Supplementary Table 1: Blood cell counts in the study cohort

blood parameters	n =	distribution median [95% CI]	Unit	Reference Range
Hemoglobin				
cancer patients	248	13.0 [12.49-12.98]	g/dl	12 - 16 (women), 14-18 (men)
non-healthy controls	42	13.35 [12.75-13.79]		
Platelets				
cancer patients	246	252.0 [261.05-289.83]	$x10^3/\mu l$	150 – 400
non-healthy controls	42	206.5 [203.72-245.33]*		
Leukocytes				
cancer patients	248	8.13 [8.44-9.42]	$x10^3/\mu l$	4 - 10
non-healthy controls	42	6.28 [6.19-7.75]**		

Reference values are from the University Medical Center Göttingen.
*p=1.1680e-04
**p=5.2840e-05

Supplementary Table 2: Univariate Analysis of overall survival in the total study cohort (n=433)

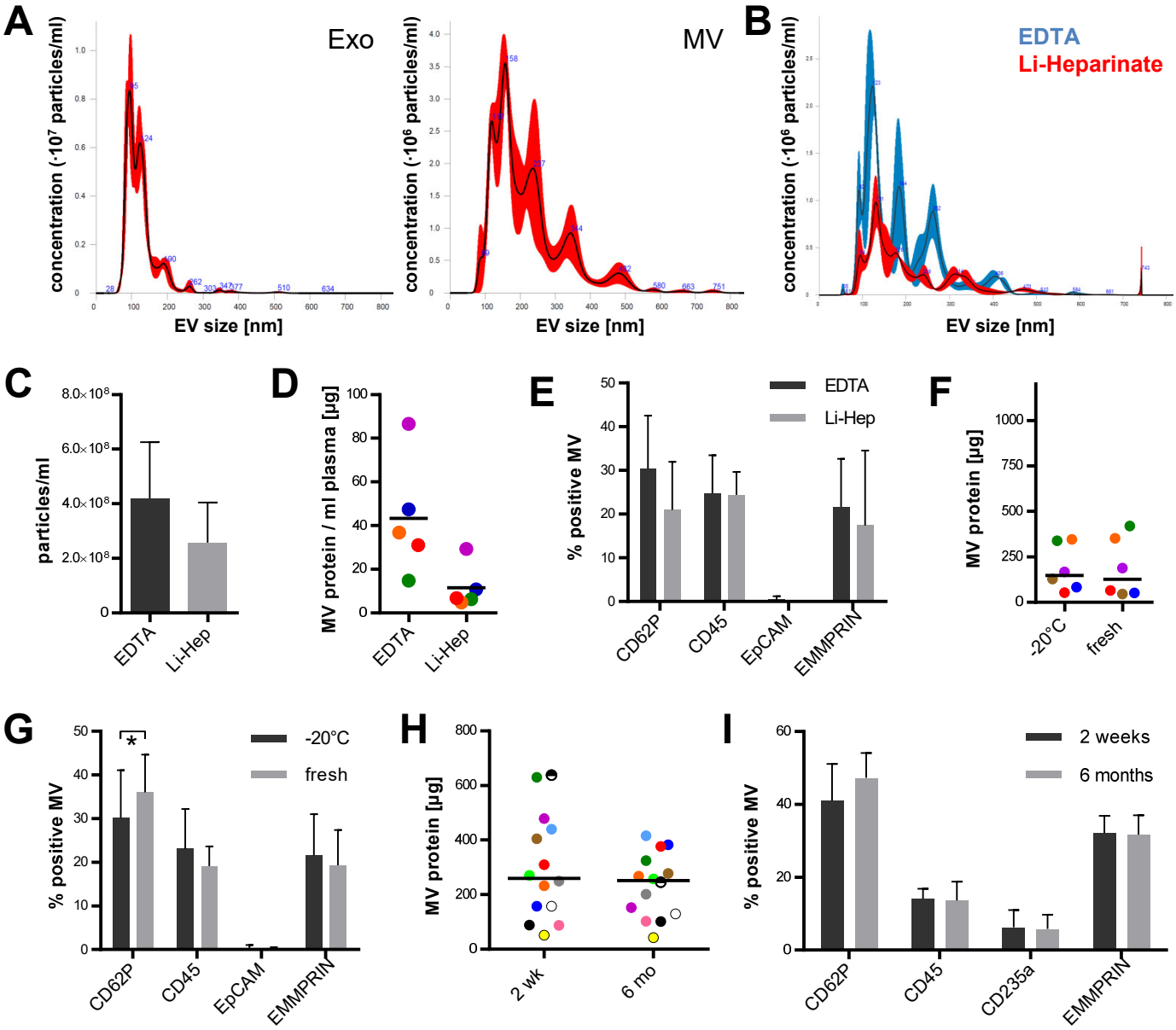
parameter	# patients	Hazard ratio [95% CI]	p-value
Age	433	1.02 [1.01-1.03]	2.250e-04
Gender			
f	192	1.09 [0.8-1.5]	0.574
m	241		
Stage			
< IV	307		
IV	126	2.17 [1.59-2.97]	1.180e-06
EMMPRIN	430	1.02 [1.0-1.04]	0.016
MUC1	423	1.03 [0.98-1.07]	0.236
EpCAM	421	1.03 [0.98-1.07]	0.245
EGFR	422	0.99 [0.94-1.06]	0.932

Univariate analysis of overall survival in the total study cohort (n=433). Besides age and tumor stage, EMMPRIN was found to be associated significantly with overall survival. Reduced patient numbers for different parameters due to missing measurement values. Shown are logrank p-values.

Supplementary Table 3: Univariate analysis for EMMPRIN in the total study cohort (n=433)

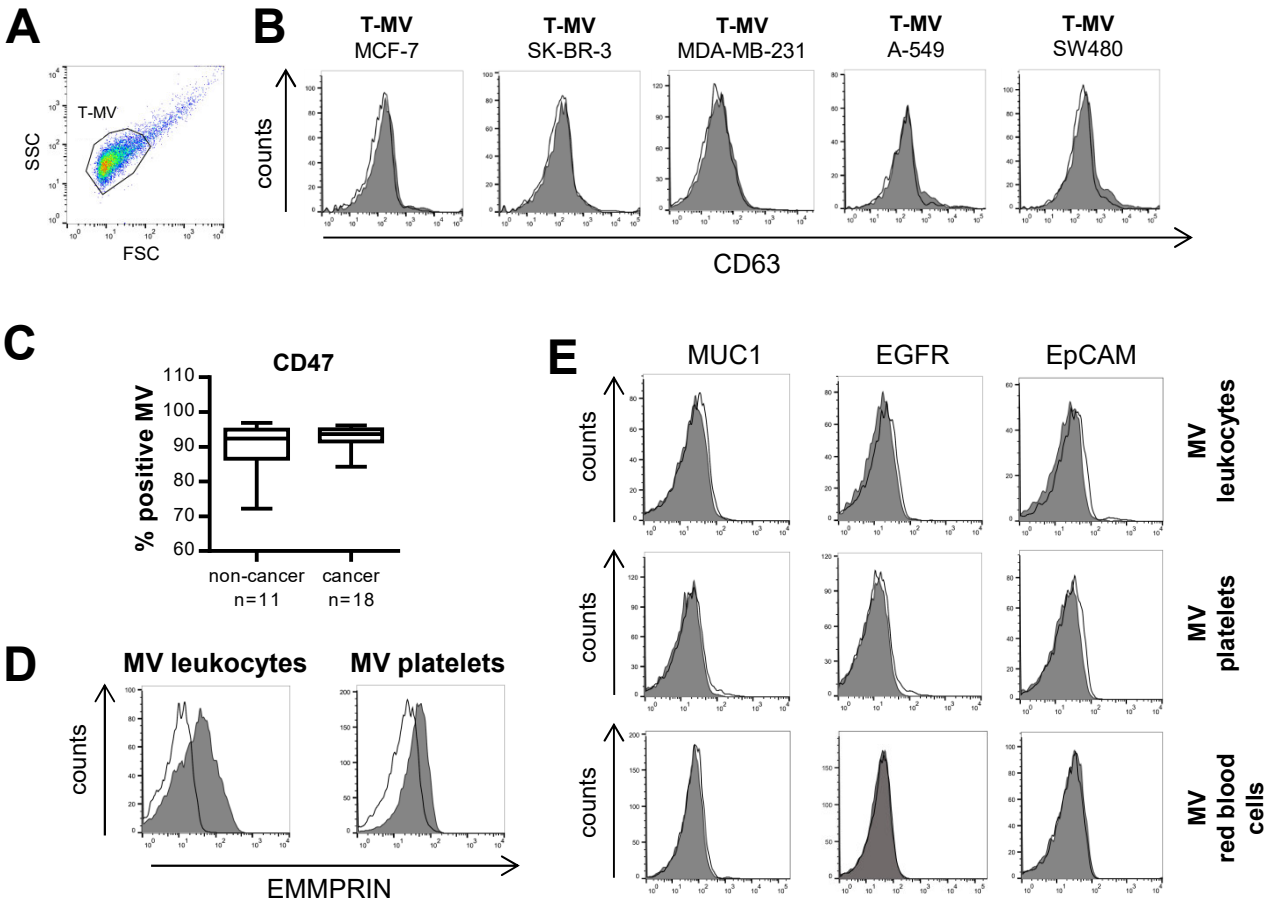
Univariate analysis					
parameter	**classification**	**threshold**	**distribution [95% CI]**	**# patients**	**p-value**
Age		>= 29.1	63.67 [61.85-65.33]	247	0.133
		< 29.1	62.1 [60.28-65.25]	183	
Gender					1.000
	f	>= 29.1		110	
	f	< 29.1		82	
	m	>= 29.1		137	
	m	<29.1		101	
Stage					0.004
	<IV	>= 29.1		161	
	<IV	< 29.1		143	
	IV	>= 29.1		86	
	IV	<29.1		40	

Supplementary Figure 1



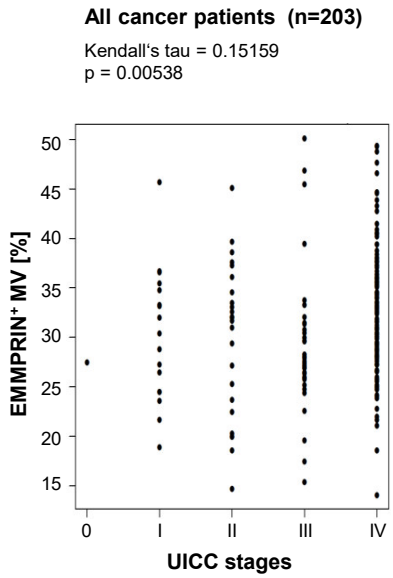
Supplementary Figure 1: Validation of the isolation protocol for MV from peripheral blood. ***A,*** MV and Exo were isolated from the same donor and resuspended in the same volume of PBS. Size distribution of EV samples was measured by nanoparticle tracking analysis (NTA) at a dilution of 1:33. ***B-E,*** Peripheral blood was drawn from each of five donors into two tubes containing EDTA and two tubes containing Li-Heparinate (Li-Hep, 16 I.E./ml blood). MV were isolated and analyzed by NTA. Shown is one representative overlay of MV from one donor (*B*) and the summary of all analyzed MV samples (*C*, n=3, mean±SD). MV protein yield (*D*) was determined (line=median) and standard markers assessed by flow cytometry (*E*, mean±SD, n=3-5). Samples from the same donor are marked in the same color. ***F+G,*** EDTA-anticoagulated blood was collected from six donors and plasma samples were divided by two. One half was directly subjected to MV isolation, the other half was stored for ≤2 weeks at -20°C and then used for MV isolation. EV yields were determined by quantification of total protein (*F*, line at median) and obtained MV analyzed by flow cytometry (*G*, mean±SD, n=6, *p<0.05). ***H+I,*** EDTA-anticoagulated plasma samples from 14 donors were divided by two and stored at -20°C for either 2 weeks (2 wk) or 6 months (6 mo) before isolating MV. Total MV protein was quantified (*H*, line at median) and MV further characterized by flow cytometry (*I*, mean±SD, n=10).

Supplementary Figure 2



Supplementary Figure 2: Establishment of markers specific for T-MV. ***A***, Flow cytometry: Example of a FSC vs SSC plot (A) that was used to gate on the MV population that was then characterized further for the expression of different antigens. ***B,*** Expression of CD63 (grey filled) was analyzed by flow cytometry on T-MV of the indicated five cell lines. The respective isotype controls are shown as black lines. Histograms are representative of at least three independent experiments. ***C,*** The percentage of $CD47^+$ MV in peripheral blood of cancer patients and non-cancer controls was measured by flow cytometry. Boxplots depict the median (line), the 25-75 percentiles (box) and the 10-90 percentiles (whiskers). ***D,*** Representative flow cytometry histograms (n=3): Expression of EMMPRIN (grey filled) on platelet- and macrophage-derived MV. ***E,*** Characterization of tumor antigens (grey filled) on blood cell-derived MV. The histograms are representative of three independent experiments.

Supplementary Figure 3



Supplementary Figure 3: The number of EMMPRIN$^+$ MV in cancer patients' blood correlates with tumor stage. Kendall-Tau correlation of the percentage of EMMPRIN$^+$ MV in cancer patients' blood with the diagnosed UICC stage at the time of sample acquisition.