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**Extracellular Matrix Secretion by Cardiac Fibroblasts:
Role of microRNA-29b and microRNA-30c**

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ABSTRACT

Rationale: MicroRNAs (miRNAs), in particular miR-29b and miR-30c, have been implicated as important regulators of cardiac fibrosis.

Objective: To perform a proteomics comparison of miRNA effects on extracellular matrix (ECM) secretion by cardiac fibroblasts (CFs).

Methods and Results: Mouse CFs were transfected with pre-/anti-miR of miR-29b and miR-30c and their conditioned medium was analysed by mass spectrometry. MiR-29b targeted a cadre of proteins involved in fibrosis, including multiple collagens, matrix metalloproteinases, and leukemia inhibitory factor (LIF), insulin-like growth factor-1 (IGF-1) and pentraxin-3, three predicted targets of miR-29b. MiR-29b even attenuated the CF response to TGF β . In contrast, miR-30c had little effect on ECM production, but opposite effects with regards to LIF and IGF-1. Both miRNAs indirectly affected cardiac myocytes: Upon transfection with pre-miR-29b, the conditioned medium of CFs lost its ability to support adhesion of rat ventricular myocytes and led to a significant reduction of cardiac myocyte proteins (alpha-actinin, cardiac myosin-binding protein C and cardiac troponin I). Similarly, cardiomyocytes derived from mouse embryonic stem cells atrophied under pre-miR-29 conditioned medium whereas pre-miR-30c conditioned medium had a prohypertrophic effect. Levels of miR-29a, miR-29c and miR-30c but not miR-29b were significantly reduced in a mouse model of pathological but not physiological hypertrophy. Treatment with antagomiRs to miR-29b induced excess fibrosis after aortic constriction without overt deterioration in cardiac function.

Conclusions: Our proteomic analysis revealed novel molecular targets of miRNAs that are linked to a fibrogenic cardiac phenotype. Such comprehensive screening methods are essential to define the concerted actions of miRNAs in cardiovascular disease.

Keywords:

microRNA, proteomics, fibroblasts, fibrosis, animal model cardiovascular disease

Nonstandard Abbreviations and Acronyms:

CF	Cardiac fibroblast
ECM	Extracellular matrix
IGF-1	Insulin-like growth factor 1
LVH	Left ventricular hypertrophy
LIF	Leukemia inhibitory factor
miRNA	microRNA
MMP	Matrix metalloproteinase
NRVM	Neonatal rat ventricular myocyte
PTX-3	Pentraxin 3
TGF β	Transforming growth factor beta

INTRODUCTION

MiRNAs have emerged as important regulators of cardiac fibrosis, a critical feature of structural myocardial remodeling in many cardiac diseases.¹⁻³ CFs communicate with cardiac myocytes via paracrine mechanisms, alterations in ECM, and direct cell-cell interactions.⁴ The miR-29 family suppresses the expression of several collagens and ECM proteins. MiR-29b is downregulated after myocardial infarction and in disease models for cardiac hypertrophy, possibly contributing to scar formation and fibrosis.⁵ Two other miRNAs, miR-30 and miR-133, display reduced expression during cardiac disease and show an inverse correlation to levels of connective tissue growth factor, collagen production, and fibrosis.⁶ Whereas miR-133 is expressed specifically in cardiac myocytes, miR-30 is present both in cardiac myocytes and CFs. MiR-21 has also been implicated in cardiac fibrosis, but its role is debated.^{7,8}

In this study, we applied a proteomics approach to investigate the targets of miR-29b and miR-30c in the secretome of CFs. Most studies rely on bioinformatic algorithms or mRNA analysis for the identification of direct targets. These algorithms are based on an incomplete understanding of miRNA-mRNA seed pairing and evolutionary conservation of miRNAs.⁹ They typically predict hundreds to thousands of target genes for one miRNA, but with limited overlap and even the most sensitive programs fail to identify known targets.¹⁰ Importantly, cell type context is not taken into consideration. The utilization of -omics methods is essential for a more comprehensive understanding of miRNA-mediated regulation of gene expression. MiRNAs function as posttranscriptional regulators of gene expression, either by inducing mRNA degradation or by blocking protein translation. A systems biology approach aiming at a global readout at the protein rather than the mRNA level may advance our insight into the coordinated regulation of direct as well as indirect targets driving cardiovascular phenotypes following miRNA manipulation³.

METHODS

An expanded Materials and Methods section is available in the online data supplement <http://circres.ahajournals.org>. Key techniques involved adaptations of previously published protocols, including those for miRNA measurements¹¹⁻¹³ and liquid chromatography tandem mass spectrometry (LC-MS/MS)¹⁴⁻¹⁵. For animal studies, procedures were performed in accordance with the Guidance on the Operation of the Animals (Scientific Procedures) Act, 1986 (United Kingdom).

RESULTS

ECM secretion by CFs.

Primary murine CFs were transfected with pre-/anti-miRs of miR-29b or miR-30c (Online Figure I) and their secretome was analysed by proteomics (Online Figure II). GO term enrichment confirmed that the majority of proteins identified belong to the extracellular region (Figure 1A), including low abundant proteins such as secreted proteases, protease inhibitors, growth factors and cytokines (Figure 1B). Online Table I lists 248 non-redundant extracellular proteins from two independent experiments. Proteins previously identified in other proteomic studies on fibroblasts, including one on CFs, are highlighted. Notably, our study provides the most detailed characterization of the CF secretome to date.

Effects of miR-29b and miR-30c.

Both, miR-29b and miR-30c are abundant miRNAs in CFs (Figure 1C). Based on three different algorithms (TargetScan, PicTar and Diana-microT), fewer common targets were predicted for miR-29b than miR-30c (Figure 1D). Yet, pre-miR-29b markedly attenuated protein secretion by CFs, whereas pre-miR-30c had comparably little effect (Figure 2A). In general, transfection with pre-miRs led to more pronounced protein changes than anti-miRs. In agreement with previous studies,¹⁶⁻¹⁹ pre-miR-29b reduced collagen (CO1A1, CO5A2) and MMP2 secretion (Figure 2B). Inhibition by anti-miR-29b also reduced the expression of other miR-29 family members (Online Figure I) but did not further stimulate collagen and MMP secretion in cultured CFs.

Proteomics for miRNA target identification.

To reveal predicted and novel targets of miR-29b and miR-30c, the normalized spectral counts of all extracellular proteins are presented in Online Table II and III. Besides conventional methods of statistical inference to detect differences in expression, we utilised a hierarchical Bayes estimation of generalized linear mixed effects model (Qspec). The false discovery rate (FDR) was calculated with a mixture model-based method of local FDR control based upon the Bayes factors (BF). Proteins with a BF>10, FDR<5% and a fold change >30% were considered to be significant. Regarding miR-30c, little is known about its extracellular targets. Recently, miR-30c has been shown to target plasminogen activator inhibitor-1 (PAI1)²⁰. Upon transfection with pre-miR-30c, plasminogen activator inhibitor-1 was decreased by 25%, but fell short of statistical significance in our analysis (BF=7, Online Table III). Instead, protein-lysine 6-oxidase (LYOX), responsible for the cross-linking of peptidyl lysine residues in precursors to fibrous collagen and elastin, displayed a significant reduction in CFs transfected with pre-miR-30c. It was only predicted as a direct target by one of the three bioinformatics algorithms (Online Figure III). Results after transfection with pre-miR-29b were much more pronounced (Online Table II, Figure 2C). Since target derepression can be stress dependent, the proteomics analysis of pre-miR-29b transfected CFs was repeated following stimulation with TGFβ. Among the 186 extracellular proteins identified (Online Table IV), 92 (≈50%) reached an unadjusted p-value (ANOVA) <0.05, including 21 out of 25 (84%) predicted targets of miR-29b (Figure 3A). Again, Qspec was used to detect differential expression. Results are shown in Figure 3B.

Confirmation of direct and indirect targets.

The quantification of low abundance proteins by proteomics can be challenging in complex biological samples. Cytokines and growth factors, such as LIF and IGF-1, as well as a member of the pentraxin superfamily, PTX3 showed weak evidence for differential expression (unadjusted p-value <0.05) in the t-test. PTX3 and LIF had a BF>4 by Qspec. For independent validation, levels of IGF-1, LIF and PTX-3 were determined using commercial ELISAs. The ELISA data correlated well to the spectral counts obtained by proteomics in the miR-29b experiment (Figure 4A-C, Spearman correlation coefficients 0.75-0.90). IGF-1 (Figure 4A), LIF (Figure 4B), and PTX3 (Figure 4C) were suppressed by pre-miR-29b and increased after inhibition by anti-miR-29b. As expected for direct targets, there was complementarity between the miR-29b seed-matching sequence and the 3'-UTR region of the target mRNAs (LIF, IGF-1, PTX3, Figure 4D). To further confirm the functionality of the seed regions of miR-29b, we fused the 3' UTR of IGF-1, LIF and PTX3 to a luciferase reporter vector. Co-expression of synthetic miR-29b decreased IGF-1 and LIF (Online Figure IV) but not PTX3 3'UTR reporter activity (data not shown). Mimics of miR-29b had the same effect as pre-miR-29b on target gene repression (Online Figure V). In contrast, miR-30c had no seed-matching sequence in the 3' UTR of IGF-1, LIF, and PTX3. Yet, overexpression of miR-30c increased levels of IGF-1 (Figure 4A) and LIF (Figure 4B). Again, PTX3 remained unaffected (Figure 4C).

In vivo validation.

Next, adult C57Bl6 mice were treated with antagomiRs directed against miR-29b (3 consecutive i.p. injections at a dose of 80mg/kg/day, Figure 4E). At day 7, successful inhibition of cardiac miR-29b was confirmed by qPCR (Figure 4F). When we evaluated cardiac mRNA expression, IGF-1 levels were increased by $\approx 50\%$ compared to respective controls (Figure 4G). In plasma, levels of IGF-1 rose by $\approx 25\%$ (Figure 4H), confirming IGF-1 as a target of miR-29b *in vitro* and *in vivo*. Neither LIF nor PTX-3 showed significant changes in unstressed hearts or in plasma following antagomiR-29b treatment (data not shown).

Effects on cell adhesion.

To investigate whether miRNA-induced changes in the secretome of CF impact on cardiac myocyte adhesion, neonatal rat ventricular myocytes (NRVM) were cultured overnight on glass-coverslips, pre-coated with conditioned medium of CFs, previously transfected with pre-miR29b (Figure 5A) or anti-miR29b (Figure 5B). Cardiac myocytes were stained for cardiac myosin-binding protein C (cMyBP-C, green) and cardiac α -actinin (red). Nuclei were counterstained with DAPI (blue). Transfection with pre-miR29b markedly reduced the ability of the conditioned medium from CFs to support adhesion of NRVM (Figure 5A, Online Figure VI). The effect of pre-miR30c on NRVM adhesion was less pronounced. Only when untransfected CFs were seeded on plates pre-coated with conditioned medium of transfected CFs, pre- as well as anti-miR-29b resulted in significant changes in early adhesion (Online Figure VII).

Effects on cardiac myocytes.

Bidirectional crosstalk between CFs and cardiac myocytes is able to regulate the CF and cardiac myocyte phenotype.⁴ NRVM cultured on plastic dishes, precoated with conditioned medium of CFs previously transfected with pre-miR-29b, displayed reduced expression of alpha-actinin, cMyBP-C and cTnI, as demonstrated by western immunoblotting (Figure 5A). These cardiac markers were unaltered by anti-miR-29b or pre-miR-30c. In contrast, pre-coating with conditioned medium from CFs transfected with anti-miR-30c reduced alpha-actinin and cTnI expression in NRVM (Figure 5B). No difference was observed for cMyBP-C. To test whether the secretomes of transfected CFs have a direct activity on cardiomyocytes, specifically on cardiomyocyte size, we exposed a pure ($>95\%$) cardiomyocyte preparation derived from mouse embryonic stem cells (ESC) modified to express a neomycin resistance under the cardiomyocyte-restricted α MHC promoter, to conditioned medium from pre-miR-29 and pre-miR30c transfected CF. Under these conditions cardiomyocytes atrophied (pre-miR-29 conditioned medium) or conversely showed hypertrophic growth (pre-miR-30c conditioned medium; Figure 5C). Conditioned media from CFs transfected with anti-miRs did not alter cardiomyocyte size.

Cross-talk between miRNAs.

Our observation that miR-30c and miR-29b induced opposite effects in several experiments (Figures 4A-C, 5A-C), prompted us to investigate the possibility of a cross-talk between miR-30c and miR-29b in CFs: Indeed, overexpression of pre-miR-29b was sufficient to reduce the endogenous levels of miR-30c in CFs to a similar extent ($\approx 50\%$) as TGF β stimulation of CFs (Online Figure VIII). Even at a moderate level of miR-29b overexpression (~ 20 fold), the difference in miR-30c remained statistically significant, while many other miRNAs were not affected (data not shown).

MiR-29b in cardiac hypertrophy.

Attenuation of miR-29b expression has previously been linked to ECM remodelling post myocardial infarction.¹⁶ MiR-29c has also been reported as down-regulated in cardiac hypertrophy.²¹ Thus, we sought to explore whether endogenous miR-29b and miR-30c levels are affected in mouse models of pathological (transverse aortic constriction, TAC) and physiological (free running exercise) left ventricular hypertrophy (LVH). RNA was isolated from 23 left ventricular samples (Sham: n=6; TAC: n=6; Sedentary: n=6; Exercise: n=5). TaqMan qPCR revealed a significant decrease of miR-29a, miR-29c and miR-30c, but not of miR-29b in pathological LVH (Figure 6A). Physiological LVH was not associated with significant alterations in any of the miRNAs tested (Figure 6A). Yet, miR-29b was abundant in non-myocytes (Figure 6B) and putative miR-29 targets were differentially expressed after TAC (Figure 6C).

In vivo silencing of miR-29b.

To establish whether miR-29b can alter ECM protein expression in pathological hypertrophy, antagomiRs to miR-29b were injected in male C57/Bl6 mice on 3 consecutive days before TAC. Hearts were obtained 14 days post surgery. AntagomiR treatment exhibited a marked repression of miR-29b without significant attenuation of other miR-29 family members (Figure 7A). Inhibition of miR-29b did not affect cardiac volumes or cardiac function and overall regional wall hypertrophy remained concentric (Online Table V). Only in mice with the most pronounced inhibition of miR-29b, the posterior papillary muscle was occasionally more echobright and its base thickened (Online Figure IX). Histologically, excess perivascular fibrosis was observed (Figure 7B). Of note, miR-29b inhibition by antagomiRs emerged as significant determinant of myocardial expression for many direct and indirect targets identified by proteomics, including LIF and IGF-1 (Figure 7C). Detailed expression data after TAC are presented in Online Figure X.

DISCUSSION

The molecular mechanisms underlying cardiac fibrosis are of intense interest. MiR-29b and miR-30c are two key miRNAs that are enriched in CFs and involved in cardiac fibrosis. In the present study, we applied a proteomics approach to identify extracellular targets of miR-29b and miR-30c. MiR-29b had a much stronger effect on the extracellular proteome of CFs than miR-30c and even blocked the response of CFs to TGF β , one of the master regulators of fibrosis. Besides its major effect on ECM proteins, miR-29b additionally altered the secretion of growth factors and cytokines, such as LIF and IGF-1. In contrast, miR-30c regulated fewer ECM proteins, but indirectly modulated the expression of LIF and IGF-1.

The secretome of mouse CFs.

Few large-scale proteomics studies focusing on the secretome of fibroblasts have been performed so far.²² Most studies investigated the secretome of feeder cells such as mouse embryonic fibroblasts, which support the growth of embryonic stem cells²³⁻²⁶ or dermal fibroblasts.^{27, 28} Thus far, only one study used CFs and profiled 24 cytokines/chemokines in their conditioned medium.²⁹ No detailed proteomics analysis has been performed to date. The recognition that cardiac fibrosis is a prominent contributor to myocardial disease and that CFs interact with cardiac myocytes via paracrine mechanisms, alterations in matrix homeostasis, and direct cell-cell interactions has resulted in a growing interest in CFs over recent years.⁴ For example, ECM promotes efficient cardiac differentiation of human pluripotent stem cells.³⁰ To the best of our knowledge, our proteomic study presents the most extensive characterization of the CF secretome published so far. Among the 248 proteins identified are important proteins for ECM-receptor

interaction, focal adhesion, the TGF β signalling pathway, and cytokine-cytokine receptor interaction. Similar to our recent study on ECM remodeling in a porcine model of cardiac ischemia/reperfusion,³¹ this comprehensive map of the CF secretome will provide an important resource for future investigations into factors involved in CF-cardiac myocyte communication.

Proteomics for miRNA target identification.

Changes in cardiovascular phenotypes following miRNA manipulation are likely to be the result of multiple interactions. As miRNAs are fine-tuners of protein expression and the regulation of their target genes tends to be in the range of 20-50%, the secretome offers the distinct advantage that miRNA-induced changes accumulate and become more readily detectable by proteomics. The levels of miR-29b expression in our study are similar to previous publications in CFs¹⁶. An obvious concern is whether transfection with precursor miRNAs interferes with the cellular processing of non-coding RNAs. To exclude off-target effects, we compared two miRNAs, both of which play an important role in CFs and are likely to be processed in a similar manner upon transfection, in parallel to respective scrambled miRNA controls. Potential explanations for the more pronounced effect of pre-miRNAs over anti-miRs are as follows: 1) Transfection with miRNA precursors will saturate the available binding sites. This is informative about the maximal effect of a particular miRNA within the proteome, but does not imply that the expression of these proteins is under the control of the endogenous miRNA. 2) A tight regulation of expression is required, in particular for proteins that have important functions. Individual miRNAs modulate the expression of several targets, which often are effectors of the same biological process. Conversely, several miRNAs can target the same effector.¹ Diverse miRNAs can also act cooperatively or redundantly to regulate the effectors of the same biological process. Thus, derepression of a protein based on inhibition of a single miRNA is more difficult to achieve. 3) Most transgenic animals for miRNAs have no baseline phenotype, but develop a phenotype in response to a stress stimulus. Stress conditions are likely to alter the susceptibility of proteins for the control by endogenous miRNAs. The abundance of the mRNA is as important for miRNA target regulation as the concentration of the endogenous miRNA itself. Thus, proteins that change following the transfection of the precursor but do not change by antagonizing the endogenous miRNA in unstimulated cells or normal hearts could still be affected during a stress response. Currently, miRNA target identification is mainly performed in unstressed cells. Our proteomics analyses were performed at baseline and after TGF β stimulation. Moreover, confirmation of target repression was obtained by using miRNA mimics and by antagomiR treatment in a mouse model of pathological LVH.

Role of miR-29b in cardiac disease.

The miR-29 family is present with four copies in the genome and mainly expressed in fibroblasts. Unlike most miRNAs that are only present in the cytosol, miR-29 is also found in the nucleus. Following myocardial infarction, miR-29b is down-regulated in the region adjacent to the infarcted area, suggesting a pertinent role of this miRNA in cardiac remodelling.¹⁶ Besides its involvement in the development of cardiac fibrosis, the miR-29 family has been implicated in aortic aneurysm formation^{32, 33} and atherosclerosis¹⁸. Its modulatory effect on ECM protein secretion and potential importance in different cardiovascular diseases has made it a lead miRNA for therapeutic intervention. Thus far, the effect of miR-29b in CFs was mainly assessed at the mRNA level. Over-expression of miR-29b reduced expression of collagens whereas down-regulation of miR-29b with anti-miRs induced the expression of collagens *in vitro* and *in vivo*.¹⁶ Our proteomic data confirm that pre-miR-29b is a potent regulator of ECM synthesis. The effect of anti-miR-29b in cultured CF, however, was not as pronounced. While we failed to observe a significant change of miR-29b expression in two mouse models of LVH, this does not negate a potential role of miR-29b for initial ECM deposition during cardiac hypertrophy, as miRNA measurements were only performed at one time point (14 days post surgery or 28 days post exercise). In fact, treatment with antagomiRs to miR-29b increased ECM deposition after aortic constriction. Previous

studies with miR-29 inhibition were done in unstressed hearts and the expression of three collagen transcripts (Col1A1, Col1A2, and Col3A1) was only modestly increased¹⁶. After TAC, we did observe target derepression and increased perivascular fibrosis in response to miR-29b inhibition.

CF – cardiac myocyte interactions.

MiRNA levels in CFs may impact on cardiac myocytes with regards to their adhesive properties and growth characteristics. Recently, Castoldi *et al.* have demonstrated that miR-133a, a miRNA expressed in cardiac myocytes and involved in cardiac hypertrophy, also targets CO1A1, a target of miR-29b.¹⁷ Their data support the concept that myocardial fibrosis could be modulated not only by miRNAs expressed in CFs, but also by muscle-specific miRNAs, through a synergistic action on CO1A1 mRNA expression. However, little is known regarding the role of miR-29b in the communication between CFs and cardiac myocytes and its involvement in myocardial hypertrophy. Our data suggest that miR-29b is not only regulating ECM protein deposition but may also contribute to development of cardiac hypertrophy by targeting important growth factors and cytokines: among the potential targets of miR-29b were IGF-1, LIF and PTX3. PTX3 is a member of the pentraxin superfamily that plays an important role at the interface of inflammation and ECM remodeling.^{34,35} It has been suggested as a novel biomarker of left ventricular dysfunction and heart failure with normal ejection fraction.³⁵ Interestingly, various inflammatory molecular cascades, in particular toll-like receptor signaling, stimulate the expression of PTX3³⁶ and the promoter region of miR-29b shows at least 4 different binding sites for NK-kappaB.³⁷ LIF is a member of the IL-6 family that is synthesized by different cell types in the myocardium including cardiac myocytes and CFs.³⁸ Previous studies have demonstrated that LIF confers both hypertrophic and cytoprotective responses in adult cardiac myocytes via the gp130 and LIF receptor signaling complex.^{39,40} IGF-1 is a key regulator of growth, survival, and differentiation. In myocardial biology, IGF-1 and its signal transduction cascade are involved in development, cardiac myocyte size and survival, action potential, and excitation-contraction coupling.^{41,42} Interestingly, miR-29b and miR-30c exerted opposite effects on IGF-1 and LIF secretion by CFs and in most functional experiments. This is in agreement with previous reports that miRNAs in the same cell type could regulate the same targets counterbalancing each other.¹ To rule out indirect effects mediated via contaminating stroma cells, we exposed a highly purified cardiomyocyte population derived from ESCs to conditioned medium and observed that the pre-miR29b and pre-miR30c CF secretomes did indeed impart opposite effects on cardiomyocyte growth, i.e. atrophy and hypertrophy, respectively. These effects were likely mediated by soluble growth factors suggesting that the observed paracrine effects on cardiomyocytes may not only be due to adhesive ECM molecules.

Conclusion.

Our proteomics study provides the most comprehensive characterization of the mouse CF secretome to date. A particular strength is the proteome-wide analysis of miRNA function, which offers unique insight into the regulation of protein networks controlled by miR-29b and miR-30c. Direct and indirect targets were identified from a broader proteomics screen and validated *in vivo*. Many of these targets would not have been anticipated based on current bioinformatics prediction models. Addressing the complexity of miRNA-regulated gene expression is an essential step to facilitate a better understanding of their concerted actions in cardiac fibrosis.

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DISCLOSURES

None.

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FIGURE LEGENDS

Figure 1: The secretome of mouse CFs. **A**, Simplified GO term enrichment graph of the proteins identified in the conditioned medium of CFs (Online Table I). The functional annotation tool “David 6.7” has been used to perform the GO term annotation. The default background dataset of *Mus Musculus* was selected for the GO term enrichment calculation. **B**, Classification of the relevant extracellular proteins identified in secretome of CFs. **C**, Expression levels of miR-29 and miR-30c compared to other selected miRNAs in mouse CFs. The higher Ct values inversely correlate with miRNA expression levels. U6 was used as normalisation control. **D**, Pie charts illustrating common targets for miR-29 and miR-30c in three target prediction algorithms (TargetScan, PicTar, Diana).

Figure 2: Comparison of miR-29b and miR-30c. **A**, Frequency distribution of protein changes after the transfection of CFs either with pre-miR-29b, anti-miR-29b, pre-miR-30c or anti-miR-30c. A log₂ fold change of -1 or 1 was used as cut-off. Protein fractions with a log₂ fold change lower than -1 or higher than 1 are highlighted in grey. Log₂ (fold change) is calculated using the normalized spectral counts and averaged for the 3 biological replicates. The data were fitted with a Gaussian function showing a normal distribution of the values in our dataset. All proteins are listed in Online Table II and III. **B**, 30 µl of conditioned medium from CFs transfected with pre-miR-29b and anti-miR-29b was separated by SDS-PAGE before validation of known targets by immunoblotting (CO1A2, CO5A2) and gel zymography (MMP-2). The corresponding silver-stained gels are presented below. **C**, The log(fold change) for each of the differentially secreted proteins on overexpression of pre-miR-29b is illustrated. The identified targets predicted by at least one prediction algorithm (TargetScan, PicTar, Diana) are highlighted.

Figure 3: TGFβ1 stimulation. **A**, Attenuation of the CF response to TGFβ1 following transfection with pre-miR-29b. Proteins identified in the conditioned medium of CFs after stimulation with TGFβ1 (10ng/ml) are listed in Online Table IV. The heat map displays only predicted miR-29b targets reaching a p-value (ANOVA) <0.05. **B**, Effect of pre-miR-29b in the presence of TGFβ1. The log(fold change) for each of the differentially secreted proteins on overexpression of pre-miR-29b is illustrated. The identified targets predicted by at least one prediction algorithm (TargetScan, PicTar, Diana) are highlighted.

Figure 4: Confirmation of miR-29b targets. Correlation between the protein concentration of IGF-1 (**A**), LIF (**B**), PTX3 (**C**) in the conditioned medium of CFs transfected by ELISA and by proteomics. The Spearman coefficients of correlations to the ELISA measurements and the normalised spectral counts (SCs) in the miR-29b experiment are given (left panel). Concentration of IGF-1, LIF, PTX3 after overexpression (middle panel) or inhibition (right panel) of miR-29b and miR-30c as measured by ELISA. **D**, Alignment of LIF, IGF-1 and PTX3 3'-UTR mRNA region with the sequence of miR-29b. The vertical bars and bold characters indicate 3' -UTR sequences of the miR-29b binding site of each target gene. **E**, Schematic representation of the antagomiR experiment. Relative expression of miR-29b (**F**) and IGF-1 (**G**) in the heart of antagomiR-treated mice. **H**, IGF-1 concentration in plasma of antagomiR-treated mice. * denotes P<0.05; ** P<0.01; *** P<0.001; “ns” non-significant; “CTL” control.

Figure 5: Functional assay on cardiac myocytes. **A**, **B** NRVM were plated onto glass-coverslips, pre-coated with conditioned medium of CFs previously transfected with control pre (Con), pre-miR-29b or pre-miR-30c or control anti (Con), anti-miR-29b or anti-miR-30c. Nuclei were labeled with DAPI (blue), cMyBP-C and α-actinin were labeled with specific antibodies (green and red, respectively). For quantitation see Online Figure VI. Representative immunoblots for cardiac α-actinin, cMyBP-C or cTnI. Bar charts reflect quantitative data of 6 independent experiments. **C**, Effect of conditioned medium of CF on cell area of ESC-derived cardiomyocytes. ** denotes P<0.05; ** P<0.01; *** P<0.001; “Con” control.

Figure 6: MiR-29b and cardiac hypertrophy. **A**, MiRNA-expression in models of pathological (TAC) and physiological hypertrophy (Exercise), with their respective controls (n=5-6 per group). **B**, In situ hybridisation for miR-29b demonstrating predominantly nuclear staining in non-myocytes of pressure-overloaded hearts. Size bar indicates 50 μ m. **C**, Heatmap of qPCR results of potential miR-29 targets. The proteins above the black line are transcripts that showed a difference in pathological hypertrophy by t-test (p-value < 0.05). The transcripts above the red line are those that remained significant after a Bonferroni correction. There were no significant differences in mRNA expression in physiological hypertrophy.

Figure 7: MiR-29b and target derepression in cardiac hypertrophy. **A**, Knock-down of miR-29 family members following antagomiR-29b treatment in two independent TAC experiments (n=9 per group, mean \pm SEM, *** P<0.001). **B**, ECM accumulation in Masson's Trichrome Staining. Size bar indicates 50 μ m. **C**, Correlation between the efficiency of miR-29b knockdown and derepression of 27 putative miR-29b targets as quantified by qPCR (upper panel). Distribution of correlations between putative miR-29b targets and the efficiency of miR-29 a,b and c knockdown (lower panel).



Circulation Research

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Novelty and Significance

What Is Known?

- MicroRNAs are involved in the pathogenesis of cardiac fibrosis.
- MicroRNA-29b suppresses extracellular matrix production.

What New Information Does This Article Contribute?

- We report proteomics analysis of the proteins secreted (secretome) from cardiac fibroblasts.
- We identify extracellular proteins that are targeted by microRNA-29b and microRNA-30c.

Comprehensive read-outs are required for assessing microRNA (miRNA) targets. We used a proteomics approach to analyze miRNA targets in the secretome of cardiac fibroblasts. We also assessed the effects of two key miRNAs (miR-29b and miR-30c) in cardiac fibroblasts side-by-side. Using this method we uncovered not only previously known direct targets, which are related to fibrosis, but also several new direct and indirect targets of miR-29b and miR-30c. Our data suggest that proteomics methods are more effective for identifying miRNA targets at the protein level than the use of mRNA profiling or bioinformatics prediction algorithms. Changes in individual miRNA targets should be interpreted in the wider context of other protein alterations, including the indirect effects of miRNAs. Studying the role of miRNAs in regulating protein secretion is a promising strategy to explore the importance of miRNAs in cardiovascular biology.

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Figure 1

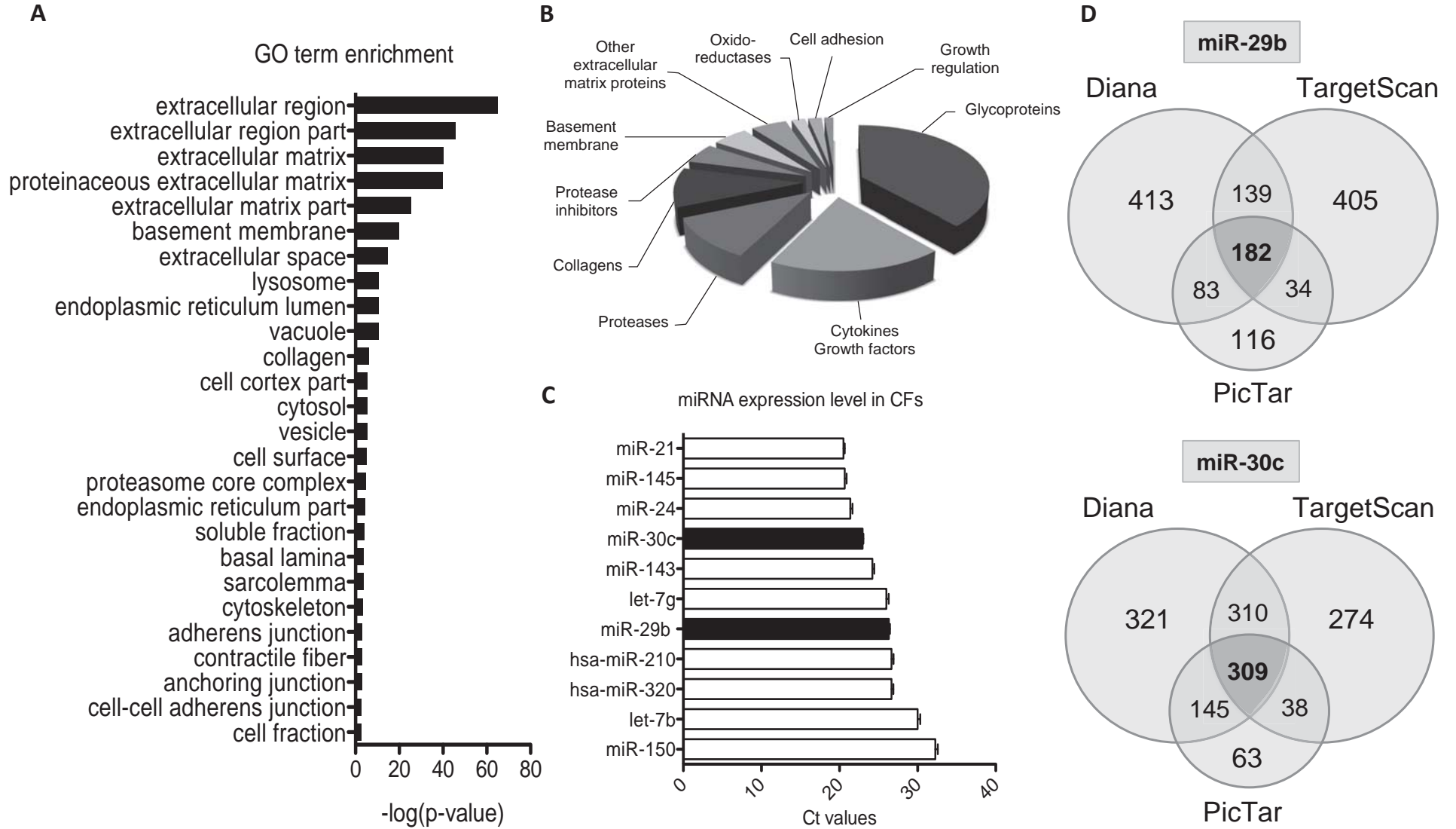
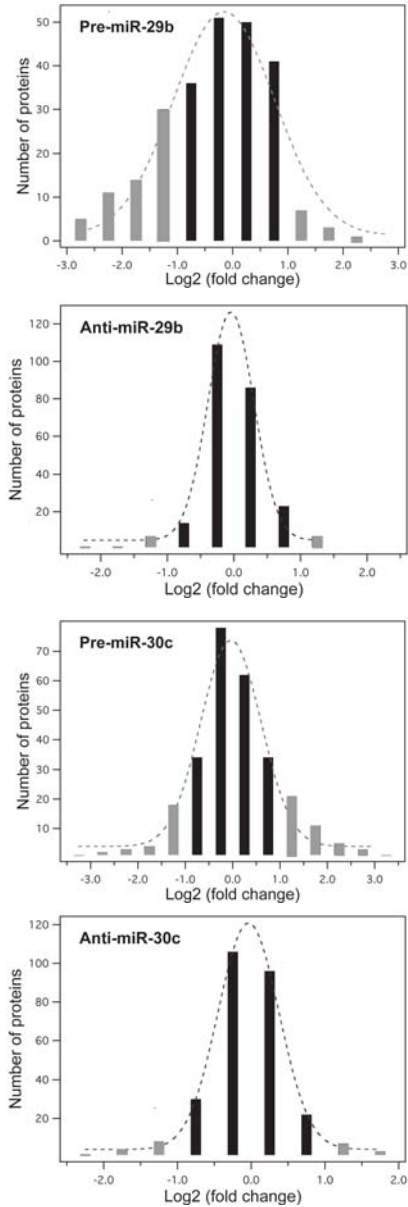
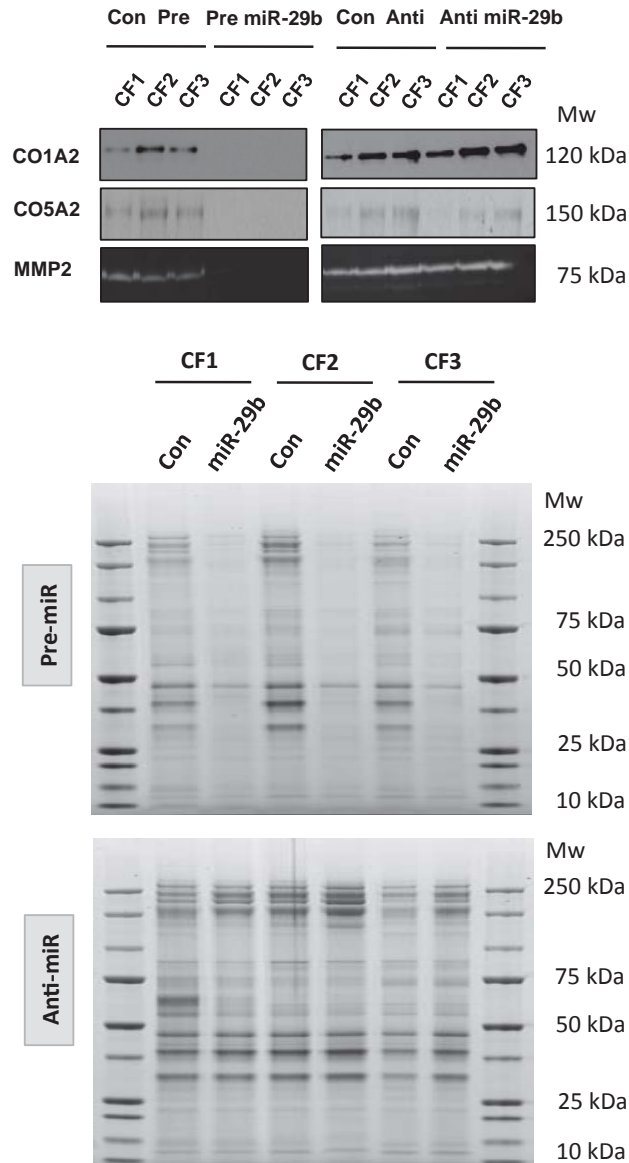


Figure 2

A



B



C

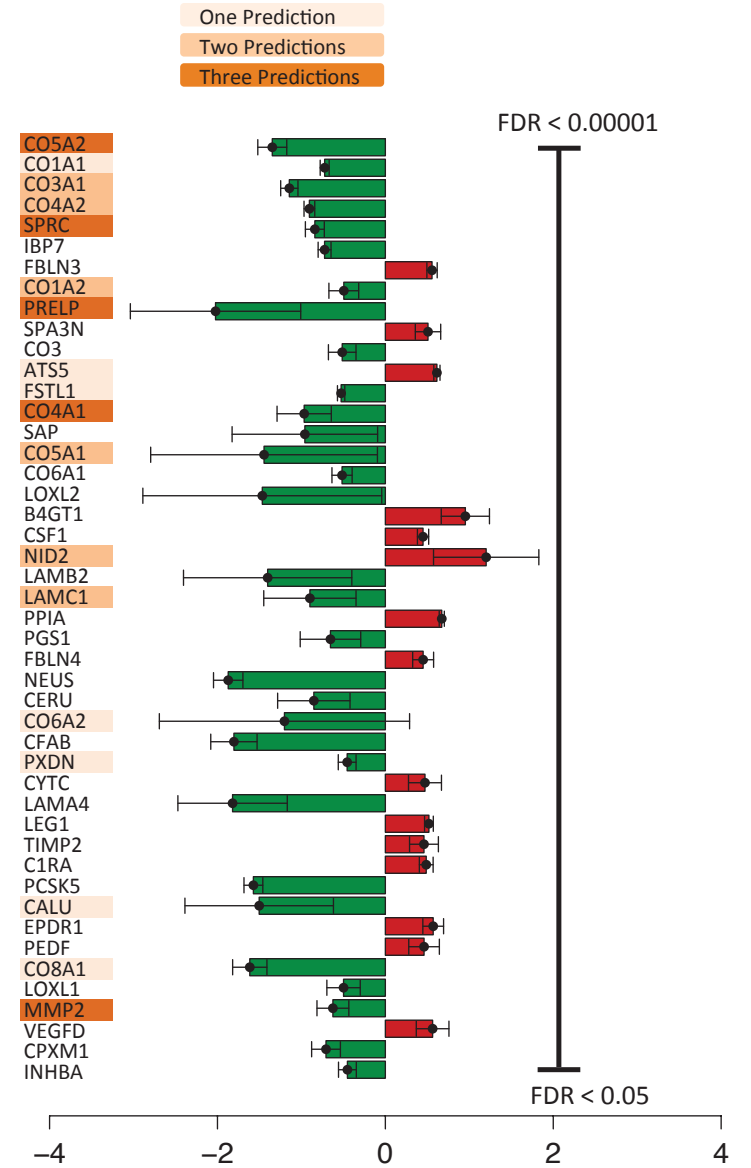


Figure 3

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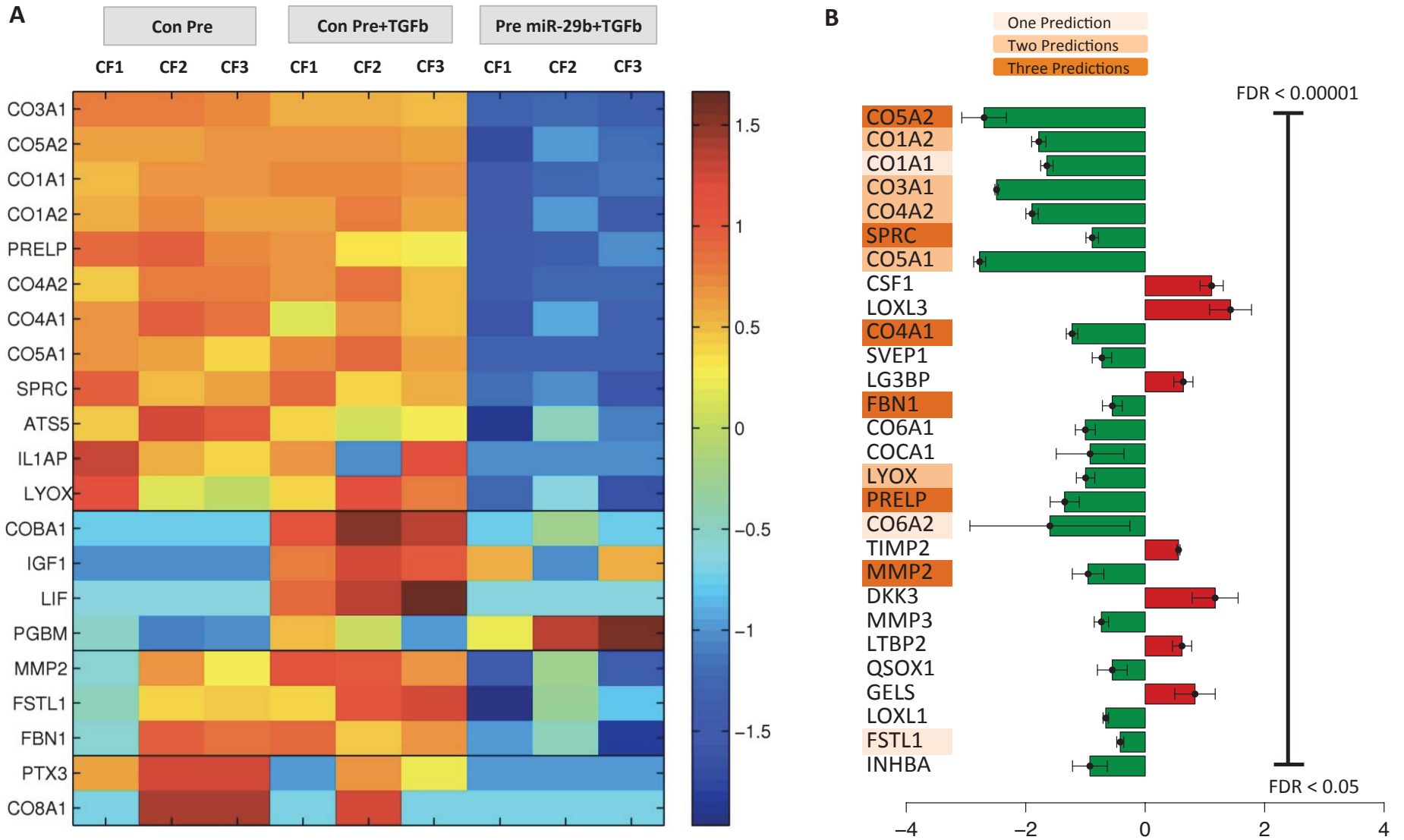


Figure 4

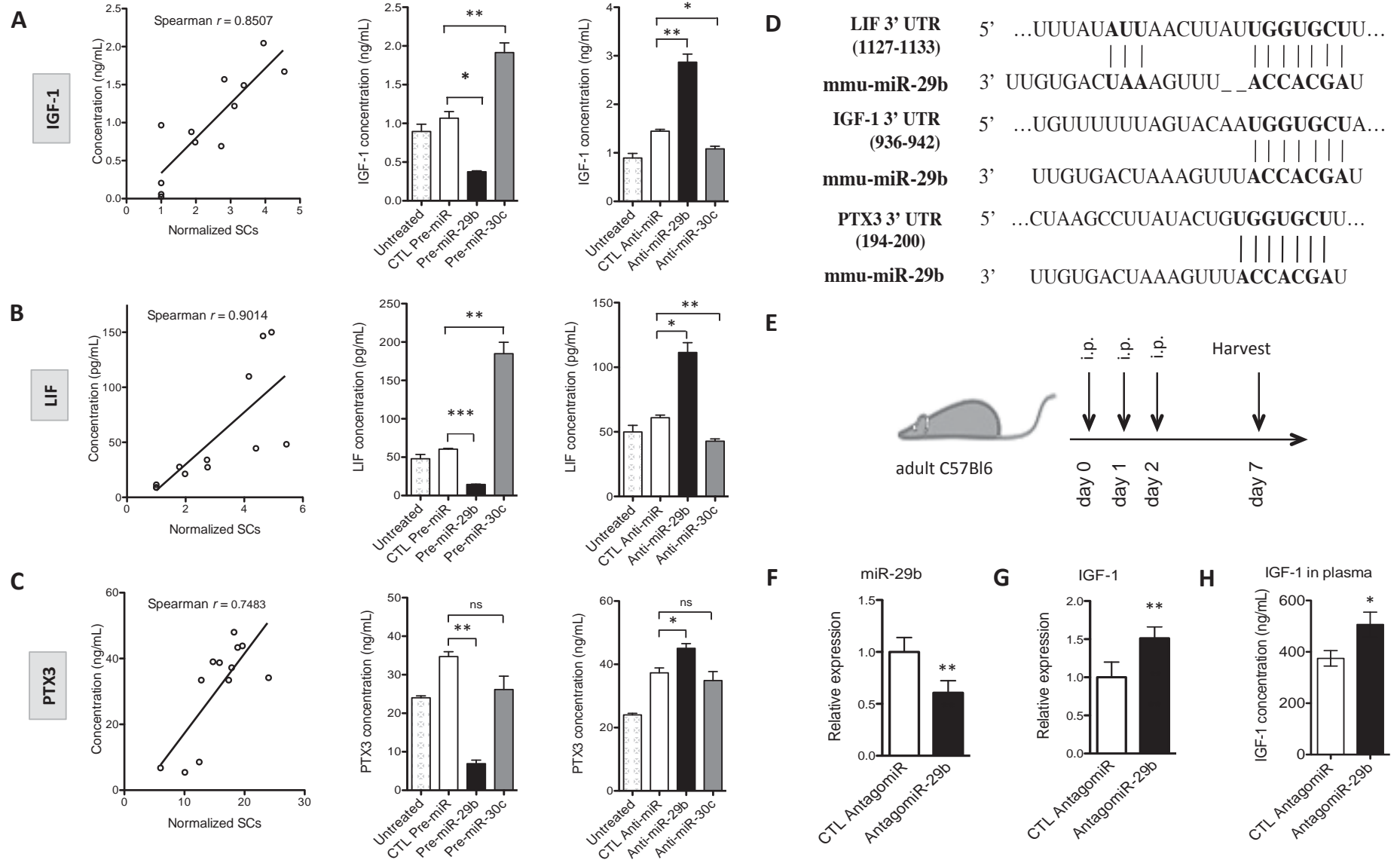


Figure 5

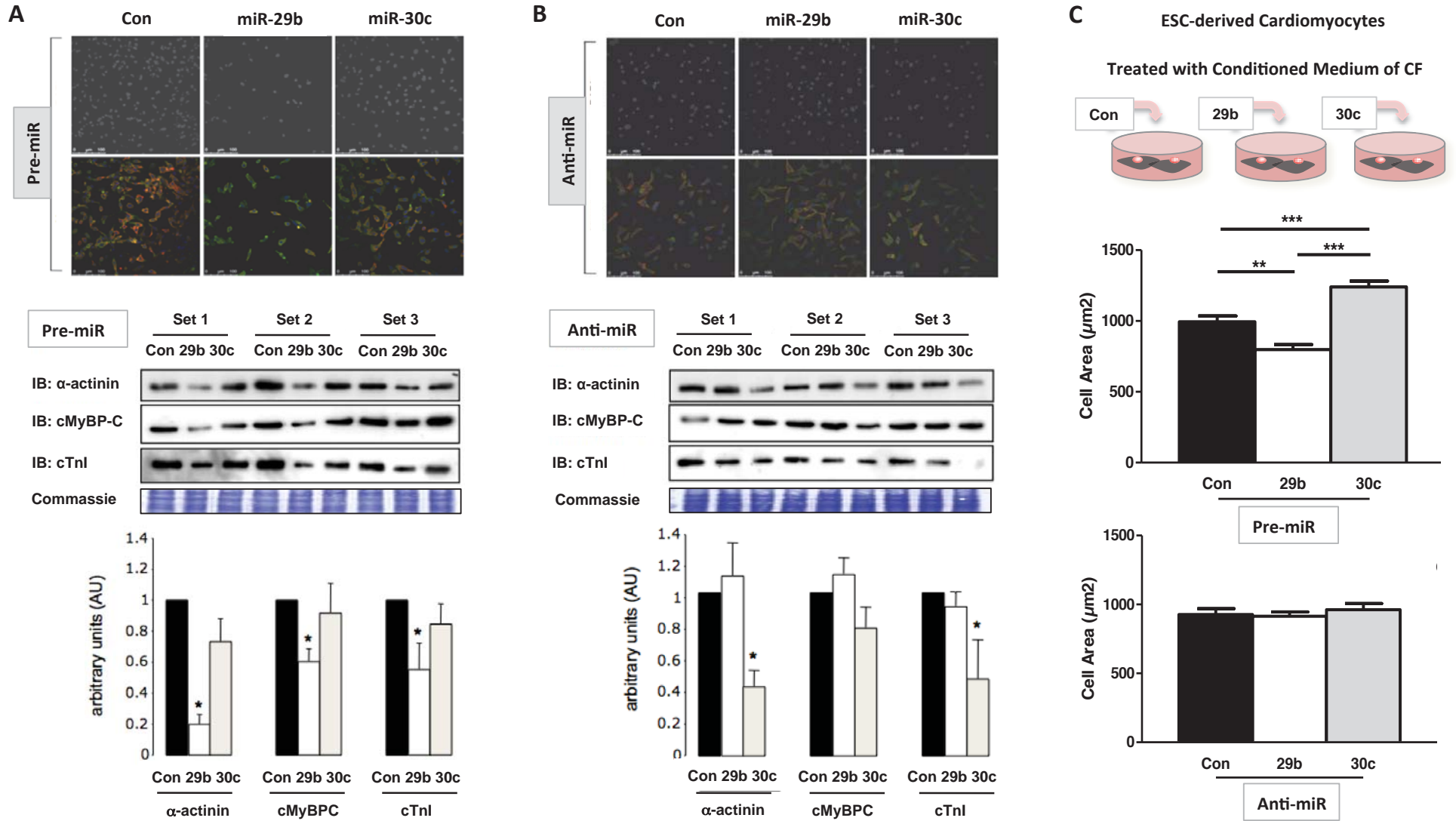


Figure 6

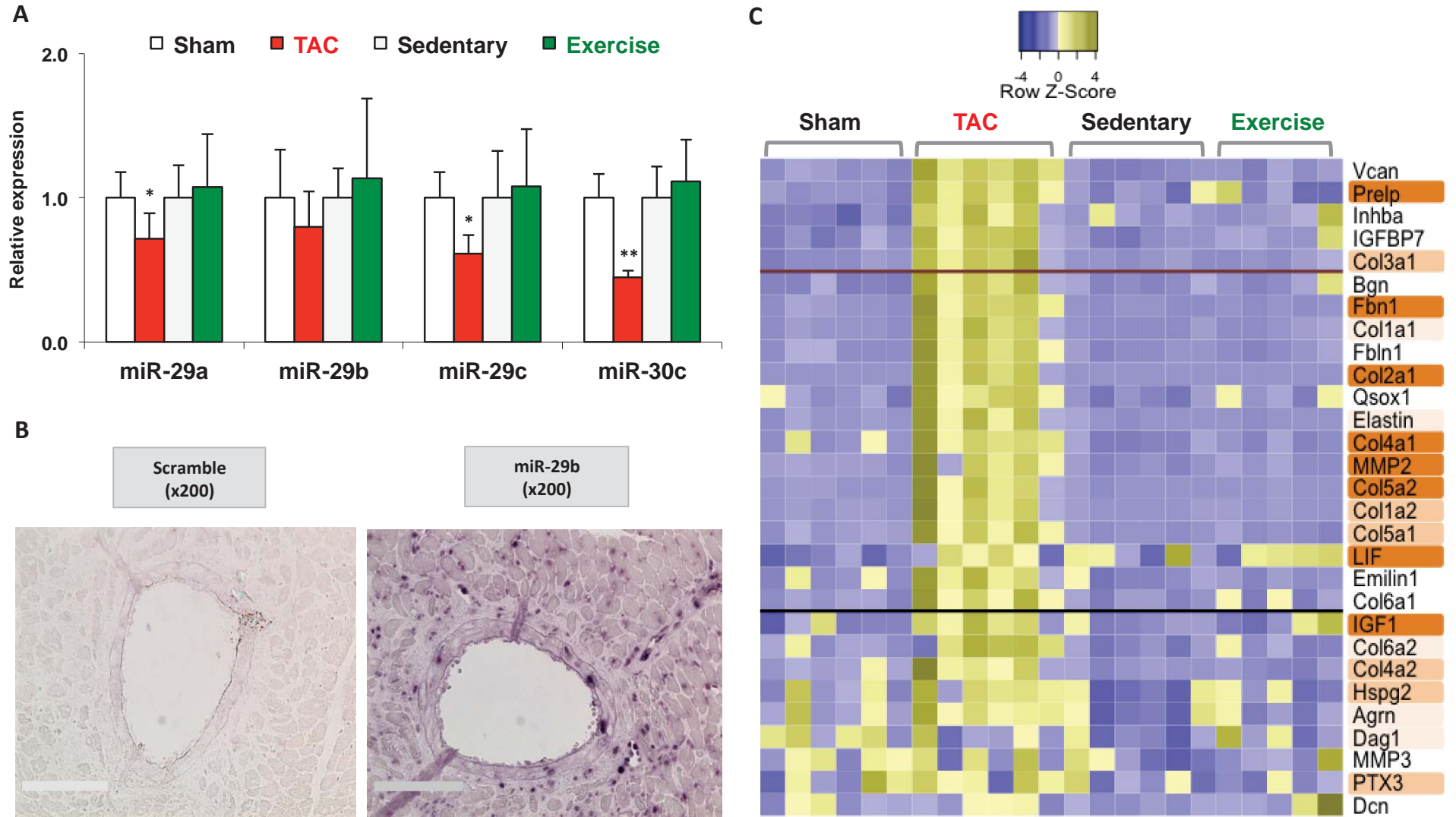
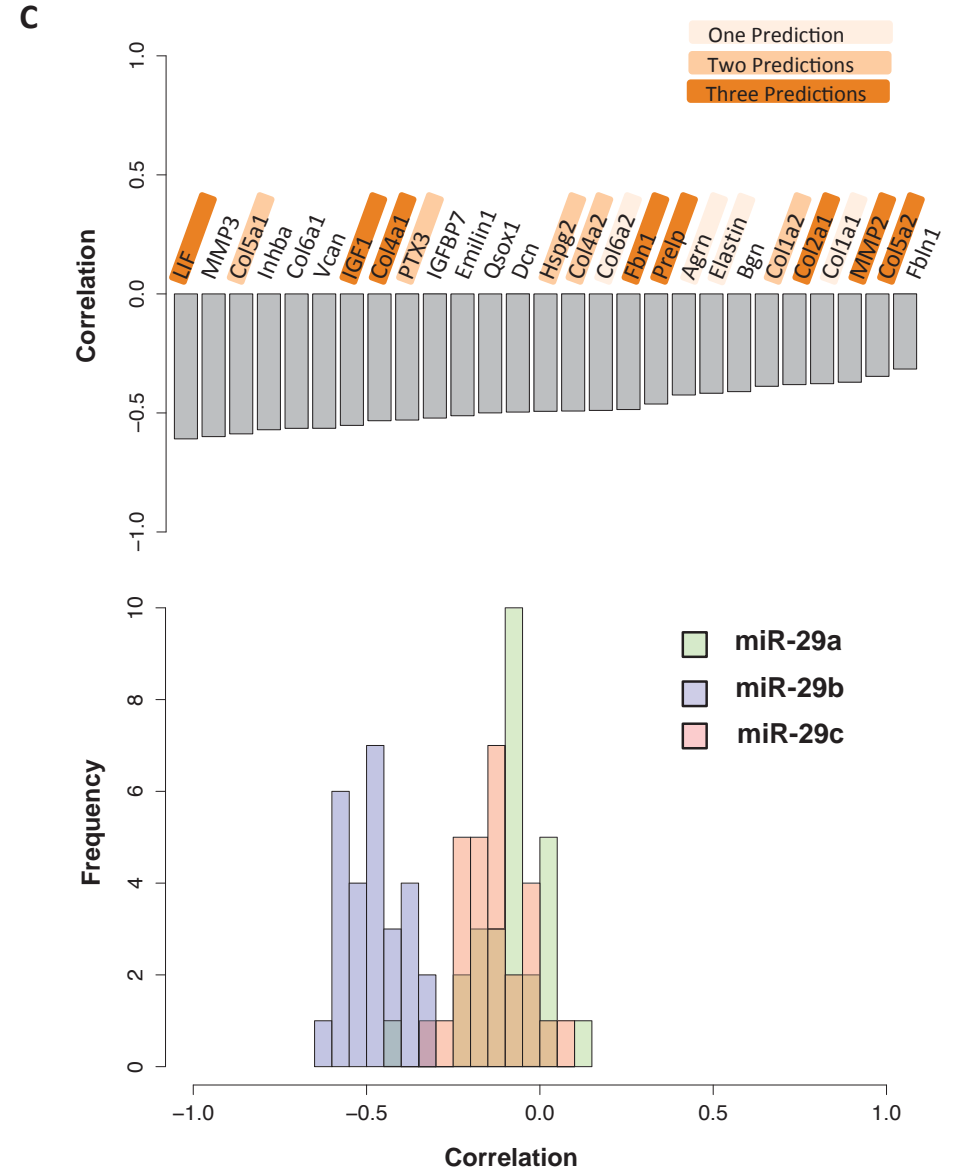
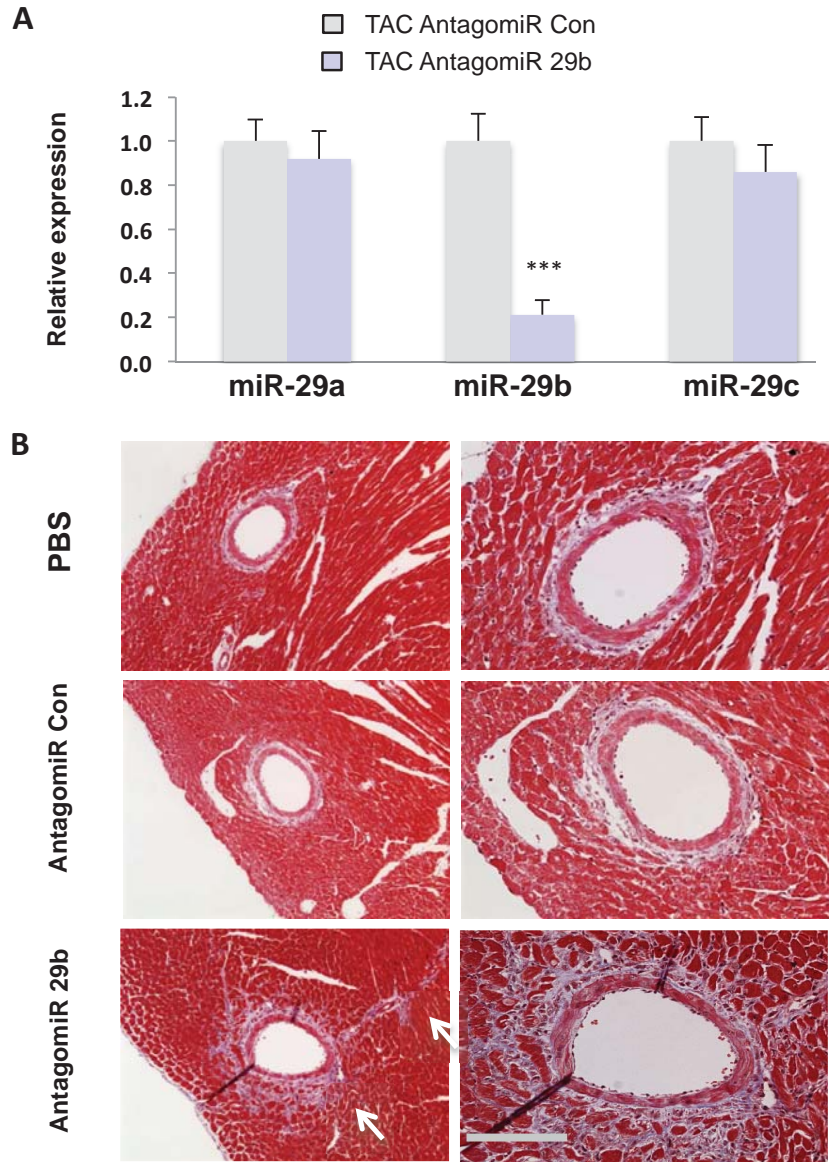


Figure 7



SUPPLEMENTAL MATERIAL

Extracellular Matrix Secretion by Cardiac Fibroblasts:

Role of microRNA-29b and microRNA-30

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Running Title: Proteomics for microRNAs in cardiac fibroblasts

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ONLINE MATERIALS AND METHODS

Isolation of mouse cardiac fibroblasts (CFs). Primary mouse CFs were isolated from the hearts of male C57BL6 mice (5-6 week-old, n=3) by standard collagenase-based digestion and maintained as separate cell lines. Two independent experiments (cardiac fibroblast isolation) were performed. Briefly, the hearts were diced into small pieces, carefully washed in ice-cold phosphate buffered saline (PBS, Sigma-Aldrich) to remove plasma contaminants. The pieces were pre-digested in collagenase II solution for 10 min. The collagenase II solution was replaced and the tissue pieces were incubated for 45 min – 1h at 37°C. The digested tissue pieces were washed in complete medium before plating. Primary mouse CFs were cultured on gelatin 0.1% and grown in DMEM medium supplemented with L-Glutamine, 10% heat-inactivated FBS and antibiotics (100 U/ml penicillin and 100 µg/ml streptomycin) at 37°C in a humidified atmosphere of 95% air / 5% CO₂. Cells were detached with 0.05% trypsin for passaging. After two passages the cell population is mainly composed of cardiac fibroblasts. Immunostaining of vimentin has been carried out at passage 2 indicating that the cell population are predominantly CFs (**Online Figure I**). Cells at passage 2-4 were used in all experiments.

Pre-miR and anti-miR transfection. Cells were plated at 60-70% confluency on the day before transfection. Mouse Pre-miRTM miRNA precursors were synthesized by Applied Biosystems/Ambion and MercuryTM LNA-antimiRs by Exiqon. The following sequences were used: LNA-29b: ACTGATTTCAAATGGRGCT; LNA-30c: TGAGAGTG TAGGATGTTTAC, LNA-CTL: GTGTAACACGTCTATACGCCCA, Pre-miR-29b: UAGCACCAUUUGAAAUCAGUGUU; Pre-miR-30c: UGUAAACAUCUACACUCUCAGC; Pre-miR-CTL2: sequence not specified. LNA inhibitors and precursor miRNA were transfected at a final concentration of 100 nM using lipofectamineTM RMAiMAX (Invitrogen) according to the manufacturer's recommendations.

TGFβ1 stimulation of CFs. The day following the transfection of CFs with the miRNA constructs, the cells were carefully washed in serum-free medium and then, stimulated with TGFβ1 (from Peprotech) at a final concentration of 10 ng/mL in serum-free medium for 72h. After stimulation, the conditioned medium and RNA were harvested for analysis.

Conditioned medium for proteomics analysis. CFs were carefully washed in serum-free medium to maximize the removal of proteins from the serum and then incubated in fresh serum-free medium for 72 hours ("conditioned medium"). The conditioned medium was collected and centrifuged at 3000 g for 10 min to remove cell debris. The supernatant was transferred into a new tube and stored at -80°C. 2 mL of conditioned medium was first desalted using Zeba Spin desalting columns (Thermo Scientific), vacuum dried and resuspended in 60 µL of ddH₂O. 30 µL was used for the proteomic analysis and 30 µL to run a SDS-PAGE gel for immunoblotting.

MicroRNA target prediction. The prediction of mir-29b and miR-30c targets was performed with the following algorithms: Targetscan 5.2 (<http://www.targetscan.org/>), PicTar (<http://pictar.mdc-berlin.de/>) and DIANA MicroT v.4.0 (<http://diana.cslab.ece.ntua.gr/>).

RNA isolation from cells. Total RNA was prepared using the miRNeasy kit (Qiagen) according to the manufacturer's recommendations. In brief, cells were lysed with 700µl of QIAzol reagent. Following a brief incubation at ambient temperature, 140 µl of chloroform were added and the solution was mixed vigorously. The samples were then centrifuged at 12,000 rpm for 15 min at 4°C. The upper aqueous phase was carefully transferred to a new tube and 1.5 volumes of ethanol were added. The samples were then applied directly to columns and washed according to the company's protocol. Total RNA was eluted in 25 µl of nuclease free H₂O.

MegaPlex reverse transcription and pre-amplification. To assess levels of specific miRNA in cells 20 ng of RNA from the 25 µl eluate were diluted in a volume of 3 µl and used as input in each reverse transcription (RT) reaction. A RT reaction and pre-amplification step were set up according to the company's recommendations. Briefly, miRNAs were reverse transcribed using the Megaplex Primer Pools (Rodent Pool A v.2.0) from Applied Biosystems. RT reaction was performed according to the company's recommendations (0.8 µl of Pooled Primers were combined with 0.2 µl of 100mmol/L dNTPs with dTTP, 0.8 µl of 10x Reverse-Transcription Buffer, 0.9 µl of MgCl₂ (25mmol/L), 1.5 µl of Multiscribe Reverse-Transcriptase and 0.1 µl of RNAsin (20U/µl) to a final volume of 7.5 µl. The RT-PCR reaction was set as follows: 16°C for 2 min, 42°C for 1 min and 50°C for 1 sec for 40 cycles and then incubation at 85°C for 5 min using a Veriti thermocycler (Applied Biosystems). The RT reaction products were further amplified using the Megaplex PreAmp Primers (Rodent Pool A v2.0). A 1.25 µl aliquot of the RT product was combined with 6.25 µl of Pre-amplification Mastermix (2x) and 1.25 µl of Megaplex PreAmp Primers (10x) to a final volume of 12.5 µl. The pre-amplification reaction was performed by heating the samples at 95°C for 10 min, followed by 12 cycles of 95°C for 15 sec and 60°C for 4 min. Finally, samples were heated at 95°C for 10 min to ensure enzyme inactivation. Pre-amplification reaction products were diluted to a final volume of 50 µl. RT-PCR and pre-amplification products were stored at -20°C.

Taqman qPCR assay. Taqman miRNA assays were used to assess the expression of individual miRNA. 0.5 µl of pre-amplification product were combined with 0.25 µl of Taqman miRNA Assay (20X) (Applied Biosystems) and 2.5 µl of the Taqman Universal PCR Master Mix No AmpErase UNG (2X) to a final volume of 5 µl. QPCR was performed on an Applied Biosystems 7900HT thermocycler at 95°C for 10 min, followed by 40 cycles of 95°C for 15 sec and 60°C for 1 min. All samples were run in duplicates and standardized to U6/sno-135/sno-202 using SDS2.2 software (Applied Biosystems).

Immunoblot analysis of CF proteins: Samples were mixed with 4X denaturing sample buffer, heated at 95°C for 10 min and separated on a Bis-Tris discontinuous 4-12% polyacrylamided gradient gels (Nupage, Invitrogen). Proteins were then transferred on nitrocellulose membranes. Membranes were blocked with 5% fat-free milk powder in PBS-Tween and probed for 16h at 4°C with primary antibodies to: CO1A2 (rabbit, Abcam ab96723), CO5A2 (mouse, Santa Cruz, sc-59903). All antibodies were used at 1:500 dilution in 5% BSA. The membranes were treated with the appropriate secondary, horseradish peroxidase (HRP) conjugated antibodies (Dako) at 1:2000 dilution. Finally, the blots were imaged using enhanced chemilluminescence (ECL, GE Healthcare) and films were developed on a Xograph

processor. The densitometry for the lanes from developed films was measured using the ImageJ software (v.1.44o, <http://imagej.nih.gov/ij> NIH, USA).

Gelatin zymography. Samples were mixed with non-reducing Tris-Glycine SDS sample buffer (2X) and applied without boiling to a Novex® 10% zymogram (gelatin, Life Technologies) gel. After electrophoresis, the gel was developed at 37°C overnight according to the manufacturer's recommendations. The gel was stained with Coomassie staining.

Enzyme-linked immunosorbent assay (ELISA). IGF-1, LIF and PTX-3 in the conditioned medium of CFs were quantified by ELISAs from R&D Systems.

Luciferase reporter assays. The 3' untranslated regions of mouse IGF-1, LIF and PTX3 harboring putative binding sites of the miR-29 family were cloned into the dual-luciferase reporter vector psiCheck2 (Promega). The following primer sets were used for this study:

Igf1 forward 'AGAGAGTTTAAACACCTCTTCCCACGTAGCTCA'
Igf1 reverse 'TATTCTCGAGGACTGAGGTCACAGGGTGGT'

LIF forward 'AGAGAGTTTAAACTAGGAGTCAGGGAAGGAGCA'
LIF reverse 'TATTCTCGAGGCCAGCTCTCTGATTTGACC'

PTX3 forward 'CGAGAGTTTAAACTGAAGGGAAGGCTTGAGAGA'
PTX3 reverse 'TATTCTCGAGCGTCCCTCTGTTCAGAGTCC'

The reporter vectors (100 ng of psiCheck2 construct) were transfected together with 30-100 nM of miR-29b mimic or the mimic negative control (CON) in triplicate into SMCs plated in 6-well plates using Lipofectamine 2000 (Lifetech) as described above. After 48 h, the Renilla and firefly luciferase activities were assessed after harvesting cells in 200 µL Glo Lysis Buffer (Promega). 30 µL of each lysate were analyzed using Dual-Glo Luciferase reagents (Promega). Renilla 3'UTR-coupled luciferase activity was normalized to constitutive firefly luciferase activity for each well.

Gel-LC-MS/MS. Samples were denatured with 4X sample loading buffer at 96°C for 5 min and then separated in Bis-Tris discontinuous 4-12% polyacrylamide gradient gels (NuPage, Invitrogen). Protein standards were run along side the samples (pre-stained All Blue, Precision Plus, BioRad Laboratories). After electrophoresis, the gels were stained using Coomassie staining. Each gel lane was cut into 16 bands. Subsequently, all gel bands were subjected to in-gel tryptic digestion using an Investigator ProGest (Digilab) robotic digestion system. Tryptic peptides were separated on a nanoflow LC system (Dionex UltiMate 3000, UK) and eluted with a 70-min gradient (4-25% B in 35 min, 25-40% B in 5 min, 100% B in 10 min and 2% B in 20min where A is 2% ACN, 0.1% formic acid in HPLC H₂O and B is 90% ACN, 0.1% formic acid in HPLC H₂O). The column (Dionex PepMap C18, 25 cm length, 75µm i.d, 3 µm particle size) was coupled to a nanospray source (Picoview). Spectra were collected from a high-mass accuracy analyzer (LTQ Orbitrap XL, ThermoFisher Scientific) using full ion scan mode over the mass-to-charge (*m/z*) range 450-1600. MS/MS was performed on the top six ions in each MS scan using the data-

dependent acquisition mode with dynamic exclusion enabled. MS/MS mass spectra were extracted by extract_msn.exe version 5.0. Charge state deconvolution and deisotoping were not performed. All MS/MS samples were analyzed using Mascot (Matrix Science, London, UK; version 2.3). Mascot was set up to search the SwissProt_57.15 database (selected for *Mus musculus*, 16230 entries) assuming the digestion enzyme trypsin. Two missed cleavages were allowed. Mascot was searched with a fragment ion mass tolerance of 0.80 Da and a parent ion tolerance of 10.0 ppm. Iodoacetamide derivative of cysteine was specified in Mascot as a fixed modification. Oxidation of methionine was specified in Mascot as a variable modification. Scaffold (version Scaffold_3_00_08, Proteome Software Inc., Portland, OR) was used to validate MS/MS based peptide and protein identifications. Peptide identifications were accepted if they could be established at greater than 95.0% probability as specified by the Peptide Prophet algorithm.¹ Protein identifications were accepted if they could be established at greater than 99.0% probability and contained at least 2 independent peptides. Protein probabilities were assigned by the Protein Prophet algorithm.² Proteins that contained similar peptides and could not be differentiated based on MS/MS analysis alone were grouped to satisfy the principles of parsimony.

Isolation and culture of neonatal rat ventricular myocytes (NRVM). Primary cultures of NRVM were prepared from neonatal (day 0-2) Sprague-Dawley rats, as described previously³. In brief, hearts were excised, the atria trimmed off and the ventricles cut into small pieces. Cardiac myocytes were dispersed by a series of incubations at 37°C in Ca²⁺-free HEPES-buffered solution containing (in mmol/L) NaCl 120, HEPES 20, NaH₂PO₄ 0.8, glucose 5, KCl 5, MgSO₄ 0.4, pancreatin (0.6 mg/mL) and 0.5 mg/mL type II collagenase (Worthington Biochemicals). The dispersed cells were pre-plated for 1 hour to reduce fibroblast contamination. Unattached NRVM were then seeded in 24-well plates or on glass coverslips, which were pre-coated overnight at 37°C with conditioned medium of CFs, previously transfected with control pre, 29b or 30c pre-miR or control anti, 29b or 30c anti-miR at a final density of 200 000 cells/well or coverslip in DMEM/M199 4:1 (v/v) supplemented with 10 % horse serum, 5 % fetal calf serum and 100 IU/mL penicillin/streptomycin. After 24 hours in culture, unattached NRVM were washed off and cells were transferred to maintenance medium (DMEM/M199 4:1 (v/v), 100 IU/mL penicillin/streptomycin) for 24 hours, before harvesting cells from 24-well plates in Laemmli sample buffer for western immunoblot analysis or fixing cells from glass coverslips for immunocytochemistry and confocal microscopy.

Immunoblot analysis of NRVM proteins. Immunoblot analysis was carried out as described previously³. In brief, NRVM protein samples were resolved by 10 % SDS-PAGE, transferred to polyvinylidene difluoride membranes and subjected to immunoblotting. Primary antibody was detected by sheep anti-mouse secondary antibody linked to HRP (GE Healthcare). Specific protein bands were detected by enhanced chemiluminescence.

Immunolabelling of cardiac myocytes. NRVM were washed twice with PBS and fixed by incubation in 4% paraformaldehyde (PFA) in PBS for 10 min and washed twice with PBS. Cells were permeabilised by incubation in 0.2% Triton X-100 in PBS for 5 min and unspecific binding sites blocked by incubation in 5 % non-specific goat serum in 1 % BSA/TBS pH 7.5 containing (in mmol/L) Trizma base 20, NaCl 155,

EGTA 2, MgCl₂ 2 for 20 min. Primary and secondary antibodies were diluted using 1 % BSA/TBS. Incubation with primary antibodies was carried out overnight at 4°C, incubation with secondary antibodies was carried out at room-temperature for 4 hours. After final washing with PBS, the cardiac myocytes were mounted with coverslips in 0.1M Tris-HCl (pH 9.5)-glycerol (3:7) including 50 mg/mL *n*-propyl gallate as an anti-fading reagent (Messerli et al. 1993).

Antibodies and fluorescent reagents. The monoclonal mouse anti cardiac α -actinin antibody was obtained from Sigma and was used at a dilution of 1:1000 for western immunoblotting and 1:100 for immunocytochemistry. The polyclonal rabbit antibody to cardiac myosin-binding protein C was a kind gift from Prof. Mathias Gautel, King's College London and was used at a dilution of 1:50 for immunocytochemistry and 1:30000 for western immunoblotting. The polyclonal rabbit antibody to cardiac troponin I was obtained from Cell Signaling Technology and was used at a dilution of 1:1000. For double immunofluorescence labeling, a combination of Cy3 anti-mouse (1:500) and Cy5 anti-rabbit (1:100) conjugated secondary antibodies was used. The secondary antibodies were purchased from Jackson ImmunoResearch. 4',6-Diamidino-2-phenylindole dihydrochloride (DAPI 1 mg/ml 1:100) was purchased from Sigma.

Confocal microscopy. The specimens were analyzed using confocal microscopy on an inverted microscope (Leica SP5 system, Mannheim, Germany) equipped with blue diode, argon and helium neon lasers, using a 63x/1.4NA oil immersion lens.

Modification and culture of murine embryonic stem cells. The murine cardiomyocyte-selectable embryonic stem cell (ESC) line (α MHC-neoR "A6-line"; R1 background⁴) was generated by electroporation of a plasmid encoding for a neomycin resistance gene (neoR), under the control of the cardiomyocyte restricted α -myosin heavy chain (α MHC) promoter, as described previously⁵. α MHC ESCs were cultured on irradiated murine embryonic fibroblasts (MEFs; 25,500 cells/cm²) in ESC culture medium consisting of: DMEM (high glucose, no pyruvate, 25 mmol/l HEPES), 15% fetal bovine serum (FBS), 1000 U/ml LIF, 2 mmol/l glutamine, 1x non-essential amino acids, 1 mmol/l Na-pyruvate, 30 μ mol/l adenosine, 30 μ mol/l cytidine, 30 μ mol/l uridine, 30 μ mol/l guanosine, 30 μ mol/l thymidine, 50 U/ml penicillin, 50 μ g/ml streptomycin, and 100 μ mol/l 2-mercaptoethanol. ES-colonies were detached every 48 hrs in 0.25% trypsin-EDTA and split at a 1:5 ratio.

Differentiation of α MHC-NeoR ESCs. ESCs were washed in phosphate buffered saline (PBS) and separated into single cells in 0.25% trypsin-EDTA. Cells were resuspended in differentiation medium consisting of: Iscove medium supplemented with 20% FBS, 2mmol/l glutamine, 1x non-essential amino acids, 50 U/ml penicillin, 50 μ g/ml streptomycin, 100 μ mol/l 2-mercaptoethanol and 0.5 mM L-ascorbic acid 2-phosphate. Spinner flasks equipped with a bulb-shaped glass stirrer (Techne) were inoculated with 50 ml of medium containing 10x10⁶ cells and stirred at 60 rpm, at 37°C in a 5% CO₂ incubator. Flasks were filled up to 100ml after 24 hrs, followed by half medium exchange every 48 hrs. Cardiomyocyte (CM) selection at day 11 was initiated by the addition of 400 μ g/ml Geneticin (G418) to eliminate non-cardiomyocytes. At day 16, CMs were harvested and dissociated into single cells with collagenase 1 for 1 hr and with 0.25% trypsin-EDTA for 3-6mins. Cells were subsequently resuspended in differentiation medium.

Treatment of ESC-derived CM with conditioned medium from transfected CF.

Purified ESC-derived CMs were cultured (8000 cells/well) for 6 days on a flat-bottom 96-well plate, coated with gelatine (0.1%). Cells were initially cultured for 24 hrs in differentiation medium, followed by 5 days with the following 50% conditioned media (Pre-miR (Control; 29b; 30c); Anti-miR (Control; 29b; 30c)) supplemented with 50% differentiation medium, with medium. Culture medium was exchanged after 48 hrs. Cells were thereafter fixed in 4% buffered formaldehyde at room temperature for 15 mins, and then subsequently washed in PBS (x2) prior to immunostaining. Fixed cells were blocked and permeabilized for 90 mins at room temperature in PBS (pH.7.4) containing 5% FBS, 1% bovine serum albumin (BSA) and 0.5% Triton X-100. Subsequent incubation with a mouse monoclonal α -actinin primary antibody (IgG1; clone: EA-53; 1:1,000 from 1 mg/ml stock; Sigma) was for 60 mins at room temperature, followed by a goat anti-mouse Alexa 488 secondary antibody (1:400 from 1 mg/ml stock; Invitrogen) and 4',6-diamidino-2-phenylindole (DAPI; 1 μ g/ml; Invitrogen) for 60 mins in the dark at room temperature. Cells were subsequently washed in buffer (x2) after each incubation step and thereafter stored in PBS. Imaging was performed with a Zeiss Axiovert 200 inverted fluorescence microscope equipped with a shutter (Visitron System; MAC 6000) and a AxioCam MRm camera (Zeiss). Image J software (National Institutes of Health) was used to determine cell area from images. Cell area was determined by measuring the α -actinin fluorescence staining of the cells. Cell clumps with >5 DAPI stained nuclei were excluded from the analysis. Data are presented as mean +/- SEM. Statistical analysis was performed using 1-way ANOVA followed by Bonferroni's multiple comparison test. A value of $P < 0.05$ was considered statistically significant.

Animal models. Procedures were performed in accordance with the Guidance on the Operation of the Animals (Scientific Procedures) Act, 1986 (United Kingdom). Pathological cardiac hypertrophy was induced by the minimally invasive transverse aortic constriction (TAC), as previously described⁶. C57BL/6 mice 8-10 weeks of age were used. Sham constriction involved identical surgery apart from band placement. Physiological cardiac hypertrophy was achieved by a voluntary wheel running program⁷. Briefly, 8-10 weeks old C57BL/6 mice were initially introduced together into the running cage to learn from each other to run on the wheel. After a 7 day training period, mice were randomly housed individually and left to run up to 4 weeks. The running wheel is connected by a light triggered counting system, running time and distance is monitored and recorded with LabChart7. The average running distance was over 4km/day. Age-matched mice were also randomly assigned to the sedentary control group. They were housed in identical cages except for a non-rotating wheel for the same amount of time. 2 weeks TAC and 4 weeks exercise running resulted in 65% and 14% increase compared to controls in terms of heart weight/tibia length ratio, respectively.

In vivo silencing of miR-29b. AntagomiR constructs from Fidelity Biosystems were resuspended in sterile PBS at 37°C and stored at -20°C. The sequences of the antagomiR constructs were: Control AntagomiR: 5'-A*A*GGCAAGCUGACCCUGAA*G*U*U* Chol*T-3', AntagomiR-29b: A*A*CACUGAUUUCAAAUGGUG*C*U*A*-Chol*T-3'. C57BL6 mice were treated by intraperitoneal injection with a dose of 80 mg/kg/day of antagomiR constructs at day 0, day 1 and day 2. Non-operated mice were sacrificed at day 7 and the plasma and

cardiac tissues were collected. For the *in vivo* model of pathological hypertrophy, pressure overload was induced at day 3 by aortic constriction in wild-type mice anesthetized with an isoflurane/O₂ mixture (2/98%). Sham surgery (n = 4) comprised an identical procedure with the exception of constriction. Cardiac tissues were obtained at 2 weeks post-surgery. Only left ventricles were used for further analysis. RNA was extracted using the RNeasy kit (Qiagen) with cDNA produced using the High Capacity Reverse transcriptase kit (Applied Biosystems). Transcript expression was quantified using TaqMan mRNA probes (Applied Biosystems).

Transthoracic echocardiography. The method for *in vivo* echocardiography was taken from Bauer et al.⁸ Studies were performed with a Vevo 2100 Imaging System (VisualSonics, Toronto, Canada) using a 22-55 MHz ultra-high frequency linear-array transducer. Mice were maintained under light anaesthesia with 1% isoflurane and 2L/min oxygen flow. Mice were fixed to a heated platform with simultaneous recording of heart rate and respiratory rate. Heart rate was maintained at >500 bpm (as described in Bauer *et al*⁸). Images were obtained in both parasternal long axis and short axis views. A B-mode image in parasternal long axis view was captured (to view both the apex and left ventricular outflow tract). In addition an M-mode of the widest part of the parasternal long axis B-mode image was taken (the midpoint between apex and base of the heart). The short axis images were obtained by a 90-degree rotation of the transducer from its long axis orientation. A B-mode image was acquired at the mid-papillary muscle level. An M-mode was also taken at this level. Conventional echocardiographic measurements were obtained from M-mode images acquired in the parasternal long axis and short axis views as described above. Measurements included left ventricular end-systolic and end-diastolic diameters and volumes, ejection fraction, fractional shortening, stroke volume and cardiac output. Short axis B-mode images taken at the papillary muscle level were used to measure interventricular septal (IVS) and left ventricular posterior wall (LVPW) thicknesses in both systole and diastole (IVS;s, IVS;d and LVPW;s, LVPW;d respectively). Measurements were taken from 3 separate cardiac cycles and then averaged (as described in Bauer *et al*⁸). Data are presented as group mean +/- SE. Group parameters (control versus antagomiR treated after TAC) were analysed with an unpaired Student's t-test. Long axis B-mode images could not be included in the analyses in view of the abnormal papillary muscle thickening leading to inaccurate values for echocardiographic parameters.

In situ hybridization. MiRNA in situ hybridisation was performed as described previously⁹. Fixed paraffin-embedded 4 µm mouse heart sections were used. After deparaffinization and proteinase K (Sigma) treatment, the sections were fixed with 4% paraformaldehyde for 10 min. Then, the slides were incubated with hybridisation buffer at 60 degree for 1h, and hybridised with 40nM DIG-labelled miR-29b or scramble probe (Exiqon) overnight. The next day, slides were incubated with anti-DIG-AP Fab fragments (Roche) in blocking buffer at the cold room overnight, and washed with PBS plus 0.1% Tween 20 and 0.1M Tris-HCL (pH9.5). MiR-29b was visualized with BM purple solution (Roche) for 1-2 days at room temperature until the staining was developed.

Statistics. Statistical analysis was performed with Graphpad Prism 5 using the Student's *t* test. A *p* value of <0.05 was considered significant. Correlations were analyzed using the Spearman method. Data are presented as mean and error bars

depict the standard deviation. Igor Pro v.6 (WaveMetrics) was used for graphics. For the generation of heatmaps, protein spectral counts were log-transformed to increase the signal of proteins with low spectral counts with respect to the “highly abundant” proteins¹⁰. Subsequently, proteins were excluded if normalized spectra counts did not exceed 5 in at least 5 samples. Overall, 51 (>30%) were retained for analysis. Co-expressions between all pairs of normalized protein spectra counts across primary cell culture and treated CFs were expressed through Pearson correlation coefficients (PCCs). Partial Correlation and an Information Theory (PCIT) algorithm was used to detect meaningful protein–protein associations from a co-expression matrix^{11, 12}. We used the Qspec software proposed by Choi *et al.*¹³ as a second measure to detect differential expression across the TGF-beta stimulated proteomics data. Qspec utilises a hierarchical Bayes estimation of generalized linear mixed effects model (GLMM) to share information across the protein levels. This eliminates some of the assumptions needed for standard statistical tests and can increase the power of the analysis when there are a limited number of replicates available. The false discovery rate (FDR) is calculated with mixture model-based method of local FDR control based upon the Bayes factors. We considered proteins with a Bayes Factor <10 and an FDR < 5%, including those with fold changes above 30%, to be significant.

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Online Table I: List of extracellular proteins identified in the secretome of mouse CFs. The secretome was prepared as described followed by a gel LC-MS/MS analysis using a LTQ-Orbitrap XL. Only the control samples are considered to characterize the proteins present in the secretome of CFs. 6 controls are used in each experiment (Exp.1 and Exp.2). The maximal value of the controls is shown in the Table.

Online Table II: List of extracellular protein changes in the secretome of CFs following overexpression or inhibition of miR-29b. The normalized spectral counts are averaged for the 3 biological replicated to calculate the ratio in protein expression. A paired t-test was used to evaluate the significance of the observed protein expression changes.

Online Table III: List of extracellular protein changes in the secretome of CFs following overexpression or inhibition of miR-30c. The normalized spectral counts are averaged for the 3 biological replicated to calculate the ratio in protein expression. A paired t-test was used to evaluate the significance of the observed protein expression changes.

Online Table IV: List of extracellular protein changes in the secretome of CFs following overexpression of miR-29b in the presence of TGF-beta. The normalized spectral counts are averaged for the 3 biological replicated to calculate the ratio in protein expression. An ANOVA test was used to evaluate the significance of the observed protein expression changes.

Online Table V: Echocardiography data of antagomiR-29b treated hearts after TAC. The analysis (n=9 per group) is based on two independent experiments.

Online-Table I: Extracellular proteins in the secretome of CFs

#	Protein name	Accession Number	Molecular Weight (kDa)	Exp. 1			Exp. 2			Cited in Ref	
				Distinct peptides, n	Unique spectra, n	% coverage	Number of total ass. Spectra, n	Distinct peptides, n	Unique spectra, n		% coverage
Cytokines & growth factors											
394	Brain-derived neurotrophic factor	BDNF_MOUSE	28	2	2	12%	4	-	-	-	-
101	Bone morphogenetic protein 1	BMP1_MOUSE	112	18	20	20%	72	8	8	9%	24
533	Bone morphogenetic protein 6	BMP6_MOUSE	56	2	2	5%	3	-	-	-	-
218	BMP-binding endothelial regulator protein	BMPER_MOUSE	76	3	3	6%	11	-	-	-	-
570	C-C motif chemokine 2	CCL2_MOUSE	16	2	2	6%	2	-	-	-	[a][g]
133	Cytokine receptor-like factor 1	CRLF1_MOUSE	47	4	4	11%	17	5	5	14%	11
24	Macrophage colony-stimulating factor 1	CSF1_MOUSE	61	6	10	15%	57	6	9	15%	49
67	Connective tissue growth factor	CTGF_MOUSE	38	12	12	32%	46	9	9	24%	24
46	EGF-containing fibulin-like extracellular matrix protein 1	FBLN3_MOUSE	55	21	28	54%	140	12	14	33%	44
58	EGF-containing fibulin-like extracellular matrix protein 2	FBLN4_MOUSE	49	13	17	33%	46	8	11	25%	41
510	Growth-regulated alpha protein	GROA_MOUSE	10	3	3	46%	4	-	-	-	-
55	Insulin-like growth factor-binding protein 2	IBP2_MOUSE	33	9	11	45%	51	5	7	26%	26
399	Insulin-like growth factor-binding protein 3	IBP3_MOUSE	32	-	-	-	-	2	2	7%	3
71	Insulin-like growth factor-binding protein 4	IBP4_MOUSE	28	4	6	23%	37	3	6	17%	18
409	Insulin-like growth factor-binding protein 6	IBP6_MOUSE	25	2	2	15%	4	-	-	-	[a][d][f]
15	Insulin-like growth factor-binding protein 7	IBP7_MOUSE	29	14	22	56%	105	14	21	58%	92
467	Insulin-like growth factor I	IGF1_MOUSE	17	2	2	16%	3	-	-	-	[a][b][d]
214	Interleukin-1 receptor accessory protein	IL1AP_MOUSE	66	3	3	4%	6	3	3	6%	6
64	Inhibin beta A chain	INHBA_MOUSE	47	10	12	28%	38	10	12	25%	29
330	Inhibin beta B chain	INHBB_MOUSE	45	3	3	12%	5	4	4	14%	6
257	Leukemia inhibitory factor	LIF_MOUSE	22	2	2	11%	4	3	3	16%	7
278	Latent-transforming growth factor beta-binding protein 1	LTBP1_MOUSE	187	3	3	2%	4	2	2	2%	4
34	Latent-transforming growth factor beta-binding protein 2	LTBP2_MOUSE	196	9	12	7%	30	11	14	7%	40
120	Latent-transforming growth factor beta-binding protein 4	LTBP4_MOUSE	179	10	10	8%	18	-	-	-	-
210	Macrophage migration inhibitory factor	MIF_MOUSE	13	2	2	17%	4	2	2	17%	4
495	Beta-nerve growth factor	NGF_MOUSE	27	2	2	8%	5	-	-	-	[a]
23	Pigment epithelium-derived factor	PEDF_MOUSE	46	13	15	33%	47	14	17	29%	56
333	Platelet-derived growth factor D	PDGFD_MOUSE	43	3	4	11%	12	3	3	11%	6
589	Retinoic acid receptor responder protein 2	RARR2_MOUSE	18	2	2	17%	2	-	-	-	-
261	Transforming growth factor beta-2	TGFβ2_MOUSE	48	3	3	9%	9	4	4	12%	8
246	Vascular endothelial growth factor A	VEGFA_MOUSE	25	2	3	14%	8	2	4	14%	6
196	Vascular endothelial growth factor C	VEGFC_MOUSE	46	3	4	9%	5	2	3	6%	6
116	Vascular endothelial growth factor D	VEGFD_MOUSE	41	4	4	13%	26	4	4	13%	14
Collagens											
1	Collagen alpha-1(I) chain	CO1A1_MOUSE	138	55	76	54%	592	56	79	53%	441
3	Collagen alpha-2(I) chain	CO1A2_MOUSE	130	46	67	48%	637	37	50	38%	350
2	Collagen alpha-1(III) chain	CO3A1_MOUSE	139	48	66	47%	447	47	67	46%	350
75	Collagen alpha-1(IV) chain	CO4A1_MOUSE	161	25	29	24%	79	3	3	3%	17
20	Collagen alpha-2(IV) chain	CO4A2_MOUSE	167	40	50	37%	268	18	21	15%	87
41	Collagen alpha-1(V) chain	CO5A1_MOUSE	184	7	8	6%	34	8	10	7%	31
5	Collagen alpha-2(V) chain	CO5A2_MOUSE	145	44	60	45%	371	36	49	38%	226
12	Collagen alpha-1(VI) chain	CO6A1_MOUSE	108	22	27	29%	143	24	31	27%	145
33	Collagen alpha-2(VI) chain	CO6A2_MOUSE	110	10	10	13%	40	17	20	20%	73
251	Collagen alpha-1(VIII) chain	CO8A1_MOUSE	74	6	6	10%	26	4	4	6%	7
105	Collagen alpha-1(XI) chain	COBA1_MOUSE	181	5	5	4%	9	4	4	4%	16
268	Collagen alpha-1(XII) chain	COCA1_MOUSE	340	24	25	10%	46	5	5	2%	6
227	Collagen alpha-1(XIV) chain	COEA1_MOUSE	193	2	2	2%	3	7	7	5%	12
93	Collagen alpha-1(XV) chain	COFA1_MOUSE	140	3	3	3%	5	8	8	7%	18
492	Collagen alpha-1(XVII) chain	COIA1_MOUSE	182	2	2	2%	5	-	-	-	-
Proteases											
259	Disintegrin and metalloproteinase domain-containing protein 10	ADA10_MOUSE	84	8	8	11%	16	4	4	5%	6
384	Disintegrin and metalloproteinase domain-containing protein 12	ADA12_MOUSE	99	-	-	-	-	2	2	3%	3
290	Disintegrin and metalloproteinase domain-containing protein 15	ADA15_MOUSE	93	3	3	4%	7	2	2	3%	4
385	Disintegrin and metalloproteinase domain-containing protein 17	ADA17_MOUSE	93	3	3	5%	4	2	2	3%	3
189	Disintegrin and metalloproteinase domain-containing protein 9	ADAM9_MOUSE	92	2	3	4%	5	2	3	4%	6
386	ADAMTS-like protein 4	ATL4_MOUSE	113	3	3	6%	5	-	-	-	-
155	A disintegrin and metalloproteinase with thrombospondin motifs 2	ATS2_MOUSE	135	4	6	6%	18	4	5	6%	9
56	A disintegrin and metalloproteinase with thrombospondin motifs 5	ATS5_MOUSE	102	9	13	10%	33	8	10	8%	24
566	A disintegrin and metalloproteinase with thrombospondin motifs 7	ATS7_MOUSE	182	2	2	2%	2	-	-	-	-
84	Carboxypeptidase E	CBPE_MOUSE	53	7	8	16%	20	8	10	22%	33
150	Probable carboxypeptidase X1	CPXM1_MOUSE	81	7	8	15%	14	7	7	12%	12
218	Serine protease HTRA1	HTRA1_MOUSE	51	5	6	15%	13	3	3	7%	10
143	Macrophage metalloelastase	MMP12_MOUSE	55	9	9	16%	21	-	-	-	-
149	Matrix metalloproteinase-19	MMP19_MOUSE	59	2	3	7%	4	5	7	15%	15
208	72 type IV collagenase	MMP2_MOUSE	74	13	15	21%	29	7	8	11%	13
90	Stromelysin-1	MMP3_MOUSE	54	16	16	29%	63	7	7	15%	17
550	Neutrophil collagenase	MMP8_MOUSE	53	2	2	5%	3	-	-	-	-
300	Pappalysin-1	PAPP1_MOUSE	181	7	7	5%	10	3	3	3%	5
274	Proprotein convertase subtilisin/kexin type 5	PCSK5_MOUSE	209	7	7	6%	17	2	3	2%	11
555	Proprotein convertase subtilisin/kexin type 9	PCSK9_MOUSE	75	2	2	4%	3	-	-	-	-
244	Serine protease 23	PRS23_MOUSE	43	3	3	10%	6	3	3	10%	6
Protease inhibitors											
354	CD109 antigen	CD109_MOUSE	162	8	8	7%	14	3	3	3%	4
42	Cystatin-C	CYTC_MOUSE	16	10	14	55%	63	6	7	34%	32
95	Glia-derived nexin	GDN_MOUSE	44	7	8	21%	17	7	9	22%	21
166	Neuroserpin	NEUS_MOUSE	46	5	5	13%	11	5	5	15%	11
9	Plasminogen activator inhibitor 1	PAI1_MOUSE	45	23	30	55%	177	23	29	55%	139
13	Serine protease inhibitor A3N	SPA3N_MOUSE	47	13	18	32%	97	17	20	42%	102
459	Tissue factor pathway inhibitor	TFPI1_MOUSE	35	2	2	7%	7	-	-	-	-
62	Metalloproteinase inhibitor 1	TIMP1_MOUSE	23	9	10	38%	48	6	7	40%	24
70	Metalloproteinase inhibitor 2	TIMP2_MOUSE	24	9	12	24%	45	7	9	24%	21
325	Metalloproteinase inhibitor 3	TIMP3_MOUSE	24	3	3	16%	5	3	3	17%	7
Basement membrane											
291	Annexin A2	ANXA2_MOUSE	39	4	4	14%	7	3	4	12%	7
355	Laminin subunit alpha-1	LAMA1_MOUSE	338	-	-	-	-	3	3	1%	4
130	Laminin subunit alpha-2	LAMA2_MOUSE	343	12	12	5%	18	21	22	8%	38
102	Laminin subunit alpha-4	LAMA4_MOUSE	202	12	12	8%	29	8	8	6%	22
65	Laminin subunit beta-1	LAMB1_MOUSE	197	6	6	4%	9	19	20	12%	40
104	Laminin subunit beta-2	LAMB2_MOUSE	196	13	14	9%	25	11	11	8%	27
18	Laminin subunit gamma-1	LAMC1_MOUSE	177	13	14	12%	31	25	36	21%	103
31	Basement membrane-specific heparan sulfate proteoglycan core protein	PGBM_MOUSE	398	14	15	4%	33	26	27	9%	53
4	SPARC	SPRC_MOUSE	34	15	20	44%	138	18	25	43%	212
248	Tetranectin	TETN_MOUSE	22	-	-	-	-	3	3	15%	9
Glycoproteins											
296	Adipocyte enhancer-binding protein 1	AEBP1_MOUSE	128	-	-	-	-	4	4	4%	9
281	Agrin	AGRIN_MOUSE	208	3	3	2%	6	5	5	3%	6

359	Acid sphingomyelinase-like phosphodiesterase 3a	ASM3A_MOUSE	50	2	2	6%	4	2	2	6%	4
194	Beta-1,4-galactosyltransferase 1	B4GT1_MOUSE	44	5	5	12%	10	5	6	12%	11
183	Biotinidase	BTD_MOUSE	58	5	5	13%	7	4	4	10%	9
106	Calumenin	CALU_MOUSE	37	5	6	18%	17	5	6	17%	22
94	Clusterin	CLUS_MOUSE	52	10	13	27%	34	6	7	20%	13
463	Cartilage oligomeric matrix protein	COMP_MOUSE	82	2	2	3%	3	-	-	-	-
344	Collagen triple helix repeat-containing protein 1	CTHR1_MOUSE	26	4	4	20%	9	2	2	8%	5
73	Dystroglycan	DAG1_MOUSE	97	7	8	9%	24	8	9	11%	19
118	Dickkopf-related protein 3	DKK3_MOUSE	38	6	7	21%	17	-	-	-	[e]
392	Dentin matrix protein 4	DMP4_MOUSE	66	-	-	-	-	2	2	5%	3
11	Extracellular matrix protein 1	ECM1_MOUSE	63	22	33	47%	182	19	25	42%	111
22	EMILIN-1	EMIL1_MOUSE	108	17	23	18%	67	20	27	20%	75
427	EMILIN-2	EMIL2_MOUSE	117	-	-	-	-	2	2	2%	2
144	Mammalian ependymin-related protein 1	EPDR1_MOUSE	25	4	4	23%	13	4	4	23%	8
505	Protein FAM20A	FA20A_MOUSE	62	3	3	7%	4	-	-	-	-
573	Protein FAM20B	FA20B_MOUSE	47	2	2	5%	2	-	-	-	-
284	Protein FAM3C	FAM3C_MOUSE	25	4	4	23%	8	3	3	17%	6
16	Fibrillin-1	FBN1_MOUSE	312	53	61	24%	127	42	46	19%	113
296	Fetuin-B	FETUB_MOUSE	43	2	3	8%	7	-	-	-	-
6	Fibronectin	FN1_MOUSE	272	58	80	31%	529	36	50	20%	220 [d][e]
44	Fibromodulin	FMOD_MOUSE	43	4	6	14%	22	6	8	18%	31
574	Follistatin	FST_MOUSE	38	2	2	8%	2	-	-	-	-
8	Follistatin-related protein 1	FSTL1_MOUSE	35	17	22	54%	85	22	29	59%	116
264	Follistatin-related protein 3	FSTL3_MOUSE	27	-	-	-	-	2	2	14%	3
157	Glypican-4	GPC4_MOUSE	63	-	-	-	-	5	5	14%	9
	Immunoglobulin superfamily containing leucine-rich										
91	repeat protein	ISLR_MOUSE	46	4	4	11%	6	6	6	16%	14
546	Integrin beta-like protein 1	ITGBL_MOUSE	54	2	2	6%	3	-	-	-	-
429	Leucine-rich repeat LGI family member 2	LGI2_MOUSE	63	4	4	8%	9	-	-	-	-
54	Lumican	LUM_MOUSE	38	6	6	16%	24	6	6	16%	24 [d][e]
212	Meteorin-like protein	METRL_MOUSE	35	4	4	15%	8	-	-	-	-
403	Microfibril-associated glycoprotein 4	MFAP4_MOUSE	29	-	-	-	-	2	2	7%	3
126	Microfibrillar-associated protein 5	MFAP5_MOUSE	19	3	4	23%	9	3	4	23%	10
77	Lactadherin	MFGM_MOUSE	51	10	11	23%	47	9	9	22%	22
204	Mimecan	MIME_MOUSE	34	4	4	11%	9	4	4	11%	6
359	Mesothelin	MSLN_MOUSE	69	4	4	7%	8	-	-	-	-
176	Neutrophil gelatinase-associated lipocalin	NGAL_MOUSE	23	3	5	17%	10	4	5	20%	14
81	Nidogen-1	NID1_MOUSE	137	11	11	10%	27	8	8	8%	27 [f]
108	Nidogen-2	NID2_MOUSE	154	6	6	5%	11	10	10	9%	33 [f]
147	Protein NOV homolog	NOV_MOUSE	39	5	5	20%	12	4	4	17%	8
158	Olfactomedin-like protein 3	OLFL3_MOUSE	46	6	6	17%	12	5	5	17%	15
406	Olfactomedin-like protein 2B	OLMB_MOUSE	84	-	-	-	-	2	2	5%	3
338	Inactive serine protease PAMR1	PAMR1_MOUSE	80	4	4	7%	5	-	-	-	-
86	Procollagen C-endopeptidase enhancer 1	PCOC1_MOUSE	50	10	14	31%	33	12	14	33%	35 [f]
21	Biglycan	PGS1_MOUSE	42	7	9	22%	66	9	11	28%	51 [e]
26	Decorin	PGS2_MOUSE	40	10	11	26%	41	9	12	25%	51 [d][e]
92	Periostin	POSTN_MOUSE	93	13	14	19%	37	7	8	10%	24 [e]
30	Prolargin	PRELP_MOUSE	43	9	13	28%	55	11	16	30%	62
409	Proteoglycan 4	PRG4_MOUSE	116	-	-	-	-	2	2	2%	3
43	Pentraxin-related protein PTX3	PTX3_MOUSE	42	9	11	29%	29	12	12	39%	44 [e]
47	Sulfated glycoprotein 1	SAP_MOUSE	61	9	10	17%	29	9	11	19%	32
527	Semaphorin-3A	SEM3A_MOUSE	89	2	2	3%	4	-	-	-	-
471	Semaphorin-3C	SEM3C_MOUSE	85	2	2	4%	4	-	-	-	-
231	Semaphorin-3D	SEM3D_MOUSE	90	4	4	6%	8	3	3	4%	5
170	Semaphorin-3E	SEM3E_MOUSE	90	7	9	11%	19	-	-	-	-
153	Semaphorin-3F	SEM3F_MOUSE	88	7	7	12%	14	-	-	-	-
159	Secreted frizzled-related protein 1	SFRP1_MOUSE	35	-	-	-	-	5	6	19%	12
141	Secreted frizzled-related protein 3	SFRP3_MOUSE	36	3	3	10%	6	3	3	10%	11
309	Slit homolog 2 protein	SLIT2_MOUSE	169	7	7	6%	10	5	5	3%	8
129	Slit homolog 3 protein	SLIT3_MOUSE	168	4	5	3%	8	4	4	3%	9
314	Spondin-2	SPON2_MOUSE	36	4	4	11%	6	3	3	9%	4 [e]
173	Sushi repeat-containing protein SRPX2	SRPX2_MOUSE	53	5	5	14%	10	3	3	8%	12
38	Tenascin	TENA_MOUSE	232	16	18	11%	32	25	30	16%	61
295	Tubulointerstitial nephritis antigen-like	TINAL_MOUSE	53	2	2	6%	8	2	2	6%	5
303	Thrombospondin-1	TSP1_MOUSE	130	20	23	23%	82	3	3	3%	4 [e]
180	Thrombospondin-2	TSP2_MOUSE	130	3	3	3%	5	4	4	4%	15
593	WNT1-inducible-signaling pathway protein 1	WISP1_MOUSE	41	2	2	8%	2	-	-	-	-
146	WNT1-inducible-signaling pathway protein 2	WISP2_MOUSE	27	9	11	31%	30	6	6	25%	11
Oxido-reductase											
364	Glutathione peroxidase 3	GPX3_MOUSE	25	2	2	13%	7	2	2	13%	4
131	Peroxidase homolog	PXDN_MOUSE	165	23	25	20%	61	6	6	5%	15
109	Superoxide dismutase [Cu-Zn]	SODC_MOUSE	16	6	9	39%	20	5	7	36%	13
49	Extracellular superoxide dismutase [Cu-Zn]	SODE_MOUSE	27	15	17	43%	52	10	13	39%	37
175	Lysyl oxidase homolog 1	LOXL1_MOUSE	67	9	11	19%	42	6	6	14%	10
228	Lysyl oxidase homolog 2	LOXL2_MOUSE	87	10	14	19%	32	4	7	8%	13
200	Lysyl oxidase homolog 3	LOXL3_MOUSE	84	10	12	18%	22	7	9	11%	16
40	Sulfhydryl oxidase 1	QSOX1_MOUSE	83	20	27	30%	114	20	26	30%	72
Extracellular matrix											
243	Transforming growth factor-beta-induced protein ig-h3	BGH3_MOUSE	75	5	5	9%	13	-	-	-	-
476	Corneodesmosin	CDSN_MOUSE	54	3	3	7%	6	-	-	-	-
479	Collectin-11	COL11_MOUSE	29	2	3	10%	6	-	-	-	-
265	Versican core protein	CSPG2_MOUSE	367	-	-	-	-	2	2	1%	4
134	Fibulin-1	FBLN1_MOUSE	78	14	15	25%	37	11	12	20%	35 [d]
7	Fibulin-2	FBLN2_MOUSE	132	24	34	24%	262	20	26	20%	158
51	Fibulin-5	FBLN5_MOUSE	50	8	10	20%	40	6	7	16%	30
66	Galectin-1	LEG1_MOUSE	15	6	8	61%	21	4	7	41%	21 [e][f]
437	Galectin-3	LEG3_MOUSE	28	3	3	16%	5	-	-	-	-
48	Galectin-3-binding protein	LG3BP_MOUSE	64	11	16	26%	47	10	14	23%	41
72	Protein-lysine 6-oxidase	LYOX_MOUSE	47	5	8	15%	25	6	7	19%	16
297	Matrilin-2	MATN2_MOUSE	107	-	-	-	-	3	3	3%	9
438	Nephronectin	NPNT_MOUSE	61	3	3	5%	4	-	-	-	-
313	Aggrecan core protein	PGCA_MOUSE	222	-	-	-	-	3	3	2%	4
Cell adhesion											
61	Coiled-coil domain-containing protein 80	CCD80_MOUSE	108	4	4	7%	7	12	12	15%	33
201	Protein CYR61	CYR61_MOUSE	42	4	6	12%	15	3	3	10%	9
114	Dermatopontin	DERM_MOUSE	24	7	7	35%	19	5	5	30%	12
	Sushi, von Willebrand factor type A, EGF and pentraxin										
29	domain-containing protein 1	SVEP1_MOUSE	387	35	45	12%	118	33	41	11%	121
Growth regulation											
314	Growth arrest-specific protein 6	GAS6_MOUSE	75	3	3	4%	8	-	-	-	-
239	Growth/differentiation factor 6	GDF6_MOUSE	51	4	4	10%	16	4	4	10%	6
Serum/Plasma											
216	Serum albumin	ALBU_MOUSE	69	2	3	4%	23	2	3	4%	5
304	Antithrombin-III	ANT3_MOUSE	52	-	-	-	-	2	2	5%	4
50	Apolipoprotein E	APOE_MOUSE	36	7	9	28%	24	8	11	30%	35
154	Beta-2-microglobulin	B2MG_MOUSE	14	3	3	23%	17	2	2	16%	14
419	Complement C1q subcomponent subunit A	C1QA_MOUSE	26	2	2	11%	6	-	-	-	-
371	Complement C1q subcomponent subunit B	C1QB_MOUSE	27	2	2	10%	8	-	-	-	-
268	Complement C1q subcomponent subunit C	C1QC_MOUSE	26	2	3	13%	9	-	-	-	-
179	Complement C1q tumor necrosis factor-related protein 5	C1QT5_MOUSE	25	4	5	23%	9	-	-	-	-
273	Complement C4-B	CO4B_MOUSE	193	10	10	7%	18	4	4	2%	11
68	Ceruloplasmin	CERU_MOUSE	121	9	10	11%	23	13	14	17%	45
69	Complement factor H	CFAH_MOUSE	139	32	45	31%	160	16	18	18%	52
571	Complement factor I	CFAI_MOUSE	67	2	2	5%	2	-	-	-	-

305 Complement C2	CO2_MOUSE	85	6	6	9%	10	-	-	-	-
97 Complement C3	CO3_MOUSE	186	58	72	38%	299	11	12	8%	32
285 Growth hormone receptor	GHR_MOUSE	73	2	2	3%	6	2	2	3%	5
57 Granulins	GRN_MOUSE	63	12	15	29%	49	11	13	26%	30
53 Haptoglobin	HPT_MOUSE	39	8	9	25%	25	11	12	27%	30
28 Plasma protease C1 inhibitor	IC1_MOUSE	56	11	12	21%	36	14	16	27%	51
199 Interferon-alpha/beta receptor beta chain	INAR2_MOUSE	57	3	3	5%	9	2	3	5%	9
521 Inter-alpha-trypsin inhibitor heavy chain H2	ITIH2_MOUSE	106	2	2	3%	4	-	-	-	-
174 Low-density lipoprotein receptor	LDLR_MOUSE	95	4	4	5%	9	3	3	4%	7
428 Mast cell protease 8	MCPT8_MOUSE	27	-	-	-	-	2	2	10%	2
60 Plasma glutamate carboxypeptidase	PGCP_MOUSE	52	8	9	19%	30	8	9	20%	22
431 Vitamin K-dependent protein S	PROS_MOUSE	75	8	8	14%	18	2	2	3%	2
286 Ribonuclease 4	RNAS4_MOUSE	17	3	4	20%	8	2	2	19%	5
375 Ribonuclease T2	RNT2_MOUSE	30	-	-	-	-	2	2	7%	4
167 Transcobalamin-2	TCO2_MOUSE	48	9	10	24%	24	6	8	18%	21
25 Serotransferrin	TRFE_MOUSE	77	36	48	46%	184	24	27	38%	61
531 Alpha-2-macroglobulin-P	A2MP_MOUSE	164	2	2	2%	3	-	-	-	-
233 Placenta-specific protein 9	PLAC9_MOUSE	11	2	2	28%	6	2	2	28%	5
Glycolysis										
140 Fructose-bisphosphate aldolase A	ALDOA_MOUSE	39	7	8	30%	22	6	7	16%	17
193 Glucose-6-phosphate isomerase	G6PI_MOUSE	63	5	6	13%	13	5	5	12%	8
Lysosome										
170 Arylsulfatase A	ARSA_MOUSE	54	2	4	8%	9	3	4	10%	7
37 Cathepsin B	CATB_MOUSE	37	10	15	28%	47	9	12	25%	33
138 Gamma-glutamyl hydrolase	GGH_MOUSE	35	3	3	11%	10	4	4	15%	9
184 Group XV phospholipase A2	PAG15_MOUSE	47	4	4	14%	10	4	4	14%	14
Membrane										
221 Calcyclin-1	CSTN1_MOUSE	109	6	6	9%	17	4	5	5%	11
369 Leukemia inhibitory factor receptor	LIFR_MOUSE	123	-	-	-	-	2	2	2%	4
Scavenger receptor cysteine-rich domain-containing protein LOC284297 homolog	SRCLR_MOUSE	145	-	-	-	-	5	5	6%	10
430 Pantetheinase	VNN1_MOUSE	57	4	4	11%	9	-	-	-	-
Epithelia-mesenchymal transition										
284 Protein FAM3C	FAM3C_MOUSE	25	4	4	23%	8	3	3	17%	6
Glycosylation										
436 Polypeptide N-acetylgalactosaminyltransferase 2	GALT2_MOUSE	65	3	3	8%	5	-	-	-	-
Lipid metabolism/transport										
447 Phospholipase A1 member A	PLA1A_MOUSE	50	3	3	9%	8	-	-	-	-
238 Phospholipid transfer protein	PLTP_MOUSE	54	5	6	12%	15	5	6	11%	16
Apoptosis										
350 Tumor necrosis factor receptor superfamily member 11B	TR11B_MOUSE	46	2	2	8%	5	2	2	8%	5
Others										
317 Cyclic AMP-dependent transcription factor ATF-6 beta	ATF6B_MOUSE	76	-	-	-	-	2	2	4%	4
336 Adenyl cyclase-associated protein 1	CAP1_MOUSE	52	2	3	6%	9	-	-	-	-
344 Macrophage-capping protein	CAPG_MOUSE	39	2	2	8%	5	-	-	-	-
407 Angiotensin-related protein 2	ANGL2_MOUSE	57	2	2	5%	4	-	-	-	-
260 Angiotensin-2	ANGP2_MOUSE	57	2	2	6%	4	5	5	12%	9
195 C-X-C motif chemokine 16	CXL16_MOUSE	27	3	3	15%	10	2	2	8%	6
491 von Willebrand factor	VWF_MOUSE	309	3	3	2%	5	-	-	-	-
177 Cofilin-1	COF1_MOUSE	19	6	7	31%	18	5	6	30%	10
302 UPF0556 protein C19orf10 homolog	CS010_MOUSE	18	2	2	16%	6	-	-	-	-
181 Gelsolin	GELS_MOUSE	86	8	11	17%	39	9	9	16%	19
220 Beta-galactosidase-1-like protein	GLB1L_MOUSE	73	5	5	9%	12	-	-	-	-
272 Epididymis-specific alpha-mannosidase	MAZB2_MOUSE	116	4	4	6%	7	5	5	7%	11
128 Epididymal secretory protein E1	NPC2_MOUSE	16	5	6	34%	16	5	5	36%	10
87 Peptidyl-prolyl cis-trans isomerase A	PPIA_MOUSE	18	7	7	35%	25	6	6	35%	16
179 Profilin-1	PROF1_MOUSE	15	8	9	59%	15	4	5	32%	11
151 Translationally-controlled tumor protein	TCTP_MOUSE	19	2	2	9%	4	3	4	16%	7
203 Thymosin beta-4	TYB4_MOUSE	6	3	5	48%	11	3	3	48%	5

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Online-Table II: ECM proteins changes in the secretome of CFs following miR-29b transfection

#	Identified Proteins	Accession Number	MW (kDa)	Control Anti-miR Sample 1	Control Anti-miR Sample 2	Control Anti-miR Sample 3	Anti-miR-29b Sample 1	Anti-miR-29b Sample 2	Anti-miR-29b Sample 3	t test (paired)	Average Control Anti-miR	Average anti-miR-29b	Ratio	Control Pre-miR Sample 1	Control Pre-miR Sample 2	Control Pre-miR Sample 3	Pre-miR-29b Sample 1	Pre-miR-29b Sample 2	Pre-miR-29b Sample 3	t test (paired)	Average Control Pre-miR	Average pre-miR-29b	Ratio	TargetScan	PiCTar	Diana
176	Cofilin-1	COF1_MOUSE	19	15.27	10.6	12.78	13.42	11.2	12.21	0.482	12.88	12.28	0.95	5.92	4.64	3.11	11.03	9.6	6.44	0.016	4.56	9.02	1.98			
126	Profilin-1	PROF1_MOUSE	15	12.89	11.48	13.76	15.2	13.76	17.39	0.025	12.71	15.45	1.22	15.75	10.09	15.75	17.3	22.49	22.78	0.155	13.86	20.86	1.50			
1	Collagen alpha-1(I) chain	CO1A1_MOUSE	138	470.41	510.94	493.75	561.85	603.92	527.21	0.066	491.70	564.33	1.15	434.68	480	455.13	204.11	214.46	244.17	0.005	456.60	220.91	0.48	X		
4	Collagen alpha-1(III) chain	CO3A1_MOUSE	139	318.96	391.31	258.17	387.91	459.36	322.77	0.000	322.81	390.01	1.21	241.94	309.13	227.54	66.2	91.25	88.11	0.016	259.54	81.85	0.32	X		X
29	Collagen alpha-1(IV) chain	CO4A1_MOUSE	161	35.89	69.98	40.26	76.43	78.39	55.35	0.161	48.71	70.06	1.44	37.39	71.9	41.04	9.78	19.62	26.41	0.104	50.11	18.60	0.37	X	X	X
8	Collagen alpha-2(IV) chain	CO4A2_MOUSE	167	196.06	218.42	177.68	194.46	217.85	205.45	0.469	197.39	205.92	1.04	174.08	244.59	173.8	63.69	95.55	79.03	0.018	197.49	79.42	0.40	X		X
85	Collagen alpha-1(V) chain	CO5A1_MOUSE	184	18.44	15.84	15.72	28.51	23.96	24.29	0.004	16.67	25.59	1.54	20.67	31.9	22.07	7.27	8.16	1	0.025	24.88	5.48	0.22	X		X
5	Collagen alpha-2(V) chain	CO5A2_MOUSE	145	295.17	303.12	268.97	276.99	369.22	288.26	0.455	289.09	311.49	1.08	219.32	269.13	254.93	39.87	85.52	68.14	0.000	247.79	64.51	0.26	X	X	X
16	Collagen alpha-1(VI) chain	CO6A1_MOUSE	108	101.7	125.86	109.96	100.39	98.79	116.59	0.450	112.51	105.26	0.94	69.84	110.07	102.15	52.4	55.44	59.07	0.073	94.02	55.64	0.59			
78	Collagen alpha-2(VI) chain	CO6A2_MOUSE	110	32.72	28.94	26.52	14.31	33.31	22.57	0.463	29.39	23.40	0.80	22.64	20.09	16.8	6.02	8.16	8.26	0.034	19.84	7.48	0.38			
113	Collagen alpha-1(VIII) chain	CO8A1_MOUSE	74	21.62	21.96	16.71	21.41	21.41	22.57	0.500	20.10	21.80	1.08	5.92	9.18	6.27	1	1	1	0.027	7.12	1.00	0.14			X
267	Collagen alpha-1(XI) chain	COBA1_MOUSE	181	4.96	7.99	5.91	8.1	12.06	9.63	0.005	6.29	9.93	1.58	4.93	10.09	5.21	2.25	3.87	6.44	0.357	6.74	4.19	0.62	X	X	X
81	Collagen alpha-1(XII) chain	COCA1_MOUSE	340	35.1	33.31	9.83	27.62	11.2	17.39	0.482	26.08	18.74	0.72	7.88	42.81	5.21	27.33	1	1	0.669	18.63	9.78	0.52			
623	Collagen alpha-1(XIV) chain	COEA1_MOUSE	193	3.38	2.75	1	1	1	1	0.193	2.38	1.00	0.42	1	1	1	2.25	1	1	0.423	1.00	1.42	1.42			
397	Collagen alpha-1(XV) chain	COFA1_MOUSE	140	4.96	2.75	2.96	2.77	1.85	1.86	0.073	3.56	2.16	0.61	1	3.73	1	1	6.73	1	0.423	1.91	2.91	1.52	X		X
121	Laminin subunit beta-2	LAMB2_MOUSE	196	10.52	22.83	19.65	15.2	21.41	12.21	0.729	17.67	16.27	0.92	15.75	22.81	11.54	4.76	5.3	1	0.029	16.70	3.69	0.22			
523	TGF-beta receptor type III	TGBR3_MOUSE	94	1	1.87	2.96	4.55	1.85	1.86	0.623	1.94	2.75	1.42	1	1	2.05	3.51	3.87	4.63	0.002	1.35	4.00	2.97			
27	Thrombospondin-1	TSBP1_MOUSE	130	66.02	66.49	31.43	74.66	53.72	23.43	0.597	54.65	50.60	0.93	69.84	63.72	23.13	98.79	95.55	39.11	0.034	52.23	77.82	1.49			
230	Adenosine deaminase	ADA_MOUSE	40	1.79	2.75	6.89	7.21	2.7	2.73	0.898	3.81	4.21	1.11	6.9	6.45	1	21.06	18.19	10.07	0.016	4.78	16.44	3.44			
153	Calumenin	CALU_MOUSE	37	12.89	14.97	13.76	13.42	15.46	14.8	0.061	13.87	14.56	1.05	17.72	6.45	11.54	4.76	1	1	0.049	11.90	2.25	0.19			
124	Beta-1,4-galactosyltransferase 1	B4GT1_MOUSE	44	7.34	9.73	8.85	6.32	10.35	9.63	0.846	8.64	8.77	1.01	4.93	8.27	7.32	19.81	18.19	17.33	0.019	6.84	18.44	2.70			
224	CD109 antigen	CD109_MOUSE	162	8.93	12.35	6.89	3.66	3.55	5.31	0.129	9.39	4.17	0.44	14.77	9.18	7.32	3.51	1	1	0.027	10.42	1.84	0.18			
31	Macrophage colony-stimulating factor 1	CSF1_MOUSE	61	46.2	41.17	51.06	43.6	35.87	33.78	0.204	46.14	37.75	0.82	46.24	42.81	37.88	64.94	74.06	60.89	0.022	42.31	66.63	1.57			
262	BMP-binding endothelial regulator protein	BMPEP_MOUSE	76	9.72	8.86	7.87	8.99	11.2	4.45	0.752	8.82	8.21	0.93	5.92	4.64	5.21	1	1	1	0.007	5.26	1.00	0.19			
618	Cell growth regulator with EF hand domain protein 1	CGRE1_MOUSE	31	1.79	1	1	4.55	2.7	2.73	0.027	1.26	3.33	2.63	1	1	1	1	1	1	NA	1.00	1.00	1.00			
516	Cartilage oligomeric matrix protein	COMP_MOUSE	82	2.59	1	3.94	1	2.7	2.73	0.758	2.51	2.14	0.85	1.98	1.91	4.16	1	1	2.81	0.016	2.68	1.60	0.60			
134	Mammalian ependymin-related protein 1	EPDR1_MOUSE	25	9.72	12.35	8.85	13.42	12.06	12.21	0.219	10.31	12.56	1.22	12.8	11	11.54	18.55	22.49	22.78	0.037	11.78	21.27	1.81			
11	EGF-containing fibulin-like extracellular matrix protein 1	FBLN3_MOUSE	55	112.01	104.04	129.59	111.04	118.35	115.73	0.985	115.21	115.04	1.00	110.16	100.07	131.65	174.02	194.4	233.29	0.017	113.96	200.57	1.76			
388	Fetuin-B	FETUB_MOUSE	43	1.79	3.62	3.94	2.77	2.7	1.86	0.529	3.12	2.44	0.78	4.93	7.36	6.27	1	1	2.81	0.036	6.19	1.60	0.26			
19	Follistatin-related protein 1	FSTL1_MOUSE	35	64.43	75.22	56.95	73.77	81.79	74.32	0.076	65.53	76.63	1.17	61.97	76.44	80.02	38.61	41.11	48.18	0.014	72.81	42.63	0.59	X		
506	Growth-regulated alpha protein	GROA_MOUSE	10	2.59	1.87	2.96	1.89	2.7	2.73	0.948	2.47	2.44	0.99	4.93	1.91	2.05	3.51	1	1	0.018	2.96	1.84	0.62			
94	Haptoglobin	HPT_MOUSE	39	13.69	16.72	25.54	9.87	10.35	15.66	0.063	18.65	11.96	0.64	8.87	11.91	24.18	28.58	28.22	50	0.018	14.99	35.60	2.38			
453	Insulin-like growth factor-binding protein 6	IBP6_MOUSE	25	3.38	2.75	4.93	1.89	2.7	5.31	0.565	3.69	3.30	0.90	2.97	1.91	4.16	1	1	2.81	0.044	3.01	1.60	0.53			
20	Insulin-like growth factor-binding protein 7	IBP7_MOUSE	29	84.26	81.33	66.77	64.89	77.53	59.66	0.167	77.45	67.36	0.87	104.26	85.53	83.19	43.63	45.41	42.74	0.020	90.99	43.93	0.48			
449	Insulin-like growth factor I	IGF1_MOUSE	17	3.38	1.87	1.98	4.55	1	2.73	0.630	2.41	2.76	1.15	3.95	2.82	3.11	1	1	1	0.021	3.29	1.00	0.30	X	X	X
68	Inhibin beta A chain	INHBA_MOUSE	47	31.13	28.07	11.8	29.4	35.02	21.7	0.286	23.67	28.71	1.21	26.57	27.36	25.23	19.81	16.76	13.7	0.022	26.39	16.76	0.64			
432	Leukemia inhibitory factor	LIF_MOUSE	22	1.79	2.75	1.98	5.44	4.4	2.73	0.143	2.17	4.19	1.93	4.93	4.64	4.16	1	1	1	0.004	4.58	1.00	0.22	X	X	X
77	Lysyl oxidase homolog 2	LOXL2_MOUSE	87	23.99	21.08	19.65	24.07	22.26	24.29	0.289	21.57	23.54	1.09	15.75	30.09	25.23	6.02	8.16	10.07	0.048	23.69	8.08	0.34			
543	Latent-transforming growth factor beta-binding protein 1	LTBP1_MOUSE	187	1	1	2.96	1.89	1.85	3.59	0.010	1.65	2.44	1.48	1.98	1.91	5.21	2.25	1	1	0.351	3.03	1.42	0.47			
227	Meteorin-like protein	METRL_MOUSE	35	7.34	6.24	5.91	5.44	5.25	3.59	0.047	6.50	4.76	0.73	6.9	8.27	8.38	7.27	18.19	19.15	0.170	7.85	14.87	1.89			
221	Neuroserpin	NEUS_MOUSE	46	8.93	7.11	9.83	5.44	7.8	11.35	0.809	8.62	8.20	0.95	9.85	7.36	12.59	3.51	1	1	0.044	9.93	1.84	0.18			
209	Neutrophil gelatinase-associated lipocalin	NGAL_MOUSE	23	7.34	3.62	8.85	6.32	1.85	7.04	0.027	6.60	5.07	0.77	9.85	9.18	11.54	8.52	5.3	8.26	0.067	10.19	7.36	0.72			
367	Pappalysin-1	PAPP1_MOUSE	181	8.93	6.24	4.93	2.77	2.7	1.86	0.047	6.70	2.44	0.36	9.85	5.54	1	1	1	1	0.223	5.46	1.00	0.18			
442	Phospholipase A1 member A	PLA1A_MOUSE	50	7.34	2.75	2.96	2.77	1.85	4.45	0.530	4.35	3.02	0.70	4.93	2.82	3.11	2.25	1	1	0.013	3.62	1.42	0.39	</		

448	Xanthine dehydrogenase/oxidase	XDH_MOUSE	147	1.79	1.87	5.91	2.77	2.7	3.59	0.889	3.19	3.02	0.95	4.93	2.82	3.11	2.25	1	1	0.013	3.62	1.42	0.39
480	Disintegrin and metalloproteinase domain-containing protein 17	ADA17_MOUSE	93	2.59	2.75	1.98	5.44	1	1	0.980	2.44	2.48	1.02	2.97	4.64	3.11	1	1	1	0.041	3.57	1.00	0.28
52	A disintegrin and metalloproteinase with thrombospondin motifs 5	ATSS_MOUSE	102	21.62	28.94	21.61	24.96	26.51	28.6	0.438	24.06	26.69	1.11	26.57	30.99	31.56	47.39	61.17	57.26	0.011	29.71	55.27	1.86 X
10	Extracellular matrix protein 1	ECM1_MOUSE	63	145.31	144.2	155.11	119.03	110.7	139.89	0.042	148.21	123.21	0.83	169.16	149.16	155.89	171.51	220.19	155.25	0.409	158.07	182.32	1.15
48	EMILIN-1	EMIL1_MOUSE	108	30.34	39.42	66.77	23.19	33.31	57.07	0.019	45.51	37.86	0.83	32.47	20.09	42.09	19.81	35.38	15.52	0.583	31.55	23.57	0.75
277	Gamma-glutamyl hydrolase	GGH_MOUSE	35	7.34	9.73	7.87	8.1	6.1	7.9	0.558	8.31	7.37	0.89	4.93	4.64	7.32	1	1	4.63	0.012	5.63	2.21	0.39
80	Galectin-1	LEG1_MOUSE	15	17.65	16.72	13.76	19.64	16.31	13.08	0.757	16.04	16.34	1.02	17.72	17.36	22.07	27.33	32.52	37.29	0.019	19.05	32.38	1.70
515	Matrix metalloproteinase-19	MMP19_MOUSE	59	4.17	1.87	3.94	1	5.25	2.73	0.879	3.33	2.99	0.90	1.98	2.82	2.05	1	1	1	0.041	2.28	1.00	0.44
101	72 type IV collagenase	MMP2_MOUSE	74	18.44	18.46	29.47	13.42	18.01	26.02	0.157	22.12	19.15	0.87	16.73	14.63	14.7	7.27	6.73	10.07	0.036	15.35	8.02	0.52 X X X
35	Stromelysin-1	MMP3_MOUSE	54	42.23	30.69	58.91	24.07	18.01	38.96	0.016	43.94	27.01	0.61	51.15	58.26	62.11	26.08	31.08	64.52	0.223	57.17	40.56	0.71
76	Nidogen-1	NID1_MOUSE	137	21.62	24.58	16.71	30.28	29.06	21.7	0.044	20.97	27.01	1.29	27.55	21.91	11.54	17.3	22.49	8.26	0.306	20.33	16.02	0.79
69	Prolargin	PRELP_MOUSE	43	44.61	28.94	25.54	22.3	35.02	27.74	0.651	33.03	28.35	0.86	26.57	23.72	14.7	4.76	3.87	4.63	0.042	21.66	4.42	0.20 X X X
33	Peroxidase homolog	PXDN_MOUSE	165	33.51	49.9	58.91	39.16	56.28	63.97	0.004	47.44	53.14	1.12	40.34	56.44	38.93	29.84	29.65	26.41	0.084	45.24	28.63	0.63 X X X
64	Sulfated glycoprotein 1	SAP_MOUSE	61	20.03	25.45	18.67	22.3	24.81	22.57	0.299	21.38	23.23	1.09	29.52	27.36	28.4	16.05	13.89	2.81	0.049	28.43	10.92	0.38
296	Spondin-2	SPON2_MOUSE	36	4.17	6.24	3.94	3.66	3.55	3.59	0.257	4.78	3.60	0.75	2.97	4.64	5.21	8.52	8.16	8.26	0.034	4.27	8.31	1.95
426	Follistatin-related protein 3	FSTL3_MOUSE	27	2.59	2.75	1.98	3.66	3.55	3.59	0.040	2.44	3.60	1.48	1	2.82	1	1	1	1	0.423	1.61	1.00	0.62
630	Alpha-2-macroglobulin-P	A2MP_MOUSE	164	3.38	1	1	1	1	1	0.423	1.79	1.00	0.56	1	1	1	1	1	1	NA	1.00	1.00	1.00
368	Disintegrin and metalloproteinase domain-containing protein 9	ADAM9_MOUSE	92	2.59	1.87	3.94	1.89	3.55	2.73	0.939	2.80	2.72	0.97	4.93	5.54	6.27	8.52	8.16	4.63	0.443	5.58	7.10	1.27
348	Agrin	AGRIN_MOUSE	208	1	2.75	6.89	1	4.4	7.9	0.206	3.55	4.43	1.25	3.95	6.45	6.27	2.25	1	6.44	0.294	5.56	3.23	0.58
183	Serum albumin	ALBU_MOUSE	69	19.24	7.11	6.89	13.42	8.65	8.76	0.779	11.08	10.28	0.93	7.88	10.09	7.32	13.54	3.87	8.26	0.974	8.43	8.56	1.02
458	Angiotensinogen-related protein 2	ANGL2_MOUSE	57	3.38	2.75	3.94	3.66	2.7	1.86	0.491	3.36	2.74	0.82	4.93	2.82	3.11	6.02	1	1	0.452	3.62	2.67	0.74
547	Angiotensin-2	ANGP2_MOUSE	57	2.59	4.49	1	3.66	2.7	1	0.801	2.69	2.45	0.91	1.98	2.82	1	1	2.43	1	0.250	1.93	1.48	0.76
409	Annxin A2	ANXA2_MOUSE	39	6.55	1	2.96	4.55	1	1	0.184	3.50	2.18	0.62	4.93	3.73	2.05	4.76	1	6.44	0.834	3.57	4.07	1.14
276	Apolipoprotein E	APOE_MOUSE	36	20.03	7.11	1.98	9.87	1.85	1	0.175	9.71	4.24	0.44	3.95	1	5.21	11.03	2.43	1	0.703	3.39	4.82	1.42
649	Sphingomyelin phosphodiesterase	ASM_MOUSE	70	1	1	1.98	1	1.85	1	0.942	1.33	1.28	0.97	3.95	1	1	1	1	1	0.423	1.98	1.00	0.50
572	Acid sphingomyelinase-like phosphodiesterase 3a	ASM3A_MOUSE	50	1	1.87	1	1.89	2.7	3.59	0.130	1.29	2.73	2.11	3.95	4.64	1	2.25	1	1	0.233	3.20	1.42	0.44
418	ADAMTS-like protein 4	ATL4_MOUSE	113	2.59	2.75	3.94	1.89	1.85	4.45	0.496	3.09	2.73	0.88	2.97	5.54	5.21	3.51	3.87	2.81	0.315	4.57	3.40	0.74
635	A disintegrin and metalloproteinase with thrombospondin motifs 1	ATS1_MOUSE	106	1	1	1	1.89	2.7	1	0.221	1.00	1.86	1.86	1	1	1	1	1	6.44	0.423	1.00	2.81	2.81
158	A disintegrin and metalloproteinase with thrombospondin motifs 2	ATS2_MOUSE	135	11.31	10.6	8.85	12.54	9.5	9.63	0.712	10.25	10.56	1.03	12.8	17.36	13.64	8.52	8.16	10.07	0.085	14.60	8.92	0.61
638	A disintegrin and metalloproteinase with thrombospondin motifs 7	ATS7_MOUSE	182	1	1	2.96	1.89	1	2.73	0.585	1.65	1.87	1.13	1	1	1	1	1	1	NA	1.00	1.00	1.00 X X X
133	Beta-2-microglobulin	B2MG_MOUSE	14	6.55	8.86	15.72	15.2	11.2	10.49	0.679	10.38	12.30	1.19	9.85	10.09	18.91	11.03	13.89	17.33	0.541	12.95	14.08	1.09
472	Brain-derived neurotrophic factor	BDNF_MOUSE	28	4.17	3.62	2.96	1	5.25	4.45	0.993	3.58	3.57	1.00	2.97	2.82	1	1	1	1	0.184	2.26	1.00	0.44
282	Transforming growth factor-beta-induced protein ig-h3	BGH3_MOUSE	75	4.96	9.73	6.89	8.99	6.1	5.31	0.879	7.19	6.80	0.95	13.78	2.82	3.11	4.76	1	1	0.208	6.57	2.25	0.34
25	Bone morphogenetic protein 1	BMP1_MOUSE	112	39.06	49.02	70.69	55.13	58.83	66.56	0.349	52.92	60.17	1.14	62.95	66.44	41.04	67.45	109.88	40.92	0.368	56.81	72.75	1.28
563	Bone morphogenetic protein 6	BMP6_MOUSE	56	2.59	3.62	3.94	2.77	4.4	1	0.625	3.38	2.72	0.80	1	2.82	2.05	1	1	1	0.211	1.96	1.00	0.51
346	Biotinidase	BTD_MOUSE	58	4.96	5.37	2.96	2.77	6.1	1	0.348	4.43	3.29	0.74	7.88	3.73	3.11	4.76	6.73	8.26	0.568	4.91	6.58	1.34
400	Complement C1q subcomponent subunit A	C1QA_MOUSE	26	5.76	4.49	2.96	2.77	2.7	3.59	0.323	4.40	3.02	0.69	3.95	2.82	3.11	3.51	6.73	8.26	0.232	3.29	6.17	1.87
284	Complement C1q subcomponent subunit B	C1QB_MOUSE	27	7.34	4.49	6.89	8.1	3.55	2.73	0.422	6.24	4.79	0.77	6.9	3.73	5.21	9.78	5.3	11.89	0.137	5.28	8.99	1.70
290	Complement C1q subcomponent subunit C	C1QC_MOUSE	26	4.17	3.62	4.93	5.44	4.4	4.45	0.421	4.24	4.76	1.12	9.85	4.64	4.16	9.78	3.87	6.44	0.655	6.22	6.70	1.08
166	Complement C1q tumor necrosis factor-related protein 5	C1QTS_MOUSE	25	8.14	7.11	7.87	6.32	6.95	9.63	0.950	7.71	7.63	0.99	9.85	8.27	10.48	13.54	12.46	11.89	0.069	9.53	12.63	1.32
528	Cadherin-13	CAD13_MOUSE	78	5.76	1	1	5.44	1	3.59	0.498	2.59	3.34	1.29	1	1	3.11	4.76	1	1	0.779	1.70	2.25	1.32
326	Adenylyl cyclase-associated protein 1	CAP1_MOUSE	52	8.14	5.37	3.94	3.66	1	2.73	0.089	5.82	2.46	0.42	4.93	3.73	1	12.28	6.73	8.26	0.055	3.22	9.09	2.82
309	Macrophage-capping protein	CAPG_MOUSE	39	3.38	3.62	5.91	4.55	4.4	5.31	0.490	4.30	4.75	1.10	3.95	5.54	4.16	9.78	6.73	8.26	0.112	4.55	8.26	1.81
42	Cathepsin B	CATB_MOUSE	37	30.34	30.69	30.45	33.83	29.91	23.43	0.684	30.49	29.06	0.95	47.22	35.54	43.15	57.42	38.25	46.37	0.156	41.97	47.35	1.13
98	Cathepsin Z	CATZ_MOUSE	34	18.44	15.84	9.8																	

650	Complement factor 1	CFAI_MOUSE	67	1	1	1	1	1	1	1	NA	1.00	1.00	1.00	1	2.82	1	1	5.3	1	0.423	1.61	2.43	1.51		
646	60 heat shock protein, mitochondrial	CH60_MOUSE	61	1	2.75	1	4.55	1	1	0.737	1.58	2.18	1.38	1	1	1	1	1	1	NA	1.00	1.00	1.00	1.00		
110	Clusterin	CLUS_MOUSE	52	27.96	7.99	17.69	16.97	7.8	21.7	0.646	17.88	15.49	0.87	17.72	5.54	23.13	19.81	3.87	15.52	0.485	15.46	13.07	0.85			
3	Collagen alpha-2(I) chain	CO1A2_MOUSE	130	506.09	506.57	393.63	463.34	542.7	399.54	0.993	468.76	468.53	1.00	333.39	418.2	449.86	220.41	330.5	196.99	0.099	400.48	249.30	0.62	X	X	
322	Complement C2	CO2_MOUSE	85	4.17	1.87	10.82	4.55	1	7.9	0.359	5.62	4.48	0.80	1	1	8.38	1	1	10.07	0.423	3.46	4.02	1.16			
7	Complement C3	CO3_MOUSE	186	146.9	191.35	237.56	128.79	148.12	276.18	0.784	191.94	184.36	0.96	179.98	272.77	301.29	146.44	157.15	140.73	0.109	251.35	148.11	0.59			
420	Collagen alpha-1(XVIII) chain	CO1A1_MOUSE	182	1.79	2.75	2.96	1.89	1.85	1.86	0.230	2.50	1.87	0.75	3.95	1.91	6.27	4.76	6.73	10.07	0.121	4.04	7.19	1.78			
531	Collectin-11	COLL11_MOUSE	29	1	1	1	2.77	1	1.86	0.228	1.00	1.88	1.88	1.98	1	7.32	1	1	11.89	0.557	3.43	4.63	1.35			
254	Probable carboxypeptidase X1	CPXM1_MOUSE	81	7.34	3.62	2.96	5.44	5.25	2.73	0.885	4.64	4.47	0.96	13.78	13.72	6.27	6.02	5.3	4.63	0.111	11.26	5.32	0.47			
548	Inactive carboxypeptidase-like protein X2	CPXM2_MOUSE	87	1.79	2.75	1	1	4.4	1	0.729	1.85	2.13	1.16	1	2.82	1	1	1	1	0.423	1.61	1.00	0.62			
170	Cytokine receptor-like factor 1	CRLF1_MOUSE	47	9.72	13.22	10.82	9.87	11.2	8.76	0.215	11.25	9.94	0.88	4.93	16.45	10.48	9.78	13.89	11.89	0.623	10.62	11.85	1.12			
333	UPF0556 protein C19orf10 homolog	CS010_MOUSE	18	3.38	4.49	4.93	2.77	6.1	4.45	0.832	4.27	4.44	1.04	6.9	4.64	3.11	11.03	3.87	4.63	0.369	4.88	6.51	1.33			
182	Calsynenin-1	CSTN1_MOUSE	109	8.14	7.99	17.69	6.32	6.1	7.04	0.244	11.27	6.49	0.58	11.82	11	9.43	6.02	8.16	13.7	0.674	10.75	9.29	0.86			
61	Connective tissue growth factor	CTGF_MOUSE	38	37.47	32.43	21.61	33.83	34.17	22.57	0.869	30.50	30.19	0.99	22.64	26.45	18.91	17.3	21.06	28.22	0.932	22.67	22.19	0.98			
229	Collagen triple helix repeat-containing protein 1	CTHR1_MOUSE	26	8.14	8.86	3.94	8.1	6.1	7.04	0.958	6.98	7.08	1.01	6.9	6.45	7.32	8.52	5.3	4.63	0.617	6.89	6.15	0.89			
196	C-X-C motif chemokine 16	CXCL16_MOUSE	27	6.55	7.11	6.89	8.1	5.25	7.9	0.846	6.85	7.08	1.03	6.9	10.09	11.54	13.54	9.6	17.33	0.219	9.51	13.49	1.42			
148	Protein CYR61	CYR61_MOUSE	42	8.93	14.1	9.83	13.42	13.76	10.49	0.390	10.95	12.56	1.15	10.83	12.82	11.54	11.03	15.33	15.52	0.180	11.73	13.96	1.19			
30	Cystatin-C	CYTC_MOUSE	16	30.34	49.02	62.84	38.27	37.57	44.13	0.450	47.40	39.99	0.84	37.39	32.81	45.25	41.12	68.33	79.03	0.142	38.48	62.83	1.63			
100	Dystroglycan	DAG1_MOUSE	97	14.48	16.72	24.56	16.09	13.76	14.8	0.379	18.59	14.88	0.80	16.73	18.27	21.02	12.28	19.62	10.07	0.318	18.67	13.99	0.75			
142	Dermatopontin	DERM_MOUSE	24	7.34	12.35	19.65	8.1	12.91	15.66	0.624	13.11	12.22	0.93	8.87	9.18	13.64	8.52	13.89	15.52	0.291	10.56	12.64	1.20			
115	Dickkopf-related protein 3	DKK3_MOUSE	38	12.1	14.1	17.69	16.09	9.5	10.49	0.522	14.63	12.03	0.82	16.73	11	12.59	24.82	23.92	13.7	0.164	13.44	20.81	1.55			
337	Dipeptidyl-peptidase 2	DPP2_MOUSE	56	4.17	5.37	6.89	6.32	4.4	3.59	0.698	5.48	4.77	0.87	6.9	1	4.16	8.52	2.43	2.81	0.615	4.02	4.59	1.14			
643	Endoglin	EGLN_MOUSE	70	3.38	1	1	1.89	1	1	0.423	1.79	1.30	0.72	1.98	1	1	1	1	1	0.423	1.33	1.00	0.75			
645	Protein FAM20A	FA20A_MOUSE	62	1	1	1	1	2.73	0.423	1.00	1.58	1.58	1	4.64	1	1	1	1	1	0.423	2.21	1.00	0.45			
225	Protein FAM3C	FAM3C_MOUSE	25	5.76	7.11	7.87	8.99	9.5	5.31	0.629	6.91	7.93	1.15	4.93	8.27	9.43	8.52	8.16	6.44	0.939	7.54	7.71	1.02			
67	Fibulin-1	FBLN1_MOUSE	78	20.82	33.31	26.52	11.65	23.96	22.57	0.052	26.88	19.39	0.72	32.47	22.81	29.45	18.55	43.98	28.22	0.863	28.24	30.25	1.07			
6	Fibulin-2	FBLN2_MOUSE	132	208.74	202.7	197.32	203.33	203.39	209.76	0.672	202.92	205.49	1.01	239.97	234.59	242.29	329.49	415.03	265.95	0.164	238.95	336.82	1.41			
36	EGF-containing fibulin-like extracellular matrix protein 2	FBLN4_MOUSE	49	37.47	40.29	42.23	37.38	42.67	37.23	0.717	40.00	39.09	0.98	36.4	38.27	37.88	47.39	56.87	73.59	0.097	37.52	59.28	1.58			
39	Fibulin-5	FBLN5_MOUSE	50	32.72	34.18	39.28	33.83	32.46	33.78	0.399	35.39	33.36	0.94	24.6	30.09	41.04	36.11	52.57	46.37	0.120	31.91	45.02	1.41			
17	Fibrillin-1	FBN1_MOUSE	312	101.7	104.91	84.43	101.28	107.3	98.48	0.351	97.01	102.35	1.06	99.34	113.71	73.7	53.66	82.66	62.7	0.101	95.58	66.34	0.69	X	X	X
2	Fibronectin	FN1_MOUSE	272	420.45	404.41	394.61	404.77	409.18	410.76	0.689	406.49	408.24	1.00	448.45	480.91	395.07	654.22	750.26	425.65	0.142	441.48	610.04	1.38			
139	Fibromodulin	FMOD_MOUSE	43	14.48	13.22	10.82	8.1	10.35	13.08	0.451	12.84	10.51	0.82	11.82	21	8.38	4.76	6.73	8.26	0.222	13.73	6.58	0.48			
662	Follistatin	FST_MOUSE	38	2.59	1	1	1	1	1	0.423	1.53	1.00	0.65	1.98	1	1	1	1	1	0.423	1.33	1.00	0.75			
222	Glucose-6-phosphate isomerase	G6PI_MOUSE	63	8.14	5.37	5.91	5.44	6.1	4.45	0.372	6.47	5.33	0.82	13.78	9.18	4.16	12.28	2.43	10.07	0.851	9.04	8.26	0.91			
488	Polypeptide N-acetylgalactosaminyltransferase 2	GALT2_MOUSE	65	1	2.75	2.96	2.77	5.25	2.73	0.241	2.24	3.58	1.60	5.92	3.73	1	1	1	1	0.215	3.55	1.00	0.28			
389	Growth arrest-specific protein 6	GAS6_MOUSE	75	1.79	7.99	4.93	2.77	5.25	1.86	0.341	4.90	3.29	0.67	1	3.73	5.21	3.51	1	2.81	0.658	3.31	2.44	0.74			
194	Growth/differentiation factor 6	GDF6_MOUSE	51	13.69	7.99	9.83	8.99	7.8	9.63	0.376	10.50	8.81	0.84	4.93	6.45	8.38	8.52	6.73	4.63	0.987	6.59	6.63	1.01			
203	Glia-derived nexin	GDN_MOUSE	44	14.48	6.24	6.89	9.87	7.8	9.63	0.968	9.20	9.10	0.99	4.93	10.09	6.27	6.02	3.87	4.63	0.401	7.10	4.84	0.68			
63	Gelsolin	GELS_MOUSE	86	31.92	28.94	18.67	14.31	22.26	18.25	0.243	26.51	18.27	0.69	19.68	28.27	23.13	34.85	32.52	28.22	0.145	23.69	31.86	1.34			
287	Growth hormone receptor	GHR_MOUSE	73	5.76	5.37	5.91	6.32	6.95	4.45	0.823	5.68	5.91	1.04	5.92	2.82	5.21	7.27	5.3	13.7	0.205	4.65	8.76	1.88			
242	Beta-galactosidase-1-like protein	GLB1L_MOUSE	73	10.52	7.99	5.91	2.77	5.25	5.31	0.223	8.14	4.44	0.55	5.92	4.64	6.27	6.02	5.3	1	0.510	5.61	4.11	0.73			
286	Glutathione peroxidase 3	GPX3_MOUSE	25	4.17	4.49	7.87	5.44	6.95	7.04	0.421	5.51	6.48	1.18	2.97	4.64	2.05	6.02	12.46	8.26	0.056	3.22	8.91	2.77	X		
34	Granulins	GRN_MOUSE	63	28.75	40.29	39.28	37.38	38.42	31.19	0.936	36.11	35.66	0.99	46.24	45.54	50.52	44.88	52.57	51.81	0.448	47.43	49.75	1.05			
656	78 glucose-regulated protein	GRP78_MOUSE	72	1	1	1	1	4.4	1	0.423	1.00	2.13	2.13	1	1	1	2.25	1	1	0.423	1.00	1.42	1.42			
40	Heat shock cognate 71 protein	HSP7C_MOUSE	71	54.13	34.18	36.34	44.48	29.06	33.78	0.108	41.55	35.77	0.86	41.32	31.9	37.88	38.61	19.62	50	0.905	37.03	36.08	0.97			
135	Serine protease HTRA1	HTRA1_MOUSE	51	11.31	9.73	13.76	12.54	18.01	13.94	0.332	11.60	14.83	1.28	9.85	10.09	7.32	6.02	25.35	4.63	0.684	9.09	12.00	1.32			
37	Insulin-like growth factor-binding protein 2	IBP2_MOUSE	33	28.75	35.93	32.41	45.37	39.27	47.58	0.108	32.36	44.07	1.36	51.15	39.17	36.82	52.4	39.68	51.81	0.357	42.38	47.96	1.13			
362	Insulin-like growth factor-binding protein 3	IBP3_MOUSE	32	3.38	2.75	2.96	5.44	4.4	7.04	0.074	3.03	5.63	1.86	4.93	1.91	5.21	3.51	1	1	0.167	4.02	1.84	0.46			
54	Insulin-like growth factor-binding protein 4	IBP4_MOUSE	28	22.41	27.2	37.32	25.85	31.61	28.6	0.952	28.98	28.69	0.99	23.62	22.81	29.45	17.3	32.52	37.29	0.537	25.29	29.04	1.15			
55	Plasma protease C1 inhibitor	IC1_MOUSE	56	21.62	25.45	34.37	24.07	22.26	34.64	0.933	27.15	26.99	0.99	23.62	29.18	38.93	28.58	43.98	42.74	0.153	30.58	38.43	1.26			
88	Intercellular adhesion molecule 1	ICAM1_MOUSE	59	20.03	20.21	23.58	21.41	17.16	19.98	0.381	21.27	19.52	0.92	20.67	13.72	19.97	23.57	25.35	30.04	0.093	18.12	26.32	1.45			
234	Interleukin-1 receptor accessory protein	IL1AP_MOUSE	66	5.76	4.49	5.91	5.44	6.95	6.18	0.442	5.39	6.19	1.15	6.9	5.54	6.27	4.76	5.3	2.81	0.173	6.24	4.29	0.69	X		
299	Interleukin-6 receptor subunit beta	IL6RB_MOUSE	102	5.76	7.11	4.93	4.55	6.1	4.45	0.054	5.93	5.03	0.85	7.88	6.45	6.27	3.51	3.87	4.63	0.070	6.87	4.00	0.58			
232	Interferon-alpha/beta receptor beta chain	INAR2_MOUSE	57	2.59	6.24	8.85	4.55	4.4	7.04	0.699	5.89	5.33	0.90	6.9	6.45	10.48	8.52	12.46	26.41	0.205	7.94	15.80	1.99			
354	Inhibin beta B chain	INHBB_MOUSE	45	3.38	5.37	2.96	2.77	1.85	1.86	0.192	3.90	2.16	0.55	5.92	2.82	4.16	3.51	6.73	10.07							

263	Immunoglobulin superfamily containing leucine-rich repeat protein	ISLR_MOUSE	46	4.96	5.37	5.91	5.44	3.55	3.59	0.293	5.41	4.19	0.77	6.9	5.54	5.21	6.02	11.03	8.26	0.303	5.88	8.44	1.43		
483	Integrin beta-1	ITB1_MOUSE	88	3.38	1	1	2.77	2.7	1	0.652	1.79	2.16	1.20	3.95	1.91	1	4.76	3.87	2.81	0.052	2.29	3.81	1.67	X	X
479	Integrin beta-like protein 1	ITGBL_MOUSE	54	3.38	4.49	2.96	2.77	4.4	3.59	0.954	3.61	3.59	0.99	1.98	1.91	3.11	2.25	1	1	0.314	2.33	1.42	0.61		
620	Inter-alpha-trypsin inhibitor heavy chain H2	ITIH2_MOUSE	106	4.17	1	1.98	3.66	1	1	0.221	2.38	1.89	0.79	1	1	1	1	1	4.63	0.423	1.00	2.21	2.21		
270	Laminin subunit alpha-2	LAMA2_MOUSE	343	1.79	9.73	4.93	3.66	3.55	7.04	0.813	5.48	4.75	0.87	1	17.36	1	1	1	1	0.423	6.45	1.00	0.15		
157	Laminin subunit alpha-4	LAMA4_MOUSE	202	3.38	17.59	13.76	13.42	9.5	17.39	0.759	11.58	13.44	1.16	4.93	27.36	6.27	2.25	2.43	1	0.259	12.85	1.89	0.15		
258	Laminin subunit beta-1	LAMB1_MOUSE	197	3.38	8.86	5.91	7.21	7.8	6.18	0.559	6.05	7.06	1.17	3.95	8.27	10.48	3.51	3.87	1	0.210	7.57	2.79	0.37		
97	Laminin subunit gamma-1	LAMC1_MOUSE	177	7.34	20.21	16.71	26.74	23.11	22.57	0.206	14.75	24.14	1.64	14.77	29.18	18.91	13.54	6.73	4.63	0.177	20.95	8.30	0.40	X	X
357	Low-density lipoprotein receptor	LDLR_MOUSE	95	1.79	5.37	9.83	1.89	3.55	8.76	0.238	5.66	4.73	0.84	1	1.91	5.21	1	1	1	0.314	2.71	1.00	0.37		
424	Galectin-3	LEG3_MOUSE	28	1.79	1.87	1.98	3.66	1	2.73	0.540	1.88	2.46	1.31	3.95	1	6.27	1	1	6.44	0.457	3.74	2.81	0.75		
44	Galectin-3-binding protein	LG3BP_MOUSE	64	27.96	37.67	41.24	19.64	19.71	40.68	0.217	35.62	26.68	0.75	36.4	41.9	50.52	41.12	54.01	64.52	0.068	42.94	53.22	1.24		
512	Leucine-rich repeat LGI family member 2	LGI2_MOUSE	63	2.59	8.86	2.96	2.77	4.4	1	0.261	4.80	2.72	0.57	1	1.91	1	1	1	1	0.423	1.30	1.00	0.77	X	X
655	Leukemia inhibitory factor receptor	LIFR_MOUSE	123	1	1	1	1	1.85	3.59	0.271	1.00	2.15	2.15	1	1	1	1	1	1	NA	1.00	1.00	1.00		
73	Lysyl oxidase homolog 1	LOXL1_MOUSE	67	11.31	21.08	16.71	16.09	20.56	22.57	0.229	16.37	19.74	1.21	21.65	39.17	30.5	9.78	21.06	24.59	0.077	30.44	18.48	0.61		
84	Lysyl oxidase homolog 3	LOXL3_MOUSE	84	18.44	16.72	22.59	17.86	12.91	22.57	0.339	19.25	17.78	0.92	16.73	19.18	17.86	19.81	29.65	24.59	0.087	17.92	24.68	1.38		
75	Latent-transforming growth factor beta-binding protein 2	LTBP2_MOUSE	196	24.79	25.45	10.82	23.19	16.31	18.25	0.839	20.35	19.25	0.95	30.5	20.09	12.59	34.85	36.82	4.63	0.602	21.06	25.43	1.21		
128	Latent-transforming growth factor beta-binding protein 4	LTBP4_MOUSE	179	15.27	13.22	15.72	6.32	9.5	2.73	0.086	14.74	6.18	0.42	15.75	11.91	10.48	24.82	29.65	2.81	0.482	12.71	19.09	1.50		
87	Lumican	LUM_MOUSE	38	13.69	19.34	15.72	8.99	14.61	16.53	0.259	16.25	13.38	0.82	12.8	22.81	24.18	22.31	46.84	20.96	0.328	19.93	30.04	1.51		
92	Protein-lysine 6-oxidase	LYOX_MOUSE	47	14.48	16.72	14.74	17.86	21.41	24.29	0.089	15.31	21.19	1.38	11.82	19.18	27.34	11.03	15.33	17.33	0.213	19.45	14.56	0.75		X
215	Lysozyme C-2	LYZ2_MOUSE	17	8.14	7.11	5.91	6.32	5.25	7.04	0.481	7.05	6.20	0.88	13.78	6.45	8.38	8.52	9.6	15.52	0.691	9.54	11.21	1.18		
338	Epididymis-specific alpha-mannosidase	MA2B2_MOUSE	116	2.59	3.62	1	1.89	4.4	6.18	0.425	2.40	4.16	1.73	6.9	7.36	7.32	7.27	2.43	6.44	0.375	7.19	5.38	0.75		
202	Microfibrillar-associated protein 5	MFAP5_MOUSE	19	3.38	4.49	5.91	9.87	7.8	5.31	0.273	4.59	7.66	1.67	9.85	5.54	10.48	8.52	8.16	6.44	0.682	8.62	7.71	0.89		
49	Lactadherin	MFGM_MOUSE	51	20.82	32.43	21.61	33.83	26.51	24.29	0.612	24.95	28.21	1.13	38.37	43.72	43.15	38.61	49.71	42.74	0.441	41.75	43.69	1.05		
532	Macrophage migration inhibitory factor	MIF_MOUSE	13	1	1	1	1.89	2.7	1	0.221	1.00	1.86	1.86	4.93	3.73	1	4.76	3.87	1	0.921	3.22	3.21	1.00		
251	Mimecan	MIME_MOUSE	34	8.14	3.62	6.89	5.44	5.25	6.18	0.682	6.22	5.62	0.90	2.97	1.91	3.11	7.27	1	4.63	0.390	2.66	4.30	1.61		
138	Macrophage metalloelastase	MMP12_MOUSE	55	17.65	9.73	4.93	16.97	6.95	7.04	0.781	10.77	10.32	0.96	20.67	5.54	6.27	14.79	5.3	8.26	0.616	10.83	9.45	0.87		
474	Neutrophil collagenase	MMP8_MOUSE	53	1	1.87	1	1.89	1	1	0.991	1.29	1.30	1.01	3.95	1	2.05	1	6.73	1	0.847	2.33	2.91	1.25		
443	Mesothelin	MSLN_MOUSE	69	1.79	1	7.87	1.89	1	7.04	0.496	3.55	3.31	0.93	1	1	9.43	1	1	6.44	0.423	3.81	2.81	0.74		
435	Beta-nerve growth factor	NGF_MOUSE	27	2.59	5.37	2.96	3.66	3.55	3.59	0.969	3.64	3.60	0.99	2.97	1	2.05	1	1	4.63	0.892	2.01	2.21	1.10		
107	Nidogen-2	NID2_MOUSE	154	9.72	4.49	11.8	6.32	11.2	12.21	0.715	8.67	9.91	1.14	11.82	7.36	12.59	41.12	68.33	15.52	0.205	10.59	41.66	3.93	X	X
259	Protein NOV homolog	NOV_MOUSE	39	5.76	7.11	2.96	1	4.4	1.86	0.114	5.28	2.42	0.46	8.87	11.91	6.27	11.03	11.03	4.63	0.927	9.02	8.90	0.99		
144	Epididymal secretory protein E1	NPC2_MOUSE	16	7.34	8.86	10.82	11.65	10.35	8.76	0.568	9.01	10.25	1.14	16.73	9.18	9.43	9.78	11.03	11.89	0.799	11.78	10.90	0.93		
536	Nephronectin	NPNT_MOUSE	61	4.17	1	1	2.77	4.4	1	0.686	2.06	2.72	1.32	4.93	2.82	2.05	1	1	1	0.119	3.27	1.00	0.31		
174	Olfactomedin-like protein 3	OLFE3_MOUSE	46	5.76	10.6	12.78	7.21	14.61	12.21	0.344	9.71	11.34	1.17	9.85	8.27	6.27	4.76	9.6	4.63	0.434	8.13	6.33	0.78		
642	Olfactomedin-like protein 2B	OLM2B_MOUSE	84	1	1	1	1	3.55	1	0.423	1.00	1.85	1.85	1	1	1	1	1	NA	1.00	1.00	1.00			
205	Group XV phospholipase A2	PAG15_MOUSE	47	4.96	7.11	10.82	8.1	8.65	9.63	0.455	7.63	8.79	1.15	7.88	10.09	5.21	3.51	9.6	6.44	0.541	7.73	6.52	0.84		
9	Plasminogen activator inhibitor 1	PAI1_MOUSE	45	113.59	131.1	153.14	134.11	140.46	158	0.131	132.61	144.19	1.09	154.41	161.88	180.12	167.75	218.76	242.36	0.104	165.47	209.62	1.27		
467	Inactive serine protease PAMR1	PAMR1_MOUSE	80	4.96	1	4.93	1	1	1	0.184	3.63	1.00	0.28	5.92	1	3.11	2.25	1	1	0.212	3.34	1.42	0.42		
70	Procollagen C-endopeptidase enhancer 1	PCOC1_MOUSE	50	27.17	21.08	33.39	16.09	27.36	20.84	0.440	27.21	21.43	0.79	22.64	21	29.45	27.33	25.35	30.04	0.135	24.36	27.57	1.13		
604	Proprotein convertase subtilisin/kexin type 9	PCSK9_MOUSE	75	1	1	1	2.77	1.85	1.86	0.063	1.00	2.16	2.16	3.95	2.82	1	1	1	1	0.205	2.59	1.00	0.39		
223	Platelet-derived growth factor D	PDGFD_MOUSE	43	6.55	5.37	6.89	6.32	5.25	6.18	0.190	6.27	5.92	0.94	6.9	11.91	8.38	4.76	3.87	4.63	0.119	9.06	4.42	0.49		
246	Phosphatidylethanolamine-binding protein 1	PEBP1_MOUSE	21	4.96	4.49	2.96	3.66	3.55	2.73	0.120	4.14	3.31	0.80	10.83	8.27	9.43	11.03	11.03	10.07	0.268	9.51	10.71	1.13		
47	Pigment epithelium-derived factor	PEDF_MOUSE	46	38.27	33.31	24.56	32.06	34.17	25.15	0.564	32.05	30.46	0.95	27.55	31.9	31.56	34.85	69.77	42.74</						

514	Retinoic acid receptor responder protein 2	RARR2_MOUSE	18	2.59	2.75	2.96	2.77	2.7	2.73	0.805	2.77	2.73	0.99	2.97	2.82	3.11	1	2.43	4.63	0.807	2.97	2.69	0.91
311	Ribonuclease 4	RNAS4_MOUSE	17	2.59	4.49	4.93	3.66	3.55	4.45	0.866	4.00	3.89	0.97	8.87	7.36	5.21	7.27	6.73	4.63	0.106	7.15	6.21	0.87
462	Semaphorin-3A	SEM3A_MOUSE	89	2.59	1.87	4.93	1	3.55	4.45	0.905	3.13	3.00	0.96	1.98	1.91	4.16	1	3.87	10.07	0.369	2.68	4.98	1.86
565	Semaphorin-3C	SEM3C_MOUSE	85	1	1	1	1.89	1	5.31	0.318	1.00	2.73	2.73	2.97	4.64	1	1	1	1	0.217	2.87	1.00	0.35
279	Semaphorin-3D	SEM3D_MOUSE	90	2.59	12.35	6.89	1	11.2	10.49	0.879	7.28	7.56	1.04	8.87	7.36	6.27	1	6.73	2.81	0.199	7.50	3.51	0.47
193	Semaphorin-3E	SEM3E_MOUSE	90	1	7.11	12.78	5.44	4.4	13.08	0.775	6.96	7.64	1.10	19.68	9.18	6.27	6.02	5.3	15.52	0.718	11.71	8.95	0.76
161	Semaphorin-3F	SEM3F_MOUSE	88	4.17	13.22	14.74	4.55	15.46	10.49	0.805	10.71	10.17	0.95	7.88	10.09	13.64	7.27	8.16	24.59	0.564	10.54	13.34	1.27
341	Secreted frizzled-related protein 3	SFRP3_MOUSE	36	4.96	2.75	6.89	5.44	6.95	3.59	0.851	4.87	5.33	1.09	2.97	4.64	1	3.51	1	1	0.514	2.87	1.84	0.64
444	Slit homolog 2 protein	SLIT2_MOUSE	169	8.93	1	1	3.66	5.25	1	0.913	3.64	3.30	0.91	5.92	2.82	1	1	1	1	0.258	3.25	1.00	0.31
214	Slit homolog 3 protein	SLIT3_MOUSE	168	3.38	7.11	7.87	8.1	8.65	9.63	0.121	6.12	8.79	1.44	4.93	8.27	8.38	6.02	2.43	11.89	0.896	7.19	6.78	0.94
90	Superoxide dismutase [Cu-Zn]	SODC_MOUSE	16	16.86	14.1	17.69	22.3	16.31	18.25	0.196	16.22	18.95	1.17	20.67	11	17.86	24.82	23.92	22.78	0.120	16.51	23.84	1.44
41	Extracellular superoxide dismutase [Cu-Zn]	SODE_MOUSE	27	35.89	46.41	47.13	33.83	33.31	45.86	0.288	43.14	37.67	0.87	28.54	25.54	43.15	16.05	39.68	44.55	0.907	32.41	33.43	1.03
24	Serine protease inhibitor A3N	SPA3N_MOUSE	47	77.91	56.88	54.01	43.6	45.22	59.66	0.365	62.93	49.49	0.79	54.1	77.35	68.43	120.11	119.91	93.55	0.064	66.63	111.19	1.67
22	Sushi, von Willebrand factor type A, EGF and pentraxin domain-containing protein 1	SVEP1_MOUSE	387	94.56	81.33	66.77	72.88	72.43	58.8	0.101	80.89	68.04	0.84	53.12	79.17	36.82	53.66	65.47	13.7	0.221	56.37	44.28	0.79
79	Transcobalamin-2	TCO2_MOUSE	48	20.03	15.84	17.69	20.52	18.01	19.12	0.107	17.85	19.22	1.08	15.75	19.18	16.8	14.79	26.79	26.41	0.237	17.24	22.66	1.31
545	Translationaly-controlled tumor protein	TCTP_MOUSE	19	4.17	2.75	1	1	2.7	2.73	0.762	2.64	2.14	0.81	1.98	1	3.11	3.51	1	1	0.872	2.03	1.84	0.90
132	Tenascin	TENA_MOUSE	232	2.59	21.08	3.94	13.42	18.01	13.94	0.319	9.20	15.12	1.64	14.77	30.09	1	19.81	9.6	1	0.577	15.29	10.14	0.66
340	Tissue factor pathway inhibitor	TFP1_MOUSE	35	2.59	7.11	2.96	5.44	6.1	4.45	0.430	4.22	5.33	1.26	4.93	4.64	5.21	4.76	1	6.44	0.613	4.93	4.07	0.83
257	Transforming growth factor beta-2	TGFB2_MOUSE	48	4.96	5.37	9.83	6.32	6.1	8.76	0.686	6.72	7.06	1.05	2.97	5.54	5.21	3.51	1	1	0.237	4.57	1.84	0.40
556	Protein-glutamine gamma-glutamyltransferase 2	TGM2_MOUSE	77	1	1	1.98	4.55	4.4	1.86	0.198	1.33	3.60	2.72	1.98	1	2.05	1	1	2.81	0.898	1.68	1.60	0.96
463	Thioredoxin OS=Mus musculus GN=Txn PE=1 SV=3	THIO_MOUSE	12	1	3.62	2.96	5.44	2.7	6.18	0.300	2.53	4.77	1.89	1.98	1.91	2.05	2.25	1	4.63	0.593	1.98	2.63	1.33
50	Metalloproteinase inhibitor 1	TIMP1_MOUSE	23	12.89	21.08	34.37	20.52	18.86	24.29	0.790	22.78	21.22	0.93	48.2	38.27	48.41	43.63	45.41	46.37	0.965	44.96	45.14	1.00
45	Metalloproteinase inhibitor 2	TIMP2_MOUSE	24	31.92	35.05	45.17	34.72	32.46	39.82	0.548	37.38	35.67	0.95	31.49	21.91	29.45	36.11	39.68	57.26	0.130	27.62	44.35	1.61
450	Metalloproteinase inhibitor 3 OS=Mus musculus GN=Timp3 PE=2 SV=1	TIMP3_MOUSE	24	4.96	1.87	1	1.89	6.1	1	0.872	2.61	3.00	1.15	4.93	2.82	2.05	1	1	1	0.119	3.27	1.00	0.31
416	Tubulointerstitial nephritis antigen-like	TINAL_MOUSE	53	1	2.75	5.91	1	4.4	6.18	0.337	3.22	3.86	1.20	1.98	4.64	9.43	1	1	1	0.184	5.35	1.00	0.19
466	Tumor necrosis factor receptor superfamily member 11B	TR11B_MOUSE	46	4.96	4.49	1	3.66	6.95	4.45	0.399	3.48	5.02	1.44	1	4.64	1	1	1	1	0.423	2.21	1.00	0.45
15	Serotransferrin	TRFE_MOUSE	77	51.75	54.26	181.61	43.6	64.78	118.32	0.456	95.87	75.57	0.79	69.84	83.71	142.19	83.75	144.26	258.69	0.165	98.58	162.23	1.65
301	Thrombospondin-2	TSP2_MOUSE	130	4.96	5.37	1.98	4.55	6.1	1	0.704	4.10	3.88	0.95	2.97	5.54	1	14.79	6.73	1	0.368	3.17	7.51	2.37
636	Thrombospondin-3	TSP3_MOUSE	104	1	1	1	1	1	1 NA	1.00	1.00	1.00	1.98	1.91	1	1	3.87	1	1	0.742	1.63	1.96	1.20
28	Vascular cell adhesion protein 1	VCAM1_MOUSE	81	46.2	36.8	48.12	49.81	42.67	47.58	0.253	43.71	46.69	1.07	54.1	50.99	75.81	68.7	74.06	75.4	0.212	60.30	72.72	1.21
272	Vascular endothelial growth factor A	VEGFA_MOUSE	25	3.38	2.75	2.96	2.77	5.25	1.86	0.837	3.03	3.29	1.09	4.93	8.27	4.16	1	8.16	2.81	0.251	5.79	3.99	0.69 X X X
118	Vascular endothelial growth factor D	VEGFD_MOUSE	41	10.52	23.7	17.69	12.54	13.76	19.12	0.634	17.30	15.14	0.87	6.9	10.09	14.7	14.79	22.49	19.15	0.070	10.56	18.81	1.78
550	Pantetheinase OS=Mus musculus GN=Vnn1 PE=1 SV=2	VNN1_MOUSE	57	1	1	2.96	1	1	2.73	0.423	1.65	1.58	0.95	9.85	1	1	6.02	1	1	0.423	3.95	2.67	0.68
607	von Willebrand factor	VWF_MOUSE	309	4.96	1	1	3.66	1	1	0.423	2.32	1.89	0.81	1	1	1	3.51	1	1	0.423	1.00	1.84	1.84
611	WNT1-inducible-signaling pathway protein 1	WISP1_MOUSE	41	1	2.75	1	1	3.55	1.86	0.184	1.58	2.14	1.35	1	1.91	1	1	1	1	0.423	1.30	1.00	0.77 X
82	WNT1-inducible-signaling pathway protein 2	WISP2_MOUSE	27	9.72	17.59	9.83	10.76	17.16	16.53	0.379	12.38	14.82	1.20	30.5	16.45	17.86	19.81	19.62	11.89	0.384	21.60	17.11	0.79
349	C-C motif chemokine 2	CCL2_MOUSE	16	1.79	2.75	1	2.77	3.55	4.45	0.178	1.85	3.59	1.94	3.95	4.64	5.21	2.25	2.43	1	0.072	4.60	1.89	0.41
105	Complement C4-B	CO4B_MOUSE	193	14.48	16.72	17.69	10.76	19.71	22.57	0.649	16.30	17.68	1.08	15.75	17.36	18.91	13.54	12.46	8.26	0.140	17.34	11.42	0.66

Online-Table III: ECM proteins changes in the secretome of CFs following miR-30c transfection

#	Identified Proteins	Accession Number	MW (kDa)	Control	Control	Anti	Control	Anti	Anti-miR-30c	Anti-miR-30c	Anti-miR-30c	Anti-miR-30c	Average		Control	Control	Pre	Control	Pre-miR-30c	Pre-miR-30c	Pre-miR-30c	Average		Average		TargetScan	PicTar	Diana		
				Anti-miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR	miR				miR	miR
228	Collagen alpha-1(XI) chain	COBA1_MOUSE	181	10.44	11.74	16.16	10.34	14.37	9.72	0.676	12.78	11.48	0.90	29.5	25.37	23.61	15.2	13.45	9.48	0.003	26.16	12.71	0.49							
173	Calumenin	CALU_MOUSE	37	11.62	2.79	8.58	1	4.34	1	0.268	7.66	2.11	0.28	13.83	36.74	12.9	5.73	3.77	3.12	0.169	21.16	4.21	0.20	X						
66	Collagen alpha-1(V) chain	COSA1_MOUSE	184	24.6	26.07	22.22	19.68	24.4	19.69	0.089	24.30	21.26	0.87	45.18	41.61	31.94	60.18	48.02	48.68	0.058	39.58	52.29	1.32							
5	Collagen alpha-2(V) chain	COSA2_MOUSE	145	134.34	182.74	134.37	103.75	163.68	170.46	0.847	150.48	145.96	0.97	315.93	272.31	269.98	177.35	169.71	191.71	0.026	286.07	179.59	0.63							
170	Collagen alpha-1(XV) chain	COFA1_MOUSE	140	22.24	9.06	17.67	17.01	8.8	14.71	0.189	16.32	13.51	0.83	18.1	10.75	14.09	19.94	14.83	6.3	0.880	14.31	13.69	0.96							
455	Leukemia inhibitory factor	LIF_MOUSE	22	1	1	1	1	1	1	NA	1.00	1.00	1.00	10.98	10.75	2.19	4.55	5.15	2.06	0.177	7.97	3.92	0.49							
	Scavenger receptor cysteine-rich domain-containing																													
402	protein LOC284297 homolog	SRCLR_MOUSE	145	4.54	3.69	4.03	7.67	6.57	3.49	0.263	4.09	5.91	1.45	15.25	4.25	8.14	6.92	6.53	6.3	0.484	9.21	6.58	0.71							
393	Placenta-specific protein 9	PLAC9_MOUSE	11	3.36	4.58	1	1	3.23	1	0.212	2.98	1.74	0.59	6.7	9.12	4.57	1	1	1	0.048	6.80	1.00	0.15							
3	Collagen alpha-1(III) chain	CO3A1_MOUSE	139	377.43	314.35	472.34	354.6	309.64	341.16	0.312	388.04	335.13	0.86	485.51	504.62	391.38	422.34	443.51	394.08	0.202	460.50	419.98	0.91							
148	Laminin subunit alpha-4	LAMA4_MOUSE	202	13.98	20.7	25.25	9.01	8.8	7.23	0.091	19.98	8.35	0.42	2.43	18.87	3.38	8.1	9.3	9.48	0.900	8.23	8.96	1.09							
454	Latent-transforming growth factor beta-binding protein 1	LTBP1_MOUSE	187	4.54	2.79	1	6.34	3.23	1	0.302	2.78	3.52	1.27	6.7	5.87	3.38	3.37	2.38	2.06	0.060	5.32	2.60	0.49							
127	Coiled-coil domain-containing protein 80	CCD80_MOUSE	108	13.98	30.54	14.64	13.01	23.28	18.44	0.690	19.72	18.24	0.93	30.93	7.5	22.42	2.18	5.15	10.54	0.205	20.28	5.96	0.29							
1	Collagen alpha-1(I) chain	CO1A1_MOUSE	138	380.97	330.46	493.56	331.92	291.81	331.19	0.170	401.66	318.31	0.79	616.61	543.61	525.87	388.01	496.06	427.98	0.147	562.03	437.35	0.78							
48	Collagen alpha-2(IV) chain	CO4A1_MOUSE	161	15.16	15.32	10.09	11.67	14.37	14.71	0.982	13.52	13.58	1.00	23.8	22.12	21.23	16.39	21.74	24.31	0.662	22.38	20.81	0.93							
7	SPARC	SPRC_MOUSE	34	251.17	114.7	313.2	269.21	221.62	215.31	0.893	226.36	235.38	1.04	261.78	319.42	204.52	259.01	288.63	207.61	0.434	261.91	251.75	0.96							
167	Collagen alpha-1(VIII) chain	CO8A1_MOUSE	74	3.36	7.27	4.03	2.33	5.46	1	0.078	4.89	2.93	0.60	3.85	2.62	5.76	1	5.24		0.132	4.08	2.41	0.59							
12	Follistatin-related protein 1	FSTL1_MOUSE	35	127.26	70.83	176.8	151.78	112.42	121.86	0.912	124.96	128.69	1.03	154.9	160.21	109.31	140.66	137.9	87.88	0.017	141.47	122.15	0.86							
321	Follistatin-related protein 3	FSTL3_MOUSE	27	4.54	2.79	5.55	5	6.57	7.23	0.179	4.29	6.27	1.46	3.85	2.62	4.57	3.37	2.38	1	0.314	3.68	2.25	0.61							
340	Ribonuclease T2	RNT2_MOUSE	30	5.72	4.58	5.55	5	7.69	4.74	0.723	5.28	5.81	1.10	6.7	7.5	4.57	4.55	5.15	4.18	0.120	6.26	4.63	0.74							
594	Proteoglycan 4	PRG4_MOUSE	116	2.18	2.79	4.03	3.67	2.11	3.49	0.910	3.00	3.09	1.03	5.28	4.25	1	3.37	1		0.299	3.51	2.71	0.77							
	Disintegrin and metalloproteinase domain-containing																													
436	protein 17	ADA17_MOUSE	93	3.36	1.9	4.03	3.67	3.23	3.49	0.568	3.10	3.46	1.12	1	4.25	4.57	3.37	3.77	1	0.775	3.27	2.71	0.83							
96	Protein-lysine 6-oxidase	LYOX_MOUSE	47	17.52	12.64	22.22	22.35	15.49	17.2	0.796	17.46	18.35	1.05	19.53	23.74	20.04	9.28	10.68	10.54	0.010	21.10	10.17	0.48							
525	Antithrombin-III	ANT3_MOUSE	52	5.72	1.9	1	3.67	3.23	5.98	0.557	2.87	4.29	1.49	3.85	7.5	2.19	1	3.77	5.24	0.636	4.51	3.34	0.74							
366	Secreted frizzled-related protein 1	SFRP1_MOUSE	35	8.08	11.74	2.52	3.67	8.8	7.23	0.785	7.45	6.57	0.88	6.7	9.12	5.76	3.37	5.15	1	0.010	7.19	3.17	0.44							
2	Collagen alpha-2(I) chain	CO2A1_MOUSE	130	296.01	274.95	352.61	322.58	269.53	323.73	0.887	307.86	305.28	0.99	499.76	399.02	369.96	345.41	431.06	360.18	0.517	422.91	378.88	0.90							
162	Integrin beta-1	ITB1_MOUSE	88	22.24	9.95	20.7	19.68	12.14	12.21	0.440	17.63	14.68	0.83	18.1	20.5	11.71	19.94	25.89	12.65	0.183	16.77	19.49	1.16							
233	Gamma-glutamyl hydrolase	GGH_MOUSE	35	5.72	9.06	13.12	11.67	9.91	8.48	0.836	9.30	10.02	1.08	9.55	14	6.95	5.73	3.77	5.24	0.177	10.17	4.91	0.48							
193	Microfibrillar-associated protein 5	MFAP5_MOUSE	19	12.8	6.37	8.58	9.01	6.57	5.98	0.223	9.25	7.19	0.78	13.83	14	9.33	9.28	6.53	6.3	0.061	12.39	7.37	0.59							
19	Insulin-like growth factor-binding protein 7	IBP7_MOUSE	29	93.04	83.37	61.62	95.74	87.91	100.68	0.322	79.34	94.78	1.19	90.78	85.48	98.6	89.76	95.03	108.01	0.230	91.62	97.60	1.07							
414	Angiopoietin-2	ANGP2_MOUSE	57	11.62	1.9	5.55	10.34	2.11	3.49	0.258	6.36	5.31	0.84	3.85	2.62	1	5.73	2.38	1	0.500	2.49	3.04	1.22							
10	Collagen alpha-2(IV) chain	CO4A2_MOUSE	167	30.5	37.71	40.4	42.37	22.17	62.05	0.644	36.20	42.20	1.17	87.93	65.98	104.55	35.32	34.19	68.81	0.024	86.15	46.11	0.54							
51	Prolargin	PRELP_MOUSE	43	56.46	56.51	43.44	46.37	38.88	43.06	0.210	52.14	42.87	0.82	33.78	23.74	28.77	30.59	27.27	26.43	0.820	28.63	28.10	0.98							
54	Collagen alpha-2(VI) chain	CO6A2_MOUSE	110	48.2	66.35	31.31	37.03	43.34	35.89	0.342	48.62	38.75	0.80	26.65	36.74	23.61	37.69	25.89	25.37	0.928	29.00	29.65	1.02							
375	Receptor-type tyrosine-protein phosphatase gamma	PTPRG_MOUSE	161	4.54	1.9	2.52	1	1	3.49	0.470	2.99	1.83	0.61	1	2.62	3.38	3.37	2.38	6.3	0.226	2.33	4.02	1.72							
142	Epididymal secretory protein E1	NPC2_MOUSE	16	12.8	6.37	7.06	15.68	9.91	7.23	0.167	8.74	10.94	1.25	15.25	12.37	9.33	6.92	9.3	7.36	0.151	12.32	7.86	0.64							
101	Dystroglycan	DAG1_MOUSE	97	15.16	11.74	16.16	10.34	15.49	12.21	0.602	14.35 </																			

492	Metalloproteinase inhibitor 3	TIMP3_MOUSE	24	1	7.27	1	1	1	7.23	0.997	3.09	3.08	1.00	1	1	1	1	1	1	NA	1.00	1.00	1.00	X	X	X
350	Tetranectin	TTN_MOUSE	22	11.62	7.27	8.58	6.34	8.8	3.49	0.319	9.16	6.21	0.68	1	1	1	4.55	5.15	6.3	0.014	1.00	5.33	5.33			
554	Galectin-3	LEG3_MOUSE	28	1	1.9	1	1	1	2.25	0.869	1.30	1.42	1.09	1	1	1	1	1	1	NA	1.00	1.00	1.00			
397	BMP-binding endothelial regulator protein	BMPER_MOUSE	76	1	1.9	1	1	1	1	0.423	1.30	1.00	0.77	1	1	1	1	1	1	NA	1.00	1.00	1.00			
688	Proprotein convertase subtilisin/kexin type 9	PCSK9_MOUSE	75	1	1.9	1	1	1	1	0.423	1.30	1.00	0.77	1	1	1	1	1	1	NA	1.00	1.00	1.00			
528	Growth arrest-specific protein 6	GAS6_MOUSE	75	1	1.9	1	1	1	1	0.423	1.30	1.00	0.77	1	1	1	1	1	1	NA	1.00	1.00	1.00			
632	Collectin-11	COLL11_MOUSE	29	2.18	1	1	1	2.11	1	0.975	1.39	1.37	0.98	1	1	1	1	1	1	NA	1.00	1.00	1.00			
642	Nephronectin	NPNT_MOUSE	61	1	2.79	1	1	2.11	1	0.423	1.60	1.37	0.86	1	1	1	1	1	1	NA	1.00	1.00	1.00			
748	Protein FAM20A	FA20A_MOUSE	62	1	2.79	1	1	1	1	0.423	1.60	1.00	0.63	1	1	1	1	1	1	NA	1.00	1.00	1.00			
600	Inactive carboxypeptidase-like protein X2	CPXM2_MOUSE	87	1	3.69	1	1	2.11	1	0.423	1.90	1.37	0.72	1	1	1	1	1	1	NA	1.00	1.00	1.00			
544	ADAMTS-like protein 4	ATL4_MOUSE	113	2.18	1	2.52	2.33	1	1	0.482	1.90	1.44	0.76	1	1	1	1	1	1	NA	1.00	1.00	1.00			
348	CD109 antigen	CD109_MOUSE	162	1	4.58	1	1	1	1	0.423	2.19	1.00	0.46	1	1	1	1	1	1	NA	1.00	1.00	1.00			
699	Laminin subunit alpha-1	LAMA1_MOUSE	338	1	4.58	1	1	1	1	0.423	2.19	1.00	0.46	1	1	1	1	1	2.06	0.423	1.00	1.35	1.35			
332	Aggrin	AGRIN_MOUSE	208	5.72	6.37	1	2.33	14.37	13.46	0.351	4.36	10.05	2.30	1	1	1	3.37	1	3.12	0.185	1.00	2.50	2.50			
605	Growth-regulated alpha protein	GROA_MOUSE	10	3.36	2.79	1	1	2.11	1	0.285	2.38	1.37	0.57	1	1	1	1	1	1	NA	1.00	1.00	1.00			
482	Acid sphingomyelinase-like phosphodiesterase 3a	ASM3A_MOUSE	50	3.36	4.58	1	3.67	3.23	3.49	0.706	2.98	3.46	1.16	1	1	2.19	2.18	1	3.12	0.189	1.40	2.10	1.50			
18	Serine protease inhibitor A3N	SPAN3_MOUSE	47	121.36	92.32	119.21	117.09	100.17	90.71	0.518	110.96	102.66	0.93	95.05	82.23	67.65	79.11	100.56	47.62	0.677	81.64	75.76	0.93			
56	Metalloproteinase inhibitor 1	TIMP1_MOUSE	23	18.7	22.49	17.67	18.35	16.6	24.67	0.952	19.62	19.87	1.01	26.65	17.25	22.42	21.12	18.98	16.89	0.327	22.11	19.00	0.86			
230	Low-density lipoprotein receptor	LDLR_MOUSE	35	6.9	6.37	11.61	9.01	11.03	5.98	0.913	8.29	8.67	1.05	5.28	4.25	8.14	12.84	12.06	7.36	0.227	5.89	10.75	1.83			
41	Cathepsin B	CATB_MOUSE	37	38.76	28.75	25.25	29.7	28.86	23.43	0.783	30.92	30.66	0.99	40.9	30.24	40.28	29.4	34.19	23.25	0.322	37.14	28.95	0.78			
217	Laminin subunit alpha-2	LAMA2_MOUSE	343	5.72	35.02	1	2.33	3.23	1	0.365	13.91	2.19	1.16	3.85	1	3.38	4.55	2.38	28.55	0.376	2.74	11.83	4.31			
110	Clusterin	CLUS_MOUSE	52	15.16	11.74	14.64	17.01	14.37	12.21	0.706	14.53	10.5	0.15	19.53	17.25	11.71	17.57	7.91	6.3	0.121	16.16	10.59	0.66			
257	Phosphatidylethanolamine-binding protein 1	PEBP1_MOUSE	21	2.18	5.48	7.06	1	1	4.74	0.111	4.91	2.25	0.46	6.7	2.62	3.38	8.1	6.53	4.18	0.166	4.23	6.27	1.48			
68	Connective tissue growth factor	CTGF_MOUSE	38	12.8	22.49	29.8	25.02	27.74	30.9	0.197	21.70	27.89	1.29	12.4	22.12	16.47	11.65	13.45	13.71	0.230	17.00	12.94	0.76			
339	Tissue factor pathway inhibitor	TFP1_MOUSE	35	3.36	2.79	7.06	3.67	3.23	1	0.496	4.40	2.63	0.60	3.85	4.25	3.38	3.37	5.15	3.12	0.912	3.83	3.88	1.01			
221	Secreted frizzled-related protein 3	SFRP3_MOUSE	36	9.26	10.85	17.67	11.67	9.91	13.46	0.680	12.59	11.68	0.93	2.43	9.12	5.76	1	3.77	1	0.088	5.77	1.92	0.33	X		X
272	Ribonuclease 4	RNAS4_MOUSE	17	5.72	3.69	4.03	3.67	5.46	2.25	0.633	4.48	3.79	0.85	8.13	7.5	6.95	3.37	6.53	3.12	0.108	7.53	4.34	0.58			
28	Laminin subunit gamma-1	LAMC1_MOUSE	177	77.7	93.21	69.2	74.39	84.57	74.51	0.641	80.04	77.82	0.97	39.48	70.86	43.85	124.09	121.31	130.26	0.024	51.40	125.22	2.44			
281	Vascular endothelial growth factor C	VEGFC_MOUSE	46	8.08	3.69	10.09	9.01	9.91	7.23	0.642	7.29	7.12	1.20	6.7	7.5	3.38	6.92	5.15	3.12	0.419	5.86	5.06	0.86			
29	EMILIN-1	EMIL1_MOUSE	108	87.14	68.15	69.2	82.4	63.4	60.81	0.039	74.83	68.87	0.92	42.33	31.87	35.52	80.3	59.08	68.81	0.009	36.57	69.40	1.90			
8	Plasminogen activator inhibitor 1	PAI1_MOUSE	45	101.3	125.44	107.09	130.43	123.57	144.29	0.213	111.28	132.76	1.19	129.25	98.48	147.39	86.21	93.65	117.55	0.147	125.04	99.14	0.79	X		X
255	Collagen triple helix repeat-containing protein 1	CTHRL_MOUSE	26	5.72	5.48	4.03	5	5.46	4.74	0.983	5.08	5.07	1.00	3.85	2.62	3.38	3.37	3.77	3.12	0.814	3.28	3.42	1.04	X		
329	C-C motif chemokine 2	CCL2_MOUSE	16	5.72	3.69	4.03	6.34	3.23	3.49	0.767	4.48	4.35	0.97	2.43	1	3.38	1	5.15	3.12	0.677	2.27	3.09	1.36			
64	Insulin-like growth factor-binding protein 4	IBP4_MOUSE	28	22.24	16.22	25.25	27.69	23.28	18.44	0.707	21.24	23.14	1.09	18.1	17.25	15.28	14.02	17.59	9.48	0.224	16.88	13.70	0.81			
231	Vascular endothelial growth factor A	VEGFA_MOUSE	25	8.08	5.48	4.03	7.67	7.69	8.48	0.276	5.86	7.95	1.36	3.05	5.87	4.57	3.37	7.91	6.3	0.301	4.76	5.86	1.23			
90	Ceruloplasmin	CERU_MOUSE	121	8.08	11.74	5.55	11.67	2.11	7.23	0.758	8.46	7.00	0.83	30.93	2.62	54.56	3.37	1	38.08	0.180	29.37	14.15	0.48			
76	Haptoglobin	HPT_MOUSE	39	36.4	10.85	25.25	21.02	9.91	12.21	0.160	24.17	14.38	0.60	40.9	31.87	15.28	37.69	28.66	14.77	0.124	29.35	27.04	0.92			
449	Fetuin-B	FETUB_MOUSE	43	1	1	4.03	3.67	3.23	3.49	0.285	2.01	3.46	1.72	1	1	2.19	1	1	2.06	0.423	1.40	1.35	0.97			
530	Monocyte differentiation antigen CD14	CD14_MOUSE	39	2.18	1	5.55	1	1	3.49	0.212	2.91	1.83	0.63	1	1	2.19	1	1	1	0.423	1.40	1.00	0.72			
216	Neuroserpin	NEUS_MOUSE	46	13.98	9.95	5.55	3.67	16.6	4.74	0.790	9.83	8.34	0.85	1	4.25	8.14	6.92	5.15	4.18	0.770	4.46	5.42	1.21			
695	Angiotensin-converting enzyme	ACE_MOUSE	151	1	1	2.52	3.67	1	1	0.784	1.51	1.89	1.25	1	1	1	4.55	1	1	0.423	1.00	2.18	2.18			
652	Protein-glutamine gamma-glutamyltransferase 2	TGM2_MOUSE	77	1	1	1	1	1	1	NA	1.00	1.00	1.00	1	1	1	1	1	1	NA	1.00	1.00	1.00			
36	Cystatin-C	CYTC_MOUSE	16	30.5	29.65	29.8	30.36	21.06	28.41	0.329	29.98	26.61	0.89	36.63	28.62	29.56	37.69	27.27	29.61	0.919	31.60	31.52	1.00			
57	Metalloproteinase inhibitor 2	TIMP2_MOUSE	24	21.06	19.8	17.67	25.02	18.83	14.71	0.997	19.51	19.52	1.00	15.25	22.12	17.66	16.39	20.36	16.89	0.641	18.34	17.88	0.97	X		
244	Protein FAM3C	FAM3C_MOUSE	25	3.36	1	4.03	7.67	2.11	4.74	0.215	2.80	4.84	1.73	6.7	4.25	8.14	3.37	1	3.12	0.022	6.36	2.50	0.39			
657	Complement factor I	CFAI_MOUSE	67	2.18	1.9	1	1	1	2.25	0.753	1.69	1.42	0.84	1	1	2.19	1	1	1	0.423	1.40	1.00	0.72			
112	Carboxypeptidase E	CPBE_MOUSE	53	17.52	30.54	14.64	9.01	17.71	14.71	0.202	20.90	13.81	0.66	10.98	7.5	9.33	14.02	13.45	11.6	0.079	9.27	13.02	1.40			
113	Cathepsin Z	CATZ_MOUSE	34	17.52	9.95	8.58	14.34	17.71	15.95	0.382	12.02	16.00	1.33	8.13	9.12	10.52	5.73	3.77	8.42	0.087	9.26	5.97	0.65			
102	Lysyl oxidase homolog 1	LOXL1_MOUSE	67	8.08	9.95	10.09	13.01	15.49</																		

570 Peroxiredoxin-4	PRDX4_MOUSE	31	6.9	3.69	1	1	4.34	8.48	0.865	3.86	4.61	1.19	1	1	1	12.84	1	13.71	0.184	1.00	9.18	9.18		
311 Epididymis-specific alpha-mannosidase	MA2B2_MOUSE	116	3.36	10.85	1	3.67	3.23	3.49	0.653	5.07	3.46	0.68	1	1	2.19	2.18	1	1	0.997	1.40	1.39	1.00		
97 Gelsolin	GELS_MOUSE	86	9.26	18.01	2.52	3.67	5.46	7.23	0.466	9.93	5.45	0.55	1	4.25	2.19	4.55	1	5.24	0.661	2.48	3.60	1.45		
117 Lysyl oxidase homolog 3	LOXL3_MOUSE	84	8.08	15.32	4.03	5	5.46	8.48	0.564	9.14	6.31	0.69	1	1	3.38	2.18	1	1	0.739	1.79	1.39	0.78		
474 Matrilin-2	MATN2_MOUSE	107	2.18	9.06	1	1	7.69	1	0.186	4.08	3.23	0.79	1	1	1	1	1	1	NA	1.00	1.00	1.00		
307 Complement factor B	CFAB_MOUSE	85	1	1	1	3.67	4.34	1	0.189	1.00	3.00	3.00	1	1	1	1	1	1	NA	1.00	1.00	1.00		
379 Angiotensin-converting enzyme 2	ANGL2_MOUSE	57	2.18	2.79	4.03	2.33	2.11	9.72	0.480	3.00	4.72	1.57	1	1	1	1	1	1	NA	1.00	1.00	1.00		
296 Pappalysin-1	PAPP1_MOUSE	181	6.9	3.69	1	6.34	3.23	5.98	0.546	3.86	5.18	1.34	1	1	1	1	1	1	NA	1.00	1.00	1.00		
99 Transcobalamin-2	TCO2_MOUSE	48	6.9	19.8	7.06	9.01	11.03	12.21	0.916	11.25	10.75	0.96	1	1	3.38	3.37	6.53	6.3	0.066	1.79	5.40	3.01		
181 Phospholipid transfer protein	PLTP_MOUSE	54	3.36	15.32	1	1	1	3.49	0.444	6.56	1.83	0.28	1	1	1	1	1	3.12	0.423	1.00	1.71	1.71		
22 Complement factor H	CFAH_MOUSE	139	21.06	47.55	7.06	15.68	12.14	14.71	0.478	25.22	14.18	0.56	2.43	1	17.66	14.02	1	5.24	0.972	7.03	6.75	0.96		
89 Nidogen-2	NID2_MOUSE	154	12.8	30.54	7.06	11.67	14.37	7.23	0.390	16.80	11.09	0.66	9.55	2.62	3.38	1	1	1	0.197	5.18	1.00	0.19	X	X
128 Complement C4-B	CO4B_MOUSE	193	2.18	10.85	1	14.34	16.6	7.23	0.060	4.68	12.72	2.72	1	1	2.19	2.18	1	6.3	0.286	1.40	3.16	2.26		
91 Collagen alpha-1(XII) chain	COCA1_MOUSE	340	3.36	6.37	1	1	5.46	3.49	0.873	3.58	3.32	0.93	1	2.62	6.95	1	1	1	0.291	3.52	1.00	0.28	X	
100 Fibulin-1	FBLN1_MOUSE	78	6.9	32.33	4.03	1	7.69	7.23	0.382	14.42	5.31	0.37	1	1	1	1	1	2.06	0.423	1.00	1.35	1.35		
203 Collagen alpha-1(XIV) chain	COEA1_MOUSE	193	6.9	11.74	1	1	5.46	3.49	0.376	6.55	3.32	0.51	1	2.62	1	1	1	1	0.423	1.54	1.00	0.65		
151 Thrombospondin-2	TSP2_MOUSE	130	5.72	14.43	11.61	6.34	24.4	8.48	0.589	10.59	13.07	1.23	1	1	1	1	1	1	NA	1.00	1.00	1.00	X	X

Online-Table IV: ECM proteins identified in the secretome of CFs after TGF-beta1 stimulation

#	Identified Proteins	Accession Number	Molecular Weight	Probability (ANOVA P-Value)	CTLPremiR1	CTLPremiR2	CTLPremiR3	CTLPremiR +TGFb1	CTLPremiR +TGFb2	CTLPremiR +TGFb3	PremiR29b +TGFb1	PremiR29b +TGFb2	PremiR29b +TGFb3	AVG CTL PremiR	STD CTL PremiR	AVG CTL PremiR +TGFb	STD CTL PremiR +TGFb	AVG PremiR29b +TGFb	STD PremiR29b +TGFb
1	Collagen alpha-2(I) chain OS=Mus musculus GN=Col1a2 PE=2 SV=2	CO1A2_MOUSE	130 kDa	95% (0.000016)	390.7	450.7	400.8	413.2	484.5	412.0	57.6	96.6	59.8	414.1	32.1	436.5	41.5	71.3	21.9
3	Collagen alpha-1(I) chain OS=Mus musculus GN=Col1a1 PE=1 SV=4	CO1A1_MOUSE	138 kDa	95% (0.000019)	309.6	362.3	353.6	368.3	383.4	365.0	56.1	70.5	80.3	341.9	28.3	372.2	9.8	69.0	12.2
7	Collagen alpha-1(III) chain OS=Mus musculus GN=Col3a1 PE=2 SV=4	CO3A1_MOUSE	139 kDa	95% (0.00000090)	268.3	271.1	249.7	202.1	193.6	183.6	14.7	15.2	13.2	263.0	11.6	193.1	9.2	14.4	1.0
6	Collagen alpha-2(V) chain OS=Mus musculus GN=Col5a2 PE=1 SV=1	CO5A2_MOUSE	145 kDa	95% (0.00000062)	242.4	257.5	278.4	276.0	271.9	254.2	8.3	24.2	17.2	259.4	18.1	267.4	11.6	16.6	7.9
2	Fibronectin OS=Mus musculus GN=Fbn1 PE=1 SV=3	FINC_MOUSE	272 kDa	95% (0.014)	207.4	302.3	304.8	315.4	317.5	309.0	429.3	366.0	409.9	271.5	55.5	314.0	4.5	401.7	32.4
4	Plasminogen activator inhibitor 1 OS=Mus musculus GN=Serpine1 PE=1 SV=1	PAI1_MOUSE	45 kDa	95% (0.025)	180.9	159.5	178.4	201.5	164.0	199.4	257.5	260.0	204.7	172.9	11.7	188.3	21.1	240.7	31.3
10	SPARC OS=Mus musculus GN=Sparc PE=1 SV=1	SPRC_MOUSE	34 kDa	95% (0.00069)	168.2	131.2	139.0	160.9	127.0	135.4	57.4	62.3	47.4	146.1	19.5	141.1	17.6	55.7	7.6
9	Collagen alpha-2(IV) chain OS=Mus musculus GN=Col4a2 PE=2 SV=4	CO4A2_MOUSE	167 kDa	95% (0.00029)	153.1	212.6	212.4	188.4	222.3	167.9	23.2	29.9	29.7	192.7	34.3	192.9	27.5	27.6	3.8
5	Fibulin-2 OS=Mus musculus GN=Fbln2 PE=1 SV=1	FBLN2_MOUSE	132 kDa	95% (0.0011)	131.6	145.1	154.3	188.1	151.2	169.2	227.9	211.9	227.9	143.7	11.4	169.5	18.4	222.6	9.2
8	Complement C3 OS=Mus musculus GN=C3 PE=1 SV=2	CO3_MOUSE	186 kDa	0% (0.98)	123.9	118.0	143.2	148.8	114.2	116.6	106.0	115.0	170.4	128.4	13.2	126.5	19.3	130.5	34.8
13	Insulin-like growth factor-binding protein 7 OS=Mus musculus GN=Igfbp7 PE=2 SV=3	IBP7_MOUSE	29 kDa	95% (0.0032)	102.6	99.5	100.4	108.5	103.8	109.0	70.8	88.9	67.9	100.8	1.6	107.1	2.9	75.9	11.4
15	Extracellular matrix protein 1 OS=Mus musculus GN=Ecm1 PE=1 SV=1	ECM1_MOUSE	63 kDa	95% (0.0057)	91.3	91.4	96.7	95.9	76.4	85.9	70.8	66.8	61.8	93.1	3.1	86.0	9.8	66.5	4.5
19	Sushi, von Willebrand factor type A, EGF and pentraxin domain-containing protein 1 OS=Mus musculus GN=Svep1 PE=1 SV=1	SVEP1_MOUSE	387 kDa	95% (0.000086)	90.4	102.7	102.5	75.6	59.8	73.5	26.5	35.9	35.6	98.5	7.0	69.7	8.6	32.7	5.3
23	EGF-containing fibulin-like extracellular matrix protein 1 OS=Mus musculus GN=Efemp1 PE=2 SV=1	FBLN3_MOUSE	55 kDa	95% (0.0013)	75.5	69.6	73.6	53.8	36.1	47.0	31.5	38.9	43.5	72.9	3.0	45.6	8.9	38.0	6.0
17	Serotransferrin OS=Mus musculus GN=Trf PE=1 SV=1	TRFE_MOUSE	77 kDa	0% (0.34)	70.9	77.1	68.3	73.3	57.1	57.0	61.0	74.7	80.9	72.1	4.5	62.5	9.4	72.2	10.2
16	Fibrillin-1 OS=Mus musculus GN=Fbn1 PE=1 SV=1	FBN1_MOUSE	312 kDa	95% (0.034)	66.3	110.0	105.7	108.2	93.1	99.9	57.8	68.7	43.5	94.0	24.1	100.4	7.6	56.6	12.6
20	Insulin-like growth factor-binding protein 2 OS=Mus musculus GN=Igfbp2 PE=2 SV=2	IBP2_MOUSE	33 kDa	0% (0.22)	64.1	43.2	51.9	59.8	46.3	65.5	69.2	77.8	59.1	53.1	10.5	57.2	9.8	68.7	9.4
25	Sulphydryl oxidase 1 OS=Mus musculus GN=Qsox1 PE=2 SV=1	QSOX1_MOUSE	83 kDa	95% (0.0072)	52.3	50.4	60.5	40.6	49.6	52.8	32.4	16.7	31.6	54.4	5.4	47.7	6.3	26.9	8.8
26	Cystatin-C OS=Mus musculus GN=Cst3 PE=2 SV=2	CYTC_MOUSE	16 kDa	0% (0.34)	51.7	33.6	30.5	45.8	49.2	46.0	40.4	57.9	48.6	38.6	11.5	47.0	1.9	49.0	8.8
43	Collagen alpha-1(XII) chain OS=Mus musculus GN=Col12a1 PE=2 SV=3	COCA1_MOUSE	340 kDa	0% (0.12)	49.4	40.9	11.8	35.3	54.5	44.6	26.0	6.6	17.7	34.0	19.8	44.8	9.6	16.8	9.7
18	Complement factor H OS=Mus musculus GN=Cfh PE=1 SV=1	CFAH_MOUSE	139 kDa	0% (0.20)	45.5	69.2	50.1	46.6	46.3	59.4	56.2	91.2	68.6	54.9	12.6	50.7	7.5	72.0	17.8
40	Serine protease inhibitor A3N OS=Mus musculus GN=Serpina3n PE=1 SV=1	SPA3N_MOUSE	47 kDa	95% (0.023)	42.2	34.5	38.6	31.2	22.7	18.0	24.4	28.2	30.2	38.4	3.8	23.9	6.7	27.6	2.9
22	Follistatin-related protein 1 OS=Mus musculus GN=Fstl1 PE=1 SV=1	FSTL1_MOUSE	35 kDa	95% (0.021)	41.6	50.6	50.8	50.3	58.8	60.9	29.6	43.5	38.4	47.6	5.3	56.6	5.6	37.2	7.0
51	Insulin-like growth factor-binding protein 4 OS=Mus musculus GN=Igfbp4 PE=2 SV=2	IBP4_MOUSE	28 kDa	0% (0.10)	37.8	28.3	26.4	22.8	21.0	21.6	24.0	29.6	21.3	30.8	6.1	21.8	0.9	24.9	4.2
50	Collagen alpha-1(IV) chain OS=Mus musculus GN=Col4a1 PE=2 SV=4	CO4A1_MOUSE	161 kDa	95% (0.00042)	37.2	47.6	43.8	25.4	38.0	34.0	6.8	11.4	8.2	42.9	5.2	32.4	6.4	8.8	2.3
29	Metalloproteinase inhibitor 1 OS=Mus musculus GN=Timp1 PE=2 SV=2	TIMP1_MOUSE	23 kDa	0% (0.30)	36.8	26.6	33.2	33.8	37.3	42.9	33.0	40.5	39.4	32.2	5.2	38.0	4.6	37.6	4.1
36	Connective tissue growth factor OS=Mus musculus GN=Ctgf PE=2 SV=2	CTGF_MOUSE	38 kDa	0% (0.24)	36.0	25.3	33.5	34.8	41.1	37.2	36.4	34.9	32.2	31.6	5.6	37.7	3.2	34.5	2.1
53	Collagen alpha-1(VI) chain OS=Mus musculus GN=Col6a1 PE=2 SV=1	CO6A1_MOUSE	108 kDa	95% (0.000039)	35.7	32.1	29.0	26.8	26.9	24.8	7.0	10.2	9.5	32.3	3.3	26.2	1.2	8.9	1.7
38	Galectin-1 OS=Mus musculus GN=Lgals1 PE=1 SV=3	LEG1_MOUSE	15 kDa	95% (0.013)	35.7	36.4	33.9	28.6	34.1	39.1	45.7	44.4	43.6	35.3	1.3	33.9	5.3	44.5	1.1
37	Extracellular superoxide dismutase [Cu-Zn] OS=Mus musculus GN=Sod3 PE=1 SV=1	SODE_MOUSE	27 kDa	0% (0.12)	34.3	34.0	25.4	33.8	39.0	44.8	31.8	33.3	29.9	31.2	5.1	39.2	5.5	31.7	1.7
24	Galectin-3-binding protein OS=Mus musculus GN=Lgals3bp PE=1 SV=1	LG3BP_MOUSE	64 kDa	95% (0.0014)	30.7	36.6	45.6	28.5	41.8	43.9	76.0	70.3	68.6	37.6	7.5	38.1	8.3	71.6	3.9
58	Profilin-1 OS=Mus musculus GN=Pfn1 PE=1 SV=2	PROF1_MOUSE	15 kDa	0% (0.75)	30.6	26.5	22.6	24.8	24.2	24.6	23.8	29.7	22.7	26.6	4.0	24.5	0.3	25.4	3.8
64	Protein-lysine 6-oxidase OS=Mus musculus GN=Lox PE=2 SV=1	LYOX_MOUSE	47 kDa	95% (0.024)	29.9	17.1	15.9	19.8	29.7	24.6	7.8	11.0	6.0	21.0	7.7	24.7	4.9	8.3	2.5
32	Plasma protease C1 inhibitor OS=Mus musculus GN=Serpinc1 PE=1 SV=2	IC1_MOUSE	56 kDa	0% (0.10)	29.8	37.6	36.2	27.1	32.1	24.5	34.8	35.9	49.0	34.5	4.2	27.9	3.9	39.9	7.9
41	Metalloproteinase inhibitor 2 OS=Mus musculus GN=Timp2 PE=1 SV=2	TIMP2_MOUSE	24 kDa	95% (0.00016)	27.5	25.3	26.5	23.8	25.1	22.2	38.7	44.5	38.9	26.4	1.1	23.7	1.5	40.7	3.3
39	Basement membrane-specific heparan sulfate proteoglycan core protein OS=Mus musculus GN=Hspg2 PE=1 SV=1	PGBM_MOUSE	398 kDa	95% (0.030)	26.9	22.2	22.8	37.1	32.1	23.2	33.8	48.9	53.1	24.0	2.6	30.8	7.0	45.3	10.2
113	Inhibin beta A chain OS=Mus musculus GN=Inhba PE=1 SV=1	INHBA_MOUSE	47 kDa	95% (0.00096)	26.8	17.0	22.4	8.9	12.3	11.9	3.8	2.7	4.4	22.1	4.9	11.0	1.8	3.6	0.9

30	Bone morphogenetic protein 1 OS=Mus musculus GN=Bmp1 PE=2 SV=1	BMP1_MOUSE 112 kDa	95% (0.011)	26.1	32.7	23.4	27.9	26.5	34.7	54.2	41.9	42.4	27.4	4.8	29.7	4.4	46.1	7.0
68	Fibromodulin OS=Mus musculus GN=Fmod PE=2 SV=1	FMOD_MOUSE 43 kDa	0% (0.93)	25.3	17.4	13.3	22.7	13.9	14.2	13.5	23.2	15.8	18.6	6.1	16.9	5.0	17.5	5.1
78	Collagen alpha-2(VI) chain OS=Mus musculus GN=Col6a2 PE=2 SV=3	CO6A2_MOUSE 110 kDa	95% (0.0078)	24.0	20.3	27.1	13.6	7.4	24.4	1.6	4.0	1.0	23.8	3.4	15.1	8.6	2.2	1.6
132	Complement C4-B OS=Mus musculus GN=C4b PE=1 SV=2	CO4B_MOUSE 193 kDa	0% (0.095)	22.1	12.3	12.9	13.6	4.6	6.1	10.3	1.0	4.3	15.8	5.5	8.1	4.8	5.2	4.7
61	Granulins OS=Mus musculus GN=Gm PE=1 SV=2	GRN_MOUSE 63 kDa	0% (0.27)	22.1	20.5	20.1	13.9	23.7	16.3	14.7	19.3	12.9	20.9	1.1	18.0	5.1	15.6	3.3
95	Prolargin OS=Mus musculus GN=Prelp PE=2 SV=2	PRELP_MOUSE 43 kDa	95% (0.00019)	22.1	23.7	18.6	17.7	12.8	12.4	2.4	2.7	3.7	21.4	2.6	14.3	3.0	2.9	0.7
52	Peptidyl-prolyl cis-trans isomerase A OS=Mus musculus GN=Ppia PE=1 SV=2	PPIA_MOUSE 18 kDa	0% (0.25)	21.1	29.2	24.9	24.8	27.3	29.4	30.6	29.6	28.0	25.1	4.1	27.2	2.3	29.4	1.3
59	Stromelysin-1 OS=Mus musculus GN=Mmp3 PE=2 SV=2	MMP3_MOUSE 54 kDa	95% (0.0087)	20.4	19.0	28.4	20.5	26.2	28.1	11.3	10.9	11.7	22.6	5.1	24.9	3.9	11.3	0.4
67	Carboxypeptidase E OS=Mus musculus GN=Cpe PE=1 SV=2	CBPE_MOUSE 53 kDa	95% (0.0050)	19.5	22.5	21.9	19.6	22.8	21.9	10.8	15.0	15.5	21.3	1.6	21.4	1.6	13.8	2.6
70	Ceruloplasmin OS=Mus musculus GN=Cp PE=1 SV=2	CERU_MOUSE 121 kDa	0% (0.23)	19.5	9.8	16.0	15.6	8.0	14.7	21.4	15.3	21.2	15.1	4.9	12.7	4.1	19.3	3.5
109	Superoxide dismutase [Cu-Zn] OS=Mus musculus GN=Sod1 PE=1 SV=2	SODC_MOUSE 16 kDa	0% (0.32)	19.0	11.5	10.9	12.4	7.5	8.7	11.0	12.7	9.0	13.8	4.5	9.5	2.5	10.9	1.8
71	WNT1-inducible-signaling pathway protein 2 OS=Mus musculus GN=Wisp2 PE=2 SV=1	WISP2_MOUSE 27 kDa	0% (0.17)	18.9	22.3	12.2	19.8	16.0	15.1	12.7	13.4	10.7	17.8	5.1	17.0	2.5	12.3	1.4
112	Collagen alpha-1(V) chain OS=Mus musculus GN=Col5a1 PE=2 SV=2	CO5A1_MOUSE 184 kDa	95% (0.00043)	18.5	16.7	12.2	20.5	25.3	17.5	1.0	1.0	1.0	15.8	3.3	21.1	3.9	1.0	0.0
45	Macrophage colony-stimulating factor 1 OS=Mus musculus GN=Csf1 PE=1 SV=2	CSF1_MOUSE 61 kDa	95% (0.000052)	18.5	19.4	20.3	18.4	12.0	14.4	44.3	51.9	43.2	19.4	0.9	14.9	3.3	46.5	4.7
103	Dystroglycan OS=Mus musculus GN=Dag1 PE=1 SV=4	DAG1_MOUSE 97 kDa	0% (0.081)	18.5	17.9	11.1	17.2	14.5	16.8	9.4	12.9	9.2	15.8	4.1	16.2	1.4	10.5	2.1
66	Lysyl oxidase homolog 1 OS=Mus musculus GN=Loxl1 PE=2 SV=3	LOXL1_MOUSE 67 kDa	0% (0.10)	18.4	25.8	10.5	19.7	30.3	22.2	10.3	14.0	12.1	18.2	7.7	24.1	5.5	12.1	1.9
56	Procollagen C-endopeptidase enhancer 1 OS=Mus musculus GN=Pcoice PE=1 SV=2	PCOC1_MOUSE 50 kDa	95% (0.031)	17.9	18.7	19.7	15.3	20.3	19.3	26.2	31.8	22.2	18.8	0.9	18.3	2.7	26.8	4.8
57	EGF-containing fibulin-like extracellular matrix protein 2 OS=Mus musculus GN=Efemp2 PE=2 SV=1	FBLN4_MOUSE 49 kDa	95% (0.0040)	16.5	19.9	17.3	19.7	15.6	19.7	27.6	25.6	32.1	17.9	1.8	18.3	2.4	28.4	3.3
85	Plasma glutamate carboxypeptidase OS=Mus musculus GN=Pgcp PE=2 SV=1	PGCP_MOUSE 52 kDa	0% (0.059)	15.3	14.1	12.4	16.3	16.5	13.1	11.1	12.7	10.8	13.9	1.5	15.3	1.9	11.6	1.0
80	A disintegrin and metalloproteinase with thrombospondin motifs 5 OS=Mus musculus GN=Adamt5 PE=2 SV=1	AT5_MOUSE 102 kDa	95% (0.0038)	15.3	21.0	19.4	15.0	13.5	14.6	6.0	10.7	8.4	18.6	2.9	14.3	0.8	8.4	2.3
92	Sulfated glycoprotein 1 OS=Mus musculus GN=Psap PE=1 SV=2	SAP_MOUSE 61 kDa	0% (0.15)	14.7	17.5	18.4	13.7	7.7	14.8	7.3	14.6	11.6	16.9	1.9	12.1	3.8	11.1	3.7
111	Cathepsin B OS=Mus musculus GN=Ctsb PE=1 SV=2	CATB_MOUSE 37 kDa	95% (0.041)	14.5	9.7	10.7	8.9	7.8	8.9	13.3	16.2	12.1	11.7	2.5	8.5	0.6	13.8	2.1
131	Coiled-coil domain-containing protein 80 OS=Mus musculus GN=Ccdc80 PE=1 SV=2	CCD80_MOUSE 108 kDa	0% (0.66)	13.7	7.5	5.5	6.7	13.6	10.4	8.3	7.0	8.0	8.9	4.3	10.2	3.4	7.8	0.7
82	Fibulin-5 OS=Mus musculus GN=Fbln5 PE=2 SV=1	FBLN5_MOUSE 50 kDa	0% (0.56)	13.6	18.1	17.3	14.7	16.3	15.2	13.4	12.3	17.4	16.3	2.4	15.4	0.8	14.4	2.6
54	Pigment epithelium-derived factor OS=Mus musculus GN=Serpinf1 PE=1 SV=2	PEDF_MOUSE 46 kDa	0% (0.21)	13.2	23.3	22.9	25.3	30.2	23.5	21.1	17.1	23.6	19.8	5.7	26.3	3.4	20.6	3.3
148	Vascular endothelial growth factor D OS=Mus musculus GN=Figf PE=2 SV=1	VEGFD_MOUSE 41 kDa	95% (0.014)	12.0	8.5	10.4	8.3	7.0	6.6	6.4	6.7	5.3	10.3	1.7	7.3	0.9	6.1	0.7
108	Gelsolin OS=Mus musculus GN=Gsn PE=1 SV=3	GELS_MOUSE 86 kDa	95% (0.029)	10.3	6.5	12.0	9.4	6.2	5.1	16.2	12.5	22.0	9.6	2.8	6.9	2.2	16.9	4.8
120	Fibulin-1 OS=Mus musculus GN=Fbln1 PE=1 SV=2	FBLN1_MOUSE 78 kDa	0% (0.48)	10.1	11.6	7.8	8.2	7.2	10.4	10.1	14.1	8.5	9.8	1.9	8.6	1.6	10.9	2.9
125	Glucose-6-phosphate isomerase OS=Mus musculus GN=Gpi PE=1 SV=4	G6PI_MOUSE 63 kDa	0% (0.11)	9.9	6.6	9.1	7.1	9.2	6.5	11.1	10.0	9.9	8.5	1.7	7.6	1.4	10.3	0.7
118	Lactadherin OS=Mus musculus GN=Mfge8 PE=1 SV=2	MFGM_MOUSE 51 kDa	0% (0.070)	9.9	4.7	4.1	11.0	5.5	12.3	13.0	12.9	12.8	6.3	3.2	9.6	3.6	12.9	0.1
145	Dermatopontin OS=Mus musculus GN=Dpi PE=2 SV=1	DERM_MOUSE 24 kDa	0% (0.39)	9.7	10.1	7.8	8.0	7.5	7.8	10.6	6.8	11.4	9.2	1.3	7.8	0.2	9.6	2.5
164	Ribonuclease 4 OS=Mus musculus GN=Rnase4 PE=2 SV=1	RNAS4_MOUSE 17 kDa	0% (0.92)	9.7	6.1	7.8	8.0	8.5	5.8	6.8	9.0	7.8	7.8	1.8	7.4	1.4	7.9	1.1
160	Transcobalamin-2 OS=Mus musculus GN=Tcn2 PE=2 SV=1	TCO2_MOUSE 48 kDa	0% (0.12)	9.7	8.0	8.1	4.1	7.8	4.5	5.8	8.6	6.6	8.6	1.0	5.4	2.0	7.0	1.5
414	Inhibin beta B chain OS=Mus musculus GN=Inhbb PE=2 SV=4	INHBB_MOUSE 45 kDa	95% (0.048)	9.5	4.1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	4.9	4.3	1.0	0.0	1.0	0.0
168	Thymosin beta-4 OS=Mus musculus GN=Tmsb4x PE=1 SV=1	TYB4_MOUSE 6 kDa	0% (0.88)	9.5	9.6	4.4	5.9	8.0	7.0	5.1	9.3	8.9	7.8	3.0	7.0	1.0	7.8	2.3
154	Epididymal secretory protein E1 OS=Mus musculus GN=Npc2 PE=2 SV=1	NPC2_MOUSE 16 kDa	0% (0.27)	9.5	8.9	6.8	13.0	9.3	5.8	6.8	4.0	6.8	8.4	1.4	9.4	3.6	5.9	1.6
218	Probable carboxypeptidase X1 OS=Mus musculus GN=Cpxm1 PE=2 SV=1	CPXM1_MOUSE 81 kDa	95% (0.0053)	9.3	8.1	5.9	5.5	5.3	2.5	1.0	1.0	1.0	7.7	1.7	4.4	1.7	1.0	0.0
128	Cofilin-1 OS=Mus musculus GN=Cfl1 PE=1 SV=3	COF1_MOUSE 19 kDa	0% (0.082)	9.2	10.3	7.9	10.2	8.5	11.1	10.4	13.0	14.6	9.1	1.2	9.9	1.3	12.6	2.1
166	Protein CYR61 OS=Mus musculus GN=Cyr61 PE=1 SV=1	CYR61_MOUSE 42 kDa	0% (0.73)	9.2	5.9	7.0	8.9	6.6	6.8	8.6	5.7	5.2	7.4	1.7	7.4	1.3	6.5	1.9
180	Spondin-2 OS=Mus musculus GN=Spon2 PE=1 SV=2	SPON2_MOUSE 36 kDa	0% (0.11)	9.1	10.7	1.0	2.2	1.0	1.0	5.7	8.4	5.5	6.9	5.2	1.4	0.7	6.5	1.6
73	Biglycan OS=Mus musculus GN=Bgn PE=2 SV=1	PGS1_MOUSE 42 kDa	95% (0.048)	9.0	11.4	11.6	11.7	20.1	14.0	24.1	15.5	27.7	10.7	1.4	15.3	4.4	22.4	6.3
165	Phospholipid transfer protein OS=Mus musculus GN=Pltp PE=1 SV=1	PLTP_MOUSE 54 kDa	0% (0.23)	8.9	5.8	8.8	1.0	7.1	3.5	4.6	13.5	8.9	7.8	1.8	3.9	3.1	9.0	4.5

Beta-2-microglobulin OS=Mus musculus GN=B2m PE=1 175 SV=1	B2MG_MOUSE 14 kDa	0% (0.79)	8.8	1.0	1.0	1.0	6.9	1.0	1.0	11.7	3.8	3.6	4.5	3.0	3.4	5.5	5.5
Peroxidase homolog OS=Mus musculus GN=Pxdn PE=2 81 SV=1	PXDN_MOUSE 165 kDa	0% (0.24)	8.8	17.6	16.7	17.8	24.1	20.1	7.3	9.5	21.0	14.4	4.9	20.7	3.2	12.6	7.4
Decorin OS=Mus musculus GN=Dcn PE=2 SV=1	PGS2_MOUSE 40 kDa	0% (0.18)	8.5	6.7	10.3	7.1	8.0	6.0	11.5	8.2	9.7	8.5	1.8	7.1	1.0	9.8	1.7
Thrombospondin-1 OS=Mus musculus GN=Thbs1 PE=1 194 SV=1	TSP1_MOUSE 130 kDa	95% (0.0091)	8.2	8.2	5.2	7.8	6.3	10.0	2.9	1.0	2.8	7.2	1.7	8.0	1.9	2.2	1.1
272 Nidogen-1 OS=Mus musculus GN=Nid1 PE=1 SV=1	NID1_MOUSE 137 kDa	0% (0.060)	8.1	3.6	6.1	4.6	1.0	4.1	1.0	1.0	1.0	5.9	2.3	3.2	1.9	1.0	0.0
72 kDa type IV collagenase OS=Mus musculus GN=Mmp2 110 PE=2 SV=1	MMP2_MOUSE 74 kDa	95% (0.0084)	7.8	15.4	12.3	19.4	18.7	15.6	4.6	9.4	4.8	11.9	3.8	17.9	2.0	6.3	2.7
Immunoglobulin superfamily containing leucine-rich repeat 212 protein OS=Mus musculus GN=Islr PE=1 SV=1	ISLR_MOUSE 46 kDa	95% (0.026)	7.6	1.0	2.7	1.0	1.0	1.0	7.0	7.5	6.5	3.8	3.4	1.0	0.0	7.0	0.5
Cytokine receptor-like factor 1 OS=Mus musculus GN=Crrf1 170 PE=1 SV=1	CRLF1_MOUSE 47 kDa	0% (0.58)	7.3	5.5	6.6	7.9	3.7	4.1	6.3	5.6	3.6	6.5	0.9	5.2	2.4	5.2	1.4
Neutrophil gelatinase-associated lipocalin OS=Mus musculus 139 GN=Lcn2 PE=1 SV=1	NGAL_MOUSE 23 kDa	95% (0.020)	6.7	8.9	6.8	12.1	9.6	9.8	3.5	4.5	7.6	7.5	1.3	10.5	1.4	5.2	2.1
Lysyl oxidase homolog 2 OS=Mus musculus GN=Loxl2 PE=2 115 SV=2	LOXL2_MOUSE 87 kDa	95% (0.029)	6.6	10.9	11.1	8.5	14.3	14.8	4.8	5.9	4.2	9.5	2.5	12.5	3.5	4.9	0.9
A disintegrin and metalloproteinase with thrombospondin 183 motifs 2 OS=Mus musculus GN=Adamts2 PE=1 SV=2	ATS2_MOUSE 135 kDa	0% (0.62)	6.4	7.5	7.2	1.0	7.7	7.8	4.3	7.1	4.4	7.0	0.5	5.5	3.9	5.3	1.6
C-X-C motif chemokine 5 OS=Mus musculus GN=Cxcl5 205 PE=1 SV=1	CXCL5_MOUSE 14 kDa	0% (0.10)	6.3	8.2	4.4	7.1	9.1	5.9	1.0	5.3	3.8	6.3	1.9	7.4	1.6	3.4	2.2
Semaphorin-3D OS=Mus musculus GN=Sema3d PE=1 210 SV=1	SEM3D_MOUSE 90 kDa	95% (0.0027)	6.3	6.5	7.8	6.9	4.5	4.9	2.4	1.0	1.8	6.9	0.8	5.4	1.3	1.7	0.7
337 Kallikrein-8 OS=Mus musculus GN=Klk8 PE=1 SV=1	KLK8_MOUSE 29 kDa	0% (0.13)	6.2	1.0	3.2	1.0	3.1	4.5	1.0	1.0	1.0	3.5	2.6	2.9	1.8	1.0	0.0
A disintegrin and metalloproteinase with thrombospondin 287 motifs 1 OS=Mus musculus GN=Adamts1 PE=1 SV=3	ATS1_MOUSE 106 kDa	95% (0.027)	6.1	3.0	3.9	1.0	5.7	3.9	1.0	1.0	1.0	4.3	1.6	3.5	2.3	1.0	0.0
Slit homolog 3 protein OS=Mus musculus GN=Slit3 PE=2 243 SV=1	SLIT3_MOUSE 168 kDa	0% (0.14)	5.8	6.0	1.0	3.1	4.3	1.8	1.0	2.9	2.8	4.3	2.8	3.1	1.3	2.2	1.1
Pentraxin-related protein PTX3 OS=Mus musculus GN=Ptx3 221 PE=1 SV=2	PTX3_MOUSE 42 kDa	95% (0.012)	5.8	12.0	11.9	1.0	6.2	3.9	1.0	1.0	1.0	9.9	3.6	3.7	2.6	1.0	0.0
Disintegrin and metalloproteinase domain-containing protein 187 9 OS=Mus musculus GN=Adam9 PE=1 SV=1	ADAM9_MOUSE 92 kDa	95% (0.048)	5.8	5.4	3.4	5.2	4.8	3.6	7.8	8.9	5.9	4.8	1.3	4.5	0.8	7.5	1.5
44 Periostin OS=Mus musculus GN=Postn PE=1 SV=2	POSTN_MOUSE 93 kDa	0% (0.16)	5.8	11.1	12.9	13.1	40.9	36.2	27.8	13.8	42.7	9.9	3.7	30.1	14.9	28.1	14.5
268 Mimecan OS=Mus musculus GN=Ogn PE=2 SV=1	MIME_MOUSE 34 kDa	0% (0.49)	5.2	1.0	1.0	3.3	5.2	4.8	3.8	4.3	1.0	2.4	2.4	4.4	1.0	3.0	1.8
Mammalian ependymin-related protein 1 OS=Mus musculus 276 GN=Epdrl PE=2 SV=1	EPDR1_MOUSE 25 kDa	0% (0.95)	5.1	2.7	1.0	1.0	1.0	4.2	4.5	1.0	1.0	2.9	2.1	2.1	1.8	2.2	2.0
Protein CTLA-2-alpha OS=Mus musculus GN=Ctla2a PE=2 242 SV=2	CTLA2_MOUSE 16 kDa	0% (0.097)	4.9	4.0	6.1	4.0	7.0	5.1	1.0	3.0	3.9	5.0	1.0	5.3	1.5	2.6	1.5
Glia-derived nexin OS=Mus musculus GN=Serpine2 PE=2 239 SV=2	GDN_MOUSE 44 kDa	0% (0.21)	4.8	5.0	3.6	1.0	3.5	2.7	1.0	5.8	2.8	4.5	0.8	2.4	1.3	3.2	2.4
Complement C1q tumor necrosis factor-related protein 5 138 OS=Mus musculus GN=C1qtnf5 PE=2 SV=1	C1QTN5_MOUSE 25 kDa	95% (0.0010)	4.8	5.4	4.3	5.2	4.8	6.6	9.5	12.1	13.1	4.8	0.6	5.5	0.9	11.5	1.8
215 Protein FAM3C OS=Mus musculus GN=Fam3c PE=1 SV=1	FAM3C_MOUSE 25 kDa	0% (0.43)	4.8	3.6	7.0	5.3	4.3	6.4	4.3	4.5	3.4	5.1	1.8	5.3	1.1	4.0	0.6
Growth-regulated alpha protein OS=Mus musculus 389 GN=Cxcl1 PE=1 SV=1	GROA_MOUSE 10 kDa	95% (0.0069)	4.8	1.0	3.3	2.4	3.4	1.0	1.0	1.0	1.0	3.0	1.9	2.3	1.2	1.0	0.0
Interleukin-1 receptor accessory protein OS=Mus musculus 277 GN=Il1rap PE=1 SV=1	IL1AP_MOUSE 66 kDa	95% (0.024)	4.5	2.8	2.5	3.1	1.0	4.1	1.0	1.0	1.0	3.3	1.1	2.7	1.6	1.0	0.0
Semaphorin-3E OS=Mus musculus GN=Sema3e PE=2 285 SV=2	SEM3E_MOUSE 90 kDa	0% (0.27)	4.5	3.8	4.1	1.0	1.0	1.0	1.0	1.0	1.0	4.1	0.4	1.0	0.0	1.0	0.0
252 Biotinidase OS=Mus musculus GN=Btd PE=1 SV=2	BTD_MOUSE 58 kDa	95% (0.024)	4.5	1.0	1.0	3.1	1.0	1.7	7.4	9.4	4.8	2.2	2.0	1.9	1.0	7.2	2.3
Protein NOV homolog OS=Mus musculus GN=Nov PE=2 413 SV=1	NOV_MOUSE 39 kDa	0% (0.27)	3.9	1.0	2.7	1.0	1.0	1.0	1.0	1.0	1.0	2.5	1.4	1.0	0.0	1.0	0.0
162 Calcitonin receptor-like receptor 1 OS=Mus musculus GN=Ctlnr1 PE=1 SV=1	CSTNR1_MOUSE 109 kDa	0% (0.14)	3.7	8.1	4.2	10.1	7.1	8.2	4.8	6.7	6.1	5.3	2.4	8.4	1.5	5.8	1.0
98 EMILIN-1 OS=Mus musculus GN=Emilin1 PE=1 SV=1	EMIL1_MOUSE 108 kDa	95% (0.0089)	3.7	8.1	4.2	13.7	18.6	13.1	11.1	15.3	16.7	5.3	2.4	15.1	3.0	14.4	2.9
Inter-alpha-trypsin inhibitor heavy chain H2 OS=Mus 353 musculus GN=Itih2 PE=1 SV=1	ITIH2_MOUSE 106 kDa	0% (0.72)	3.7	1.8	1.0	7.2	1.0	1.0	1.0	1.0	1.0	2.2	1.4	3.1	3.6	1.0	0.0
Beta-nerve growth factor OS=Mus musculus GN=Ngf PE=1 371 SV=2	NGF_MOUSE 27 kDa	0% (0.42)	3.7	3.0	1.0	1.0	1.0	5.7	1.0	1.0	1.0	2.6	1.4	2.6	2.7	1.0	0.0
Serine protease 23 OS=Mus musculus GN=Prss23 PE=2 274 SV=2	PRSS23_MOUSE 43 kDa	0% (0.79)	3.7	1.0	2.9	3.0	1.0	4.1	3.9	3.0	2.9	2.5	1.4	2.7	1.6	3.3	0.5
Polypeptide N-acetylgalactosaminyltransferase 2 OS=Mus 420 musculus GN=Galt2 PE=2 SV=1	GALT2_MOUSE 65 kDa	95% (0.0056)	3.6	1.0	3.3	1.0	1.0	1.0	1.0	1.0	1.0	2.6	1.4	1.0	0.0	1.0	0.0
Microfibrillar-associated protein 5 OS=Mus musculus 193 GN=Mfap5 PE=2 SV=1	MFAP5_MOUSE 19 kDa	0% (0.24)	3.1	1.0	5.5	5.6	6.2	4.6	1.0	4.8	5.6	3.2	2.2	5.5	0.8	3.8	2.4
Fructose-bisphosphate aldolase A OS=Mus musculus 94 GN=Aldoa PE=1 SV=2	ALDOA_MOUSE 39 kDa	95% (0.0023)	2.9	7.3	12.5	7.5	12.0	10.7	25.2	21.3	22.9	7.6	4.8	10.0	2.3	23.1	2.0
222 Calumenin OS=Mus musculus GN=Calu PE=1 SV=1	CALU_MOUSE 37 kDa	95% (0.0020)	2.9	2.0	3.6	8.3	8.9	6.3	2.9	1.0	1.0	2.8	0.8	7.8	1.4	1.6	1.1
122 Haptoglobin OS=Mus musculus GN=Hp PE=1 SV=1	HPT_MOUSE 39 kDa	95% (0.0064)	2.9	10.5	6.2	8.1	7.7	8.8	16.6	21.7	15.4	6.5	3.8	8.2	0.6	17.9	3.3
Disintegrin and metalloproteinase domain-containing protein 294 15 OS=Mus musculus GN=Adam15 PE=1 SV=2	ADA15_MOUSE 93 kDa	0% (0.44)	2.9	4.7	1.0	1.0	1.0	1.0	1.7	5.8	1.0	2.9	1.9	1.0	0.0	2.8	2.6
Transitionally-controlled tumor protein OS=Mus musculus 231 GN=Tpt1 PE=1 SV=1	TCTP_MOUSE 19 kDa	0% (0.63)	2.9	5.4	4.3	5.2	4.8	3.6	1.0	1.0	5.6	4.2	1.2	4.5	0.8	2.5	2.6
Olfactomedin-like protein 3 OS=Mus musculus GN=Olfm3 198 PE=2 SV=2	OLFL3_MOUSE 46 kDa	95% (0.0059)	2.7	1.9	3.4	4.1	2.8	2.5	5.7	9.1	10.0	2.7	0.8	3.1	0.9	8.3	2.3

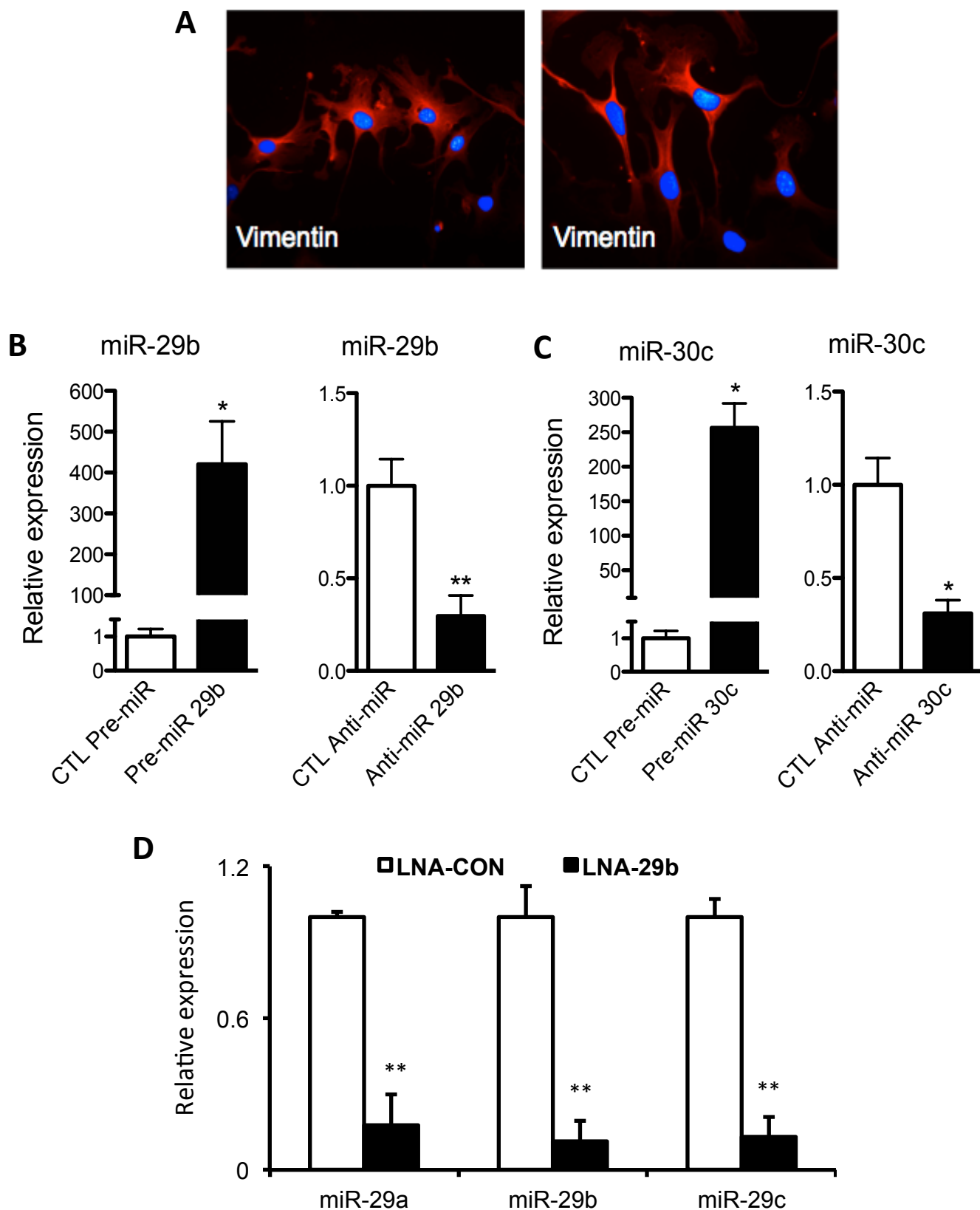
Follistatin-related protein 3 OS=Mus musculus GN=Fstl3 178 PE=1 SV=1	FSTL3_MOUSE 27 kDa	0% (0.17)	2.6	4.8	4.3	7.7	7.3	3.6	5.6	9.7	6.4	3.9	1.2	6.2	2.3	7.3	2.1
UPF0556 protein C19orf10 homolog OS=Mus musculus 384 GN=D17Wsu104e PE=2 SV=1	CS010_MOUSE 18 kDa	0% (0.093)	2.4	1.0	2.9	1.0	1.0	1.0	2.9	2.0	1.0	2.1	1.0	1.0	0.0	2.0	1.0
Disintegrin and metalloproteinase domain-containing protein 400 19 OS=Mus musculus GN=Adam19 PE=2 SV=2	ADA19_MOUSE101 kDa	95% (0.0074)	1.9	1.0	2.6	2.6	1.0	2.7	1.0	1.0	1.0	1.8	0.8	2.1	0.9	1.0	0.0
Acid sphingomyelinase-like phosphodiesterase 3a OS=Mus 495 musculus GN=Smpd3a PE=2 SV=1	ASM3A_MOUSE50 kDa	95% (0.0047)	1.8	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.3	0.5	1.0	0.0	1.0	0.0
Disintegrin and metalloproteinase domain-containing protein 381 10 OS=Mus musculus GN=Adam10 PE=1 SV=1	ADA10_MOUSE84 kDa	95% (0.035)	1.0	1.0	1.0	1.0	1.0	1.0	3.2	7.3	1.8	1.0	0.0	1.0	0.0	4.1	2.8
365 Agrin OS=Mus musculus GN=Agrn PE=2 SV=1	AGRIN_MOUSE208 kDa	95% (0.050)	1.0	1.0	3.4	1.0	1.0	3.6	1.0	1.0	1.0	1.8	1.4	1.9	1.5	1.0	0.0
Apolipoprotein A-I-binding protein OS=Mus musculus 391 GN=Apoa1bp PE=1 SV=1	AIBP_MOUSE 31 kDa	95% (0.027)	1.0	1.8	1.0	1.0	1.0	1.0	3.5	1.8	3.4	1.3	0.5	1.0	0.0	2.9	0.9
Aminoacyl tRNA synthetase complex-interacting multifunctional protein 1 OS=Mus musculus GN=Aimp1 453 PE=1 SV=2	AIMP1_MOUSE 34 kDa	95% (0.0083)	1.0	1.0	1.0	1.0	1.0	1.0	2.6	1.8	1.0	1.0	0.0	1.0	0.0	1.8	0.8
151 Serum albumin OS=Mus musculus GN=Alb PE=1 SV=3	ALBU_MOUSE 69 kDa	0% (0.22)	1.0	9.0	5.9	1.0	1.0	1.0	12.5	1.0	8.1	5.3	4.0	1.0	0.0	7.2	5.8
Angiopoietin-related protein 2 OS=Mus musculus 449 GN=Angptl2 PE=2 SV=1	ANGL2_MOUSE57 kDa	0% (0.31)	1.0	1.0	1.0	1.0	3.1	1.0	1.0	1.0	1.8	1.0	0.0	1.7	1.2	1.3	0.5
279 Arylsulfatase A OS=Mus musculus GN=Arsa PE=2 SV=1	ARSA_MOUSE 54 kDa	0% (0.20)	1.0	1.0	1.0	1.0	1.0	1.0	2.4	1.0	2.7	1.0	0.0	1.0	0.0	2.0	0.9
Beta-1,4-galactosyltransferase 1 OS=Mus musculus 340 GN=B4gal1 PE=2 SV=1	B4GT1_MOUSE44 kDa	0% (0.18)	1.0	1.0	1.0	1.0	2.6	1.0	2.7	1.9	5.6	1.0	0.0	1.5	0.9	3.4	2.0
Brain-derived neurotrophic factor OS=Mus musculus 442 GN=Bdnf PE=1 SV=1	BDNF_MOUSE 28 kDa	0% (0.60)	1.0	1.0	1.0	1.0	1.0	1.9	1.0	1.0	1.0	1.0	0.0	1.3	0.5	1.0	0.0
Adenylyl cyclase-associated protein 1 OS=Mus musculus 439 GN=Cap1 PE=1 SV=3	CAP1_MOUSE 52 kDa	0% (0.20)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	4.5	1.0	0.0	1.0	0.0	2.2	2.0
Macrophage-capping protein OS=Mus musculus GN=Capg 293 PE=1 SV=2	CAPG_MOUSE 39 kDa	95% (0.048)	1.0	1.0	1.0	1.0	4.3	3.6	4.8	4.8	2.8	1.0	0.0	3.0	1.7	4.1	1.1
485 CD109 antigen OS=Mus musculus GN=Cd109 PE=2 SV=1	CD109_MOUSE162 kDa	0% (0.61)	1.0	1.0	1.0	1.0	1.0	1.0	3.1	1.0	1.0	1.0	0.0	1.0	0.0	1.7	1.2
Complement factor B OS=Mus musculus GN=Cfb PE=1 421 SV=2	CFAB_MOUSE 85 kDa	0% (0.46)	1.0	1.0	1.0	1.0	1.0	1.0	3.2	1.0	1.0	1.0	0.0	1.0	0.0	1.7	1.3
208 Clusterin OS=Mus musculus GN=Clu PE=1 SV=1	CLUS_MOUSE 52 kDa	0% (0.54)	1.0	9.7	7.5	1.0	5.2	7.2	3.8	10.8	9.2	6.1	4.5	4.5	3.2	7.9	3.7
Collagen alpha-1(VIII) chain OS=Mus musculus GN=Col8a1 220 PE=1 SV=3	COBA1_MOUSE74 kDa	95% (0.032)	1.0	8.7	8.7	1.0	7.3	1.0	1.0	1.0	1.0	6.2	4.5	3.1	3.6	1.0	0.0
Collagen alpha-1(XI) chain OS=Mus musculus GN=Col11a1 246 PE=1 SV=1	COBA1_MOUSE181 kDa	95% (0.00089)	1.0	1.0	1.0	7.9	13.3	11.3	1.0	1.8	1.0	1.0	0.0	10.8	2.8	1.3	0.5
Collagen triple helix repeat-containing protein 1 OS=Mus 214 musculus GN=Cthrc1 PE=2 SV=1	CTHR1_MOUSE26 kDa	95% (0.021)	1.0	3.6	3.4	1.0	4.2	3.7	5.3	7.6	7.1	2.7	1.4	2.9	1.7	6.7	1.2
C-X-C motif chemokine 16 OS=Mus musculus GN=Cxcl16 248 PE=1 SV=2	CXL16_MOUSE27 kDa	95% (0.013)	1.0	1.0	1.0	1.0	1.0	1.0	6.4	7.9	7.0	1.0	0.0	1.0	0.0	7.1	0.7
Dickkopf-related protein 3 OS=Mus musculus GN=Dkk3 176 PE=1 SV=1	DKK3_MOUSE 38 kDa	95% (0.00038)	1.0	2.8	2.5	1.0	1.0	4.9	9.6	11.0	12.7	2.1	1.0	2.3	2.3	11.1	1.6
451 Elastin OS=Mus musculus GN=Eln PE=2 SV=1	ELN_MOUSE 72 kDa	95% (0.00024)	1.0	1.0	1.0	1.0	1.0	1.0	1.9	3.1	2.9	1.0	0.0	1.0	0.0	2.6	0.7
Growth/differentiation factor 15 OS=Mus musculus 377 GN=Gdf15 PE=2 SV=1	GDF15_MOUSE33 kDa	95% (0.0026)	1.0	4.1	4.4	1.0	4.6	1.0	1.0	1.0	1.0	3.2	1.9	2.2	2.1	1.0	0.0
Gamma-glutamyl hydrolase OS=Mus musculus GN=Ggh 447 PE=1 SV=1	GGH_MOUSE 35 kDa	95% (0.021)	1.0	2.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.3	0.6	1.0	0.0	1.0	0.0
Serine protease HTRA1 OS=Mus musculus GN=Htra1 PE=2 362 SV=1	HTRA1_MOUSE51 kDa	0% (0.72)	1.0	1.0	2.9	1.0	1.0	1.8	1.0	1.0	1.0	1.6	1.1	1.3	0.5	1.0	0.0
Insulin-like growth factor-binding protein 6 OS=Mus 440 musculus GN=Igfbp6 PE=2 SV=1	IBP6_MOUSE 25 kDa	0% (0.48)	1.0	1.0	1.0	1.7	1.0	1.0	1.0	1.0	1.0	1.0	0.0	1.2	0.4	1.0	0.0
Insulin-like growth factor 1 OS=Mus musculus GN=Igf1 PE=2 227 SV=2	IGF1_MOUSE 17 kDa	95% (0.0076)	1.0	1.0	1.0	4.8	6.9	5.9	3.8	1.0	3.8	1.0	0.0	5.8	1.1	2.9	1.6
344 Interleukin-6 OS=Mus musculus GN=Il6 PE=1 SV=1	IL6_MOUSE 24 kDa	0% (0.84)	1.0	1.8	1.0	3.2	1.0	1.0	1.0	1.0	4.3	1.8	0.8	1.7	1.3	2.1	1.9
Interferon-alpha/beta receptor beta chain OS=Mus musculus 327 GN=Ifnar2 PE=1 SV=1	INAR2_MOUSE 57 kDa	0% (0.53)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	6.4	1.0	1.0	0.0	1.0	0.0	2.8	3.1
Laminin subunit alpha-1 OS=Mus musculus GN=Lama1 490 PE=1 SV=1	LAMA1_MOUSE338 kDa	0% (0.42)	1.0	1.0	1.0	1.0	2.1	1.0	1.0	1.0	1.0	1.0	0.0	1.4	0.6	1.0	0.0
Laminin subunit alpha-2 OS=Mus musculus GN=Lama2 259 PE=1 SV=1	LAMA2_MOUSE343 kDa	0% (0.11)	1.0	4.6	1.0	8.1	4.2	1.0	1.0	1.0	1.0	2.2	2.0	4.4	3.5	1.0	0.0
Laminin subunit alpha-5 OS=Mus musculus GN=Lama5 348 PE=1 SV=3	LAMA5_MOUSE404 kDa	0% (0.36)	1.0	8.0	1.0	1.0	6.3	1.0	1.0	1.0	1.0	3.3	4.0	2.8	3.1	1.0	0.0
Laminin subunit beta-2 OS=Mus musculus GN=Lamb2 PE=2 497 SV=1	LAMB2_MOUSE196 kDa	0% (0.62)	1.0	1.0	1.0	1.0	2.2	1.0	1.0	1.0	2.7	1.0	0.0	1.4	0.7	1.6	1.0
Laminin subunit gamma-1 OS=Mus musculus GN=Lamc1 403 PE=1 SV=2	LAMC1_MOUSE177 kDa	0% (0.27)	1.0	1.0	1.0	2.1	1.0	1.0	6.3	1.0	1.8	1.0	0.0	1.4	0.6	3.0	2.8
Leukemia inhibitory factor OS=Mus musculus GN=Lif PE=1 305 SV=1	LIF_MOUSE 22 kDa	95% (0.0093)	1.0	1.0	1.0	3.1	4.3	5.4	1.0	1.0	1.0	1.0	0.0	4.3	1.2	1.0	0.0
Lysyl oxidase homolog 3 OS=Mus musculus GN=Loxl3 PE=2 83 SV=1	LOXL3_MOUSE84 kDa	95% (0.00074)	1.0	2.7	3.4	3.7	8.0	9.0	30.5	40.0	24.1	2.4	1.2	6.9	2.8	31.5	8.0
Latent-transforming growth factor beta-binding protein 1 321 OS=Mus musculus GN=Ltbp1 PE=2 SV=2	LTBP1_MOUSE 187 kDa	95% (0.0051)	1.0	1.0	1.0	4.8	4.6	4.7	1.0	4.0	3.8	1.0	0.0	4.7	0.1	2.9	1.7
Latent-transforming growth factor beta-binding protein 2 60 OS=Mus musculus GN=Ltbp2 PE=1 SV=2	LTBP2_MOUSE 196 kDa	95% (0.00021)	1.0	1.0	1.0	11.8	23.1	19.5	30.5	33.9	39.9	1.0	0.0	18.1	5.8	34.8	4.7
Latent-transforming growth factor beta-binding protein 4 206 OS=Mus musculus GN=Ltbp4 PE=2 SV=1	LTBP4_MOUSE 179 kDa	95% (0.0064)	1.0	1.0	1.0	3.1	4.2	1.0	6.3	14.2	13.7	1.0	0.0	2.8	1.6	11.4	4.4
217 Lumican OS=Mus musculus GN=Lum PE=1 SV=2	LUM_MOUSE 38 kDa	0% (0.084)	1.0	2.9	1.0	1.0	4.5	4.2	5.0	10.7	4.6	1.6	1.1	3.2	1.9	6.8	3.4

320	Mesencephalic astrocyte-derived neurotrophic factor OS=Mus musculus GN=Manf PE=1 SV=1	MANF_MOUSE 20 kDa	95% (0.038)	1.0	1.0	1.0	4.2	1.0	1.0	2.9	1.0	1.0	1.0	0.0	2.1	1.8	1.6	1.1
406	Multiple epidermal growth factor-like domains protein 6 OS=Mus musculus GN=Megf6 PE=2 SV=3	MEGF6_MOUSE 165 kDa	95% (0.0012)	1.0	1.0	1.0	1.0	1.0	1.0	4.8	3.8	2.3	1.0	0.0	1.0	0.0	3.6	1.3
302	Meteorin-like protein OS=Mus musculus GN=Metrl PE=2 SV=1	METRL_MOUSE 35 kDa	95% (0.040)	1.0	1.0	2.2	1.0	4.2	1.0	3.8	4.3	4.6	1.4	0.7	2.1	1.8	4.2	0.4
300	Microfibril-associated glycoprotein 4 OS=Mus musculus GN=Mfap4 PE=1 SV=1	MFAP4_MOUSE 29 kDa	95% (0.010)	1.0	1.0	1.0	1.0	3.1	1.0	4.7	8.6	4.6	1.0	0.0	1.7	1.2	6.0	2.3
251	Macrophage migration inhibitory factor OS=Mus musculus GN=Mif PE=1 SV=2	MIF_MOUSE 13 kDa	0% (0.16)	1.0	1.0	4.4	3.6	1.0	4.7	6.4	6.7	3.8	2.1	2.0	3.1	1.9	5.6	1.6
350	Matrix metalloproteinase-19 OS=Mus musculus GN=Mmp19 PE=2 SV=1	MMP19_MOUSE 59 kDa	0% (0.47)	1.0	1.0	1.8	1.0	1.8	2.6	1.9	3.1	1.9	1.3	0.4	1.8	0.8	2.3	0.7
428	Neuroserpin OS=Mus musculus GN=Serpini1 PE=1 SV=1	NEUS_MOUSE 46 kDa	95% (0.00026)	1.0	1.0	1.0	2.0	2.8	2.5	1.0	1.0	1.0	1.0	0.0	2.4	0.4	1.0	0.0
322	Nidogen-2 OS=Mus musculus GN=Nid2 PE=1 SV=1	NID2_MOUSE 154 kDa	0% (0.11)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	3.9	9.1	1.0	0.0	1.0	0.0	4.7	4.1
304	Pappalysin-1 OS=Mus musculus GN=Pappa PE=2 SV=2	PAPP1_MOUSE 181 kDa	95% (0.0069)	1.0	1.0	2.1	1.0	1.0	2.2	6.3	3.8	7.3	1.4	0.6	1.4	0.7	5.8	1.8
317	Protein convertase subtilisin/kexin type 5 OS=Mus musculus GN=Pcsk5 PE=1 SV=2	PCSK5_MOUSE 209 kDa	0% (0.25)	1.0	1.0	1.0	1.0	5.3	1.0	4.0	3.8	3.0	1.0	0.0	2.4	2.5	3.6	0.5
323	Platelet-derived growth factor D OS=Mus musculus GN=Pdgfrd PE=2 SV=1	PDGFRD_MOUSE 143 kDa	95% (0.010)	1.0	3.0	3.6	3.1	2.6	2.7	1.0	1.0	1.0	2.5	1.4	2.8	0.3	1.0	0.0
379	Phospholipase A1 member A OS=Mus musculus GN=Pla1a PE=2 SV=2	PLA1A_MOUSE 50 kDa	95% (0.041)	1.0	2.8	1.0	1.0	3.7	3.3	1.0	1.0	1.0	1.6	1.0	2.6	1.4	1.0	0.0
310	Placenta-specific protein 9 OS=Mus musculus GN=Plac9 PE=2 SV=1	PLAC9_MOUSE 11 kDa	95% (0.00025)	1.0	1.0	3.2	5.6	6.5	5.5	1.0	1.0	1.0	1.7	1.2	5.8	0.5	1.0	0.0
271	Vitamin K-dependent protein S OS=Mus musculus GN=Pros1 PE=2 SV=1	PROS_MOUSE 75 kDa	0% (0.099)	1.0	2.9	3.5	4.1	1.0	1.0	3.7	6.3	5.7	2.5	1.3	2.0	1.8	5.2	1.3
241	Secreted frizzled-related protein 3 OS=Mus musculus GN=Frzb PE=1 SV=1	SFRP3_MOUSE 36 kDa	0% (0.11)	1.0	2.4	1.0	1.0	5.2	2.4	1.0	1.0	1.8	1.5	0.8	2.9	2.1	1.3	0.5
436	Slit homolog 2 protein OS=Mus musculus GN=Slit2 PE=2 SV=1	SLIT2_MOUSE 169 kDa	0% (0.19)	1.0	1.0	1.0	1.0	1.0	2.7	1.0	1.0	1.0	1.0	0.0	1.6	1.0	1.0	0.0
318	Sushi repeat-containing protein SRPX2 OS=Mus musculus GN=Srxp2 PE=2 SV=1	SRPX2_MOUSE 53 kDa	0% (0.12)	1.0	1.0	1.0	1.0	1.0	1.0	5.6	1.0	6.7	1.0	0.0	1.0	0.0	4.4	3.0
455	Tenascin OS=Mus musculus GN=Tnc PE=1 SV=1	TENA_MOUSE 232 kDa	0% (0.065)	1.0	1.0	1.0	1.0	1.0	1.0	4.2	1.0	1.0	1.0	0.0	1.0	0.0	2.1	1.8
335	Transforming growth factor beta-2 OS=Mus musculus GN=Tgfb2 PE=2 SV=1	TGFB2_MOUSE 48 kDa	95% (0.029)	1.0	4.1	4.4	1.0	4.6	4.4	1.0	1.0	1.0	3.2	1.9	3.3	2.0	1.0	0.0
370	Tumor necrosis factor receptor superfamily member 11B OS=Mus musculus GN=Trnrf11b PE=2 SV=1	TR11B_MOUSE 46 kDa	95% (0.028)	1.0	1.0	1.0	1.0	1.0	4.9	1.0	1.0	1.0	1.0	0.0	2.3	2.2	1.0	0.0
481	Ubiquitin cross-reactive protein OS=Mus musculus GN=Ucrp15 PE=1 SV=4	UCRP_MOUSE 18 kDa	0% (0.53)	1.0	1.0	1.0	1.0	2.8	1.0	1.0	1.0	1.0	1.0	0.0	1.6	1.1	1.0	0.0
501	Pantetheinase OS=Mus musculus GN=Vnn1 PE=1 SV=2	VNN1_MOUSE 57 kDa	0% (0.42)	1.0	1.0	1.0	1.0	1.0	1.6	1.0	1.0	1.0	1.0	0.0	1.2	0.4	1.0	0.0

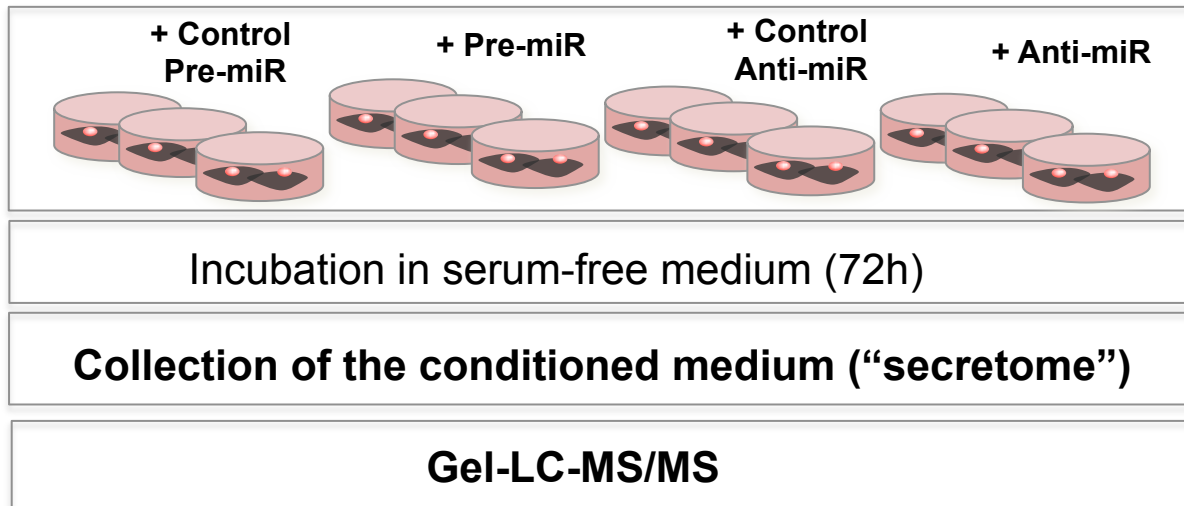
Online-Table V: Echocardiography data of antagomiR-29b treated hearts after TAC (n=9 per group)

	Control			antagomir			T-test
	Mean (9)	SD	SE	Mean (9)	SD	SE	
Body weight (baseline)	20.2	2.6	0.9	20.1	2.4	0.8	0.81
Body weight (2 week)	22.6	2.9	1.0	22.9	3.2	1.1	0.99
HW/T	9.0	1.8	0.6	9.9	1.5	0.5	0.28
M-mode (combined PSLAX and SAX)							
Heart Rate	517.8	54.8	18.3	513.2	51.6	17.2	0.82
Diameter;s	3.3	0.3	0.1	3.3	0.5	0.2	0.84
Diameter;d	4.1	0.2	0.1	4.1	0.4	0.1	0.96
Volume;s	43.4	11.0	3.7	46.1	15.7	5.2	0.77
Volume;d	73.6	9.8	3.3	74.9	17.2	5.7	0.95
Stroke Volume	30.2	4.6	1.5	28.8	3.1	1.0	0.41
Ejection Fraction	41.7	7.8	2.6	39.7	7.1	2.4	0.64
Fractional Shortening	20.3	4.3	1.4	19.2	3.8	1.3	0.62
Cardiac Output	15.6	2.5	0.8	14.8	2.0	0.7	0.41
B-mode (SAX)							
IVS;d	0.9	0.1	0.0	0.9	0.1	0.0	0.46
IVS;s	1.2	0.2	0.1	1.2	0.1	0.0	0.97
LVID;d	4.2	0.5	0.2	4.3	0.5	0.2	0.81
LVID;s	3.2	0.5	0.2	3.4	0.5	0.2	0.45
LVPW;d	0.9	0.1	0.0	1.1	0.2	0.1	0.13
LVPW;s	1.2	0.1	0.0	1.2	0.1	0.0	0.91

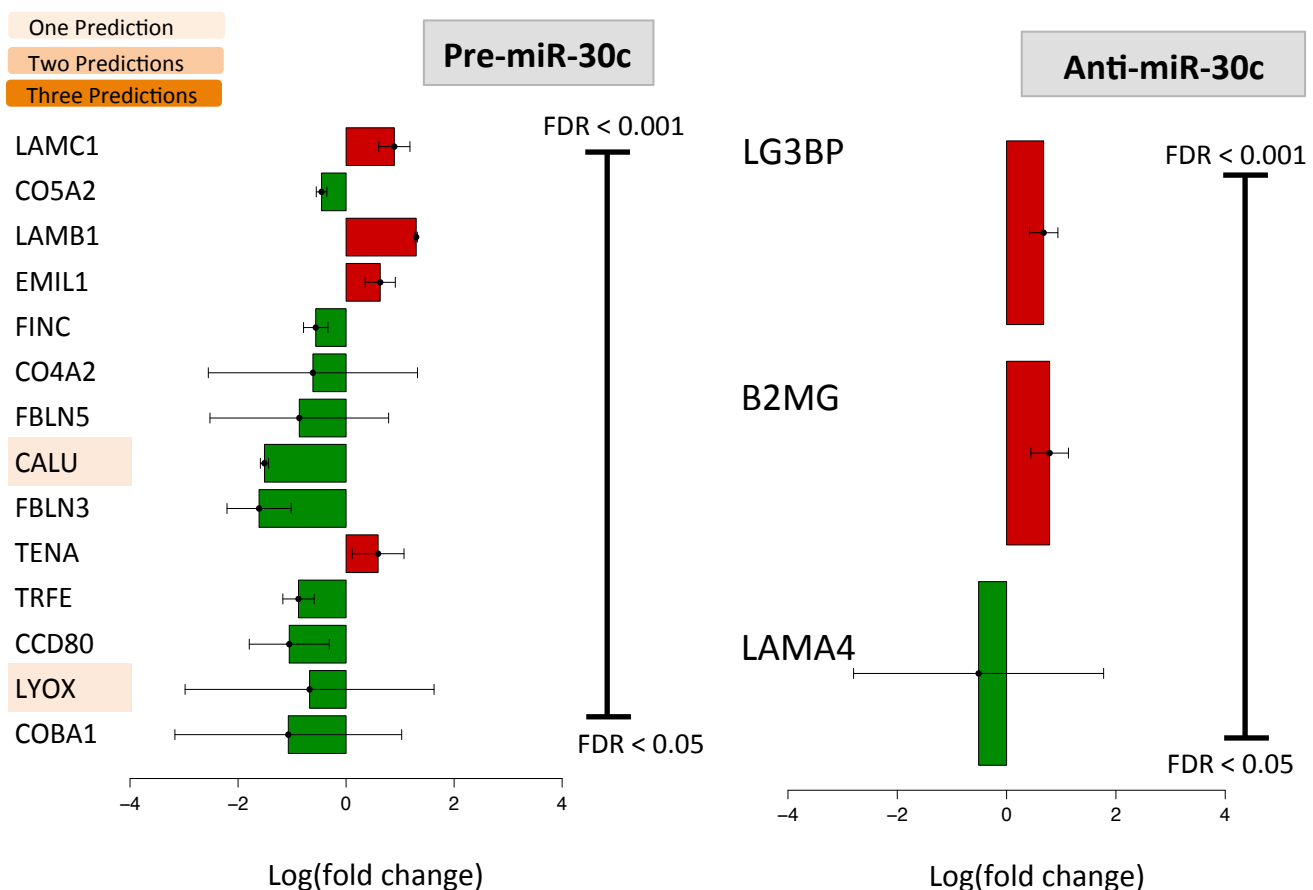
Online Figure I: A) Vimentin immunostaining after collagenase-based digestion of mouse hearts. Following collagenase-based digestion of mouse hearts, primary mouse CFs were cultured on gelatin 0.1% and grown in DMEM medium supplemented with L-Glutamine, 10% heat-inactivated FBS and antibiotics (100 U/ml penicillin and 100 µg/ml streptomycin) at 37°C in a humidified atmosphere of 95% air / 5% CO₂. Cells were detached with 0.05% trypsin for passaging. At passage 2, the cells were plated on 8-well chamber slides for immunostaining (Vimentin: red, DAPI:blue). **B, C)** Confirmation of over-expression and inhibition of miR-29b and miR-30c by qPCR. **D)** LNA-anti-miRs to miR-29b also reduced the expression of the other miR-29 family members. *P<0.05, **P<0.01.



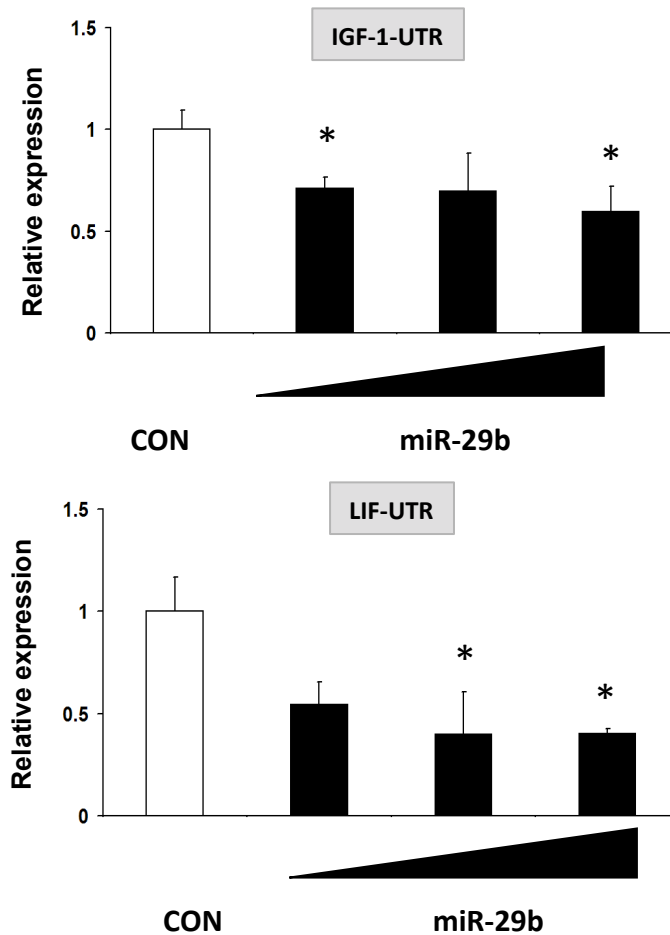
Online Figure II: Schematic description of the proteomics workflow. CFs were isolated from mouse heart by collagenase-based digestion. At passage 2-3, CFs (3 biological replicates per experimental condition) were transfected with a miRNA construct and then, incubated in serum-free medium. After 72h, the conditioned medium was collected, cleared from cell debris by centrifugation, desalted, and resuspended in loading buffer. An equal volume of sample (30 μ l) was separated on a SDS-PAGE gel, digested with trypsin and analysed by LC-MS/MS using a high mass accuracy LTQ-Orbitrap XL.



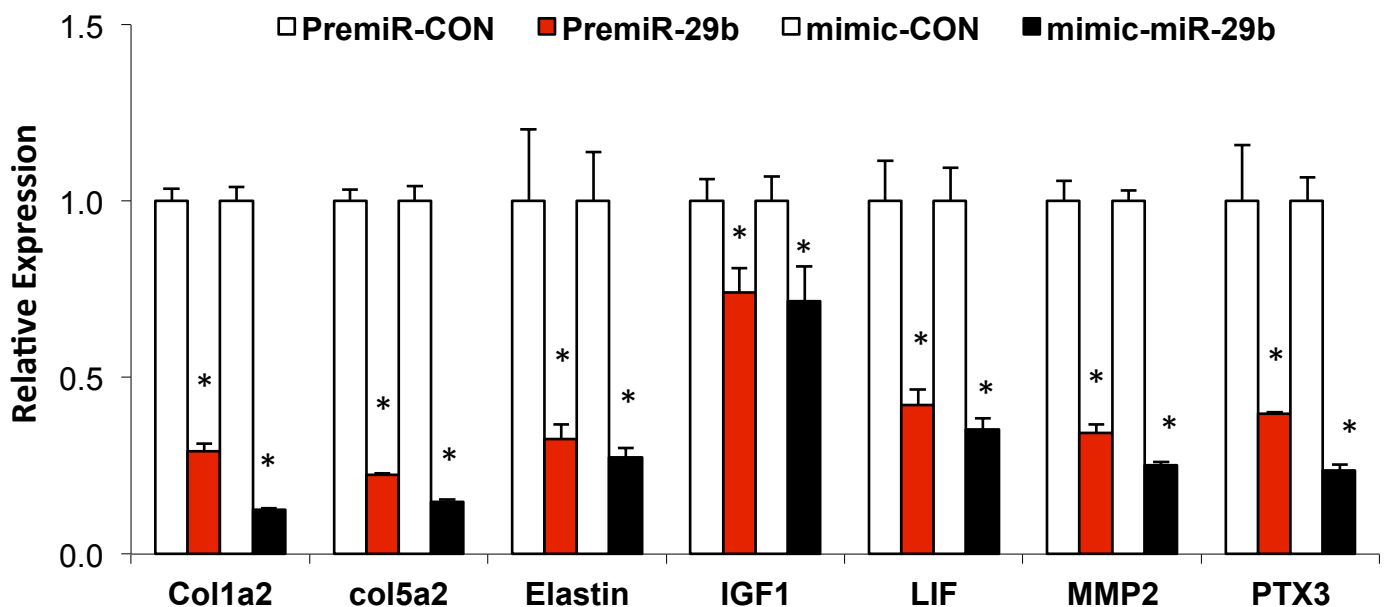
Online Figure III: The log(fold change) for each of the differentially released proteins in the miR-30c experiment is illustrated. The proteins are ordered from the smallest to largest False Discovery Rate (FDR) with significant differential expression set at a FDR 5% (<0.05). The differential release and corresponding FDR was calculated using the Qspec method which utilises a model based on a hierarchical Bayes estimation of generalized linear mixed effects model (GLMM). The FDR, as per the Qspec method, was calculated using the Bayes Factors and a mixture model-based method of controlling the local FDR. All protein identifications are listed in **Online Table III**.



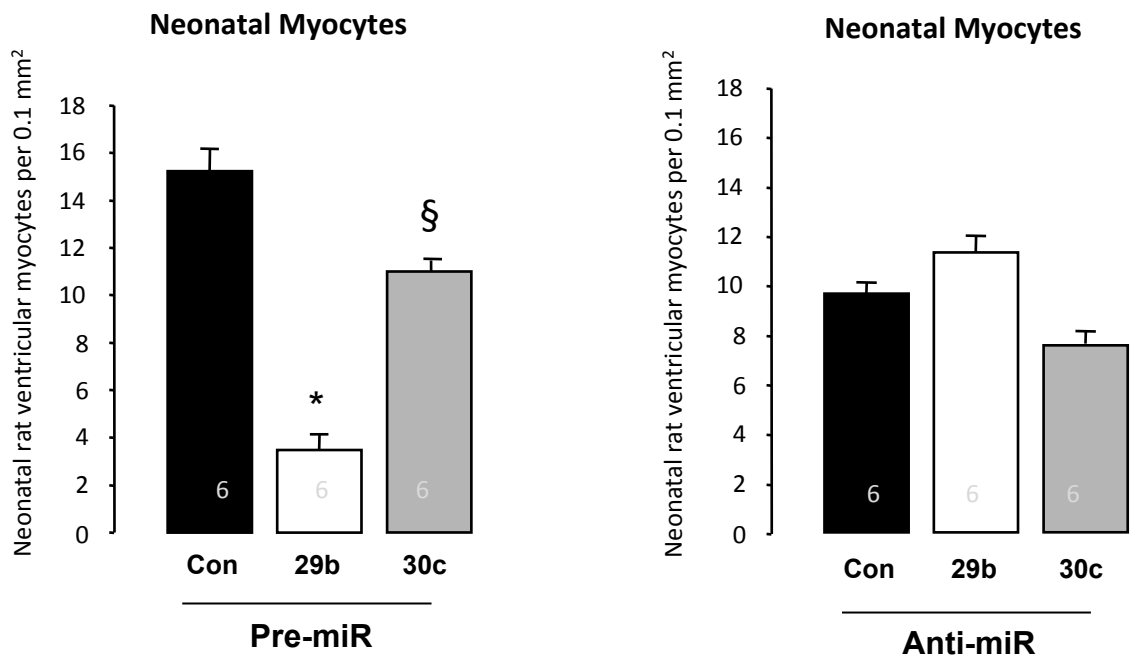
Online Figure IV: Luciferase reporter assay. The 3' untranslated regions of mouse IGF-1, LIF and PTX3 harboring putative binding sites of the miR-29 family were cloned into the dual-luciferase reporter vector psiCheck2 (Promega). The reporter vectors (100 ng of psiCheck2 construct) were transfected together with 30-100 nM of miR-29b mimic or the mimic negative control (CON) in triplicate into mouse aortic smooth muscle cells using Lipofectamine 2000 (Lifetechnologies). Renilla 3'UTR-coupled luciferase activity was normalized to constitutive firefly luciferase activity for each well. Unlike IGF-1 and LIF, no significant inhibition was obtained for PTX3 (data not shown). *, denotes $P < 0.05$ compared to respective CON.



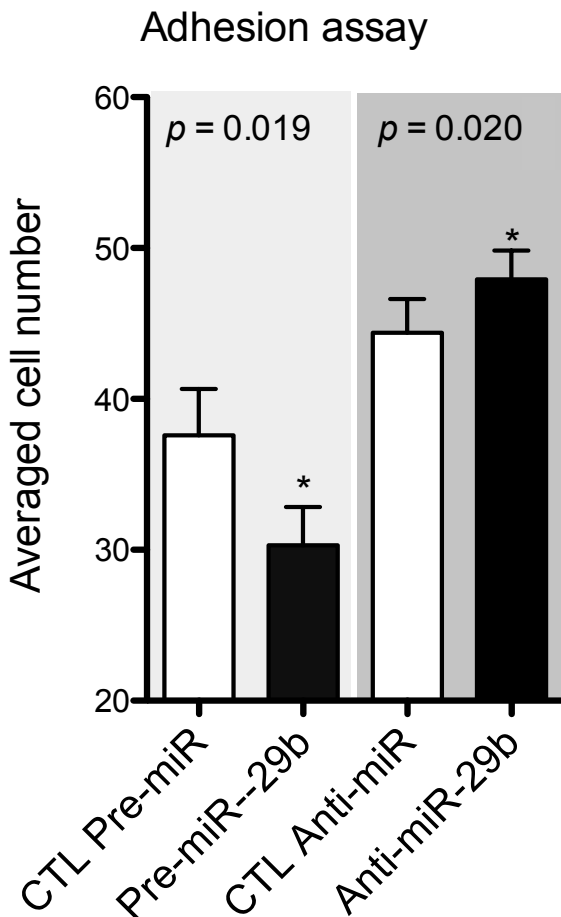
Online Figure V: Effect of miR-29b mimics on expression of miR-29b targets in CFs as assessed by qPCR (minimum of n=3 per group). * denotes $P < 0.05$.



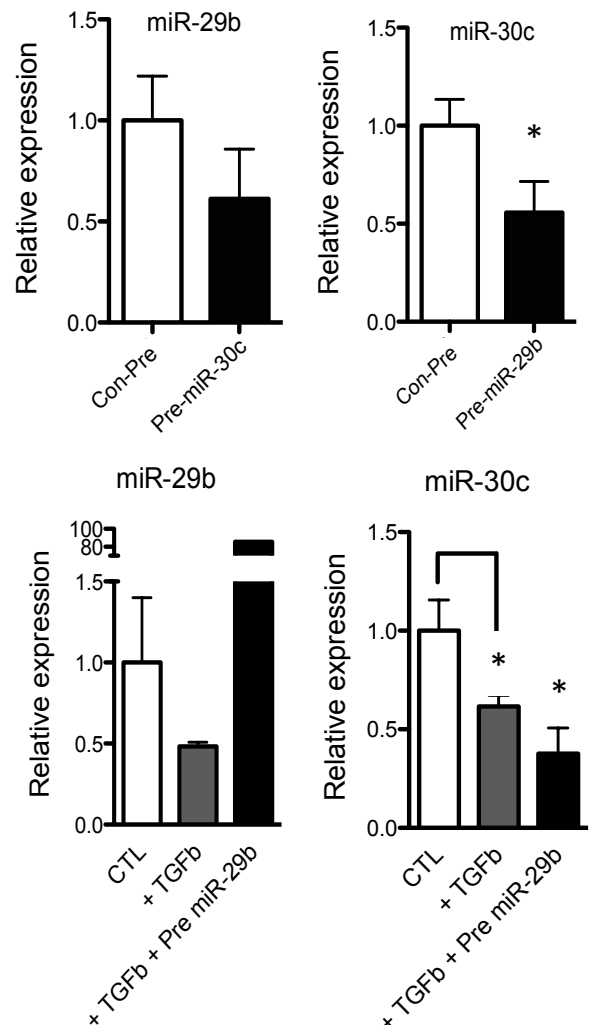
Online Figure VI: Number of adherent NRVM is displayed by the bar chart per 0.1 mm². The bar chart demonstrates the myocyte count of 3 areas per coverslip in 6 independent experiments. §*P<0.05 vs corresponding control group (CON).



Online Figure VII: Number of adherent CFs is displayed as averaged cell number per 0.1 mm². *P<0.05 vs control (CON) for the averaged CF count of 3 areas per coverslip.

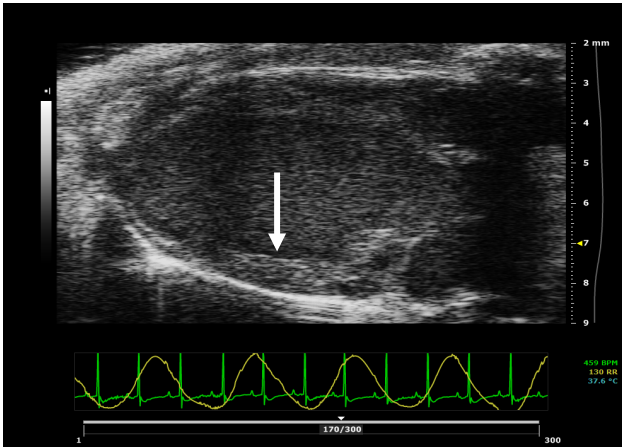


Online Figure VIII: Cross-talk between miR-29b and miR-30c in CFs as assessed by qPCR. *P<0.05 vs control (CON) in three independent experiments.

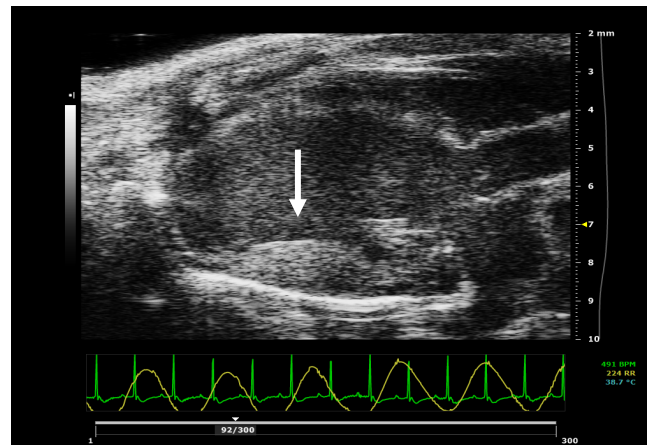


Online Figure IX: Representative parasternal long axis B mode image from antagomiR-treated mice that showed the most pronounced inhibition of miR-29b after TAC. A cross section of the papillary muscle (white arrows) is in view rather than the true inferolateral (posterior) wall. The latter (*) has the same thickness as revealed in the short axis B-mode but the papillary muscle was abnormally thickened and hyperechogenic.

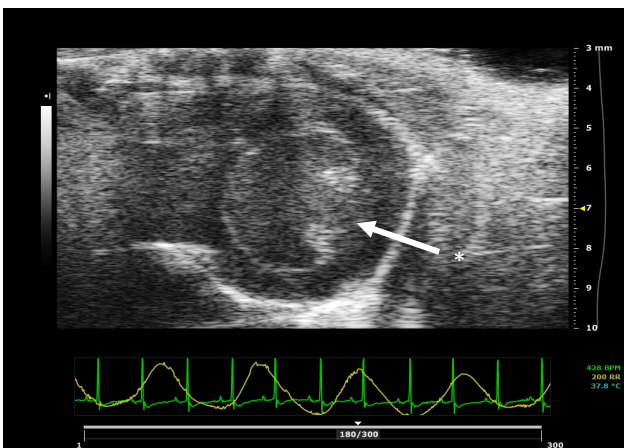
**TAC AntagomiR
Con**



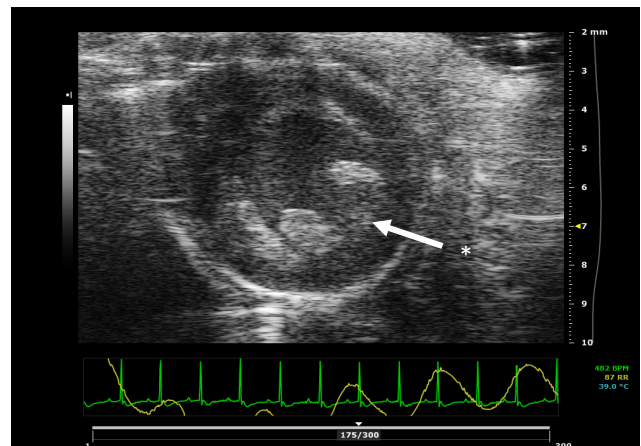
**TAC
AntagomiR-29b**



**TAC AntagomiR
Con**



**TAC
AntagomiR-29b**



Online Figure X: Q-PCR. Bean plots visualizing 27 transcript levels in LVH normalized to U6.

