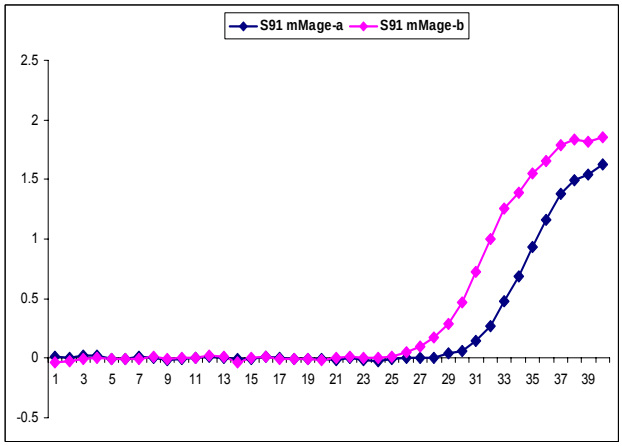
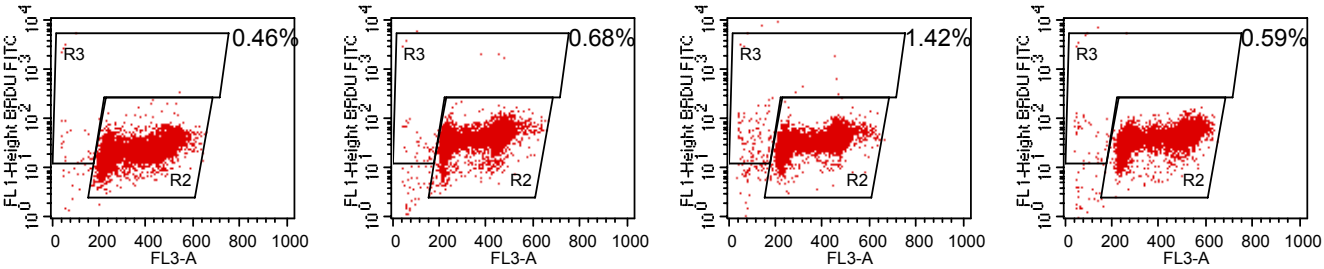
Supplementary Fig: 1



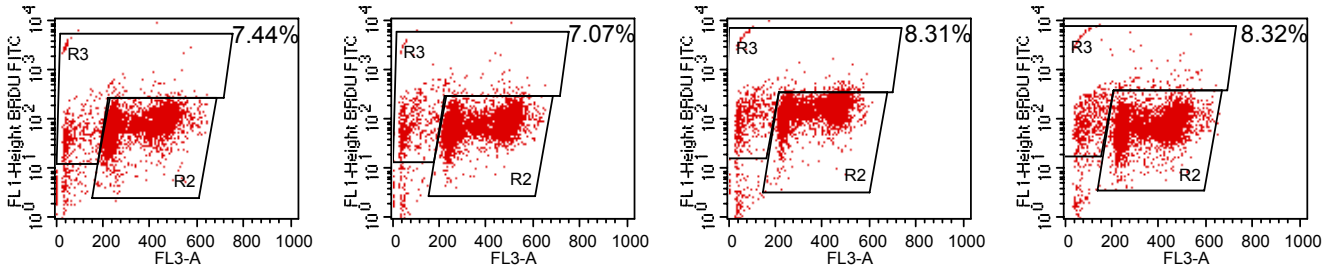
Real time RT-PCR quantification of murine mMage-a and mMage-b mRNA. mMage-b has higher expression than mMage-a at mRNA level in S91 cells.

Supplementary Fig: 2 TUNEL Analysis

A. Hs-294T cells

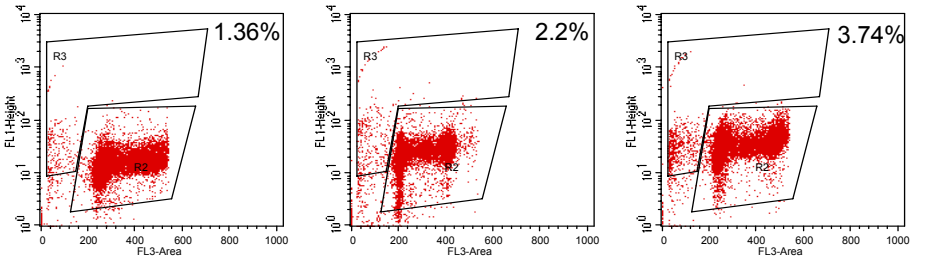


Mock-transfection | FMK | Non-specific siRNA | FMK+Non-specific siRNA

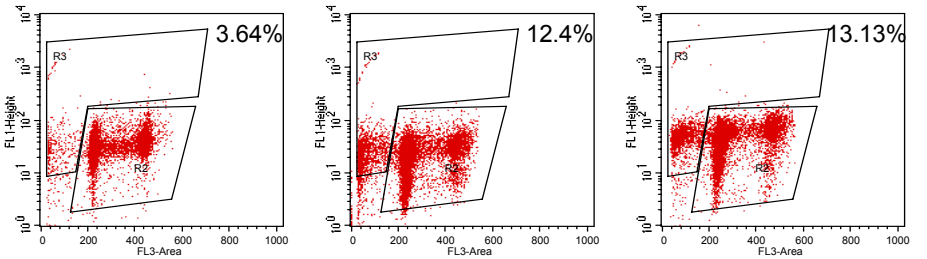


pan MAGE-A siRNA | FMK+ pan MAGE-A siRNA | C2 siRNA | FMK+C2 siRNA

B. S91 cells



Mock-transfection | FMK | Non-specific siRNA



FMK+Non-specific siRNA | mMage-b siRNA | FMK+mMage-b siRNA

MAGE siRNAs induced caspase-independent apoptosis in melanoma cells (TUNEL Analysis). Flow cytometry shows that apoptosis induced by MAGE siRNA in human Hs-294T **(A)** and murine S91 cells **(B)** is not inhibited by the general caspase inhibitor zVAD-FMK. Apoptotic cells are in upper, L-shaped window. The percentage of apoptotic cells is shown for each condition in the upper right corner of the individual panels.

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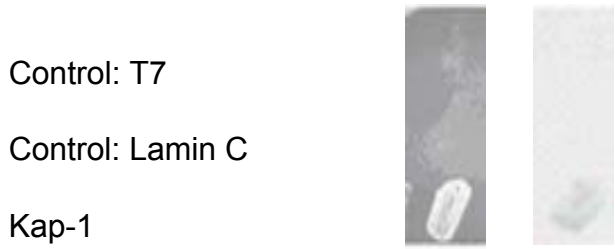
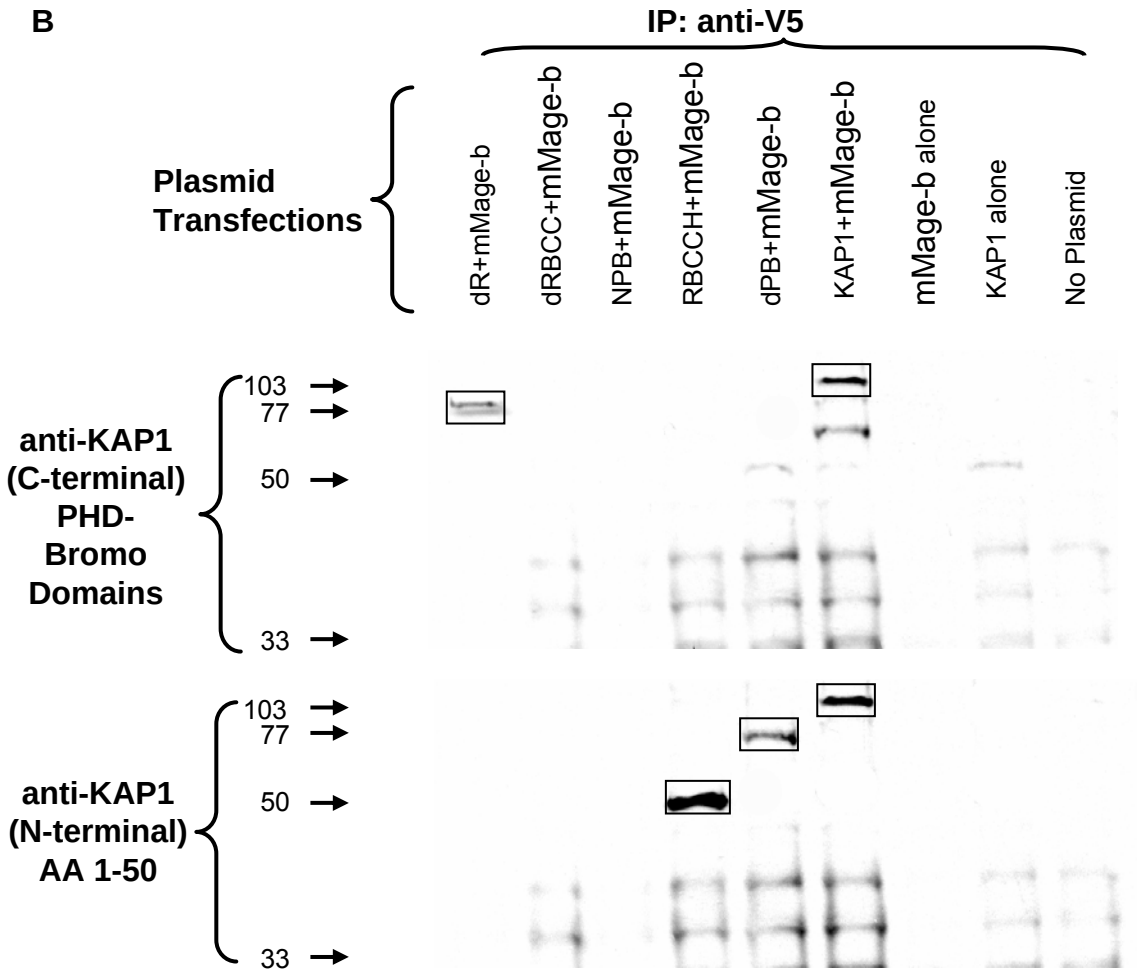
Supplementary Fig: 3

A



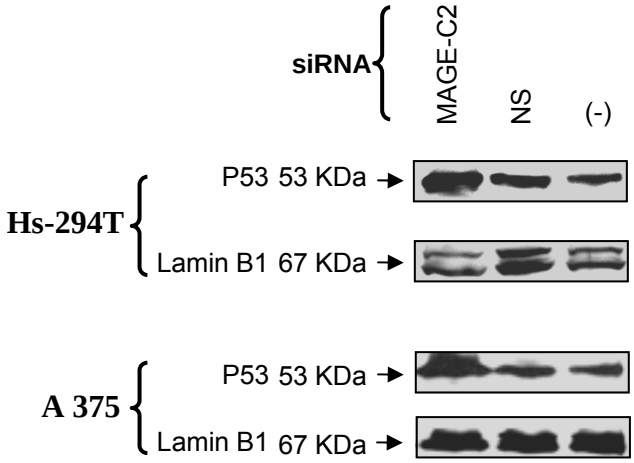
Yeast two hybrid assay identifies MAGE-C2as a Kap-1 binding partner. Yeast were co-transformed with KAP1 or control protein expression plasmids and grown on selection medium (left panel). Colonies were transferred and assayed for β–galactosidase activity (blue-green color, right panel). T7= yeast co-transformed with irrelevant bait, pGBK-T7; LaminC= yeast co-transformed with irrelevant bait, pGBKT7-LaminC; KAP1=yeast co-transformed with pGBKT7-KAP1. Note that β–galactosidase activity was only seen in the presence of Kap-1, confirming Kap-1 MAGE-C2 binding.

B



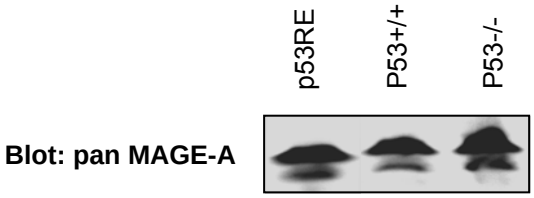
Kap-1 and mMage-b protein Co-immunoprecipitate. V5-Tagged mMage-b and KAP1 deletion expression plasmids were co-transfected into COS7 cells and lysates were immunoprecipitated with anti-V5 antibody and immunoblotted with anti-KAP1 antibodies recognizing either N-terminal or C-terminal Kap-1 peptides. The pattern is identical to that seen with MAGE-C2 (Figure 3c) indicating that mMage-b also binds to the Kap-1 BB-Coiled coil region

Supplementary Fig: 4



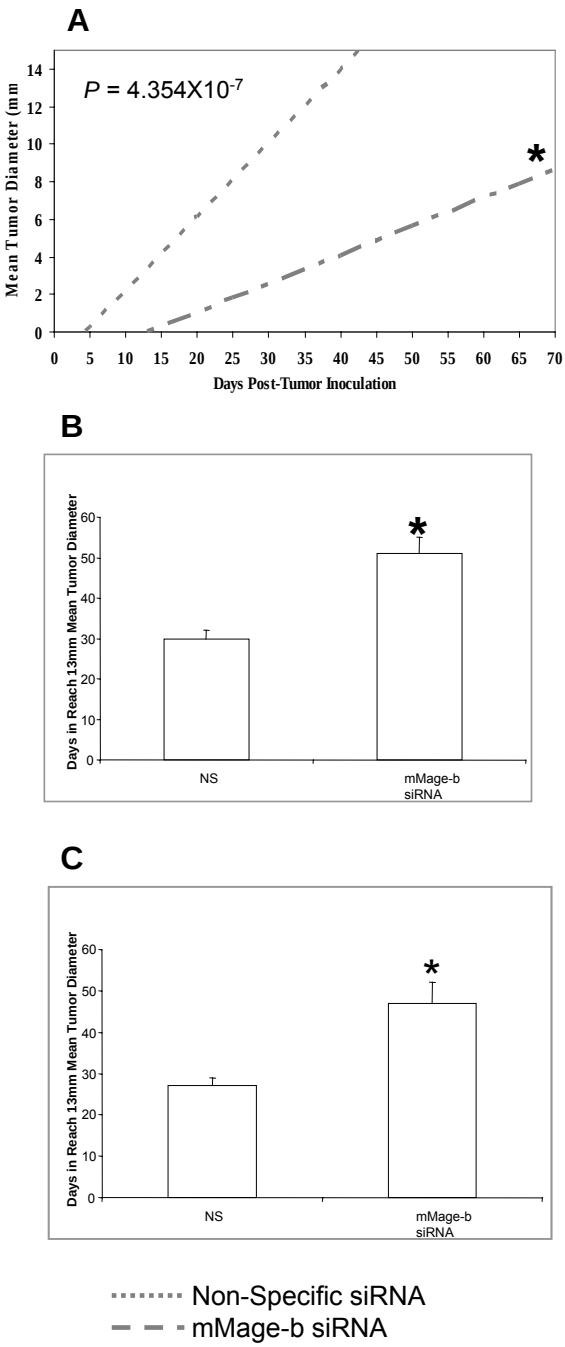
Immunoblotting shows an increase in immunoreactive p53 in the nuclear fractions of the Hs-294T and A375 human melanoma cell lines 24h after knockdown of MAGE-C2 compared to non-specific siRNA and no siRNA controls. Immunoblot of the nuclear protein Lamin B1 shows the purity of fractionation and serves as a protein loading control.

Supplementary Fig: 5



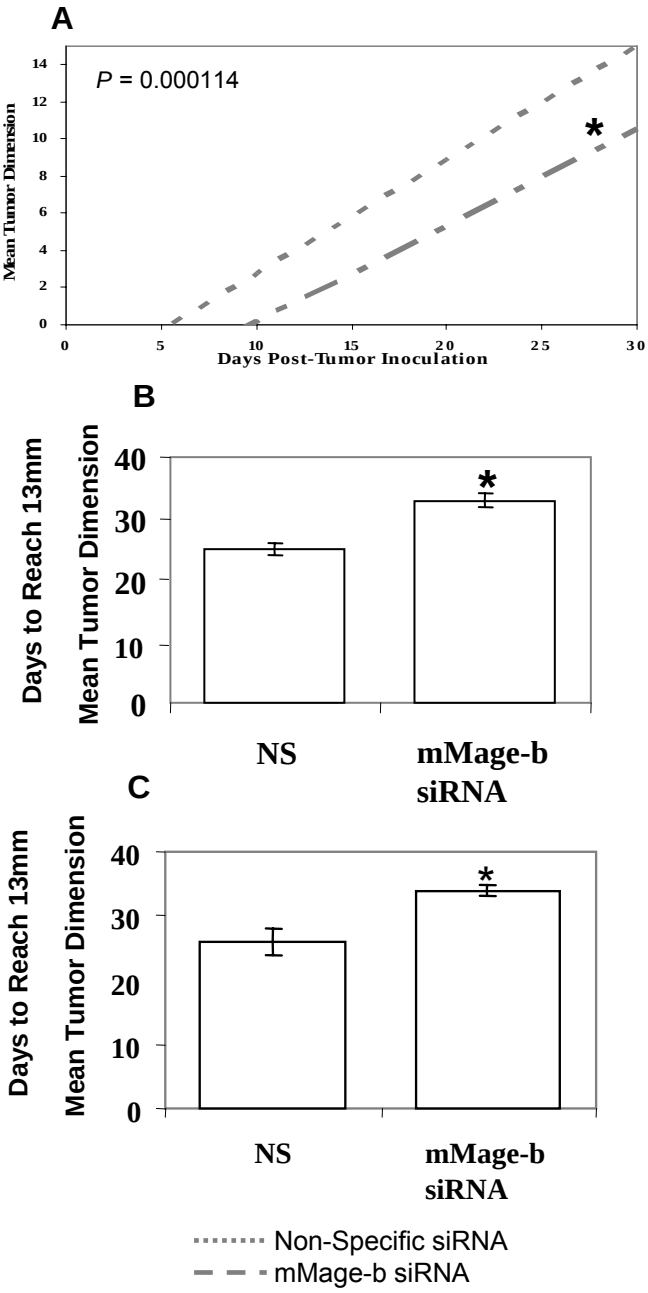
MAGE-A protein expressed in all three HCT 116 cell variants.

Supplementary Fig: 6



Analysis of Growth of mMage-b siRNA Transfected S91 Cells in Syngenic Mice. (Compare with Figure 6a) **A.** Linear regression analysis with tumor growth averaging 0.38mm/d for nonspecific siRNA and 0.15mm/d for mMage-b siRNA ($p < 0.001$). **B, C.** Log-Rank analysis in Kaplan-Meier mean and median survival between non-specific and mMage-b siRNA. ($p < 0.001$).

Supplementary Fig: 7



Analysis of Growth of S91 Cells in Syngenic Mice Treated with Intraperitoneal Injections of Cholesterol Conjugated siRNA. (Compare with Figure 6b) **A.** Linear Regression analysis, tumor diameter increases averaged 0.61mm/d with nonspecific siRNA and 0.51mm/d with mMage-b siRNA. ($p < 0.01$, $n=5$ for both mMage-b and control siRNA groups). **B, C.** Log-Rank analysis, significant difference in Kaplan-Meier mean and median survival between non-specific and mMage-b siRNA ($p < 0.002$). * = statistically significant difference from control siRNA.

Supplementary Table 1: siRNA sequences

siRNA sequences: Human Pan MAGE-A siRNA SmartPool duplex1: sense 5'-GAAACCAGCUAUGUGAAAG-3', antisense 5'-CUUUCACAUAGCUGGUUUC-3'; duplex 2: sense 5'-UGAAACCAGCUAUGUGAAA-3', antisense 5'-UUUCACAUAGCUGGUUUCA-3'; duplex3: sense 5'-UGAAACCAGCUAUGUGAAA-3', antisense 5'-UUUCACAUAGCUGGUUUCA-3'; duplex4: sense 5'-GGUCACAAAGGCAGAAAUG-3', antisense 5'-CAUUUCUGCCUUUGUGACC-3'. Human MAGE-A1 siRNA SmartPool duplex1: sense 5'-CUAAGAAGGUGGCUGAUUU-3', antisense 5'-AAAUCAGCCACCUUCUUAG-3'; duplex2: sense 5'-UGAAAGUCCUUGAGUAUGU-3', antisense 5'-ACAUACUCAAGGACUUUCA-3'; duplex3: sense 5'-UGGCUGAUUUGGUUGGUUU-3', antisense 5'-AAACCAACCAAAUCAGCCA-3'; duplex4 : sense 5'-CAAGGUCAGUGCAAGAGUU-3', antisense 5'-AACUCUUGCACUGACCUUG- 3'. Human MAGE-A2 siRNA SmartPool duplex1: sense 5'- GAGAGUGUCCUCAGAAAUU-3', antisense 5'-AAUUUCUGAGGACACUCUC-3'; duplex2: sense 5'- GAGAACCUCACAUUUCCUA-3', antisense 5'-UAGGAAAUGUGAGGUUCUC-3'; duplex3: sense 5'- GCACUGCAAGCCUGAAGAA-3', antisense 5'-UUCUUCAGGCUUGCAGUGC-3'; duplex4: sense 5'-UGAAACCAGCUAUGUGAAA-3', antisense 5'-UUUCACAUAGCUGGUUUCA-3'. Human MAGE-A3 siRNA SmartPool duplex1: sense 5'-GAAACCAGCUAUGUGAAAG-3', antisense 5'-CUUUCACAUAGCUGGUUUC-3'; duplex2: sense 5'- UGAAACCAGCUAUGUGAAA-3', antisense 5'-UUUCACAUAGCUGGUUUCA-3'; duplex3 : sense 5'- UGAAACCAGCUAUGUGAAA-3', antisense 5'-UUUCACAUAGCUGGUUUCA-3'; duplex4 : sense 5'-GGUCACAAAGGCAGAAAUG-3', antisense 5'-CAUUUCUGCCUUUGUGACC-3'. Human MAGE-A5 siRNA SmartPool duplex1: sense 5'- CCAUUAAGGGCUCCAGCAA-3', antisense 5'-UUGCUGGAGCCCUUAAUGG-3', duplex2: sense 5'-CGAGCAGCACUCAGUAAGA-3', antisense 5'-UCUUACUGAGUGCUGCUCG-3'; duplex3: sense 5'- GAGCAGCACUCAGUAAGAA-3', antisense 5'-UUCUUACUGAGUGCUGCUC-3'; duplex4: sense 5'-GAAGGUGGCUGACUUGAUU-3', antisense 5'-AAUCAAGUCAGCCACCUUC-3'. Human MAGE-A6 siRNA SmartPool duplex1: sense 5'-GAGAAGAUCUGUAAGUAAG-3', antisense 5'-CUUACUUACAGAUCUUCUC-3', duplex2: sense 5'-GCACGUGAGUCCUGAGGUU-3', antisense 5'-AACCUCAGGACUCACGUGC-3', duplex3: sense 5'-GGACUUCAAUAAAUUUGGA-3', antisense 5'-UCCAAAUUUAUUGAAGUCC-3', duplex4: sense 5'-GGGCAGGGCUGGUUAGAAG-3', antisense 5'-CUUCUAACCAGCCCUGCCC-3'. Human MAGE-A12 siRNA SmartPool duplex1: sense 5'-GGACAGUGUCUUUGCGCAU-3', antisense 5'-AUGCGCAAAGACACUGUCC-3', duplex2: sense 5'-CAACUAUACUCUCUGGAGU-3', antisense 5'-ACUCCAGAGAGUAUAGUUG-3'; duplex3: sense 5'- GAGACGAGCUUCCAAGUAG-3', antisense 5'-CUACUUGGAAGCUCGUCUC-3', duplex4: sense 5'-CCACUACCAUCAACUAUAC-3', antisense 5'-GUAUAGUUGAUGGUAGUGG-3'. Human MAGE-B2 siRNA SmartPool duplex1: sense 5'- AGAGAAAGCCGGAGUCUGA-3', antisense 5'-UCAGACUCCGGCUUUCUCU-3'; duplex2: sense 5'- GAGGAGCACUCAGUCUUUG-3', antisense 5'-CAAAGACUGAGUGCUCCUC-3'; duplex3: sense 5'-GCCUUGAGCUGAAUAAAGU-3', antisense 5'-ACUUUAUUCAGCUCAAGGC-3'; duplex4: sense 5'-AGGAAUCCCUGCUCAGUUC-3', antisense 5'-GAACUGAGCAGGGAUUCCU-3'. Human MAGE-C2 siRNA SmartPool duplex1: sense 5'-GAGAACAGCCUCCUGAUUA-3', antisense 5'-UAAUCAGGAGGCUGUUCUC-3', duplex2: sense 5'-CAAGAGAGCCCGUGAGUUC-3', antisense 5'-GAACUCACGGGCUCUCUUG-3'; duplex3:sense 5'-GGUGUGAUACCAAAUCUUA-3', antisense 5'-UAAGAUUUGGUAUCACACC-3'; duplex4: sense 5'- ACAGUUCUCCUCCAUAUUA-3', antisense 5'-UAAUAUGGAGGAGAACUGU. Mouse Mage-a complex siRNA SmartPool duplex1: sense 5'- CCAGGAAGCUCAUCUCUGA-3', antisense 5'-UCAGAGAUGAGCUUCCUGG-3'; duplex2: sense 5'- GAAGGGAAACUAUGUCAGU-3', antisense 5'-ACUGACAUAGUUUCCCUUC-3'; duplex3: sense 5'- UACCAAAGCAGAAAUGUUG-3', antisense 5'-CAACAUUUCUGCUUUGGUA-3'; duplex4: sense 5'- GUAGAGAGUAUGAGGAGUA-3', antisense 5'-UACUCCUCAUACUCUCUAC-3'. Mouse Mage-b complex siRNA SmartPool duplex1: sense 5'-UGGCAGUAGUUAACAAGAA-3', antisense 5'-UUCUUGUUAACUACUGCCA-3'; duplex2: sense 5'-CAGCACUCAUUCCUAUUUG-3', antisense 5'-CAAAUAGGAAUGAGUGCUG-3'; duplex3: sense 5'-CAAGAGGUCUGGCAAUUUC-3', antisense 5'-GAAAUUGCCAGACCUCUUG-3'; duplex4: sense 5'-GCAAGGGUGUUCAUUCCAA-3', antisense 5'-UUGGAAUGAACACCCUUGC. Mage-b siSTABLE Plus siRNA sequence: Sense: 5'-GCAAGGGUGUUCAUUCCAAUU;Anti-sense: 5'-PUUGGAAUGAACACCCUUGCUU.