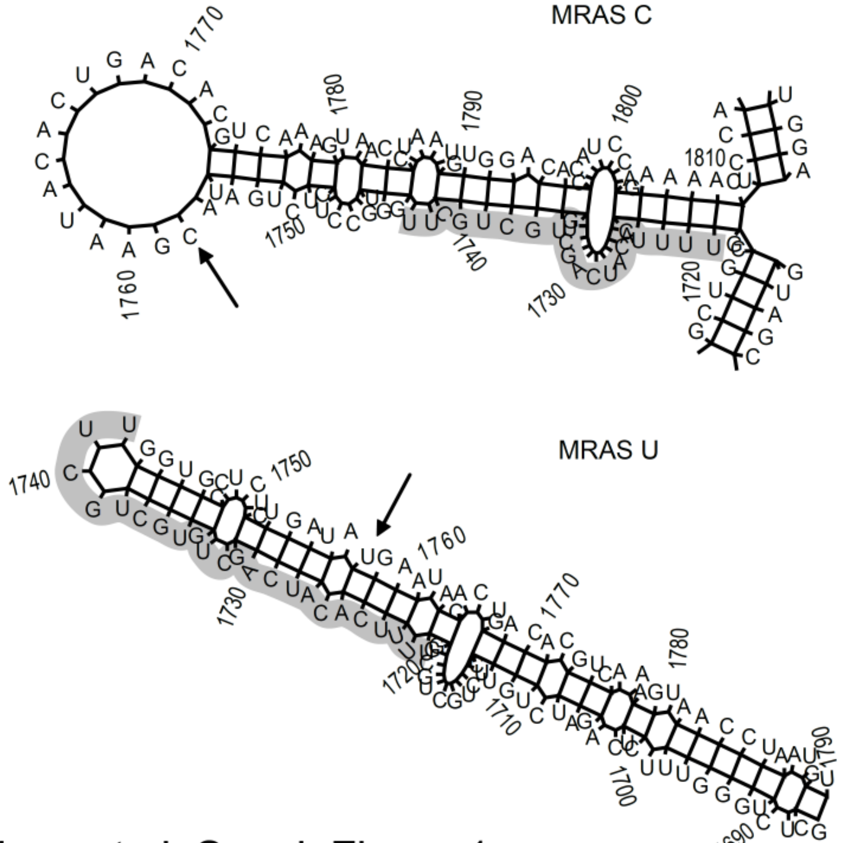
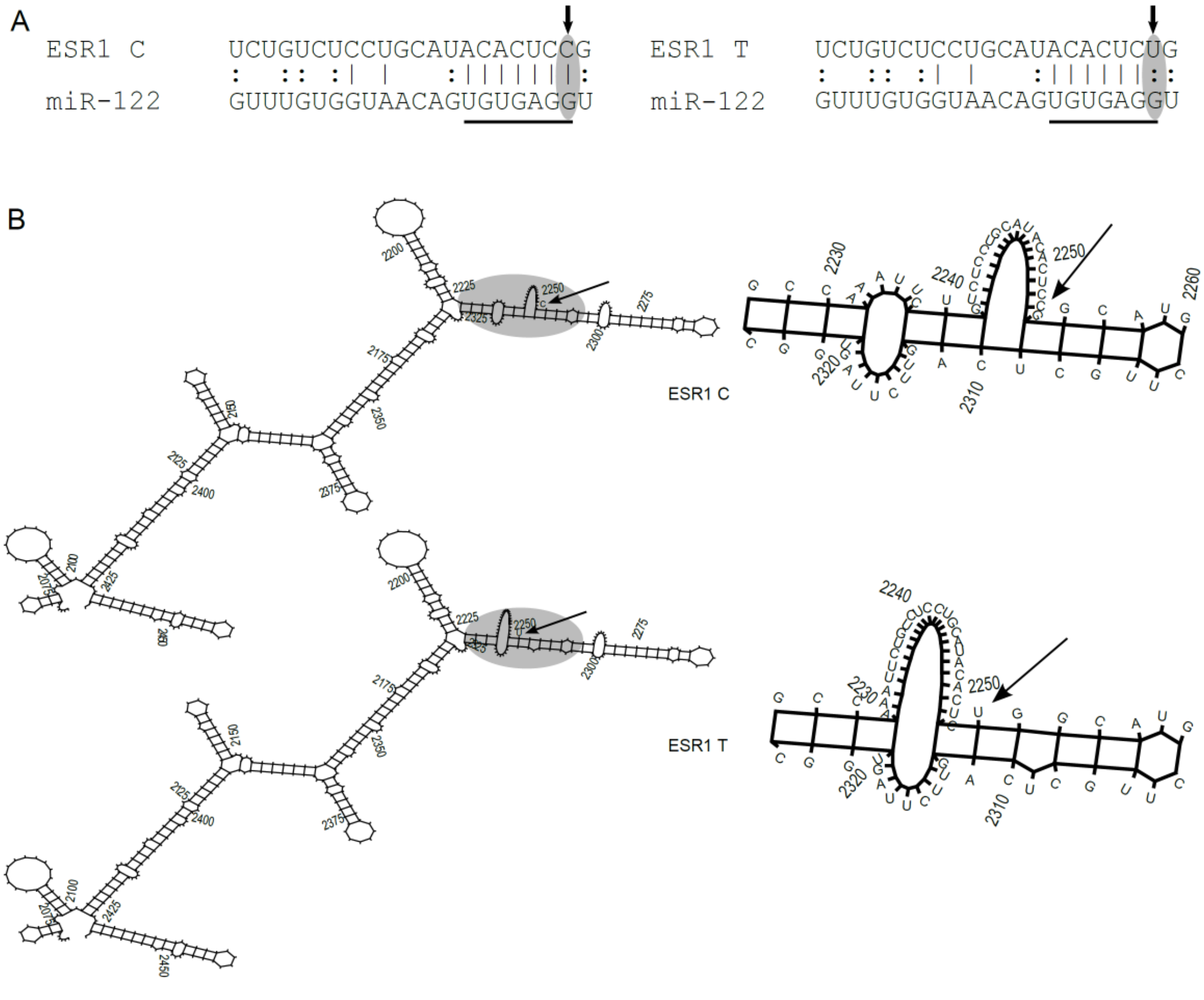


Haas et al. Suppl. Figure 1

Supplementary Figure 1.

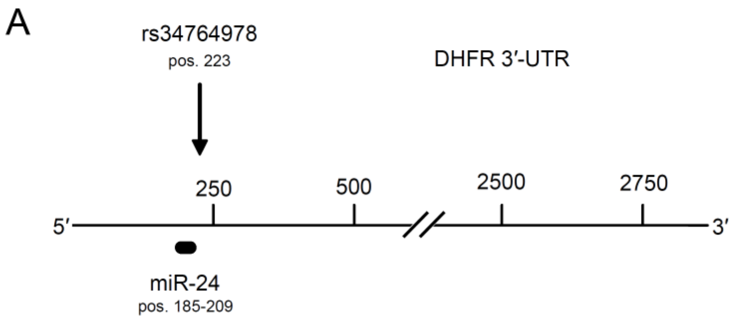
Predicted secondary structures for MRAS variants C (upper panel) and U (lower panel). The arrow indicates the position of the SNP rs9818870 and the miR-195 target site is highlighted in grey. The numbering is according to the position in the *MRAS* mRNA (see Figure 5).
The structures exemplarily illustrate differences in local RNA structure predictions between the two MRAS variants (see Figure 5) which affect the SNP site as well as the miRNA binding site (highlighted in grey) that is located directly upstream of the SNP.



Haas et al. Suppl. Figure 2

Supplementary Figure 2.

We performed further experiments to study miR-SNPs and their influence on miRNA regulation by analyzing a SNP (rs3798577) in the estrogen receptor 1 gene (*ESR1*) that is located at position 96 of the *ESR1* 3′ -UTR within a potential binding site for miR-122. Whereas the C variant is characterized by a seed match, the U variant leads to one G:U mismatch between mRNA and miRNA **(A)**. Overall, we performed identical experiments as for the *AGTR1*/miR-155 system. Reporter gene assays show that both variant target sites, C and U, were regulated by miR-122 and miR-122_SNP, respectively (data not shown). Independent of the length of the ESR1 construct, repression was stronger with the matching miRNA. *In silico* secondary structure analyses of the two *ESR1* mRNA variants yielded a lot of different local structures. However, some structures show repeating local RNA elements that differ only slightly in the vicinity of the SNP **(B)**. For the C variant this local structure was observed in 35% and for the U in 21% of all analysed structures. Subsequently performed RNA probing experiments illustrate indistinguishable cleavage patterns with only minor differences of the cleavage patterns (data not shown). In summary, these results suggest that the analyzed miR-SNP in the *ESR1* 3′ -UTR does not significantly influence miR-122 regulation. Firstly, this can be explained by the fact that the T allele induces only a wobble mismatch between mRNA and miR-122. Secondly, our results indicate that this SNP does not cause a structural change and hence does not affect mRNA accessibility or miRNA regulation.



B

Local structure context of miR-24 site	DHFR C	DHFR U
Loop	32	66
Junction	74	22
Stem	91	96
Others	3	16

Haas et al. Suppl. Figure 3

Supplementary Figure 3.

(A) schematically shows the *DHFR* 3′-UTR with the SNP rs34764978 at position 223 and the miR-24 target site located 14 nt upstream of the polymorphic site. Secondary structures of the miR-24 target site-containing polymorphic RNAs were predicted via mfold and results are listed in **(B)**.