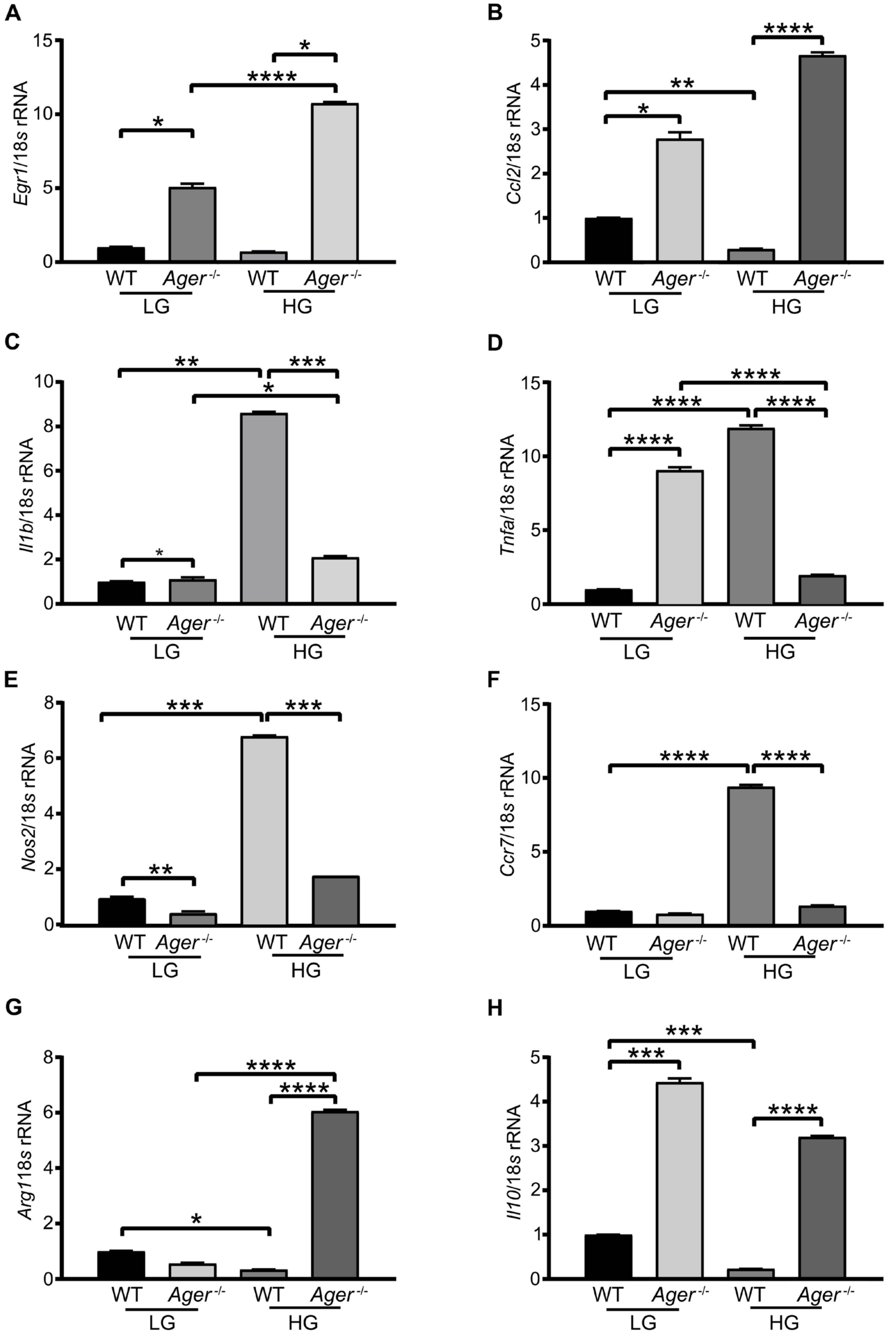


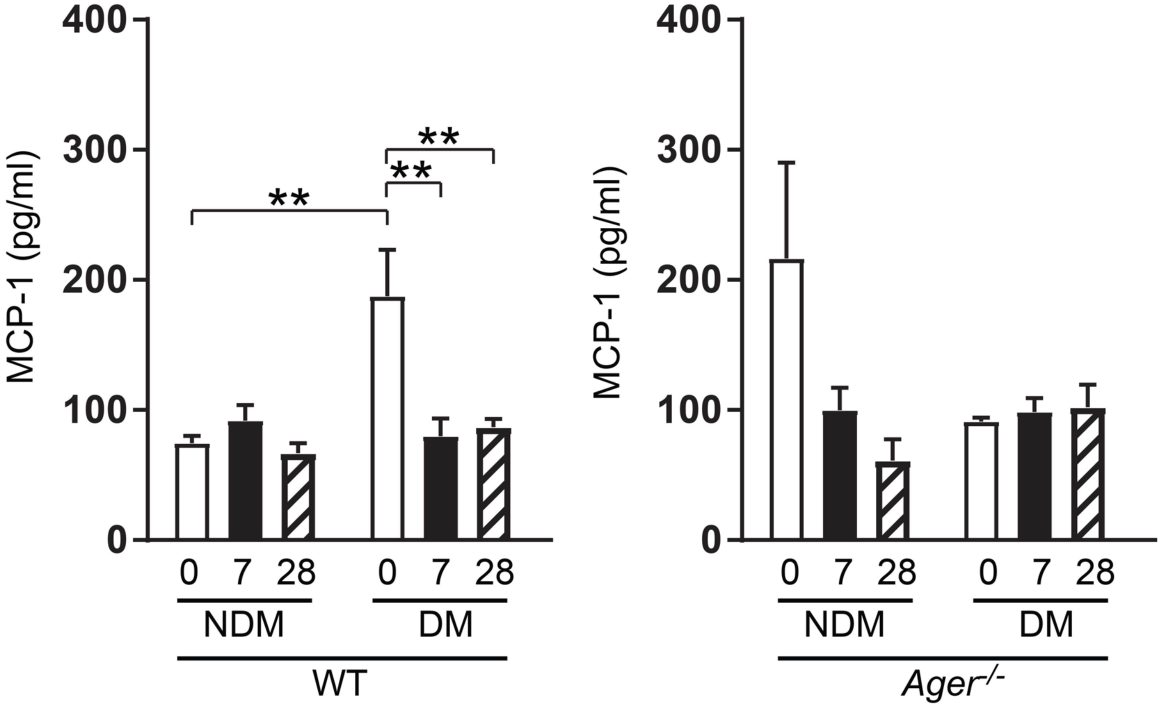
**Supplemental Figure I. Gene expression in hind limb ischemia, day 28: effect of RAGE. (A-B)** Total RNA was isolated from the indicated muscles and subjected to real-time PCR analysis. *Ccl2* mRNA (A) and *Egr1* (B) mRNA was detected on day 28 after FAL vs. sham and normalized to 18*s* rRNA. R denotes right leg/sham control and L denotes left leg/femoral artery ligation (FAL). NDM denotes non-diabetes and DM denotes diabetes. Numbers of mice per group is as follows: For detection of *Egr1*: WT/NDM/Sham, 4; WT/NDM/FAL, 4; WT/DM/Sham, 4; WT/DM/FAL, 4; *Ager*$^{-/-}$/NDM/Sham, 5; *Ager*$^{-/-}$/NDM/FAL, 5; *Ager*$^{-/-}$/DM/Sham, 5; and *Ager*$^{-/-}$/DM/FAL 4. For detection of Ccl2: WT/NDM/Sham, 4; WT/NDM/FAL, 4; WT/DM/Sham, 4; WT/DM/FAL, 4; *Ager*$^{-/-}$/NDM/Sham, 5; *Ager*$^{-/-}$/NDM/FAL, 5; *Ager*$^{-/-}$/DM/Sham, 5; and *Ager*$^{-/-}$/DM/FAL 5. Error bars represent ±SEM. *$p<0.05$, **$p<0.01$



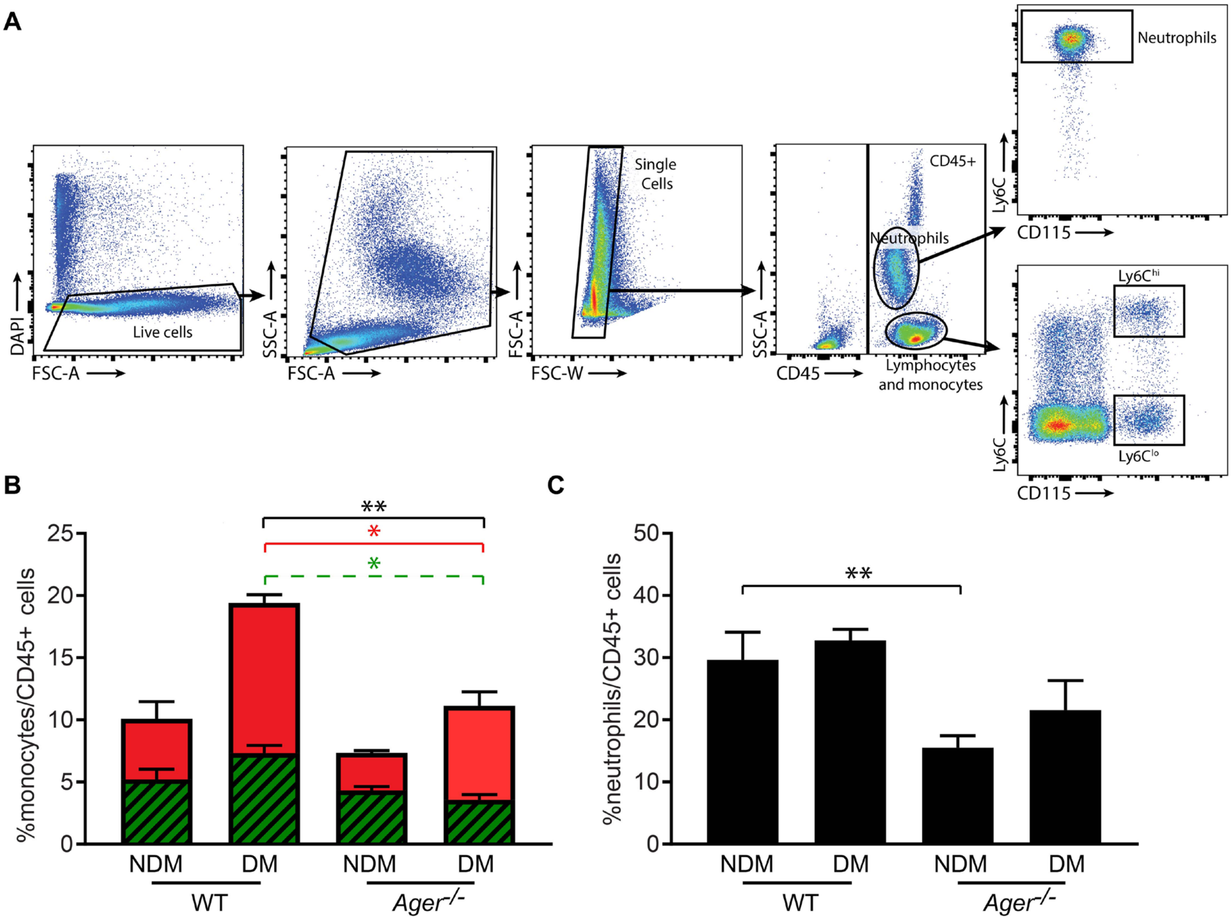
**Supplemental Figure II. Expression levels of GLO1 and S100B in skeletal muscle after hind limb ischemia.** Proteins from the indicated muscles on day 7 after FAL were subjected to Western blotting for detection of GLO1 **(A)** or S100B **(B)** and normalized to β-Actin (n=4 mice/group). R denotes right leg/sham control and L denotes left leg/femoral artery ligation (FAL). NDM denotes non-diabetes and DM denotes diabetes. Error bars represent ±SEM.



**Supplemental Figure III. Expression levels of inflammatory markers in bone marrow-derived macrophages (BMDMs): effect of RAGE. (A-H)** Total RNA was isolated from BMDMs cultured in either low glucose (LG) (5.5 mM) or high glucose (HG) (25 mM) for 7 days, and subjected to real-time PCR analysis for detection of *Egr1* (A); *Ccl2* (B); *Il1b* (C); *Tnfa* (D); *Nos2* (E); *Ccr7* (F); *Arg1* (G); and *Il10* (H) and normalized to 18*s* rRNA (n = BMDMs retrieved from n=4 mice/genotype). Error bars represent ±SEM. *$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$



**Supplemental Figure IV. Levels of plasma MCP1.** Plasma levels of MCP1 were analyzed by ELISA in WT and *Ager*$^{-/-}$ mice at baseline (0), day 7 and day 28 after FAL (n=6 mice/group). NDM denotes non-diabetes and DM denotes diabetes. FAL indicates femoral artery ligation. Error bars represent ±SEM. $^{**}p<0.01$



**Supplemental Figure V. Peripheral monocytes and neutrophils.** **(A)** Monocytes and neutrophil populations were analyzed by flow cytometry in peripheral blood. Flow cytometry approach. **(B-C)** Relative quantification of Ly6C$^{hi}$ and Ly6C$^{lo}$ monocytes subpopulations (B) and neutrophils (C) in WT and *Ager* $^{-/-}$ baseline samples (16 weeks old). NDM denotes non-diabetes and DM denotes diabetes. Red bars denote Ly6C$^{hi}$ monocyte subpopulation; Green bars denote Ly6C$^{lo}$ monocyte subpopulation. N=5-14/group as follows: WT/NDM, 8; WT/DM, 5; *Ager* $^{-/-}$/NDM, 14; and *Ager* $^{-/-}$/DM, 6. Statistical analysis was performed from the total population (Ly6C$^{hi}$ + Ly6C$^{lo}$/CD45+ cells) (black); Ly6C$^{hi}$ population (red) and Ly6C$^{lo}$ population (dashed green) and the differences reported in this figure only reflect comparisons performed between WT vs. the *Ager* $^{-/-}$ genotype. All intra-genotype comparisons are illustrated in Figure 6B and 6C. Error bars represent ±SEM. **p*<0.05, ***p*<0.01

**Supplemental Table I. Levels of plasma glucose for nondiabetic and diabetic WT, *Ager-/-* and Tg(*Glo1*) mice.** Levels of plasma glucose were obtained after two months of hyperglycemia induced by streptozotocin. The number of animals per experimental group is shown in the Table in parentheses following the genotype indicator. Results are expressed as mean ± SEM.

| | Nondiabetic | | | Diabetic | | |
|---|---|---|---|---|---|---|
| | WT (16) | *Ager* $^{-/-}$(17) | Tg(*Glo1*) (13) | WT (15) | *Ager* $^{-/-}$(14) | Tg(*Glo1*) (11) |
| Plasma glucose (mg/dL) | 141.88±7.63 | 139.56±6.87 | 140.72±7.46 | 414.17±16.15 | 405.33±23.14 | 407.92±15.43 |

**Supplemental Table II**. Gene expression profiling by angiogenesis $RT^2$ Profiler$^{TM}$ PCR array in muscle RNA of non-diabetic (NDM) or diabetic (DM) WT or *Ager*$^{-/-}$ mice at day 3 after femoral artery ligation (FAL) compared to that of NDM WT-sham controls (defined as 1.0-fold in each case).

| Gene Symbol | Gene Description | Mean of fold regulation in NDM WT mice after FAL vs. NDM WT-sham | Mean of fold regulation in DM WT mice after FAL vs. NDM WT-sham | Mean of fold regulation in NDM *Ager*$^{-/-}$ mice after FAL vs. NDM WT-sham | Mean of fold regulation in DM *Ager*$^{-/-}$ mice after FAL vs. NDM WT-sham |
|---|---|---|---|---|---|
| *Angpt1* | Angiopoietin 1 | -3.0 | -1.0 | -3.0 | -3.0 |
| *Angpt2* | Angiopoietin 2 | 6.0 | 3.0 | 4.0 | 4.0 |
| *Ccl2* | Chemokine (C-C motif) ligand 2 | 9.0 | 1.6 | 14.0 | 26.0 |
| *Cxcl2* | Chemokine (C-X-C motif) ligand 2 | 8.0 | 3.6 | 14.0 | 26.0 |
| *Cxcl5* | Chemokine (C-X-C motif) ligand 5 | 10.1 | 2.7 | 16.9 | 92.0 |
| *Il1β* | Interleukin 1 beta | 9.6 | 2.4 | 5.3 | 4.6 |
| *Mmp19* | Matrix metallopeptidase 19 | 3.7 | 6.2 | 4.1 | 6.5 |
| *Mmp9* | Matrix metallopeptidase 9 | 5.2 | 28.0 | 5.2 | 5.2 |
| *Pdgfα* | Platelet derived growth factor-α | -3.8 | -1.6 | -3.8 | -2.1 |
| *Pgf* | Placental growth factor | 7.5 | 5.9 | 2.4 | 9.1 |
| *Thbs1* | Thrombospondin-1 | 9.7 | 6.7 | 3.7 | 11.3 |
| *Vegfa* | Vascular endothelial growth factor-a | -11.0 | -1.0 | -5.8 | -8.0 |
| *Vegfb* | Vascular endothelial growth factor-b | -12.0 | -2.1 | -2.7 | -3.7 |
| *Vegfc* | Vascular endothelial growth factor-c | 1.4 | 1.9 | 2.4 | 1.4 |

**Supplemental Table III**. Gene expression profiling by angiogenesis RT$^2$ Profiler$^{TM}$ PCR array in muscle RNA of non-diabetic (NDM) or diabetic (DM) WT or *Ager*$^{-/-}$ mice at day 5 after femoral artery ligation (FAL) compared to that of NDM WT-sham controls (defined as 1.0-fold in each case).

| Gene Symbol | Gene Description | Mean of fold regulation in NDM WT mice after FAL vs. NDM WT-sham | Mean of fold regulation in DM WT mice after FAL vs. NDM WT-sham | Mean of fold regulation in NDM *Ager*$^{-/-}$ mice after FAL vs. NDM WT-sham | Mean of fold regulation in DM *Ager*$^{-/-}$ mice after FAL vs. NDM WT-sham |
|---|---|---|---|---|---|
| *Angpt1* | Angiopoietin 1 | -1.9 | 1.1 | -1.3 | -5.0 |
| *Angpt2* | Angiopoietin 2 | -1.4 | 1.0 | 3.0 | 19.0 |
| *Ccl2* | Chemokine (C-C motif) ligand 2 | 1.0 | -4.0 | 35.0 | 21.0 |
| *Cxcl2* | Chemokine (C-X-C motif) ligand 2 | 4.0 | -1.0 | 32.0 | 38,679.0 |
| *Cxcl5* | Chemokine (C-X-C motif) ligand 5 | 4.0 | -1.5 | 134.0 | 798.0 |
| *Il1β* | Interleukin 1 beta | 1.2 | -3.0 | 31.0 | 2,428.0 |
| *Mmp19* | Matrix metallopeptidase 19 | 3.6 | -1.7 | 9.5 | 7.8 |
| *Mmp9* | Matrix metallopeptidase 9 | -2.4 | -5.9 | 116.0 | 49 |
| *Pdgfα* | Platelet derived growth factor-α | -1.6 | 1.0 | 1.0 | -3.4 |
| *Pgf* | Placental growth factor | 1.7 | 1.8 | 9.4 | 14.7 |
| *Thbs1* | Thrombospondin-1 | 2.0 | -2.7 | 22.0 | 14.0 |
| *Vegfa* | Vascular endothelial growth factor-a | -1.9 | 1.0 | -6.0 | -6.0 |
| *Vegfb* | Vascular endothelial growth factor-b | -1.5 | 2.5 | -2.0 | -23.0 |
| *Vegfc* | Vascular endothelial growth factor-c | -1.5 | 1.4 | 3.5 | 1.4 |

**Supplemental Table IV**. Gene expression profiling by angiogenesis RT$^2$ Profiler$^{TM}$ PCR array in muscle RNA of non-diabetic (NDM) or diabetic (DM) WT or *Ager*$^{-/-}$ mice at day 7 after femoral artery ligation (FAL) compared to that of NDM WT-sham controls (defined as 1.0-fold in each case).

| Gene Symbol | Gene Description | Mean of fold regulation in NDM WT mice after FAL vs. NDM WT-sham | Mean of fold regulation in DM WT mice after FAL vs. NDM WT-sham | Mean of fold regulation in NDM *Ager*$^{-/-}$ mice after FAL vs. NDM WT-sham | Mean of fold regulation in DM *Ager*$^{-/-}$ mice after FAL vs. NDM WT-sham |
|---|---|---|---|---|---|
| *Angpt1* | Angiopoietin 1 | 1.05 | -1.3 | -1.2 | -1.5 |
| *Angpt2* | Angiopoietin 2 | 2.3 | 2.3 | 6.4 | 8.1 |
| *Ccl2* | Chemokine (C-C motif) ligand 2 | 6.1 | 3.5 | 22.9 | 14.9 |
| *Cxcl2* | Chemokine (C-X-C motif) ligand 2 | 2.3 | 3.4 | 11.8 | 16.1 |
| *Cxcl5* | Chemokine (C-X-C motif) ligand 5 | 2.8 | 1.5 | 4.3 | 6.3 |
| *Hgf* | Hepatocyte growth factor | 2.3 | 3.4 | 11.8 | 16.1 |
| *Hif1α* | Hypoxia inducible factor 1, alpha | 1.9 | 1.4 | 5.1 | 4.6 |
| *Il1β* | Interleukin 1 beta | 1.8 | 1.7 | 4.0 | 6.4 |
| *Itgβ3* | Integrin beta 3 | 1.5 | 1.2 | 6.3 | 5.8 |
| *Mdk* | Midikine | 4.3 | 10.6 | 45.8 | 69.1 |
| *Mmp19* | Matrix metallopeptidase 19 | 1.3 | 1.5 | 10.2 | 6.4 |
| *Mmp2* | Matrix metallopeptidase 2 | 1.9 | 2.3 | 7.7 | 5.6 |
| *Mmp9* | Matrix metallopeptidase 9 | -1.3 | -2.3 | 4.6 | 3.3 |
| *Pecam1* | Platelet endothelial cell adhesion molecule 1 | 1.3 | 1.5 | 2.2 | 2.9 |
| *Pgf* | Placental growth factor | 2.3 | 4.5 | 9.9 | 11.2 |
| *Sphk1* | Sphingosine kinase 1 | 1.9 | 1.3 | 5.8 | 5.5 |
| *Thbs1* | Thrombospondin-1 | 1.1 | -2.3 | 4.7 | 2.3 |
| *Tgfb1* | Transforming growth factor beta 1 | 3.3 | 2.4 | 17.1 | 10.3 |
| *Vegfa* | Vascular endothelial growth factor-a | -2.1 | -2.1 | -3.8 | -3.8 |
| *Vegfb* | Vascular endothelial growth factor-b | -1.6 | -2.1 | -2.7 | -3.7 |
| *Vegfc* | Vascular endothelial growth factor-c | -1.6 | -2.1 | -2.7 | -3.7 |