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MicroRNAs in farm animals

X. Wang[1,2], Z. Gu[1†] and H. Jiang[3†]

[1]*Department of Life Science and Technology, Changshu Institute of Technology, Changshu 215500, P R China;* [2]*College of Animal Science and Technology, Yangzhou University, Yangzhou 225509, P R China;* [3]*Department of Animal and Poultry Sciences, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA*

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MicroRNAs (miRNAs) are a class of ~22 nucleotide-long small noncoding RNAs that target mRNAs for translational repression or degradation. miRNAs target mRNAs by base-pairing with the 3′-untranslated regions (3′-UTRs) of mRNAs. miRNAs are present in various species, from animals to plants. In this review, we summarize the identification, expression, and function of miRNAs in four important farm animal species: cattle, chicken, pig and sheep. In each of these species, hundreds of miRNAs have been identified through homology search, small RNA cloning and next generation sequencing. Real-time RT-PCR and microarray experiments reveal that many miRNAs are expressed in a tissue-specific or spatiotemporal-specific manner in farm animals. Limited functional studies suggest that miRNAs have important roles in muscle development and hypertrophy, adipose tissue growth, oocyte maturation and early embryonic development in farm animals. Increasing evidence suggests that single-nucleotide polymorphisms in miRNA target sites or miRNA gene promoters may contribute to variation in production or health traits in farm animals.

Keywords: microRNAs, cattle, chickens, pigs, sheep

Implications

MicroRNAs (miRNAs) are predicted to regulate the expression of 20% to 30% of the genes in a genome. Studies in laboratory animals have revealed that miRNAs play critical roles in many aspects of animal development and physiology. Hundreds of miRNAs have been also identified in various farm animal species. Understanding the functions of miRNAs in farm animals is essential to know how the various biological processes are regulated and to developing novel strategies to improve production efficiency in farm animals.

Introduction

MicroRNAs (miRNAs) are a class of small (~22 nucleotides) single-stranded noncoding RNAs that inhibit gene expression post-transcriptionally (Bartel, 2004). The first miRNA was discovered in *Caenorhabditis elegans*, and was called lin-4 because it represses the expression of protein-coding gene *lin-14* (Lee *et al.*, 1993). Since then hundreds of miRNAs have been identified in various animal and plant species, and miRNAs have been shown to play roles in many biological processes, including cell proliferation, differentiation, apoptosis and development (Bartel, 2004; Wienholds and Plasterk, 2005). This review will focus on the identification, expression, function and regulation of miRNAs in major farm animals.

† E-mail: zhilianggu88@hotmail.com; hojiang@vt.edu

Biogenesis of miRNAs

In animals miRNAs are generated from miRNA genes located in intergenic regions or introns of protein-coding genes (Bartel, 2004) (Figure 1). Non-protein-coding miRNA genes are transcribed by RNA polymerase II to generate primary miRNAs (pri-miRNAs). In the nucleus, pri-miRNAs are processed by the RNase III Drosha to form ~70-nucleotide (nt) precursor miRNAs (pre-miRNAs), which are characterized by the stem-loop structure (Lee *et al.*, 2003; Kim, 2005). Pre-miRNAs are transported from the nucleus to the cytoplasm by the shuttle protein Exportin-5 with the assistance of the G-protein Ran. In the cytoplasm, pre-miRNAs are recognized and cleaved by the RNase III Dicer to form ~22 nt double-stranded RNAs (Hutvagner *et al.*, 2001; Lund *et al.*, 2004). When the double strands unwind, one strand enters the RNA-induced silencing complex (RISC), and this strand becomes mature miRNA and can exercise its gene silencing function (Khvorova *et al.*, 2003). Generation of miRNAs from introns of protein-coding genes, termed *mirtrons*, follows a slightly different procedure. When pri-miRNAs are transcribed from *mirtrons*, they accurately imitate the structures of pre-miRNAs without involving Drosha (Carthew and Sontheimer, 2009).

Like mRNAs, miRNA expression is controlled at the transcriptional level by gene-specific transcription factors (Li *et al.*, 2011d; Wang *et al.*, 2011). miRNA expression can also be regulated by epigenetic mechanisms. Many miRNA

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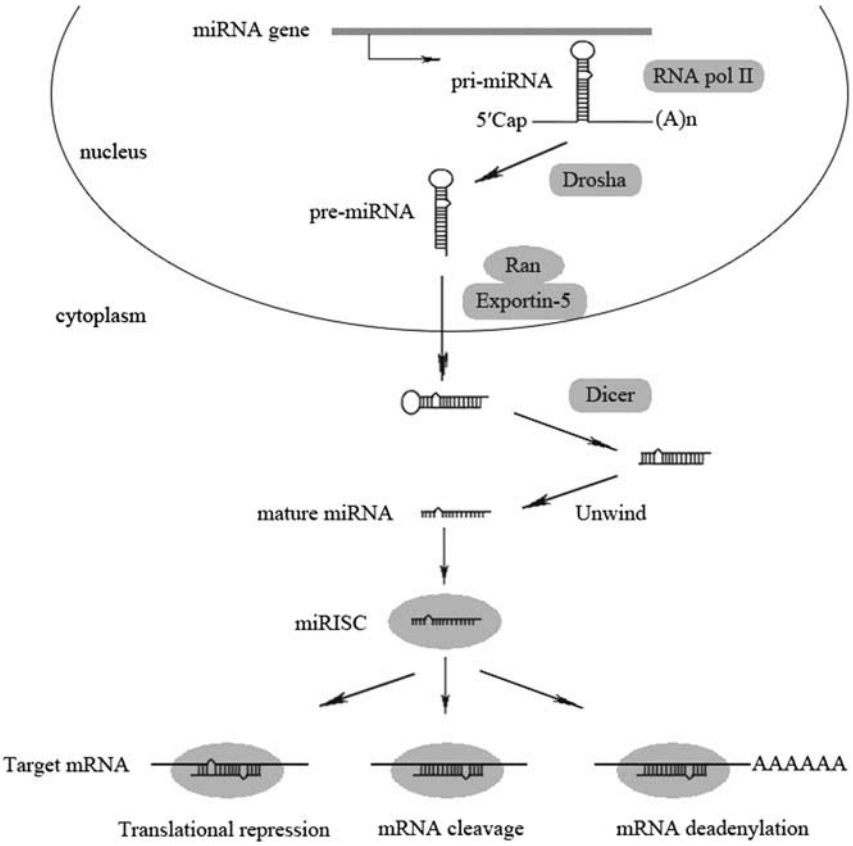


Figure 1 Biogenesis and mechanism of action of miRNAs. Primary miRNA (pri-miRNA), precursor miRNA (pre-miRNA), Drosha and Dicer are nuclear and cytoplasmic RNase III, respectively; miRISC, miRNA containing RNA-induced silencing complex. See text for details modified from references (Hutvagner *et al*., 2001; Khvorova *et al*., 2003; Lee *et al*., 2003; Lund *et al*., 2004; Kim, 2005) and (Lee *et al*., 1993; Bartel, 2004; Guo *et al*., 2005; Giraldez *et al*., 2006; Wu *et al*., 2006).

genes contain CpG islands in the promoters, and methylation of these islands represses the transcription of the miRNA genes (Bueno *et al*., 2008). miRNA expression can be also induced or inhibited by histone acetylation and/or methylation (Chen *et al*., 2012b; Saito *et al*., 2012). Some miRNA genes are regulated by CpG island methylation as well as histone modification (Saito and Saito, 2012). miRNA biogenesis can be also regulated at the post-transcriptional level (Siomi and Siomi, 2010).

Mechanism of miRNA action

A miRNA regulates the expression of its target mRNA in three manners (Figure 1), depending on the degree of complementarity between them. An imperfect complementarity leads to translational repression whereas a perfect or nearly perfect complementarity leads to cleavage of the target mRNA. Animal miRNAs are often imperfectly complementary to their target sites; so translational repression is the predominant mechanism by which miRNAs inhibit mRNA expression in animal cells (Lee *et al*., 1993). Plant miRNAs in general have perfect or nearly perfect complementarity to their target sites. As such, cleavage of target mRNAs is the major consequence of miRNA–mRNA binding in plants (Guo *et al*., 2005). Some animal miRNAs can cause the cleavage of their target mRNAs despite imperfect complementarity between them. This is how miR-196 regulates the expression of homeobox protein HOXB8 in mouse embryos (Yekta *et al*., 2004). The third manner by which miRNA regulates mRNA expression involves mRNA deadenylation. When binds to the imperfectly complementary target site of mRNA, miRNA accelerates the poly(A) tail to be deadenylated. This manner seems to be exclusive to animal miRNAs, and this is how zebrafish miR-430 accelerates the degradation of maternal mRNAs (Giraldez *et al*., 2006), and mammalian miR-125b and let-7 regulate the expression of their target mRNAs (Wu *et al*., 2006). Although the complementarity between a miRNA and its target mRNA does not have to be perfect, nucleotides 2 to 8 from the 5′ end of the miRNA, also called seed sequence, must be perfectly complementary to the target mRNA (Bartel, 2004).

miRNA target prediction and validation

miRNA target genes can be predicted by computational methods. These methods include miRanda and TargetScan, which are mainly based on sequence complementarity (Enright *et al*., 2003; Lewis *et al*., 2005), and PicTar, DIANA-microT, RNAhybrid, microInspector, RNA22 and SVMicrO, which use different algorithms (Liu *et al*., 2010). It is difficult

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to rate the accuracy of these programs, but a target predicted by multiple programs has greater potential to be a true miRNA target than a target predicted by one program. miRNA target genes predicted by computational methods need to be validated by experiments. A common experiment to validate miRNA targets involves overexpression or knockdown of the miRNA and subsequent detection of the predicted target mRNAs using qRT-PCR or luciferase reporter assays. miRNA knockdown is usually achieved by antisense oligonucleotides (ASO), which bind to the complementary miRNAs so that the latter can not bind to their target mRNAs. 2′-O-methyl antisense oligonucleotides (AMO) and locked nucleic acids (LNA) are two kinds of chemically modified ASO. Compared with AMO, LNA have a higher inhibition efficiency (Naguibneva *et al*., 2006b). Another kind of ASO is miRNA sponges. miRNA sponges are RNA sequences transcribed from expression vectors, containing multiple tandem binding sites to miRNAs. miRNA sponges competitively bind to miRNAs, and thereby prevent them from binding to their targets (Ebert *et al*., 2007; Ebert and Sharp, 2010). Large-scale miRNA target validation can be achieved through proteomic approaches. For example, using selected reaction monitoring (SRM) and isotope-coded affinity tag quantification, hundreds of potential let-7 target proteins extracted from wild-type and let-7 mutant *C. elegans* were screened. One hundred and sixty-one proteins can be quantified, and of these, 29 showed significant changes in abundance between wild-type and let-7 mutant. The results of SRM were similar to those of independent experimental downstream analyses such as genetic interaction, as well as polysomal profiling and luciferase assays, indicating that SRM-based validation of miRNA targets is effective and efficient (Jovanovic *et al*., 2010).

miRNAs in cattle

Extensive work has been conducted to identify bovine miRNAs, and a total of 755 mature miRNAs processed from 766 pre-miRNAs have been identified in cattle by various labs (Table 1; (Kozomara and Griffiths-Jones, 2011)). By cloning small RNAs from bovine embryo, thymus, small intestine and lymph node, Coutinho and colleagues identified 129 bovine miRNAs (Coutinho *et al*., 2007). Using a similar approach, Gu *et al*. identified 59 miRNAs from bovine adipose tissue and mammary gland (Gu *et al*., 2007), and Jin *et al*. discovered 101 bovine miRNAs from 11 bovine tissues (Jin *et al*., 2009). Using computational methods, a total of 496 miRNA genes were predicted from bovine genome (Bovine Genome Sequencing and Analysis Consortium, 2009). More recently, deep sequencing was used to detect miRNAs in primary bovine retinal microvascular endothelial cells, resulting in the identification of 255 known bovine miRNAs. Interestingly, there were multiple new members of the miR-2284/2285 family detected, suggesting this family of miRNAs may play important roles in angiogenesis (Guduric-Fuchs *et al*., 2012).

Table 1 *Numbers of identified miRNAs in four farm animal species**

Species	miRNA precursors	Mature miRNAs
Cattle	766	755
Chicken	684	791
Pig	271	306
Sheep	55	103

*Based on *miRBase* 19.

Functional studies of bovine miRNAs have concentrated on the roles of miRNAs in adipose, skeletal muscle, oocyte and early embryonic developments (Table 2). Jin *et al*. compared the expression of 89 bovine miRNAs in adipose tissues between three crossbreeds differing in backfat thickness, and found that 42 miRNAs were differentially expressed, of which miR-378 was most differentiated (Jin *et al*., 2010). miR-378 has been shown to play a role in lipogenesis in mice (Gerin *et al*., 2010). Thus, miR-378 might participate in the control of subcutaneous growth in cattle. Expression of miR-143 is upregulated during differentiation of bovine intramuscular preadipocytes into mature adipocytes. Transfection of miR-143 antisense oligonucleotide represses the differentiation of bovine intramuscular preadipocytes (Li *et al*., 2011b). These observations further support a role of miR-143 in intramuscular fat development in cattle. Romao and colleagues reported that adipose tissue expression of 8 miRNAs, including miR-19a, -92a, -92b, -101, -103, -106, -142-5p and -296, was responsive to high-fat diet feeding (Romao *et al*., 2012). Thus, these miRNAs might be parts of the gene regulatory network that mediates high-fat diet-induced adipogenesis in cattle.

miR-1 and miR-206 are two muscle-specific miRNAs that play an important role in muscle cell differentiation (Townley-Tilson *et al*., 2010). Miretti and colleagues analyzed the expression of miR-1 and miR-206 in skeletal muscle of Piedmontese and Friesian cattle, of which the former are 'double-muscled' because of a point mutation in the myostatin gene (Berry *et al*., 2002). Expression of miR-1 was not different between the two breeds or sexes, whereas miR-206 was expressed significantly higher in female Piedmontese than in female Friesian cattle (Miretti *et al*., 2011), suggesting that upregulated expression of miR-206 might contribute to muscle hypertrophy in female Piedmontese cattle. miR-181b is known to be involved in myoblast differentiation (Naguibneva *et al*., 2006a). In Angus cattle, after acute stress (anesthetization and placement of a rumen catheter), miR-181b was upregulated in the muscle, implying it may play a role in myogenesis in Angus cattle (Zhao *et al*., 2012a).

Six miRNAs enriched in oocytes, including miR-205, -150, -122, -96, -146a and -146b-5p, were found to decrease dramatically in expression from 0 to 22 h of maturation (Abd El Naby *et al*., 2011). These miRNAs might therefore play a role in bovine oocyte maturation. Expression of miR-106a was greater in bovine oocytes than in cumulus–oocyte complexes (COCs), whereas expression of the miR-106a target gene WEE1 homolog (*Schizosaccharomyces pombe*) (WEE1A) was less in oocytes compared with COCs (Miles *et al*., 2012). These differences suggest that miR-106a might

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Table 2 *miRNAs with different functions in farm animals*

Species	miRNA	Expression pattern	Target gene	Function	Reference
Cattle	miR-143	Intramuscular preadipocytes		Preadipocyte differentiation and proliferation	Li *et al.*, (2011b)
	miR-378	CL	IFNGR1	Apoptosis	Ma *et al.*, (2011)
	miR-196a	Oocytes	NOBOX	Folliculogenesis	Tripurani *et al.*, (2011)
	miR-181a	Oocytes	NPM2	Early embryogenesis	Lingenfelter *et al.*, (2011)
	miR-21	RMECs		Angiogenesis	Guduric-Fuchs *et al.*, (2012)
Chicken	miR-26a	Cone photoreceptors	L-VGCCα1C	Circadian rhythm of cone photoreceptors	Shi *et al.*, (2009)
		Lymphocytes	Interleukin-2	Lymphocyte proliferation	Xu *et al.*, (2010)
	miR-150	Leukocytes	MYB	Leukaemogenesis	Guillon-Munos *et al.*, (2010)
	miR-143	Embryonic chick splenocytes	PYCR2, PSTPIP1, PDCD5, KLF5	Cell proliferation and apoptosis	Trakooljul *et al.*, (2010)
	miR-302, miR-456	Blastoderm	SOX11	Maintain undifferentiated stage	Lee *et al.*, (2011)
	miR-181a*	PGCs	HOXA1, NR6A1	Somatic and meiotic differentiation	Lee *et al.*, (2011)
	miR-221, miR-142-3p	Limb mesenchymal cells	Mdm2, ADAM9	Chondrogenesis	Kim *et al.*, (2010)
	miR-365	Primary chondrocytes	HDAC4	Chondrogenesis	Guan *et al.*, (2011)
	miR-34a	Limb mesenchymal cells	EphA5	Chondrogenesis	Kim *et al.*, (2011a); Kim *et al.*, (2012)
	miR-1	Skeletal muscle	ACVR2B	Skeletal muscle development	Li *et al.*, (2011c)
Pig	miR-378	Granulosa cells	Aromatase	Estradiol production	Xu *et al.*, (2011)
	miR-155	Skeletal muscle	OLFML3	Skeletal muscle development	Zhao *et al.*, (2012b)
		Spleen		Immune function	Li *et al.*, (2013)
Sheep	miR-22	Sertoli cells		Fetal testicular development	Torley *et al.*, (2011)
	miR-1, miR-206	Skeletal muscle	MSTN in Texel	Muscular hypertrophy	Clop *et al.*, (2006); Takeda *et al.*, (2010)

play a role in bovine oocyte development by downregulating the WEE1A gene. Similarly, miR-196a and miR-181a may regulate bovine oocyte development by targeting the newborn ovary homeobox gene (NOBOX) and the nucleoplasmin 2 (NPM2) gene, respectively, which are essential for folliculogenesis and nuclear and nucleolar organization, respectively (Lingenfelter *et al.*, 2011; Tripurani *et al.*, 2011). Expression of miR-21 and miR-130a in bovine embryos was increased from the 1-cell to 8-cell stage. These two miRNAs might be involved in early bovine embryonic development (Mondou *et al.*, 2012).

miRNAs in chickens

The first study of chicken miRNAs was conducted in 2006, which identified 25 miRNAs from chicken embryos and adult chickens through small RNA cloning and sequencing (Xu *et al.*, 2006). Using the same cloning strategy, Wang *et al.* identified 47 miRNAs from chicken adipose tissue and skeletal muscle (Wang *et al.*, 2012). Using deep sequencing, 123 miRNAs were discovered from embryonic chick livers at embryonic days 15 (E15) and E20 (Hicks *et al.*, 2010), 121 known chicken miRNAs, 449 new chicken miRNAs and 39 mirtrons were identified from E5, E7 and E9 chicken embryos (Glazov *et al.*, 2008), and 63 and 33 novel chicken miRNAs were identified from chicken preadipocytes and skeletal muscle, respectively (Li *et al.*, 2011c; Yao *et al.*, 2011).

Microarrays were used to profile the expression of chicken miRNAs at different stages of gonadal sex differentiation. The study showed that miR-202*, a sexually dimorphic miRNA, was upregulated in male gonads, and this result was validated by *in situ* hybridization and Northern blot, indicating a potential role of miR-202* in male gonad development (Bannister *et al.*, 2009). miR-363 was identified to be another sexually dimorphic miRNA, whose expression in chicken gonads was different between sexes at E4.5 and E6.5 (Huang *et al.*, 2010). Using *in situ* hybridization, 111 miRNAs were profiled in chicken embryos and 75 of them were differentially expressed during embryonic development, suggesting these miRNAs might play roles in chicken embryonic development (Darnell *et al.*, 2006). MiR-302 and miR-456 maintain the undifferentiated stage of blastoderm by targeting the sex-determining region Y box 11 (SOX11). MiR-181a* inhibits the somatic differentiation of primordial germ cells (PGCs) by targeting homeobox A1 and prevents PGCs from entering meiosis by inhibiting the nuclear receptor subfamily 6, group A, member 1 (NR6A1) gene (Lee *et al.*, 2011). Also in PGCs the gene controlling DNA methylation DNA (cytosine-5-)-methyltransferase 3 beta (DNMT3B) is regulated by miR-15c, -29b, -383 and -222 (Rengaraj *et al.*, 2011).

Wang *et al.* found that 10 miRNAs including miR-1a, -133a and -122 were differentially expressed in chicken adipose tissue or skeletal muscle at different developmental stages, suggesting a potential role of these miRNAs in chicken adipose tissue and skeletal muscle development (Wang *et al.*, 2012). Li and colleagues further identified the activin receptor 2B (ACVR2B) gene as a miR-1 target in chicken muscle (Li *et al.*, 2011c).

Several chicken miRNAs were reported to be involved in chondrogenesis. In chicken limb mesenchymal cells, miR-221 inhibits slug degradation by targeting mdm2 to regulate chondrogenic differentiation (Kim *et al.*, 2010), and miR-142-3p regulates chondrogenesis by directly modulating the disintegrin and metalloprotease 9 (ADAM9) gene (Kim *et al.*, 2011b). In primary chicken chondrocytes, miR-365 is a mechanically responsive miRNA that stimulates chondrocyte differentiation by targeting histone deacetylase 4 (HDAC4), an inhibitor of chondrocyte hypertrophy (Guan *et al.*, 2011). miR-34a negatively regulates chondrogenesis by targeting EphA5 and suppressing the migration of chondroblasts (Kim *et al.*, 2011a) or the reorganization of the actin cytoskeleton, which is essential for chondrocyte differentiation (Kim *et al.*, 2012).

In chicken cone photoreceptors, the expression of miR-26a is diurnally rhythmic; miR-26a regulates the expression of L-type voltage-gated calcium channel α1C subunit (L-VGCCα1C) according to its own diurnal rhythm to allow retinal photoreceptors to exercise rhythmic function (Shi *et al.*, 2009). As a tumor suppressor, miR-26a targets interleukin-2, and the downregulation of miR-26a contributes to proliferation of lymphoma cells (Xu *et al.*, 2010). Interestingly, a few miRNAs identified in avian herpes viruses including Marek's disease virus might also have regulatory functions (immune evasion, anti-apoptosis and proliferation) in chickens (Burnside and Morgan, 2011).

miRNAs in pigs

The first set of porcine miRNAs identified included miR-17, miR-18a, miR-19a, miR-20a, miR-19b and miR-92a, and they all belong to the miR17-92 cluster and were identified based on sequence homology search with known human miRNAs (Sawera *et al.*, 2005). Using small RNA cloning, Sharbati-Tehrani *et al.* identified 11 miRNAs from various pig tissues (Sharbati-Tehrani *et al.*, 2008). Combining deep sequencing and computational analysis, 777 unique miRNAs were identified from six prenatal and four postnatal pigs, including 30 tissue-specific miRNAs (Li *et al.*, 2010). Using similar approaches, 15 novel pig-specific miRNAs and 56 novel candidate miRNAs were identified from pig testis (Lian *et al.*, 2012); 57 miRNAs were identified from pig skeletal muscle (Xie *et al.*, 2010); 293 miRNAs were identified from pig adipose tissue (Li *et al.*, 2011a); 215 miRNAs were identified from the backfat of Large White and Chinese Meishan pigs (Chen *et al.*, 2012a); and 89 miRNAs were identified from pig skeletal muscle and adipose tissue (Cho *et al.*, 2010).

Expression profiles of porcine miRNAs were mostly analyzed by miRNA microarrays. Using microarrays based on known porcine and human miRNAs, 332 miRNAs, 201 of which were potentially novel porcine miRNAs, were found to be expressed in pig intestine (Sharbati *et al.*, 2010). Between the sexually immature and mature porcine testes, 129 miRNAs are differentially expressed. In the mature testes, 51 miRNAs are upregulated and 78 are downregulated, suggesting that a large number of miRNAs participate in spermatogenesis

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(Luo *et al.*, 2010). The expression levels of let-7a, let-7d, let-7e and miR-22 were higher whereas that of miR-15b lower in abnormal sperm compared with normal sperm (Curry *et al.*, 2011); thus, these miRNAs might be involved in sperm development. MiR-122 is an important regulator of lipid metabolism. The expression level of miR-122 is lower in minipigs fed a high-cholesterol diet than those fed a standard diet, implying a potential role of miR-122 in obesity (Cirera *et al.*, 2010). Using deep sequencing, Chen *et al.* found that the expression of miR-215, -135, -224 and -146b is higher, whereas the expression of miR-1a, -133a, -122, -204 and -183 is lower in the Large White pigs than in the Meishan pigs (Chen *et al.*, 2012a). The Meishan pigs are known to have more fat than the Large White pigs. Differential expression of these miRNAs suggests the potential involvement of these miRNAs in adipose tissue development and growth in pigs.

Functions of porcine miRNAs are beginning to be revealed. MiR-148b potentially targets integrin alpha 5 (ITGA5), which is related to splay leg in piglets. The miR-148b gene has two SNPs, one of which alters a potential miRNA core promoter sequence. This SNP has different frequencies between different breeds of pig, but is not associated with splay leg condition (Maak *et al.*, 2010). One T/C SNP in miR-27a gene, detected in Large White and Dam line of Chinese lean-type new lines (DIV) pigs, is associated with litter size (Lei *et al.*, 2011). Between different genotypes, there is a significant difference of litter size in DIV but no significant difference of litter size in Large White pigs, implying the specific role of miR-27a in litter size in DIV pigs (Lei *et al.*, 2011). In the ovarian granulosa cells, miR-378 downregulates aromatase expression and estradiol production by targeting the 3′-UTR of the aromatase mRNA (Xu *et al.*, 2011). Thus, miRNA-378 might play a role in ovarian follicular development (Xu *et al.*, 2011). Zhao *et al.* analyzed the expression of Olfactomedin-like 3 (OLFML3) in developmental skeletal muscle and found it was regulated by miR-155 (Zhao *et al.*, 2012b). MiR-155 was also highly expressed in spleen and was upregulated after lipopolysaccharide and poly (I:C) stimulation, and it positively regulated TLR3/TLR4 signaling pathways. These imply a role of miR-155 in regulating porcine immunity (Li *et al.*, 2013).

miRNAs in sheep

MiR-431, -433, -127, -434, -432 and -136 were first sheep miRNAs identified through sequence homology search from the Callipyge sheep, which display the muscle hypertrophy phenotype (Davis *et al.*, 2005). From the same sheep, 747 miRNAs representing 472 miRNA precursors were identified from the skeletal muscle of callipyge sheep through deep sequencing (Caiment *et al.*, 2010). Using small RNA cloning, Sheng and colleagues reported the identification of 31 sheep miRNAs (Sheng *et al.*, 2011). More recently, McBride *et al.* reported the identification of 212 sheep miRNAs by sequencing small RNA libraries from sheep ovarian follicles and corpus lutea at various reproductive stages (McBride *et al.*, 2012).

Using miRNA microarrays, Wenguang *et al.* compared the expression of 159 miRNAs in body skin and ear skin from sheep, finding that 19 miRNAs were specifically expressed or greatly enriched in body side skin (Wenguang *et al.*, 2007). This raises the possibility that these miRNAs play a role in hair growth in sheep. Torley *et al.* compared the expression of 128 miRNAs in sheep ovaries and testes at gestational day (GD) 42 and GD75 by real-time qRT-PCR, finding that 24 miRNAs were differentially expressed between ovaries and testes at GD42 while 43 miRNAs at GD75. *Using in situ* hybridization, Torley *et al.* revealed that miR-22 was located in Sertoli cells and proposed that this miRNA might play a role in suppressing the estrogen-signaling pathway during fetal testicular development (Torley *et al.*, 2011). Prenatal testosterone treatment leads to ovarian pathology. In the fetal ovaries from gestational ewes treated with testosterone, miR-497 and miR-15b were upregulated, suggesting that these two miRNAs might have a role in testosterone-induced ovarian pathology (Luense *et al.*, 2011). Clop *et al.* found that the *myostatin* (MSTN) gene of Texel sheep had a G to A mutation in the 3′-UTR, and they further found that this mutation created a target site for miR-1 and miR-206, and thereby repressed the expression of MSTN protein and resulted in muscular hypertrophy in Texel sheep (Clop *et al.*, 2006).

Conclusions and perspectives

MicroRNAs are important regulators in biology. Hundreds of miRNAs have been identified in cattle, chickens, pigs and sheep. Many of these miRNAs are found to be expressed in a spatiotemporal-specific manner, which indicates that miRNAs play roles in specific tissue types or at specific developmental stages. Although limited functional studies of farm animal miRNAs have been conducted, these studies indicate that miRNAs play important roles in muscle development and hypertrophy, adipose tissue growth, oocyte maturation and early embryonic development in farm animals. The key to understanding the functions of miRNAs is to identify their mRNA targets. Therefore, future studies of miRNAs in farm animals should focus on the identification of mRNAs targeted by miRNAs and the physiological processes where the mRNA–miRNA interactions take place. Recent genome-wide association studies have shown that complex traits are often strongly associated with noncoding SNPs (Easton *et al.*, 2007; Greenman *et al.*, 2007; Saxena *et al.*, 2007; Scott *et al.*, 2007; Yeager *et al.*, 2007; Stefansson *et al.*, 2009; Ellinor *et al.*, 2010). Given the role of miRNAs in gene expression, one possible explanation for such trait-noncoding SNP associations is that the associated SNPs are parts of miRNA binding sites or miRNA sequences. Therefore, another potential direction of future miRNA studies in farm animals is to identify SNPs that overlap with miRNA binding sites or miRNA sequences and are associated with production or health traits in farm animals. Such studies could have immediate implications for selecting farm animals with superior production or health traits and for improving genetics in farm animals.

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References

Abd El Naby WS, Hagos TH, Hossain MM, Salilew-Wondim D, Gad AY, Rings F, Cinar MU, Tholen E, Looft C, Schellander K, Hoelker M and Tesfaye D 2011. Expression analysis of regulatory microRNAs in bovine cumulus oocyte complex and preimplantation embryos. Zygote 11, 1–21.

Bannister SC, Tizard ML, Doran TJ, Sinclair AH and Smith CA 2009. Sexually dimorphic microRNA expression during chicken embryonic gonadal development. Biology of Reproduction 81, 165–176.

Bartel DP 2004. MicroRNAs: genomics, biogenesis, mechanism, and function. Cell 116, 281–297.

Berry C, Thomas M, Langley B, Sharma M and Kambadur R 2002. Single cysteine to tyrosine transition inactivates the growth inhibitory function of Piedmontese myostatin. American Journal of Physiology Cell Physiology 283, C135–C141.

Bovine Genome Sequencing and Analysis Consortium 2009. The genome sequence of taurine cattle: a window to ruminant biology and evolution. Science 324, 522–528.

Bueno MJ, Perez de Castro I, Gomez de Cedron M, Santos J, Calin GA, Cigudosa JC, Croce CM, Fernandez-Piqueras J and Malumbres M 2008. Genetic and epigenetic silencing of microRNA-203 enhances ABL1 and BCR-ABL1 oncogene expression. Cancer Cell 13, 496–506.

Burnside J and Morgan R 2011. Emerging roles of chicken and viral microRNAs in avian disease. BMC Proceedings 5 (suppl. 4), S2.

Caiment F, Charlier C, Hadfield T, Cockett N, Georges M and Baurain D 2010. Assessing the effect of the CLPG mutation on the microRNA catalog of skeletal muscle using high-throughput sequencing. Genome Research 20, 1651–1662.

Carthew RW and Sontheimer EJ 2009. Origins and mechanisms of miRNAs and siRNAs. Cell 136, 642–655.

Chen C, Deng B, Qiao M, Zheng R, Chai J, Ding Y, Peng J and Jiang S 2012a. Solexa sequencing identification of conserved and novel microRNAs in backfat of Large White and Chinese Meishan pigs. PLoS One 7, e31426.

Chen KC, Liao YC, Hsieh IC, Wang YS, Hu CY and Juo SH 2012b. OxLDL causes both epigenetic modification and signaling regulation on the microRNA-29b gene: novel mechanisms for cardiovascular diseases. Journal of Molecular and Cellular Cardiology 52, 587–595.

Cho IS, Kim J, Seo HY, Lim do H, Hong JS, Park YH, Park DC, Hong KC, Whang KY and Lee YS 2010. Cloning and characterization of microRNAs from porcine skeletal muscle and adipose tissue. Molecular Biology Reports 37, 3567–3574.

Cirera S, Birck M, Busk PK and Fredholm M 2010. Expression profiles of miRNA-122 and its target CAT1 in minipigs (Sus scrofa) fed a high-cholesterol diet. Comparative Medicine 60, 136–141.

Clop A, Marcq F, Takeda H, Pirottin D, Tordoir X, Bibe B, Bouix J, Caiment F, Elsen JM, Eychenne F, Larzul C, Laville E, Meish F, Milenkovic D, Tobin J, Charlier C and Georges M 2006. A mutation creating a potential illegitimate microRNA target site in the myostatin gene affects muscularity in sheep. Nature Genetics 38, 813–818.

Coutinho LL, Matukumalli LK, Sonstegard TS, Van Tassell CP, Gasbarre LC, Capuco AV and Smith TP 2007. Discovery and profiling of bovine microRNAs from immune-related and embryonic tissues. Physiological Genomics 29, 35–43.

Curry E, Safranski TJ and Pratt SL 2011. Differential expression of porcine sperm microRNAs and their association with sperm morphology and motility. Theriogenology 76, 1532–1539.

Darnell DK, Kaur S, Stanislaw S, Konieczka JH, Yatskievych TA and Antin PB 2006. MicroRNA expression during chick embryo development. Developmental Dynamics 235, 3156–3165.

Davis E, Caiment F, Tordoir X, Cavaille J, Ferguson-Smith A, Cockett N, Georges M and Charlier C 2005. RNAi-mediated allelic trans-interaction at the imprinted Rtl1/Peg11 locus. Current Biology 15, 743–749.

Easton DF, Pooley KA, Dunning AM, Pharoah PD, Thompson D, Ballinger DG, Struewing JP, Morrison J, Field H, Luben R, Wareham N, Ahmed S, Healey CS, Bowman R, Meyer KB, Haiman CA, Kolonel LK, Henderson BE, Le Marchand L, Brennan P, Sangrajrang S, Gaborieau V, Odefrey F, Shen CY, Wu PE, Wang HC, Eccles D, Evans DG, Peto J, Fletcher O, Johnson N, Seal S, Stratton MR, Rahman N, Chenevix-Trench G, Bojesen SE, Nordestgaard BG, Axelsson CK, Garcia-Closas M, Brinton L, Chanock S, Lissowska J, Peplonska B, Nevanlinna H, Fagerholm R, Eerola H, Kang D, Yoo KY, Noh DY, Ahn SH, Hunter DJ, Hankinson SE, Cox DG, Hall P, Wedren S, Liu J, Low YL, Bogdanova N, Schurmann P, Dork T, Tollenaar RA, Jacobi CE, Devilee P, Klijn JG, Sigurdson AJ, Doody MM, Alexander BH, Zhang J, Cox A, Brock IW, MacPherson G, Reed MW, Couch FJ, Goode EL, Olson JE, Meijers-Heijboer H, van den Ouweland A, Uitterlinden A, Rivadeneira F, Milne RL, Ribas G, Gonzalez-Neira A, Benitez J, Hopper JL, McCredie M, Southey M, Giles GG, Schroen C, Justenhoven C, Brauch H, Hamann U, Ko YD, Spurdle AB, Beesley J, Chen X, Mannermaa A, Kosma VM, Kataja V, Hartikainen J, Day NE, Cox DR and Ponder BA 2007. Genome-wide association study identifies novel breast cancer susceptibility loci. Nature 447, 1087–1093.

Ebert MS and Sharp PA 2010. MicroRNA sponges: progress and possibilities. RNA 16, 2043–2050.

Ebert MS, Neilson JR and Sharp PA 2007. MicroRNA sponges: competitive inhibitors of small RNAs in mammalian cells. Nature Methods 4, 721–726.

Ellinor PT, Lunetta KL, Glazer NL, Pfeufer A, Alonso A, Chung MK, Sinner MF, de Bakker PI, Mueller M, Lubitz SA, Fox E, Darbar D, Smith NL, Smith JD, Schnabel RB, Soliman EZ, Rice KM, Van Wagoner DR, Beckmann BM, van Noord C, Wang K, Ehret GB, Rotter JI, Hazen SL, Steinbeck G, Smith AV, Launer LJ, Harris TB, Makino S, Nelis M, Milan DJ, Perz S, Esko T, Kottgen A, Moebus S, Newton-Cheh C, Li M, Mohlenkamp S, Wang TJ, Kao WH, Vasan RS, Nothen MM, MacRae CA, Stricker BH, Hofman A, Uitterlinden AG, Levy D, Boerwinkle E, Metspalu A, Topol EJ, Chakravarti A, Gudnason V, Psaty BM, Roden DM, Meitinger T, Wichmann HE, Witteman JC, Barnard J, Arking DE, Benjamin EJ, Heckbert SR and Kaab S 2010. Common variants in KCNN3 are associated with lone atrial fibrillation. Nature Genetics 42, 240–244.

Enright AJ, John B, Gaul U, Tuschl T, Sander C and Marks DS 2003. MicroRNA targets in Drosophila. Genome Biology 5, R1.

Gerin I, Bommer GT, McCoin CS, Sousa KM, Krishnan V and MacDougald OA 2010. Roles for miRNA-378/378* in adipocyte gene expression and lipogenesis. American Journal of Physiology Endocrinology and Metabolism 299, E198–E206.

Giraldez AJ, Mishima Y, Rihel J, Grocock RJ, Van Dongen S, Inoue K, Enright AJ and Schier AF 2006. Zebrafish MiR-430 promotes deadenylation and clearance of maternal mRNAs. Science 312, 75–79.

Glazov EA, Cottee PA, Barris WC, Moore RJ, Dalrymple BP and Tizard ML 2008. A microRNA catalog of the developing chicken embryo identified by a deep sequencing approach. Genome Research 18, 957–964.

Greenman C, Stephens P, Smith R, Dalgliesh GL, Hunter C, Bignell G, Davies H, Teague J, Butler A, Stevens C, Edkins S, O'Meara S, Vastrik I, Schmidt EE, Avis T, Barthorpe S, Bhamra G, Buck G, Choudhury B, Clements J, Cole J, Dicks E, Forbes S, Gray K, Halliday K, Harrison R, Hills K, Hinton J, Jenkinson A, Jones D, Menzies A, Mironenko T, Perry J, Raine K, Richardson D, Shepherd R, Small A, Tofts C, Varian J, Webb T, West S, Widaa S, Yates A, Cahill DP, Louis DN, Goldstraw P, Nicholson AG, Brasseur F, Looijenga L, Weber BL, Chiew YE, DeFazio A, Greaves MF, Green AR, Campbell P, Birney E, Easton DF, Chenevix-Trench G, Tan MH, Khoo SK, Teh BT, Yuen ST, Leung SY, Wooster R, Futreal PA and Stratton MR 2007. Patterns of somatic mutation in human cancer genomes. Nature 446, 153–158.

Gu Z, Eleswarapu S and Jiang H 2007. Identification and characterization of microRNAs from the bovine adipose tissue and mammary gland. FEBS Letters 581, 981–988.

Guan YJ, Yang X, Wei L and Chen Q 2011. MiR-365: a mechanosensitive microRNA stimulates chondrocyte differentiation through targeting histone deacetylase 4. FASEB Journal 25, 4457–4466.

Guduric-Fuchs J, O'Connor A, Cullen A, Harwood L, Medina RJ, O'Neill CL, Stitt AW, Curtis TM and Simpson DA 2012. Deep sequencing reveals predominant expression of miR-21 amongst the small non-coding RNAs in retinal microvascular endothelial cells. Journal of Cellular Biochemistry 113, 2098–2111.

Guillon-Munos A, Dambrine G, Richerioux N, Coupeau D, Muylkens B and Rasschaert D 2010. The chicken miR-150 targets the avian orthologue of the functional zebrafish MYB 3'UTR target site. BMC Molecular Biology 11, 67.

Guo HS, Xie Q, Fei JF and Chua NH 2005. MicroRNA directs mRNA cleavage of the transcription factor NAC1 to downregulate auxin signals for arabidopsis lateral root development. The Plant Cell 17, 1376–1386.

Hicks JA, Trakooljul N and Liu HC 2010. Discovery of chicken microRNAs associated with lipogenesis and cell proliferation. Physiological Genomics 41, 185–193.

https://doi.org/10.1017/S1751731113001183 Published online by Cambridge University Press

Huang P, Gong Y, Peng X, Li S, Yang Y and Feng Y 2010. Cloning, identification, and expression analysis at the stage of gonadal sex differentiation of chicken miR-363 and 363*. Acta Biochimica et Biophysica Sinica 42, 522–529.

Hutvagner G, McLachlan J, Pasquinelli AE, Balint E, Tuschl T and Zamore PD 2001. A cellular function for the RNA-interference enzyme Dicer in the maturation of the let-7 small temporal RNA. Science 293, 834–838.

Jin W, Grant JR, Stothard P, Moore SS and Guan LL 2009. Characterization of bovine miRNAs by sequencing and bioinformatics analysis. BMC Molecular Biology 10, 90.

Jin W, Dodson MV, Moore SS, Basarab JA and Guan LL 2010. Characterization of microRNA expression in bovine adipose tissues: a potential regulatory mechanism of subcutaneous adipose tissue development. BMC Molecular Biology 11, 29.

Jovanovic M, Reiter L, Picotti P, Lange V, Bogan E, Hurschler BA, Blenkiron C, Lehrbach NJ, Ding XC, Weiss M, Schrimpf SP, Miska EA, Grosshans H, Aebersold R and Hengartner MO 2010. A quantitative targeted proteomics approach to validate predicted microRNA targets in C. Elegans. Nature Methods 7, 837–842.

Khvorova A, Reynolds A and Jayasena SD 2003. Functional siRNAs and miRNAs exhibit strand bias. Cell 115, 209–216.

Kim VN 2005. MicroRNA biogenesis: coordinated cropping and dicing. Nature Reviews Molecular Cell Biology 6, 376–385.

Kim D, Song J and Jin EJ 2010. MicroRNA-221 regulates chondrogenic differentiation through promoting proteosomal degradation of slug by targeting Mdm2. Journal of Biological Chemistry 285, 26900–26907.

Kim D, Song J, Kim S, Chun CH and Jin EJ 2011a. MicroRNA-34a regulates migration of chondroblast and IL-1beta-induced degeneration of chondrocytes by targeting EphA5. Biochemical and Biophysical Research Communications 415, 551–557.

Kim D, Song J, Kim S, Kang SS and Jin EJ 2011b. MicroRNA-142-3p regulates TGF-beta3-mediated region-dependent chondrogenesis by regulating ADAM9. Biochemical and Biophysical Research Communications 414, 653–659.

Kim D, Song J, Kim S, Park HM, Chun CH, Sonn J and Jin EJ 2012. MicroRNA-34a modulates cytoskeletal dynamics through regulating RhoA/Rac1 cross-talk in chondroblasts. Journal of Biological Chemistry 287, 12501–12509.

Kozomara A and Griffiths-Jones S 2011. miRBase: integrating microRNA annotation and deep-sequencing data. Nucleic Acids Research 39, D152–D157.

Lee RC, Feinbaum RL and Ambros V 1993. The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. Cell 75, 843–854.

Lee SI, Lee BR, Hwang YS, Lee HC, Rengaraj D, Song G, Park TS and Han JY 2011. MicroRNA-mediated posttranscriptional regulation is required for maintaining undifferentiated properties of blastoderm and primordial germ cells in chickens. Proceedings of the National Academy of Sciences of the United States of America 108, 10426–10431.

Lee Y, Ahn C, Han J, Choi H, Kim J, Yim J, Lee J, Provost P, Radmark O, Kim S and Kim VN 2003. The nuclear RNase III Drosha initiates microRNA processing. Nature 425, 415–419.

Lei B, Gao S, Luo LF, Xia XY, Jiang SW, Deng CY, Xiong YZ and Li FE 2011. A SNP in the miR-27a gene is associated with litter size in pigs. Molecular Biology Reports 38, 3725–3729.

Lewis BP, Burge CB and Bartel DP 2005. Conserved seed pairing, often flanked by adenosines, indicates that thousands of human genes are microRNA targets. Cell 120, 15–20.

Li C, He H, Zhu M, Zhao S and Li X 2013. Molecular characterisation of porcine miR-155 and its regulatory roles in the TLR3/TLR4 pathways. Developmental and Comparative Immunology 39, 110–116.

Li G, Li Y, Li X, Ning X, Li M and Yang G 2011a. MicroRNA identity and abundance in developing swine adipose tissue as determined by Solexa sequencing. Journal of Cellular Biochemistry 112, 1318–1328.

Li H, Zhang Z, Zhou X, Wang Z, Wang G and Han Z 2011b. Effects of microRNA-143 in the differentiation and proliferation of bovine intramuscular preadipocytes. Molecular Biology Reports 38, 4273–4280.

Li T, Wu R, Zhang Y and Zhu D 2011c. A systematic analysis of the skeletal muscle miRNA transcriptome of chicken varieties with divergent skeletal muscle growth identifies novel miRNAs and differentially expressed miRNAs. BMC Genomics 12, 186.

Li ZY, Xi Y, Zhu WN, Zeng C, Zhang ZQ, Guo ZC, Hao DL, Liu G, Feng L, Chen HZ, Chen F, Lv X, Liu DP and Liang CC 2011d. Positive regulation of hepatic miR-122 expression by HNF4alpha. Journal of Hepatology 55, 602–611.

Li M, Xia Y, Gu Y, Zhang K, Lang Q, Chen L, Guan J, Luo Z, Chen H, Li Y, Li Q, Li X, Jiang AA, Shuai S, Wang J, Zhu Q, Zhou X and Gao X 2010. MicroRNAome of porcine pre- and postnatal development. PLoS One 5, e11541.

Lian C, Sun B, Niu S, Yang R, Liu B, Lu C, Meng J, Qiu Z, Zhang L and Zhao Z 2012. A comparative profile of the microRNA transcriptome in immature and mature porcine testes using Solexa deep sequencing. FEBS Journal 279, 964–975.

Lingenfelter BM, Tripurani SK, Tejomurtula J, Smith GW and Yao J 2011. Molecular cloning and expression of bovine nucleoplasmin 2 (NPM2): a maternal effect gene regulated by miR-181a. Reproductive Biology and Endocrinology 9, 40.

Liu H, Yue D, Chen Y, Gao SJ and Huang Y 2010. Improving performance of mammalian microRNA target prediction. BMC Bioinformatics 11, 476.

Luense LJ, Veiga-Lopez A, Padmanabhan V and Christenson LK 2011. Developmental programming: gestational testosterone treatment alters fetal ovarian gene expression. Endocrinology 152, 4974–4983.

Lund E, Guttinger S, Calado A, Dahlberg JE and Kutay U 2004. Nuclear export of microRNA precursors. Science 303, 95–98.

Luo L, Ye L, Liu G, Shao G, Zheng R, Ren Z, Zuo B, Xu D, Lei M, Jiang S, Deng C, Xiong Y and Li F 2010. Microarray-based approach identifies differentially expressed microRNAs in porcine sexually immature and mature testes. PLoS One 5, e11744.

Ma T, Jiang H, Gao Y, Zhao Y, Dai L, Xiong Q, Xu Y, Zhao Z and Zhang J 2011. Microarray analysis of differentially expressed microRNAs in non-regressed and regressed bovine corpus luteum tissue; microRNA-378 may suppress luteal cell apoptosis by targeting the interferon gamma receptor 1 gene. Journal of Applied Genetics 52, 481–486.

Maak S, Boettcher D, Komolka K, Tetens J, Wimmers K, Reinsch N, Swalve HH and Thaller G 2010. Exclusion of sequence polymorphisms in the porcine ITGA5 and MIR148B loci as causal variation for congenital splay leg in piglets. Animal Genetics 41, 447–448.

McBride D, Carre W, Sontakke S, Hogg CO, Law AS, Donadeu FX and Clinton M 2012. Identification of miRNAs associated with the follicular-luteal transition in the ruminant ovary. Reproduction 144, 221–233.

Miles JR, McDaneld TG, Wiedmann RT, Cushman RA, Echternkamp SE, Vallet JL and Smith TP 2012. MicroRNA expression profile in bovine cumulus-oocyte complexes: possible role of let-7 and miR-106a in the development of bovine oocytes. Animal Reproduction Science 130, 16–26.

Miretti S, Martignani E, Taulli R, Bersani F, Accornero P and Baratta M 2011. Differential expression of microRNA-206 in skeletal muscle of female Piedmontese and Friesian cattle. Veterinary Journal 190, 412–413.

Mondou E, Dufort I, Gohin M, Fournier E and Sirard MA 2012. Analysis of microRNAs and their precursors in bovine early embryonic development. Molecular Human Reproduction 18, 425–434.

Naguibneva I, Ameyar-Zazoua M, Polesskaya A, Ait-Si-Ali S, Groisman R, Souidi M, Cuvellier S and Harel-Bellan A 2006a. The microRNA miR-181 targets the homeobox protein Hox-A11 during mammalian myoblast differentiation. Nature Cell Biology 8, 278–284.

Naguibneva I, Ameyar-Zazoua M, Nonne N, Polesskaya A, Ait-Si-Ali S, Groisman R, Souidi M, Pritchard LL and Harel-Bellan A 2006b. An LNA-based loss-of-function assay for micro-RNAs. Biomedicine Pharmacotherapy 60, 633–638.

Rengaraj D, Lee BR, Lee SI, Seo HW and Han JY 2011. Expression patterns and miRNA regulation of DNA methyltransferases in chicken primordial germ cells. PLoS One 6, e19524.

Romao JM, Jin W, He M, McAllister T and Guan le L 2012. Altered microRNA expression in bovine subcutaneous and visceral adipose tissues from cattle under different diet. PLoS One 7, e40605.

Saito Y and Saito H 2012. Role of CTCF in the regulation of microRNA expression. Frontiers in Genetics 3, 186.

Saito Y, Suzuki H, Taya T, Nishizawa M, Tsugawa H, Matsuzaki J, Hirata K, Saito H and Hibi T 2012. Development of a novel microRNA promoter microarray for ChIP-on-chip assay to identify epigenetically regulated microRNAs. Biochemical and Biophysical Research Communications 426, 33–37.

Sawera M, Gorodkin J, Cirera S and Fredholm M 2005. Mapping and expression studies of the mir17-92 cluster on pig chromosome 11. Mammalian Genome 16, 594–598.

Saxena R, Voight BF, Lyssenko V, Burtt NP, de Bakker PI, Chen H, Roix JJ, Kathiresan S, Hirschhorn JN, Daly MJ, Hughes TE, Groop L, Altshuler D, Almgren P, Florez JC, Meyer J, Ardlie K, Bengtsson Bostrom K, Isomaa B, Lettre G, Lindblad U,

https://doi.org/10.1017/S1751731113001183 Published online by Cambridge University Press

Lyon HN, Melander O, Newton-Cheh C, Nilsson P, Orho-Melander M, Rastam L, Speliotes EK, Taskinen MR, Tuomi T, Guiducci C, Berglund A, Carlson J, Gianniny L, Hackett R, Hall L, Holmkvist J, Laurila E, Sjogren M, Sterner M, Surti A, Svensson M, Tewhey R, Blumenstiel B, Parkin M, Defelice M, Barry R, Brodeur W, Camarata J, Chia N, Fava M, Gibbons J, Handsaker B, Healy C, Nguyen K, Gates C, Sougnez C, Gage D, Nizzari M, Gabriel SB, Chirn GW, Ma Q, Parikh H, Richardson D, Ricke D and Purcell S 2007. Genome-wide association analysis identifies loci for type 2 diabetes and triglyceride levels. Science 316, 1331–1336.

Scott LJ, Mohlke KL, Bonnycastle LL, Willer CJ, Li Y, Duren WL, Erdos MR, Stringham HM, Chines PS, Jackson AU, Prokunina-Olsson L, Ding CJ, Swift AJ, Narisu N, Hu T, Pruim R, Xiao R, Li XY, Conneely KN, Riebow NL, Sprau AG, Tong M, White PP, Hetrick KN, Barnhart MW, Bark CW, Goldstein JL, Watkins L, Xiang F, Saramies J, Buchanan TA, Watanabe RM, Valle TT, Kinnunen L, Abecasis GR, Pugh EW, Doheny KF, Bergman RN, Tuomilehto J, Collins FS and Boehnke M 2007. A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants. Science 316, 1341–1345.

Sharbati-Tehrani S, Kutz-Lohroff B, Scholven J and Einspanier R 2008. Concatameric cloning of porcine microRNA molecules after assembly PCR. Biochemical and Biophysical Research Communications 375, 484–489.

Sharbati S, Friedlander MR, Sharbati J, Hoeke L, Chen W, Keller A, Stahler PF, Rajewsky N and Einspanier R 2010. Deciphering the porcine intestinal microRNA transcriptome. BMC Genomics 11, 275.

Sheng X, Song X, Yu Y, Niu L, Li S, Li H, Wei C, Liu T, Zhang L and Du L 2011. Characterization of microRNAs from sheep (Ovis aries) using computational and experimental analyses. Molecular Biology Reports 38, 3161–3171.

Shi L, Ko ML and Ko GY 2009. Rhythmic expression of microRNA-26a regulates the L-type voltage-gated calcium channel alpha1C subunit in chicken cone photoreceptors. Journal of Biological Chemistry 284, 25791–25803.

Siomi H and Siomi MC 2010. Posttranscriptional regulation of microRNA biogenesis in animals. Molecular Cell 38, 323–332.

Stefansson H, Ophoff RA, Steinberg S, Andreassen OA, Cichon S, Rujescu D, Werge T, Pietilainen OP, Mors O, Mortensen PB, Sigurdsson E, Gustafsson O, Nyegaard M, Tuulio-Henriksson A, Ingason A, Hansen T, Suvisaari J, Lonnqvist J, Paunio T, Borglum AD, Hartmann A, Fink-Jensen A, Nordentoft M, Hougaard D, Norgaard-Pedersen B, Bottcher Y, Olesen J, Breuer R, Moller HJ, Giegling I, Rasmussen HB, Timm S, Mattheisen M, Bitter I, Rethelyi JM, Magnusdottir BB, Sigmundsson T, Olason P, Masson G, Gulcher JR, Haraldsson M, Fossdal R, Thorgeirsson TE, Thorsteinsdottir U, Ruggeri M, Tosato S, Franke B, Strengman E, Kiemeney LA, Melle I, Djurovic S, Abramova L, Kaleda V, Sanjuan J, de Frutos R, Bramon E, Vassos E, Fraser G, Ettinger U, Picchioni M, Walker N, Toulopoulou T, Need AC, Ge D, Yoon JL, Shianna KV, Freimer NB, Cantor RM, Murray R, Kong A, Golimbet V, Carracedo A, Arango C, Costas J, Jonsson EG, Terenius L, Agartz I, Petursson H, Nothen MM, Rietschel M, Matthews PM, Muglia P, Peltonen L, St Clair D, Goldstein DB, Stefansson K and Collier DA 2009. Common variants conferring risk of schizophrenia. Nature 460, 744–747.

Takeda H, Charlier C, Farnir F and Georges M 2010. Demonstrating polymorphic miRNA-mediated gene regulation in vivo: application to the g+6223G->A mutation of Texel sheep. RNA 16, 1854–1863.

Torley KJ, da Silveira JC, Smith P, Anthony RV, Veeramachaneni DN, Winger QA and Bouma GJ 2011. Expression of miRNAs in ovine fetal gonads: potential role in gonadal differentiation. Reproductive Biology and Endocrinology 9, 2.

Townley-Tilson WH, Callis TE and Wang D 2010. MicroRNAs 1, 133, and 206: critical factors of skeletal and cardiac muscle development, function, and disease. The International Journal of Biochemistry & Cell Biology 42, 1252–1255.

Trakooljul N, Hicks JA and Liu HC 2010. Identification of target genes and pathways associated with chicken microRNA miR-143. Animal Genetics 41, 357–364.

Tripurani SK, Lee KB, Wee G, Smith GW and Yao J 2011. MicroRNA-196a regulates bovine newborn ovary homeobox gene (NOBOX) expression during early embryogenesis. BMC Developmental Biology 11, 25.

Wang XG, Yu JF, Zhang Y, Gong DQ and Gu ZL 2012. Identification and characterization of microRNA from chicken adipose tissue and skeletal muscle. Poultry Science 91, 139–149.

Wang Z, Lin S, Li JJ, Xu Z, Yao H, Zhu X, Xie D, Shen Z, Sze J, Li K, Lu G, Chan DT, Poon WS, Kung HF and Lin MC 2011. MYC protein inhibits transcription of the microRNA cluster MC-let-7a-1~let-7d via noncanonical E-box. Journal of Biological Chemistry 286, 39703–39714.

Wenguang Z, Jianghong W, Jinquan L and Yashizawa M 2007. A subset of skin-expressed microRNAs with possible roles in goat and sheep hair growth based on expression profiling of mammalian microRNAs. OMICS 11, 385–396.

Wienholds E and Plasterk RH 2005. MicroRNA function in animal development. FEBS Letters 579, 5911–5922.

Wu L, Fan J and Belasco JG 2006. MicroRNAs direct rapid deadenylation of mRNA. Proceedings of the National Academy of Sciences of the United States of America 103, 4034–4039.

Xie SS, Huang TH, Shen Y, Li XY, Zhang XX, Zhu MJ, Qin HY and Zhao SH 2010. Identification and characterization of microRNAs from porcine skeletal muscle. Animal Genetics 41, 179–190.

Xu H, Wang X, Du Z and Li N 2006. Identification of microRNAs from different tissues of chicken embryo and adult chicken. FEBS Letters 580, 3610–3616.

Xu H, Yao Y, Smith LP and Nair V 2010. MicroRNA-26a-mediated regulation of interleukin-2 expression in transformed avian lymphocyte lines. Cancer Cell International 10, 15.

Xu S, Linher-Melville K, Yang BB, Wu D and Li J 2011. Micro-RNA378 (miR-378) regulates ovarian estradiol production by targeting aromatase. Endocrinology 152, 3941–3951.

Yao J, Wang Y, Wang W, Wang N and Li H 2011. Solexa sequencing analysis of chicken pre-adipocyte microRNAs. Bioscience Biotechnology and Biochemistry 75, 54–61.

Yeager M, Orr N, Hayes RB, Jacobs KB, Kraft P, Wacholder S, Minichiello MJ, Fearnhead P, Yu K, Chatterjee N, Wang Z, Welch R, Staats BJ, Calle EE, Feigelson HS, Thun MJ, Rodriguez C, Albanes D, Virtamo J, Weinstein S, Schumacher FR, Giovannucci E, Willett WC, Cancel-Tassin G, Cussenot O, Valeri A, Andriole GL, Gelmann EP, Tucker M, Gerhard DS, Fraumeni JF Jr, Hoover R, Hunter DJ, Chanock SJ and Thomas G 2007. Genome-wide association study of prostate cancer identifies a second risk locus at 8q24. Nature Genetics 39, 645–649.

Yekta S, Shih IH and Bartel DP 2004. MicroRNA-directed cleavage of HOXB8 mRNA. Science 304, 594–596.

Zhao C, Tian F, Yu Y, Liu G, Zan L, Updike MS and Song J 2012a. miRNA-dysregulation associated with tenderness variation induced by acute stress in Angus cattle. Journal of Animal Science and Biotechnology 3, 12.

Zhao S, Zhang J, Hou X, Zan L, Wang N, Tang Z and Li K 2012b. OLFML3 expression is decreased during prenatal muscle development and regulated by microRNA-155 in pigs. International Journal of Biological Sciences 8, 459–469.

https://doi.org/10.1017/S1751731113001183 Published online by Cambridge University Press