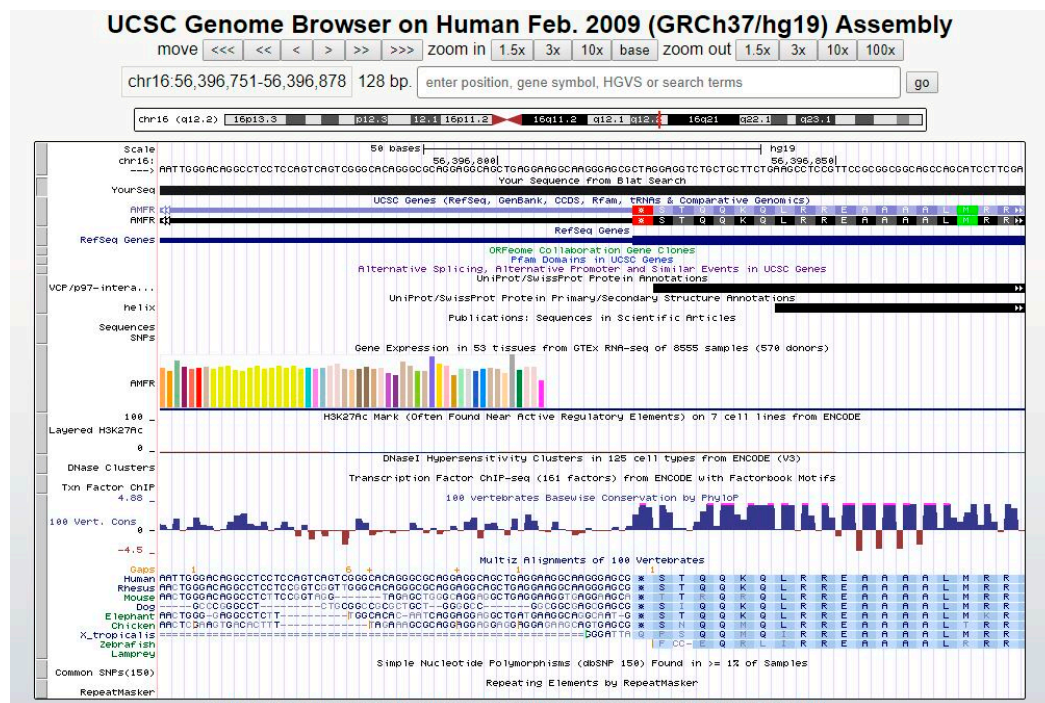
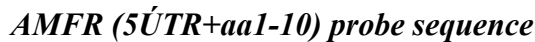


*ATM (aa63-109) probe sequence*



**UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly**

move <<< << < > >> >>> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x 100x

chr6:74,446,106-74,446,231 126 bp. enter position, gene symbol, HGVS or search terms go

chr6 (q13) epd2c3 h19

Scale chr6 74,446,106 74,446,280 hg19  
--- Your Sequence from BAC Search

YourSeq UCSC Genes (RefSeq, GENBANK, CCDS, Rfam, tRNAs & Comparative Genomics)  
CD199 F K S N L I Q Q H L S Q Q S D L G V I S K T F Q L S S N P I L G D H S S I Q V Q V N  
CD199 F K S N L I Q Q H L S Q Q S D L G V I S K T F Q L S S N P I L G D H S S I Q V Q V N  
CD199 F K S N L I Q Q H L S Q Q S D L G V I S K T F Q L S S N P I L G D H S S I Q V Q V N

RefSeq Genes ORFome Collaboration Gene Clones  
BC143504 Ex In  
BC182996 Ex In  
Pfam Domains in UCSC Genes  
RAH\_N Alternative Splicing, Alternative Probesets and Similar Events in UCSC Genes  
CD199 antigen UniProt/SwissProt Protein Primary Structure Annotations  
Uniprot/SwissProt Protein Secondary Structure Annotations  
Publications: Sequences in Scientific Articles

Sequences SNPs  
Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (576 donors)

CD199  
100  
0  
Layered H3K27ac  
H3K27ac Mark (Often Found Near Active Regulatory Elements) on 7 cell lines from ENCODE

DNAse Clusters  
Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs  
100 Vert. Cons.  
100 Vert. Cons. Baseuse Conservation by PhyloP

HuTiz Alignments of 100 Vertebrates  
GapD  
Human  
Rhesus  
Mouse  
Dog  
Elephant  
Chicken  
X\_tropicalis  
Zebrafish  
Lancelet  
Common SNPs (150)  
RepeatsMasker  
Simple Nucleotide Polymorphisms (dbSNP 150) Found in >= 1% of Samples  
Repeating Elements by RepeatMasker

UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly

move <<< << < > >> >>> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x 100x

chr2:39,237,725-39,237,844 120 bp. enter position, gene symbol, HGVS or search terms go

chr2 (p22.1) 31 14 12p12 13 34 35

Scale 50 bases 39,237,800 hg19

chr2: 39,237,750  
 ----> TTCTCAACACACAGATGAGGTTGGTGTATGTCGATCATTTTCAGAGATATGAGAGATTAACTTTTCCTCTTTTGTCCACAGACTTCACACTTAATTCGTGATGGCTACAGCT

YourSeq  
 Your Sequence from Blast Search

UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics)

SOS1  
 SOS1

RefSeq Genes  
 RefSeq Genes

BC140215  
 ORFeome Collaboration Gene Clones

RasGEF  
 Pfam Domains in UCSC Genes

Ras-GEF  
 Alternative Splicing, Alternative Promoter, and Similar Events in UCSC Genes  
 UniProt/SwissProt Protein Annotations

UniProt/SwissProt Protein Primary/Secondary Structure Annotations

helix  
 helix  
 helix  
 helix

Publications: Sequences in Scientific Articles

Sequences  
 SNPs

Gene Expression in 53 tissues from GTEx RNA-seq of 8555 samples (578 donors)

SOS1

H3K27Ac Mark (Often Found Near Active Regulatory Elements) on 7 cell lines from ENCODE

Layered H3K27Ac

DNase Clusters  
 DNase Hypersensitivity Clusters in 125 cell types from ENCODE (V3)

Txn Factor ChIP  
 Transcription Factor ChIP-seq (161 factors) from ENCODE with Factorbook Motifs

100 Vert. Cons  
 100 vertebrates Basewise Conservation by PhyloP

Multiz Alignments of 100 Vertebrates

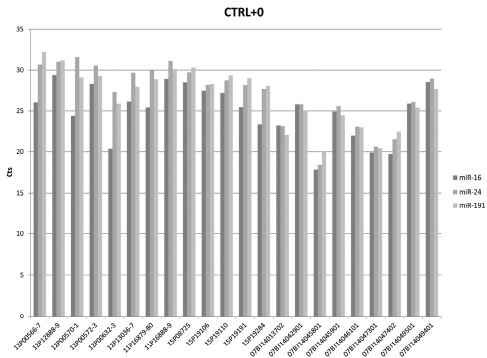
Common SNPs (150)  
 Simple Nucleotide Polymorphisms (dbSNP 150) Found in >= 1% of Samples

RepeatMasker  
 Repeating Elements by RepeatMasker

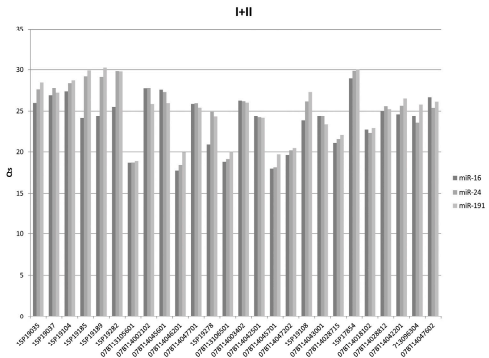
A

| Gene name            | Stability value | Best gene                                         | miR-191            |
|----------------------|-----------------|---------------------------------------------------|--------------------|
| miR-24               | 0.036           | Stability value                                   | 0.002              |
| miR-36               | 0.011           |                                                   |                    |
| miR-191              | 0.009           | Best combination of two genes                     | miR-24 and miR-191 |
|                      |                 | Stability value for best combination of two genes | 0.002              |
| Intragroup variation |                 |                                                   |                    |
| Group identifier     | 0               | 1                                                 | 2                  |
| miR-24               | 0.006           | 0.004                                             | 0.002              |
| miR-36               | 0.001           | 0.000                                             | 0.001              |
| miR-191              | 0.001           | 0.002                                             | 0.001              |
| Intragroup variation |                 |                                                   |                    |
| Group identifier     | 0               | 1                                                 | 2                  |
| miR-24               | -0.011          | 0.012                                             | -0.001             |
| miR-36               | 0.011           | -0.012                                            | 0.000              |
| miR-191              | 0.000           | 0.000                                             | 0.000              |

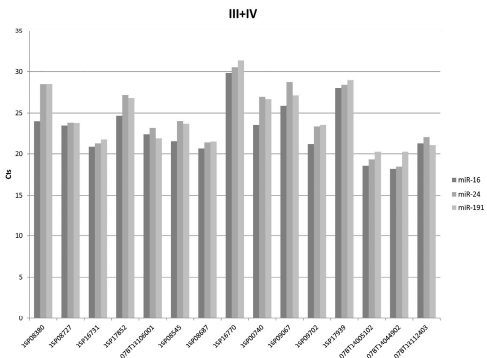
B



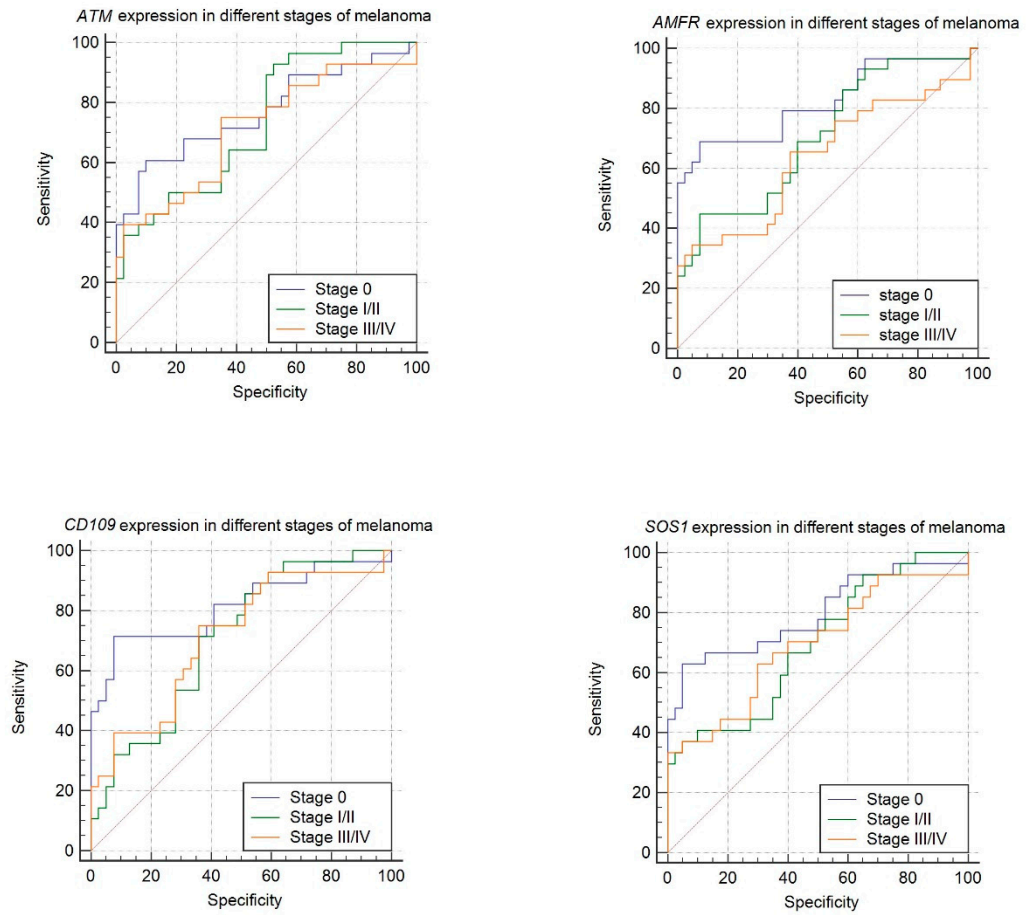
C



D



**Supplementary Figure S2. Variation of Ct values in levels of miRNA reference genes in selected cohort measured by qRT-PCR.** (A) NormFinder analysis of levels of *miR-16*, *miR-24* and *miR-191*. (B) Levels of miRNAs in healthy and stage 0 patient cohort, (C) in stage I/II cohort and stage III/IV cohort.



**Supplementary Figure S3. ROC analysis of mRNA expression in different melanoma stage cohorts. (A) *ATM*, (B) *AMFR*, (C) *CD109*, (D) *SOS1* expression.**

**Table S1. Clinical details of patients used for NGS cohort. NK- not known.**

| ID          | Gender | Age | Stage | TMN                     |
|-------------|--------|-----|-------|-------------------------|
| pool-0#1    | Female | 79  | 0     | Melanoma in situ        |
| pool-0#2    | Female | 80  | 0     | Melanoma in situ        |
| pool-0#3    | Male   | 65  | 0     | Melanoma in situ        |
| pool-0#4    | Female | 58  | 0     | Lentigo maligna in situ |
| pool-0#5    | Male   | 76  | 0     | Lentigo maligna in situ |
| pool-I/II#1 | Female | 62  | IA    | T1aN0M0                 |
| pool-I/II#2 | Male   | 60  | IA    | T1aN0M0                 |
| pool-I/II#3 | Male   | 82  | IA    | T1aN0M0                 |
| pool-I/II#4 | Male   | 35  | IA    | T1aN0M0                 |
| pool-I/II#5 | Female | 61  | IA    | T1aN0M0                 |
| pool-I/II#6 | Female | 81  | IA    | T1aN0M0                 |
| pool-I/II#7 | Male   | 84  | IIIB  | T4bN0M0                 |
| pool-I/II#8 | Female | 64  | IA    | T1aN0M0                 |
| pool-III#1  | Female | 83  | IIIB  | T2bN2cM0                |
| pool-III#2  | Female | 67  | IIIC  | TxN3M0                  |
| pool-III#3  | Female | 48  | IIIB  | T2xN2cM0                |
| pool-III#4  | Male   | 55  | IIIC  | T2aN3M0                 |
| pool-III#5  | Male   | 80  | IIIB  | T2aN2cM0                |
| pool-III#6  | Female | 68  | IIIC  | T4aN0M0                 |
| pool-III#7  | Female | 89  | IIIA  | T3aN2cM0                |
| pool-III#8  | Male   | 61  | IIIA  | T3aN2cM0                |
| pool-IV#1   | Female | 54  | IV    | T3bN0M1                 |
| pool-IV#2   | Female | 79  | IV    | T4bN1M1                 |
| pool-IV#3   | Male   | 73  | IV    | T3aN3M1                 |
| pool-IV#4   | Female | 53  | IV    | T4bN1bM1                |
| pool-IV#5   | Male   | 58  | IV    | T4bN3M1                 |
| pool-IV#6   | Male   | 51  | IV    | T3bN3M1                 |
| pool-IV#7   | Female | 60  | IV    | TxN3m1                  |
| pool-IV#8   | Female | 82  | IV    | TxNxM1                  |
| pool-cont#1 | Female | 60  | -     | -                       |
| pool-cont#2 | Female | 65  | -     | -                       |
| pool-cont#3 | Male   | 57  | -     | -                       |
| pool-cont#4 | Male   | 58  | -     | -                       |
| pool-cont#5 | Male   | 53  | -     | -                       |
| pool-cont#6 | Male   | 58  | -     | -                       |
| pool-cont#7 | Female | 62  | -     | -                       |
| pool-cont#8 | Female | 58  | -     | -                       |



**Table S2. Clinical details of patients used in mRNA validation cohort.** NK- not known.

| <b>ID</b> | <b>Origin</b> | <b>Gender</b> | <b>Age</b> | <b>Stage</b> | <b>TNM</b> |
|-----------|---------------|---------------|------------|--------------|------------|
| Cont#1    | Biobanco      | Female        | 64         | Control      | -          |
| Cont#2    | Biobanco      | Female        | 70         | Control      | -          |
| Cont#3    | Biobanco      | Female        | 67         | Control      | -          |
| Cont#4    | Biobanco      | Female        | 56         | Control      | -          |
| Cont#5    | Biobanco      | Female        | 68         | Control      | -          |
| Cont#6    | Biobanco      | Male          | 62         | Control      | -          |
| Cont#7    | Biobanco      | Male          | 57         | Control      | -          |
| Cont#8    | Biobanco      | Male          | 60         | Control      | -          |
| Cont#9    | Biobanco      | Male          | 63         | Control      | -          |
| Cont#10   | Biobanco      | Male          | 67         | Control      | -          |
| Cont#11   | Biobanco      | Female        | 59         | Control      | -          |
| Cont#12   | Biobanco      | Female        | 53         | Control      | -          |
| Cont#13   | Biobanco      | Female        | 55         | Control      | -          |
| Cont#14   | Biobanco      | Female        | 64         | Control      | -          |
| Cont#15   | Biobanco      | Male          | 54         | Control      | -          |
| Cont#16   | Biobanco      | Male          | 55         | Control      | -          |
| Cont#17   | Biobanco      | Male          | 54         | Control      | -          |
| Cont#18   | Biobanco      | Male          | 53         | Control      | -          |
| Cont#19   | Biobanco      | Female        | 29         | Control      | -          |
| Cont#20   | Biobanco      | Female        | 24         | Control      | -          |
| Cont#21   | Biobanco      | Female        | 26         | Control      | -          |
| Cont#22   | Biobanco      | Male          | 22         | Control      | -          |
| Cont#23   | Biobanco      | Male          | 28         | Control      | -          |
| Cont#24   | Biobanco      | Female        | 43         | Control      | -          |
| Cont#25   | Biobanco      | Female        | 31         | Control      | -          |
| Cont#26   | Biobanco      | Female        | 33         | Control      | -          |
| Cont#27   | Biobanco      | Female        | 34         | Control      | -          |
| Cont#28   | Biobanco      | Female        | 50         | Control      | -          |
| Cont#29   | Biobanco      | Male          | 42         | Control      | -          |
| Cont#30   | Biobanco      | Male          | 30         | Control      | -          |
| Cont#31   | Biobanco      | Female        | 45         | Control      | -          |
| Cont#32   | Biobanco      | Male          | 35         | Control      | -          |
| Cont#33   | Biobanco      | Male          | 50         | Control      | -          |
| Cont#34   | Biobanco      | Female        | 31         | Control      | -          |
| Cont#35   | Biobanco      | Male          | NK         | Control      | -          |
| Cont#36   | Biobanco      | Female        | NK         | Control      | -          |

|         |               |        |    |         |                          |
|---------|---------------|--------|----|---------|--------------------------|
| Cont#37 | Biobanco      | Male   | 59 | Control | -                        |
| Cont#38 | Biobanco      | Female | 54 | Control | -                        |
| Cont#39 | Biobanco      | Female | 60 | Control | -                        |
| Cont#40 | Biobanco      | Male   | 53 | Control | -                        |
| Cont#41 | Biobanco      | Female | 62 | Control | -                        |
| mRNA#1  | Madrid        | Male   | 77 | 0       | -                        |
| mRNA#2  | Madrid        | Male   | 46 | 0       | TisN0M0                  |
| mRNA#3  | Madrid        | Female | 57 | 0       | TisN0M0                  |
| mRNA#4  | Madrid        | Female | 68 | 0       | TisN0M0                  |
| mRNA#5  | Madrid        | Male   | 45 | 0       | TisN0M0                  |
| mRNA#6  | Madrid        | Female | 85 | 0       | TisN0M0                  |
| mRNA#7  | Madrid        | Female | 78 | 0       | TisN0M0                  |
| mRNA#8  | Madrid        | Male   | 56 | 0       | TisN0M0                  |
| mRNA#9  | Madrid        | Male   | 84 | 0       | TisN0M0                  |
| mRNA#10 | Madrid        | Male   | 40 | 0       | Melanoma in situ         |
| mRNA#11 | Madrid        | Male   | 66 | 0       | Léntigo maligno. In situ |
| mRNA#12 | Madrid        | Male   | 52 | 0       | Léntigo maligno. In situ |
| mRNA#13 | Madrid        | Female | 84 | 0       | Léntigo maligno. In situ |
| mRNA#14 | Madrid        | Male   | 43 | 0       | Léntigo maligno. In situ |
| mRNA#15 | Madrid        | Female | 33 | 0       | TisN0M0                  |
| mRNA#16 | San Sebastián | Male   | 64 | 0       | pT1sN0                   |
| mRNA#17 | San Sebastián | NK     | 67 | 0       | pT1sN0M0                 |
| mRNA#18 | San Sebastián | female | 68 | 0       | pT1sN0                   |
| mRNA#19 | San Sebastián | Female | 73 | 0       | pT1sN0M0                 |
| mRNA#20 | San Sebastián | Female | 60 | 0       | pT1sN0M0                 |
| mRNA#21 | San Sebastián | Female | 70 | 0       | pT1sN0M0                 |
| mRNA#22 | San Sebastián | Male   | 57 | 0       | pT1sN0M0                 |
| mRNA#23 | San Sebastián | Female | 59 | 0       | pT1sN0M0                 |
| mRNA#24 | San Sebastián | Female | 71 | 0       | pT1sN0M0                 |
| mRNA#25 | San Sebastián | Female | 46 | 0       | pT1sN0M0                 |
| mRNA#26 | San Sebastián | Female | 64 | 0       | pT1sN0M0                 |
| mRNA#27 | San Sebastián | Female | 76 | 0       | TisN0M0                  |
| mRNA#28 | San Sebastián | Female | 75 | 0       | TisN0M0                  |
| mRNA#29 | San Sebastián | Female | 40 | 0       | TisN0M0                  |
| mRNA#30 | Madrid        | Male   | 47 | IA      | T1aN0M0                  |
| mRNA#31 | Madrid        | Female | 72 | IA      | T1aN0M0                  |
| mRNA#32 | Madrid        | Female | 81 | IA      | T1aN0M0                  |
| mRNA#33 | Madrid        | Female | 43 | IA      | T1aN0M0                  |
| mRNA#34 | Madrid        | Female | 37 | IA      | T1aN0M0                  |
| mRNA#35 | Madrid        | Male   | 42 | IA      | T1aN0M0                  |

|         |         |        |    |      |         |
|---------|---------|--------|----|------|---------|
| mRNA#36 | Madrid  | Male   | 57 | IA   | T1aN0M0 |
| mRNA#37 | Madrid  | Male   | 70 | IB   | T2aN0M0 |
| mRNA#38 | Madrid  | Female | 80 | IB   | T1bN0M0 |
| mRNA#39 | Madrid  | Female | 69 | IB   | T1bN0M0 |
| mRNA#40 | Madrid  | Male   | 40 | IB   | T2aN0M0 |
| mRNA#41 | Madrid  | Male   | 86 | IB   | T2aN0M0 |
| mRNA#42 | Madrid  | Female | 37 | IB   | T2aN0M0 |
| mRNA#43 | Madrid  | Female | 51 | IIA  | T2bN0M0 |
| mRNA#44 | Madrid  | Male   | 79 | IIA  | T3aN0M0 |
| mRNA#45 | AVAST-M | Female | 61 | IIB  | NK      |
| mRNA#46 | AVAST-M | Male   | 47 | IIB  | NK      |
| mRNA#47 | AVAST-M | Male   | 72 | IIB  | NK      |
| mRNA#48 | AVAST-M | Male   | 38 | IIB  | NK      |
| mRNA#49 | AVAST-M | Female | 36 | IIB  | NK      |
| mRNA#50 | AVAST-M | Female | 48 | IIB  | NK      |
| mRNA#51 | AVAST-M | Male   | 58 | IIB  | NK      |
| mRNA#52 | AVAST-M | Male   | 40 | IIB  | NK      |
| mRNA#53 | AVAST-M | Male   | 43 | IIB  | NK      |
| mRNA#54 | AVAST-M | Female | 54 | IIB  | NK      |
| mRNA#55 | Madrid  | Male   | 75 | IIB  | T4aN0M0 |
| mRNA#56 | Madrid  | Female | 64 | IIB  | T3bN0M0 |
| mRNA#57 | Madrid  | Female | 85 | IIB  | T3bN0M0 |
| mRNA#58 | Madrid  | Female | 79 | IIB  | T3bN0M0 |
| mRNA#59 | AVAST-M | Female | 60 | IIC  | NK      |
| mRNA#60 | AVAST-M | Female | 45 | IIC  | NK      |
| mRNA#61 | AVAST-M | Female | 56 | IIC  | NK      |
| mRNA#62 | AVAST-M | Female | 65 | IIC  | NK      |
| mRNA#63 | AVAST-M | Male   | 70 | IIC  | NK      |
| mRNA#64 | AVAST-M | Male   | 67 | IIC  | NK      |
| mRNA#65 | AVAST-M | Female | 57 | IIC  | NK      |
| mRNA#66 | AVAST-M | Female | 54 | IIC  | NK      |
| mRNA#67 | AVAST-M | Female | 62 | IIC  | NK      |
| mRNA#68 | AVAST-M | Male   | 52 | IIC  | NK      |
| mRNA#69 | AVAST-M | Male   | 63 | IIC  | NK      |
| mRNA#70 | Madrid  | Female | 84 | IIC  | T4bN0M0 |
| mRNA#71 | Madrid  | Female | 46 | IIC  | T4bN0M0 |
| mRNA#72 | Madrid  | Male   | 58 | IIC  | T4bN0M0 |
| mRNA#73 | Madrid  | Female | 84 | IIC  | T4bN0M0 |
| mRNA#74 | AVAST-M | Female | 40 | IIIA | NK      |
| mRNA#75 | AVAST-M | Female | 40 | IIIA | NK      |



|          |         |        |    |        |          |
|----------|---------|--------|----|--------|----------|
| mRNA#76  | AVAST-M | Female | 43 | IIIA   | NK       |
| mRNA#77  | AVAST-M | Male   | 60 | IIIA   | NK       |
| mRNA#78  | AVAST-M | Male   | 35 | IIIA   | NK       |
| mRNA#79  | AVAST-M | Male   | 54 | IIIA   | NK       |
| mRNA#80  | AVAST-M | Male   | 65 | IIIA   | NK       |
| mRNA#81  | AVAST-M | Female | 37 | IIIA   | NK       |
| mRNA#82  | AVAST-M | Male   | 59 | IIIA   | NK       |
| mRNA#83  | AVAST-M | Female | 37 | IIIA   | NK       |
| mRNA#84  | AVAST-M | Male   | 37 | IIIA   | NK       |
| mRNA#85  | AVAST-M | Male   | 24 | IIIA   | NK       |
| mRNA#86  | AVAST-M | Male   | 62 | IIIA   | NK       |
| mRNA#87  | AVAST-M | Male   | 65 | IIIA   | NK       |
| mRNA#88  | AVAST-M | Male   | 56 | IIIA   | NK       |
| mRNA#89  | AVAST-M | Male   | 61 | IIIA   | NK       |
| mRNA#90  | AVAST-M | Female | 37 | IIIA   | NK       |
| mRNA#91  | Madrid  | Male   | 69 | IIIA   | NK       |
| mRNA#92  | AVAST-M | Female | 45 | IIIB   | NK       |
| mRNA#93  | AVAST-M | Female | 51 | IIIB   | NK       |
| mRNA#94  | AVAST-M | Male   | 62 | IIIB   | NK       |
| mRNA#95  | AVAST-M | Female | 70 | IIIB   | NK       |
| mRNA#96  | AVAST-M | Female | 54 | IIIB   | NK       |
| mRNA#97  | AVAST-M | Female | 65 | IIIB   | NK       |
| mRNA#98  | AVAST-M | Female | 41 | IIIB   | NK       |
| mRNA#99  | AVAST-M | Male   | 66 | IIIB   | NK       |
| mRNA#100 | AVAST-M | Female | 72 | IIIB   | NK       |
| mRNA#101 | AVAST-M | Male   | 55 | IIIB   | NK       |
| mRNA#102 | AVAST-M | Male   | 43 | IIIB   | NK       |
| mRNA#103 | AVAST-M | Male   | 57 | IIIB   | NK       |
| mRNA#104 | AVAST-M | Female | 65 | IIIB   | NK       |
| mRNA#105 | AVAST-M | Female | 29 | IIIB   | NK       |
| mRNA#106 | AVAST-M | Female | 49 | IIIB   | NK       |
| mRNA#107 | AVAST-M | Male   | 61 | IIIB   | NK       |
| mRNA#108 | AVAST-M | Male   | 59 | IIIB   | NK       |
| mRNA#109 | AVAST-M | Male   | 61 | IIIB   | NK       |
| mRNA#110 | AVAST-M | Male   | 50 | IIIB   | NK       |
| mRNA#111 | AVAST-M | Male   | 23 | IIIB   | NK       |
| mRNA#112 | AVAST-M | Female | 62 | IIIB   | NK       |
| mRNA#113 | Madrid  | Male   | 88 | IIIB   | T1aN2cM0 |
| mRNA#114 | Madrid  | Female | 70 | IIIB   | T1aN2cM0 |
| mRNA#115 | Oxford  | NK     | NK | IIIB-C | NK       |

|          |         |        |    |      |                     |
|----------|---------|--------|----|------|---------------------|
| mRNA#116 | AVAST-M | Female | 33 | IIIC | NK                  |
| mRNA#117 | AVAST-M | Female | 76 | IIIC | NK                  |
| mRNA#118 | AVAST-M | Male   | 55 | IIIC | NK                  |
| mRNA#119 | AVAST-M | Male   | 63 | IIIC | NK                  |
| mRNA#120 | AVAST-M | Male   | 48 | IIIC | NK                  |
| mRNA#121 | AVAST-M | Male   | 53 | IIIC | NK                  |
| mRNA#122 | AVAST-M | Male   | 50 | IIIC | NK                  |
| mRNA#123 | AVAST-M | Female | 46 | IIIC | NK                  |
| mRNA#124 | AVAST-M | Male   | 27 | IIIC | NK                  |
| mRNA#125 | AVAST-M | Female | 80 | IIIC | NK                  |
| mRNA#126 | AVAST-M | Female | 73 | IIIC | NK                  |
| mRNA#127 | AVAST-M | Female | 64 | IIIC | NK                  |
| mRNA#128 | AVAST-M | Female | 53 | IIIC | NK                  |
| mRNA#129 | AVAST-M | Female | 41 | IIIC | NK                  |
| mRNA#130 | AVAST-M | Male   | 58 | IIIC | NK                  |
| mRNA#131 | AVAST-M | Male   | 59 | IIIC | NK                  |
| mRNA#132 | Madrid  | Female | 81 | IIIC | T4bN3M0             |
| mRNA#133 | Madrid  | Male   | 85 | IIIC | T3bN3M0             |
| mRNA#134 | Madrid  | Female | 80 | IIIC | T3bN2cM0            |
| mRNA#135 | Madrid  | Male   | 74 | IIIC | T2bN3M0             |
| mRNA#136 | Madrid  | Male   | 70 | IV   | T4aN2M1             |
| mRNA#137 | Madrid  | Female | 55 | IV   | T4aN2M1             |
| mRNA#138 | Madrid  | Male   | 46 | IV   | TxN3M1              |
| mRNA#139 | Madrid  | Female | 71 | IV   | TxN2cM1             |
| mRNA#140 | Madrid  | Male   | 58 | IV   | Metástasis melanoma |
| mRNA#141 | Madrid  | Female | 55 | IV   | T3aN0M1             |
| mRNA#142 | Madrid  | Male   | 61 | IV   | T4aN3M1             |
| mRNA#143 | Oxford  | NK     | NK | IV   | NK                  |

---

**Table S3. Clinical details of patients used in miRNA validation cohort.** NK- not known.

| <b>ID</b> | <b>Cohort</b> | <b>Gender</b> | <b>Age</b> | <b>Stage</b> | <b>TNM</b>      |
|-----------|---------------|---------------|------------|--------------|-----------------|
| Cont#1    | Biobanco      | female        | 59         | Control      | -               |
| Cont#2    | Biobanco      | male          | 55         | Control      | -               |
| Cont#3    | Biobanco      | female        | 65         | Control      | -               |
| Cont#4    | Biobanco      | female        | 68         | Control      | -               |
| Cont#5    | Biobanco      | female        | 64         | Control      | -               |
| Cont#6    | Biobanco      | male          | 60         | Control      | -               |
| Cont#7    | Biobanco      | male          | 57         | Control      | -               |
| Cont#8    | Biobanco      | male          | 51         | Control      | -               |
| Cont#9    | Biobanco      | male          | 51         | Control      | -               |
| Cont#10   | Biobanco      | male          | 56         | Control      | -               |
| Cont#11   | Biobanco      | male          | 62         | Control      | -               |
| Cont#12   | Biobanco      | female        | 56         | Control      | -               |
| Cont#13   | Biobanco      | female        | 60         | Control      | -               |
| Cont#14   | Biobanco      | female        | 58         | Control      | -               |
| Cont#15   | Biobanco      | NK            |            | Control      | -               |
| Cont#16   | Biobanco      | NK            |            | Control      | -               |
| Cont#17   | Biobanco      | female        | 64         | Control      | -               |
| Cont#18   | Biobanco      | female        | 54         | Control      | -               |
| Cont#19   | Biobanco      | male          | 53         | Control      | -               |
| Cont#20   | Biobanco      | female        | 55         | Control      | -               |
| Cont#21   | Biobanco      | male          | 59         | Control      | -               |
| Cont#22   | Biobanco      | Female        | 57         | Control      | -               |
| Cont#23   | Biobanco      | Male          | 58         | Control      | -               |
| Cont#24   | Biobanco      | Female        | 60         | Control      | -               |
| Cont#25   | Biobanco      | female        | 60         | Control      | -               |
| Cont#26   | Biobanco      | female        | 56         | Control      | -               |
| Cont#27   | Biobanco      | male          | 55         | Control      | -               |
| Cont#28   | Biobanco      | male          | 58         | Control      | -               |
| miRNA#1   | San Sebastián | male          | 66         | 0            | pT1sN0M0        |
| miRNA#2   | San Sebastián | female        | 41         | 0            | pTisN0M0        |
| miRNA#3   | San Sebastián | female        | 45         | 0            | pTisN0M0        |
| miRNA#4   | San Sebastián | female        | 51         | 0            | pTisN0M0        |
| miRNA#5   | San Sebastián | female        | 62         | 0            | pT1sN0M0        |
| miRNA#6   | Madrid        | male          | 66         | 0            | Léntigo maligno |
| miRNA#7   | Madrid        | NK            | 75         | 0            | TisN0M0         |

|          |               |        |    |    |                          |
|----------|---------------|--------|----|----|--------------------------|
| miRNA#8  | Madrid        | male   | 52 | 0  | Léntigo maligno. In situ |
| miRNA#9  | Madrid        | NK     | 52 | 0  | Léntigo maligno. In situ |
| miRNA#10 | Madrid        | female | 84 | 0  | Léntigo maligno. In situ |
| miRNA#11 | Madrid        | male   | 43 | 0  | Léntigo maligno. In situ |
| miRNA#12 | Madrid        | female | 33 | 0  | TisN0M0                  |
| miRNA#13 | Madrid        | NK     | 61 | 0  | TisN0M0                  |
| miRNA#14 | Madrid        | NK     | 43 | 0  | TisN0M0                  |
| miRNA#15 | San Sebastián | female | 55 | 0  | pT1sN0M0                 |
| miRNA#16 | San Sebastián | female | 77 | 0  | pT1a Melanoma in situ    |
| miRNA#17 | San Sebastián | Female | 47 | 0  | pT1sN0M0                 |
| miRNA#18 | San Sebastián | female | 15 | 0  | pT1sN0M0                 |
| miRNA#19 | San Sebastián | female | 43 | 0  | pT1sN0M0                 |
| miRNA#20 | San Sebastián | female | 59 | 0  | pT1sN0M0                 |
| miRNA#21 | San Sebastián | female | 49 | 0  | pT1sN0M0                 |
| miRNA#22 | San Sebastián | female | 51 | 0  | pT1s                     |
| miRNA#23 | San Sebastián | female | 65 | 0  | pT1sN0M0                 |
| miRNA#24 | San Sebastián | female | 51 | 0  | pT1sN0M0                 |
| miRNA#25 | San Sebastián | male   | 72 | 0  | pT1sN0M0                 |
| miRNA#26 | San Sebastián | female | 52 | 0  | pT1sN0M0                 |
| miRNA#27 | San Sebastián | female | 48 | 0  | pT1sN0M0                 |
| miRNA#28 | San Sebastián | female | 40 | 0  | pT1sN0M0                 |
| miRNA#29 | San Sebastián | male   | 51 | 0  | pT1sN0M0                 |
| miRNA#30 | San Sebastián | female | 43 | IA | pT1aN0M0                 |
| miRNA#31 | San Sebastián | female | 48 | IA | pT1aN0M0                 |
| miRNA#32 | San Sebastián | female | 33 | IA | pT1aN0M0                 |
| miRNA#33 | San Sebastián | female | 48 | IA | pT1aN0M0                 |
| miRNA#34 | San Sebastián | male   | 44 | IA | pT1aN0M0                 |
| miRNA#35 | San Sebastián | male   | 31 | IA | pT1aN0M0                 |
| miRNA#36 | Madrid        | female | 37 | IA | T1aN0M0                  |
| miRNA#37 | Madrid        | NK     | 75 | IA | T1aN0M0                  |
| miRNA#38 | Madrid        | NK     | NK | IA | T1aN0M0                  |
| miRNA#39 | Madrid        | male   | 57 | IA | T1aN0M0                  |
| miRNA#40 | Madrid        | NK     | 80 | IA | T1aN0M0                  |
| miRNA#41 | San Sebastián | male   | 67 | IB | PT2aN0M0                 |
| miRNA#42 | Madrid        | male   | 86 | IB | T2aN0M0                  |
| miRNA#43 | Madrid        | NK     | 67 | IB | T2aN0M0                  |
| miRNA#44 | Madrid        | NK     | 60 | IB | T2aN0M0                  |
| miRNA#45 | Madrid        | female | 37 | IB | T2aN0M0                  |

|          |               |        |    |      |           |
|----------|---------------|--------|----|------|-----------|
| miRNA#46 | Madrid        | NK     | 76 | IB   | T1bN0M0   |
| miRNA#47 | San Sebastián | female | 68 | IIA  | pT2bN0M0  |
| miRNA#48 | Madrid        | NK     | 71 | IIA  | T3aN0M0   |
| miRNA#49 | Madrid        | male   | 79 | IIA  | T3aN0M0   |
| miRNA#50 | San Sebastián | female | 71 | IIA  | pT3a      |
| miRNA#51 | San Sebastián | female | 69 | IIA  | pT2bN0    |
| miRNA#52 | San Sebastián | male   | 48 | IIB  | pT4N0M0   |
| miRNA#53 | Madrid        | female | 85 | IIB  | T3bN0M0   |
| miRNA#54 | Madrid        | female | 79 | IIB  | T3bN0M0   |
| miRNA#55 | San Sebastián | female | 83 | IIB  | pT4aN0M0. |
| miRNA#56 | San Sebastián | male   | 51 | IIB  | pT3bN0M0  |
| miRNA#57 | Madrid        | NK     | 64 | IIC  | T4bN0M0   |
| miRNA#58 | Madrid        | female | 84 | IIC  | T4bN0M0   |
| miRNA#59 | Madrid        | NK     | 87 | IIC  | T4bN0M0   |
| miRNA#60 | San Sebastián | female | 53 | IIC  | t4bn0M0   |
| miRNA#61 | San Sebastián | male   | 62 | IIC  | t4bn0M0   |
| miRNA#62 | San Sebastián | NK     | 47 | IIC  | pT4bN0M0  |
| miRNA#63 | San Sebastián | female | 55 | III  | TxN1M0    |
| miRNA#64 | San Sebastián | female | 20 | IIIA | pT3N1aM0  |
| miRNA#65 | San Sebastián | male   | 62 | IIIA | pT3aN2aM0 |
| miRNA#66 | San Sebastián | male   | 42 | IIIA | pT2N1aM0  |
| miRNA#67 | Madrid        | NK     | 54 | IIIA | T4aN2aM0  |
| miRNA#68 | San Sebastián | female | 58 | IIIA | T2aN1aM0  |
| miRNA#69 | San Sebastián | female | 40 | IIIA | -         |
| miRNA#70 | San Sebastián | male   | 45 | IIIA | txn2m0    |
| miRNA#71 | San Sebastián | male   | 57 | IIIA | t4an1am0  |
| miRNA#72 | San Sebastián | female | 52 | IIIA | t3an1m0   |
| miRNA#73 | AVAST-M       | male   | 53 | IIIA |           |
| miRNA#74 | San Sebastián | Female | 41 | IIIA | pT3bN1cM0 |
| miRNA#75 | San Sebastián | female | 65 | IIIB | pT2bN2aM0 |
| miRNA#76 | San Sebastián | female | 62 | IIIB | T3bN2cM0  |
| miRNA#77 | San Sebastián | female | 38 | IIIB | T2aN2aM0  |
| miRNA#78 | San Sebastián | female | 60 | IIIB | T2aN1bM0  |
| miRNA#79 | AVAST-M       | female | 55 | IIIB |           |
| miRNA#80 | AVAST-M       | female | 60 | IIIB |           |
| miRNA#81 | AVAST-M       | male   | 33 | IIIB |           |
| miRNA#82 | AVAST-M       | male   | 48 | IIIB |           |
| miRNA#83 | AVAST-M       | female | 46 | IIIB |           |
| miRNA#84 | San Sebastián | Female | 62 | IIIB | pT3N2aM0  |
| miRNA#85 | San Sebastián | male   | 69 | IIIC | pT3aN3M0  |
| miRNA#86 | Madrid        | NK     | 44 | IIIC | T2bN3M0   |

|          |               |        |    |      |            |
|----------|---------------|--------|----|------|------------|
| miRNA#87 | Madrid        | male   | 74 | IIIC | T2bN3M0    |
| miRNA#88 | San Sebastián | Female | 41 | IIIC | pT3aN3M0   |
| miRNA#89 | Madrid        | Female | 80 | IIIC | T3bN2cM0   |
| miRNA#90 | Madrid        | Female | 71 | IV   | TxN2cM1    |
| miRNA#91 | Madrid        | Male   | 61 | IV   | T4aN3M1    |
| miRNA#92 | Madrid        | Female | 55 | IV   | T3aN0M1    |
| miRNA#93 | Madrid        | NK     |    | IV   | metastatic |
| miRNA#94 | San Sebastián | male   | 59 | IV   | t4bn0m1a   |
| miRNA#95 | San Sebastián | Female | 48 | IV   | E.IV (M1b) |
| miRNA#96 | Madrid        | Male   | 58 | IV   | metastatic |

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**Table S4. Clinical details of patients used in yRNA validation cohort.** NK- not known.

| ID      | Origin | Gender | Age | Stage   | TNM      |
|---------|--------|--------|-----|---------|----------|
| Cont#1  |        | male   | 53  | Control | -        |
| Cont#2  |        | male   | 51  | Control | -        |
| Cont#3  |        | male   | 56  | Control | -        |
| Cont#4  |        | male   | 62  | Control | -        |
| Cont#5  |        | female | 56  | Control | -        |
| Cont#6  |        | female | 60  | Control | -        |
| Cont#7  |        | female | 60  | Control | -        |
| Cont#8  |        | female | 58  | Control | -        |
| Cont#9  |        | Female | 64  | Control | -        |
| Cont#10 |        | Female | 54  | Control | -        |
| Cont#11 |        | Male   | 53  | Control | -        |
| Cont#12 |        | Female | 55  | Control | -        |
| Cont#13 |        | Male   | 59  | Control | -        |
| Cont#14 |        | Female | 57  | Control | -        |
| Cont#15 |        | Male   | 58  | Control | -        |
| Cont#16 |        | Female | 60  | Control | -        |
| Cont#17 |        | Female | 60  | Control | -        |
| Cont#18 |        | Female | 56  | Control | -        |
| Cont#19 |        | Male   | 55  | Control | -        |
| Cont#20 |        | Male   | 58  | Control | -        |
| Cont#21 |        | Male   | 60  | Control | -        |
| Cont#22 |        | Male   | 53  | Control | -        |
| yRNA#1  |        | Male   | 45  | 0       | TisN0M0  |
| yRNA#2  |        | NK     | 41  | 0       | TisN0M0  |
| yRNA#3  |        | NK     | 45  | 0       | TisN0M0  |
| yRNA#4  |        | NK     | 51  | 0       | TisN0M0  |
| yRNA#5  |        | NK     | 62  | 0       | T1sN0M0  |
| yRNA#6  |        | Male   | 84  | 0       | TisN0M0  |
| yRNA#7  |        | Male   | 56  | 0       | TisN0M0  |
| yRNA#8  |        | Female | 47  | 0       | pT1sN0M0 |
| yRNA#9  |        | female | 15  | 0       | pT1sN0M0 |
| yRNA#10 |        | female | 43  | 0       | pT1sN0M0 |
| yRNA#11 |        | female | 59  | 0       | pT1sN0M0 |
| yRNA#12 |        | female | 49  | 0       | pT1sN0M0 |
| yRNA#13 |        | female | 51  | 0       | pT1s     |
| yRNA#14 |        | female | 65  | 0       | pT1sN0M0 |
| yRNA#15 |        | female | 51  | 0       | pT1sN0M0 |



|         |        |    |      |           |
|---------|--------|----|------|-----------|
| yRNA#16 | male   | 71 | 0    | pT1sN0M0  |
| yRNA#17 | female | 52 | 0    | pT1sN0M0  |
| yRNA#18 | female | 48 | 0    | pT1sN0M0  |
| yRNA#19 | female | 40 | 0    | pT1sN0M0  |
| yRNA#20 | male   | 51 | 0    | pT1sN0M0  |
| yRNA#21 | Female | 39 | IA   | T1N0M0    |
| yRNA#22 | Female | 43 | IA   | T1aN0M0   |
| yRNA#23 | Female | 48 | IA   | T1aN0M0   |
| yRNA#24 | Female | 33 | IA   | T1aN0M0   |
| yRNA#25 | Female | 48 | IA   | T1aN0M0   |
| yRNA#26 | Male   | 44 | IA   | T1aN0M0   |
| yRNA#27 | Male   | 31 | IA   | T1aN0M0   |
| yRNA#28 | Male   | 16 | IB   | T2aN0M0   |
| yRNA#29 | Male   | 67 | IB   | T2aN0M0   |
| yRNA#30 | Male   | 79 | IIA  | T3N0M0    |
| yRNA#31 | Female | 68 | IIA  | T2bN0M0   |
| yRNA#32 | Male   | 72 | IIB  | T4aN0M0   |
| yRNA#33 | Male   | 67 | IIB  | T4aN0M0   |
| yRNA#34 | Male   | 48 | IIB  | T4N0M0    |
| yRNA#35 | Female | 46 | IIC  | T4bN0M0   |
| yRNA#36 | Male   | 58 | IIC  | T4bN0M0   |
| yRNA#37 | Female | 84 | IIC  | T4bN0M0   |
| yRNA#38 | Female | 55 | III  | NK        |
| yRNA#39 | Female | 41 | IIIA | T3bN1cM0  |
| yRNA#40 | Female | 49 | IIIA | T4N1M0    |
| yRNA#41 | Male   | 62 | IIIA | T3aN2aM0  |
| yRNA#42 | Male   | 42 | IIIA | T2N1aM0   |
| yRNA#43 | Male   | 69 | IIIA | T4aN1M0   |
| yRNA#44 | Female | 40 | IIIA | NK        |
| yRNA#45 | Female | 60 | IIIA | pT2aN1aM0 |
| yRNA#46 | Female | 40 | IIIB | pT2aN2aM0 |
| yRNA#47 | Female | 65 | IIIB | T2bN2aM0  |
| yRNA#48 | Male   | 88 | IIIB | T1aN2cM0  |
| yRNA#49 | Female | 62 | IIIB | pT3bN2c   |
| yRNA#50 | Female | 60 | IIIB | pT2aN1bM0 |
| yRNA#51 | Male   | 69 | IIIC | T3bN2cM0  |
| yRNA#52 | Male   | 69 | IIIC | T3aN3M0   |
| yRNA#53 | Female | 81 | IIIC | T4bN3M0   |
| yRNA#54 | Female | 80 | IIIC | T3bN2cM0  |
| yRNA#55 | Male   | 61 | IV   | T4aN3M1   |
| yRNA#56 | Female | 71 | IV   | TxN2cM1   |
| yRNA#57 | Female | 55 | IV   | T3aN0M1   |

yRNA#58

Male

58

IV

Metastasis

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**Table S5. Characteristics of selected differentially protein-encoding gene fragment probe sets**

| <i>probe<br/>set ID</i> | <i>Gene</i>  | <i>Exon (Amino<br/>acid<br/>position)*</i> | <i>Length</i> | <i>Sequence</i>                                                                                                                                                       |
|-------------------------|--------------|--------------------------------------------|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>2648985</b>          | <b>ATM</b>   | <b>1 (63-109)</b>                          | <b>143</b>    | ATTTTACAGAAATATATTCAGAAAGA<br>AACAGAATGTCTGAGAATAGCAAAAC<br>CAAATGTATCAGCCTCAACACAAGCC<br>TCCAGGCAGAAAAAGATGCAGGAAAT<br>CAGTAGTTTGGTCAAATACTTCATCAA<br>ATGTGCAAACAGAA |
| <b>667389</b>           | <b>AMFR</b>  | <b>1<br/>(59nt(5'UTR)<br/>1-10)</b>        | <b>104</b>    | AATTGGGACAGGCCTCCTCCAGTCA<br>GTCGGGCACAGGGCGCAGGAGGCA<br>GCTGAGGAAGGCAAGGGAGCGCTAG<br>GAGGTCTGCTGCTTCTGAAGCCTCC<br>GTTCCG                                             |
| <b>731164</b>           | <b>CD109</b> | <b>5 (170-211)</b>                         | <b>125</b>    | GACCCCAAATCAAATTTGATCCAACA<br>GTGGTTGTCACAACAAAGTGATCTTG<br>GAGTCATTTCCAAAACTTTTAGCTAT<br>CTTCCCATCCAATACTTGGTGACTGG<br>TCTATTCAAGTTCAAGTGAAT                         |
| <b>730641</b>           | <b>SOS1</b>  | <b>8 (798-836)</b>                         | <b>119</b>    | TTCTCAAACCACAGAGTGAGGTTGGT<br>GGTATGTCGAATCATTTTCAGAAGATT<br>AGGAGAGTTAATTTCTTTGTCTTCTTT<br>TGTCCACACACTTCCAATAATTCTGA<br>TGGCTGTACAGCT                               |

\*positions and exon number relative to refseq transcript

**Supplementary Table S6. Summary of NGS results from pooled RNA samples.**

\*sRNA (shortRNA) was defined as sequences between 18-43 nt.

| <b>Pool (n, µg (RNA))</b> | <b>Reads (10<sup>6</sup>)</b> | <b>Phread score</b> | <b>Mapped (10<sup>6</sup>)</b> | <b>Mapped sRNA* (10<sup>6</sup>)</b> |
|---------------------------|-------------------------------|---------------------|--------------------------------|--------------------------------------|
| Cont. (8, 2.96)           | 49.79                         | 37.93               | 27.83 (55%)                    | 14.38 (29%)                          |
| Stage 0 (5, 2.07)         | 57.91                         | 37.89               | 31.94 (55%)                    | 11.68 (20%)                          |
| Stage I/II (8, 3.45)      | 49.37                         | 37.86               | 24.97 (51%)                    | 13.14 (27%)                          |
| Stage III (7, 3.20)       | 49.15                         | 37.87               | 26.54 (54%)                    | 12.20 (25%)                          |
| Stage IV (8, 2.96)        | 41.45                         | 37.89               | 20.69 (50%)                    | 9.14 (23%)                           |

|                    | <b>Cont.</b>                            | <b>Stage 0</b>                          | <b>Stage I/II</b>                       | <b>Stage III</b>                        | <b>Stage IV</b>                         |
|--------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| <b>RNY/RNY4*</b>   | 1,494,240 (25.6%)<br>/1,399,490 (24%)   | 1,233,516 (26.2%)<br>/1,185,336 (25.2%) | 1,141,496(25.3%)<br>/1,085,019 (24.1%)  | 1,284,278 (26.4%)<br>/1,175,099 (24.2%) | 1,179,907 (27.1%)<br>/1,120,159 (25.7%) |
| <b>RNYP/RNYP4*</b> | 2,833,938 (48.6%)<br>/2,830,682 (48.5%) | 2,290,363 (48.7%)<br>/2,288,302 (48.7%) | 2,190,406 (48.6%)<br>/2,187,535 (48.5%) | 2,313,285 (47.6%)<br>/2,310,512 (47.6%) | 2,113,392 (48.5%)<br>/2,111,236 (48.4%) |
| <b>Rfam YRNA*</b>  | 1,511,724 (25.9%)                       | 1,176,482 (25%)                         | 1,176,210 (26.1%)                       | 1,258,188 (25.9%)                       | 1,065,461 (24.4%)                       |
| <b>Total reads</b> | <b>5,839,905</b>                        | <b>4,700,362</b>                        | <b>4,508,112</b>                        | <b>4,855,751</b>                        | <b>4,358,760</b>                        |

**Supplementary Table S7. YRNA reads from NGS. \*% of total YRNA counts.**