

## Supplementary Material

## Supplementary Table 1. Patient characteristics

	BM total cells	MSCs
Patients	Number	Number
MDS	48	21
Gender Male/Female	27/23	15/6
Age (years), media (range)	70 (15-86)	70 (16-90)
WHO 2016 classification		
RS-SLD / RS-MLD / del(5q) / SLD / MLD EB-1/EB-2	1/11/1/0/20 5/10	3/1/0/1/10 2/4
R-IPSS		
Very low / Low	6 / 20	2/7
Intermediate	9	7
Not available	3	1/3
Cytogenetic risk <sup>1</sup>		
Good	36	15
Intermediate	8	2
Poor	1	3
No growth	3	1
AML	50	18
de novo AML / AML-MRC	42/8	12/6
Gender Male/Female	33/17	9/9
Age (years), median (range)	69 (22-90)	66 (30-86)
BM blasts (%), median (range)	70 (22-96)	50 (20-89)
Cytogenetic risk <sup>2</sup>		
Good	5	10
Intermediate/Poor	26/9	0/8
No growth	10	0

Abbreviations: MDS, myelodysplastic syndromes; MDS-MLD: MDS with multilineage dysplasia; MDS-SLD: MDS with single lineage dysplasia; MDS-RS: MDS with ring sideroblasts; MDS-EB: MDS with excess blasts; MDS with isolated del(5q); WHO, World Health Organization; R-IPSS, Revised International Prognostic Scoring System; BM, bone marrow; AML, acute myeloid leukemia; AML-MRC, acute myeloid leukemia with myelodysplasia-related changes. <sup>1</sup>Cytogenetic risk for MDS was defined according to R-IPSS (Arber et al. 2016). <sup>2</sup>Cytogenetic risk for AML was defined according to Grimwade et al. (Grimwade et al. 2016)

Gene	<b>Primers (5' – 3')</b>	Product length	Concentration
ARHGAP21	AGGCAAACTTTGCTTGGTGCTA	07	300nM
(human)	ACTGAGAAGTTTCCTTTCCGACTC	87	
HPRT	GAACGTCTTGCTCGAGATGTGA	101	150nM
(human)	TCCAGCAGGTCAGCAAAGAAT	101	
Arhgap21	GAGGAAAGCTTCAAGCACCA	121	150nM
(mouse)	GATGACAGCAGATGCAGGAA	121	
Collal	AGCACGTCTGGTTTGGAGAG	110	150 14
(mouse)	GACATTAGGCGCAGGAAGGT	112	1501101
Ocn	GGCCCAGACCTAGCAGACAC	0.9	150nM
(mouse)	CTGGGCTTGGCATCTGTGAG	98	
Opn	TGGCTGAATTCTGAGGGACTAAC	150	150
(mouse)	TATAGGATCTGGGTGCAGGCT	147	150nM
Rank	TTGCACGGCTGGCTACCACT	117	150 14
(mouse)	GCACACCGTATCCTTGTTGAGCTG	115	1501101
Trap	AGCCACATACGGGGTCACTG	01	150 14
(mouse)	TAGCCCACACCGTTCTCGTC	81	150nM
Gapdh	TGACCACCAACAACTGCTTA	170	150nM
(mouse)	GGATGCAGGGATGATGTTC	1/9	

Supplementary Table 2. Sequence and concentration of primers used for quantitative PCR



**Supplementary Figure 1.** Levels of IFN- $\gamma$ , M-CSF, G-CSF, TGF- $\beta$ 1, IL-1 $\alpha$ , IL-1 $\beta$ , IL-4, IL-10, IL-17, and VEGF-A in the bone marrow supernatant measured using Luminex xMAP assay. No difference was found in the levels of the tested cytokines between bone marrow supernatant from Arhgap21+/- and WT. Each dot represents an individual mouse. For all graphs 2-tailed Student's t test statistical analysis were used, mean and standard error of the mean are shown.



**Supplementary Figure 2. Increased expression of ARHGAP21 mRNA in MSCs and total bone marrow samples from** *de novo* **AML patients.** Quantitative PCR analysis of ARHGAP21 expression in MSCs (A) and (B) total bone marrow samples from healthy donors and patients with MDS (RS-SLD, RS-MLD, del(5q), SLD, MLD), MDS (EB-1, EB-2), AML-MRC and *de novo* AML. Each dot represents one subject and horizontal lines indicate medians. The number of subjects and P values are indicated (Mann–Whitney test). mRNA expression levels of *ARHGAP21* were normalized by *HPRT* endogenous control.

## References

- Arber DA, Orazi A, Hasserjian R, Borowitz MJ, Beau MM Le, Bloomfield CD, et al. The 2016 revision to the World Health Organization classi fi cation of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391–406.
- Grimwade D, Ivey A, Huntly BJP. Molecular landscape of acute myeloid leukemia in younger adults and its clinical relevance. Vol. 127, Blood. 2016. p. 29–41.