

**Supplementary Table 1: List of oligonucleotide sequences used for PCR mutagenesis**

Primer	Sequence (5'-3')	Mutagenesis	Reference
DH <sub>mut</sub> for	GGCTTACCTGTCCACTTGCATGGATCAATTTCCGTCGTCC	D116H	[18]
DH <sub>mut</sub> rev	CCGGACGACGGAAAATTGATCCATGCAAGTGGACAGGTA		
HA <sub>mut</sub> for	GGATAACTCCAGGTACACAGCCTTCCCTGACCCAGCACTAT	H8A	[16]
HA <sub>mut</sub> rev	GCATCATAGTGCTGGGTCAGGAAGGCTGTGTACCTGGAG		
RA <sub>mut</sub> for	CGAGTCTAGACAGGATAACTCCGCGTACACACACTTCCTG	R5A	[15]
RA <sub>mut</sub> rev	GGGTCAGGAAGTGTGTGTACGCGGAGTTATCCTGTCTAGA		
KQ <sub>mut</sub> for	GCCTGACCTCACCTGCCAAGACATCAACACATTTATTCA	K40Q	[15, 16]
KQ <sub>mut</sub> rev	GCCATGAATAAATGTGTTGATGTCTTGGCAGGGTGAGGTC		
5'-SfiI_for	TCGTCCGCCAGCCGCC	-	-
Hinterhis_rev	CCAACAGCTGGCCCTCGCAGACAG	-	-

**Supplementary Table 2: Cytotoxicity of H22-Ang variants against stimulated HL-60 cells and hM1Φ cells**

hCFP	EC <sub>50</sub> on		Improvement compared to H22-Ang wild type (fold change)	
	HL-60 (nM)	hM1Φ (pM)	HL-60	hM1Φ
H22-Ang wild type	6.01 ± 1.81	0.89 ± 0.01	-	-
H22-Ang GRR <sub>mut</sub>	0.74 ± 0.33	0.50 ± 0.04	5 - 12	≤ 2
H22-Ang GRR/QG/RA <sub>mut</sub>	1.83 ± 0.59	0.79 ± 0.14	2 - 5	-
H22-Ang GRR/QG/HA <sub>mut</sub>	1.16 ± 0.45	0.45 ± 0.07	3 - 7	2
H22-Ang GRR/QG/DH <sub>mut</sub>	0.30 ± 0.17	0.32 ± 0.08	13 - 32	2 - 3
H22-Ang GRR/QG/KQ <sub>mut</sub>	1.13 ± 0.35	0.72 ± 0.17	4 - 7	-

**Supplementary Table 3: Relevant patient data**

Patient characteristics	Number	Specimen condition
Total patient number	4	
Average age	71 ± 17	
Gender		
Male	2	
Female	2	
WHO subtype		
CMML	1	bone marrow
AML-M4	2	peripheral blood
AML-M5	1	peripheral blood
WBC (g/l)	95 ± 15	
Monocytes (%)	1 - 6	
Hemoglobin (g/l)	90 ± 18	
Platelet count (g/l)	31 - 128	

WHO: World Health Organization, CMML: chronic myelomonocytic leukemia, AML: acute myeloid leukemia, WBC: white blood cells