

Supplementary figure 1. RBP precipitation by the 3'UTR of MICB from HEK293T cell cytoplasmic extract

Coomassie staining of RNA binding proteins precipitated from cytoplasmic extracts of HEK293T cells via RNA-AP. The specific bands that were cut and sent for mass spectrometry analysis are marked by red arrowheads. BG-background, stands for purification in the presence of streptavidin beads only (without a labeled RNA). Un-MICA/un-MICB stands for the 3'UTR of either MICA or MICB, which was not labeled with biotinylated UTPs. MICA/MICB stands for the 3' UTR of either MICA or MICB labeled with biotinylated UTPs. AS stands for antisense 3'UTR. Ctrl-A is the 3'UTR of TAF6. Ctrl-B is the 3'UTR of CASQ2.



Supplementary figure 2. Validation of KD efficiency

(a) WB analysis of confirming the knockdown of various RBPs in RKO cells. The shRNAs are indicated above the target and the various antibodies used for the WB are indicated on the left. The specific KD is marked with a red asterisk. Tubulin served as a loading control. (b) WB analysis quantification of RBP KD efficiency relative to the control shRNA (Ctrl) that was set to 1 (marked by the dashed line). (c) WB analysis of the known target of CUGBP1, cJUN, in CUGBP1-KD cells. CJUN showed increased expression due to depletion of CUGBP1 relative to control-shRNA and sh-hnRNPM as an additional control.



Supplementary figure 3. The RBPs regulate specifically MICB and do not alter the expression of MICA on HEK293T cells (a and b) FACS analysis of the expression of MICA on HEK293T cells transduced with either shRNAs against the various RBPs (a) or with lentiviral vectors expressing the various RBPs (b). The empty black histogram represents the indicated shRNA (a) or RBP (b), the empty grey histogram represents a control-shRNA (a) or STAU2 as a control RBP (b), the dashed dark grey histogram represents background of the specific cell and the filled grey histogram represents background staining. Data are representative of six independent experiments.



Supplementary figure 4. The identified RBPs do not affect the relative abundance of MICA mRNA.

Relative mRNA abundance of MICA in the various shRNA-transduced (a) or RBP-transduced (b) RKO cells was evaluated by qRT-PCR. hGAPDH was used as a reference gene. Shown are mean±SEM of triplicates. Data are representative of three independent experiments. (a) The abundance of MICA in cells transduced with a control-shRNA was set as 1. (b) The abundance of MICA in cells transduced with STAU2 was set as 1.

а

b

1 ACUCUACAGCCAGGCAGCUGGGAUUCAAUUCCCUGCCUGGAUCUCACGAGCACUUUCCCUCUUGGUGCCUCAGUUUCCUG 81 ACCUAUGAAACAGAGAAAAUAAAAGCACUUAUUUAUUGUUGUUGGAGGCUGCAAAAUGUUAGUAGAUAUGAGGCGUUUGC 161 AGCUGUACCAUAUU

Supplementary figure 5. Analysis of RBP binding elements in the 3'UTRs of MICA

The sequence of the 3' UTR of MICA. One AU-rich element (possible HuR binding regions) is highlighted in dark grey and white letters.



Supplementary figure 6. MICA and MICB expression by HEK293T cells

FACS analysis of the levels of MICA (filled black histogram) and MICB (empty black histogram) on HEK293T cells. Filled grey histogram represents background staining.



Supplementary figure 7. Doxorubicin treatment induces MICB expression.

HFF cells were treated with 2 μ g/ml of Doxorubicin for 48 hrs and then the levels of MICB were analyzed by FACS. The empty grey histogram represents MICB levels prior to Doxorubicin treatment, the black histogram represents MICB levels following Doxorubicin and the filled grey histogram represents background staining.

81 UCUGCCCCACACCCAGCCAGCUCCUUUCCCUUUUCCAUCAUCUUUUCCCACUCCCUUUGCGUCAGGAGCAGCAUCAUU 161 CAGCAAAUGCCUUUUCAAAUGCAGCAAUCCCACUUAGCAGGGACAGGAGAAAAUUAUUCCCAUGUUGACUGUCUUGACU 241 GUCACGGAACAGAUCUUGUUGCUGGACCAUCAAGGGUCAUGGCAGUGCCUGAACAUGGCAGUCUAGGGUGAACAAU 321 CCCCUAACACAAGUUUACUUGUCUUUGAUUAUGACAGUAACAAAUUGACAGCUUUCUAACUCACAGGCAUAGAGUGACC 481 CCAGCCAAGAUGAUCCUUCUUAGAGAAGGCUCAGCCUUGGAAGCAAACUUAUAAAUCAUAUUCUCAUGGCUUUGUUAAAC 561 UUAUUUCAAGUGAUGGUCAUUCAUAUCACUAUGAACUUGGAUAUUCAAGCCUUUGGAUGGCUAUGGAGAGGGCUUGAAAU 641 GUGUACAGGUGUCACCAUCAUUUCUAGUAUAUUAGGAAACUGGGAUGGGAGGUUGAUUUGCUCUCUAAACUUCCCUCUAG 721 UUGGCAAGUCUCACAUAUUCAUCAGCAGGAGUGGAGGGUGGGGGAAAACUAGAAAGAUGAAAACUUUUACAUUUUUCUGA 801 UGGGUUCAUGUCUCUGAUUGGGUCAGCUGGCUUCCUAGCCUAAGCUGGGAUCUGAAUACCCCUUCUCUGUAGCUGCUAGU 881 GAGCCUUCCCAUUUAGAUUAAAGAUUGCUUUAUCCAGCAGUCAAUUAACUCUCCAGUUAUCAGUACUCCCACAAUUGGCC 1041 CUAAAAGUUACAUUGUGCUUGGUAGAUUUAGUGUUAAGUGUGCAGUAUAAUUUUCUAAUUUUCUCAAUCUUUUAGC 1201 AAACUCAUAUUUUGAAAAUAUUCAGACAAUGUUGAA

Supplementary figure 8. Analysis of putative RBP binding elements in the 3'UTR of CASQ2

The sequence of the 3' UTR of CASQ2. RBP binding elements are highlighted. One AU-rich element (possible HuR binding regions) is highlighted in dark grey and white letters. MATR3 binding sequences are marked in red. IGF2BP2 binding sequences are marked in blue.

1 ACUCUACAGCCAGGCGGCCAGGAUUCAACUCCCUGCCUGGAUCUCACCAGCACUUUCCCUCUGUUUCCUGACCUAUGAAA 81 161 CGUAGAGAGCCAGCAAAGGGAUCAUGACCAACUCAACAUUCCAUUGGAGGCUAUAUGAUCAAACAGCAAAUUGUUUAUCA UGAAUGCAGGAUGUGGGCAAACUCACGACUGCUCCUGCCAACAGAAGGUUUGCUGAGGGCAUUCACUCCAUGGUGCUCAU 241 321 UGGAGUUAUCUACUGGGUCAUCUAGAGCCUAUUGUUUGAGGAAUGCAGUCUUACAAGCCUACUCUGGACCCAGCAGCUGA 401 GAGAAGCAAGAAGCCCCCUGACCCCUUGUUCCAAAUAUACUCUUUUGUCUUUUCUCUUUAUUCCCACGUUCGCCCUUUGUU 481 CAGUCCAAUACAGGGUUGUGGGGCCCUUAACAGUGCCAUAUUAAUUGGUAUCAUUAUUUCUGUUGUUUUUGUUUUUGUUUUUGUUU 561 641 UUGUUUUUGUUUUUGAGACAGAGUCUCACUCUGUCACCCAGGCUGCAGUUCACUGGUGUGAUCUCAGCUCACUGCAACCU 721 801 UAAUUUUUUGUAUUUUUUGUAGAGACGGGGUUUCGCCAAGUUGACCAGCCCAGUUUCAAACUCCUGACCUCAGGUGAUCUG CCUGCCUUGGCAUCCCAAAGUGCUGGGAUUACAAGAAUGAGCCACCGUGCCUGGCCUAUUUUAUUAUUAUUGCCACCAUGC 881 1041 CUCCUGACCAGCCCAGGACCAGCUUUCUUGUCACCUUGAGGUCCCCUCGCCCCGUCACACCGUUAUGCAUUACUCUGUGU

b

1 ACUCUACAGCCAGGCGGCCAGGAUUCAACUCCCUGCCUGGAUCUCACCAGCACUUUCCCUCUGUUUCCUGACCUAUGAAA 81 CAGAGAAAAUAACAUCACUUAUUUAUUGUUGUUGGAUGCUGCAAAGUGUUAGUAGGUAUGAGGUGUUUGCUGCUGCCA 161 CGUAGAGAGCCAGCAAAGGGAUCAUGACCAACUCAACAUUCCAUUGGAGGCUAUAUGAUCAAACAGCAAAUUGUUUAUCA 241 UGAAUGCAGGAUGUGGGCAAACUCACGACUGCUCCUGCCAACAGAAGGUUUGCUGAGGGCAUUCACUCCAUGGUGCUCAU 321 UGGAGUUAUCUACUGGGUCAUCUAGAGCCUAUUGUUUGAGGAAUGCAGUCUUACAAGCCUACUCUGGACCCAGCAGCUGA 481 GAGAAGCAAGAAGCCCCCUGACCCCUUGUUCCAAAUAUACUCUUUUGUCUUUUCUCUUUAUUCCCACGUUCGCCCUUUGUU CAGUCCAAUACAGGGUUGUGGGGCCCUUAACAGUGCCAUAUUAAUUGGUAUCAUUAUUUCUGUUUUUGUUUUGUUU 561 641 UUGUUUUUGUUUUUGAGACAGAGUCUCACUCUGUCACCCAGGCUGCAGUUCACUGGUGUGUCUCAGCUCACUGCAACCU 721 801 UAAUUUUUGUAUUUUUUGUAGAGACGGGGUUUCGCCAAGUUGACCAGCCCAGUUUCAAACUCCUGACCUCAGGUGAUCUG CCUGCCUUGGCAUCCCAAAGUGCUGGGAUUACAAGAAUGAGCCACCGUGCCUGGCCUAUUUUAUUAUUAUUGCCACCAUGC 881 CUCCUGACCAGCCCAGGACCAGCUUUCUUGUCACCUUGAGGUCCCCUCGCCCCGUCACACCGUUAUGCAUUACUCUGUGU 1041

Supplementary figure 9. Comparison of RBP binding elements and cellular or viral miRNA binding sites in the 3'UTR of MICB All RBP consensus sequences are marked in blue. Cellular miRNA (a) and viral miRNA (b) binding sites are marked in red. The binding site of only miR-10b overlaps with a possible binding site of MATR3 at positions 561-578. No overlap is observed between viral miRNAs and RBPs.



Supplementary figure 10. KD of FUBP3 and of HuR does not effect MICB on untreated HFF cells. HFF cells were transduced with shRNAs against FUBP3, HuR or a control vector and MICB levels were subsequently analyzed by FACS. The empty grey histogram represents

Gene	Orientation	Sequence (5'-3')
TAF6	Fw	TGCTCCACCTGCCAGCCC
	Rv	TCAGAACTTACAAACCAAACTTTTA
CASQ2	Fw	CCCAACTCCAAACAATTCTGATG
	Rv	TTCAACATTGTCTGAATATTTTC
MICA	Fw	ACTCTACAGCCAGGCAGCTGGGATTC
	Rv	AATATGGTACAGCTGCAAACGCCTC
MICB	Fw	ACTCTACAGCCAGGCGGCCAGG
	Rv	AGAGTAAACATTTACGGTATAAATTATGC

Supplementary Table 1. Primers for amplification of 3'UTRs

	Orientation	Sequence (5'-3')
FUBP3	Fw	ATGGCGGAGCTGGTGCAGG
	Rv	CTACTGCTCCTGGCTGTGGG
HuR	Fw	ATGTCTAATGGTTATGAAGACCACATG
	Rv	TTTATTTGTGGGACTTGTTGGTTTT
XRN2	Fw	ATGGGAGTCCCGGCGTTCTT
	Rv	TTAATTCCAATTGTATCTTCCTGAG
MATR3	Fw	ATGTCCAAGTCATTCCAGCAGT
	Rv	TTAAGTTTCCTTCTTCTGTCTGC
CUGBP1	Fw	ATGAACGGCACCCTGGACCA
	Rv	TCAGTAGGGCTTGCTGTCATTC
IGF2BP2	Fw	ATGATGAACAAGCTTTACATCGG
	Rv	TTCACTTGCTGCGCTGTGAGG
STAU2	Fw	ATGCTTCAAATAAATCAGATGTTC
	Rv	TCATACCTGAAAGCCTTGAATCC
hnRNP-M	Fw	ATGGCGGCAGGGGTCGAAG
	Rv	TTAAGCGTTTCTATCAATTCGAAC
GUmut	Fw	GGTATCATTATTTCTGTTGTTGTTGTTGTTG
		TTGTTGTTGTTGTTGTTGAGACAGAG
	Rv	CTCTGTCTCAACAACAACAACAACAACAACA
		ACAACAACAACAGAAATAATGATACC

Supplementary Table 2. Primers for amplification of RBPs and mutagenesis

	Supplementary	Table 3. Primers f	for the detection	of the transcript	s in qRT-PCR
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	Orientation	Sequence (5'-3')
MICB	Fw	CTGCTGTTTCTGGCCGTC
	Rv	ACAGATCCATCCTGGGACAG
MICA	Fw	ATCTTCCCTTTTGCACCTCC
	Rv	AACCCTGACTGCACAGATCC
FUBP3	Fw	GGAGCAGACAAGCCTCTTCGTA
	Rv	CCATTCGAGAGTTGAAATCGCCG
HuR	Fw	AGCAGCATTGGTGAAGTTGA
	Rv	GCGGTCACGTAGTTCACAAA
XRN2	Fw	GCAAGTACCCGTCCATCATAG
	Rv	TGGATTAGGTTTACTGGCATCA
MATR3	Fw	GGGGGATTGTGGGAGTCT
	Rv	TTCAAGCTGAGAACCAGCAG
CUGBP1	Fw	CATCTGTGTGGGGGAAACCTT
	Rv	GTGTTGAGGTTCCCAGAGGA
IGF2BP2	Fw	AAAGTGGAATTGCATGGGAA
	Rv	CAGGTGAGGAGGGATGTTTC
hnRNP-M	Fw	CAAAATGGAGGAAGAGAGCG
	Rv	TTCTCATTCTGAGCAGGTCG
STAU2	Fw	GCCATTAGATCCAAAGCCAT
	Rv	CTTAGGCACTGGGCAATGAT
GAPDH	Fw	AAGGTGAAGGTCGGAGTCAA
	Rv	AATGAAGGGGTCATTGATGG