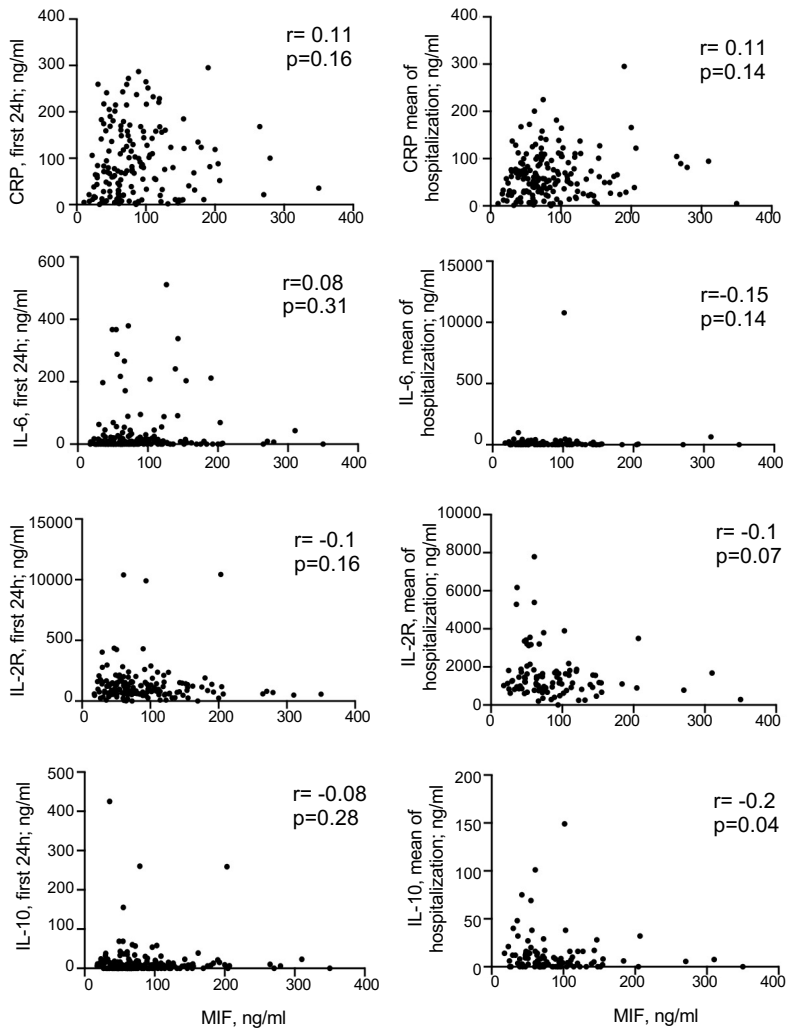


Supplementary Figure 1. A. Scheme employed for the creation of humanized *MIF* mice by vector-based recombinant replacement of the endogenous *Mif* gene with a human high-expresser -794 CATT₇ (7xCATT=CATT₇, shown) or low-expresser -794 CATT₅ *MIF* allele, yielding the *MIF*^{CATT7} and *MIF*^{CATT5} C57BL/6J strains. **B.** Validation of human MIF mRNA expression by PCR of splenic leukocytes from *MIF*^{CATT5} and *MIF*^{CATT7} strains but not C57BL/6 wild-type (*Mif*^{+/+}) mice (n=2 mice per group). HuPBLs: human peripheral blood leukocytes. **C.** Plasma human MIF levels before (-) and 5 hrs after (+) intraperitoneal injection of the model stimulus lipopolysaccharide (LPS, 2.5 mg/kg) in *MIF*^{CATT5} and *MIF*^{CATT7} mice (n=6-9 per group). Mean ± SD, **p*<0.01 for +LPS vs -LPS, #*p*<0.05 for *MIF*^{CATT5} versus *MIF*^{CATT7} mouse strains.



Supplementary Figure 2. Correlations between serum MIF and CRP, IL-6, IL-2R and IL-10 levels in 163 COVID-19 patients measured in the first 24 hrs of hospital admission and as a mean of hospitalization duration.

A.

	Healthy Controls	US Patients	Hungary Patients	Spain Patients	All Patients
Total	617	284	128	580	992
-794 CATT_{5,6}	501 (81%)	250 (88%)	114 (90%)	517 (89%)	881 (89%)
-794 CATT_{7,8}	116 (19%)	34 (12%)	14 (10%)	63 (11%)	111 (11%)
Odds ratio		0.59	0.53	0.53	0.54
95% CI		0.39, 0.88	0.28, 0.94	0.38, 0.73	0.41, 0.72
<i>p</i> value		0.01	0.04	0.0001	<0.0001

B.

	Healthy Controls	US Patients	Hungary Patients	Spain Patients	All Patients
Total	579	191	220	367	778
-173 G	548 (95%)	181 (95%)	213 (97%)	350 (96%)	744 (96%)
-173 C	31 (5%)	10 (5%)	7 (3%)	17 (4%)	34 (4%)
Odds ratio		0.97	0.61	0.86	0.81
95% CI		0.47, 2.01	0.27, 1.34	0.48, 1.54	0.49, 1.33
<i>p</i> value		0.99	0.26	0.65	0.44

Supplementary Table 1. Frequencies of the *MIF* -794 CATT₅₋₈ (A) and -173 G/C alleles (B) in healthy controls and COVID-19 patients by study sites and in all patients. The -794 CATT₅₋₈ alleles are grouped into low-expresser (CATT_{5,6}) and high-expresser (CATT_{7,8}) variants.

A.

	US Patients		Hungary Patients		Spain Patients		All Patients	
Total	284		128		580		992	
Total	Inpatient	Outpatient	Inpatient	Outpatient	Inpatient	Outpatient	Inpatient	Outpatient
	177	107	108	20	520	60	805	187
-794 CATT_{5,6}	147 (83%)	103 (96%)	95 (89%)	19 (95%)	461 (89%)	56 (93%)	703 (87%)	178 (95%)
-794 CATT_{7,8}	30 (17%)	4 (4%)	13 (11%)	1 (5%)	59 (11%)	4 (7%)	102 (13%)	9 (5%)
<i>p</i>	0.0009		0.4		0.02		0.002	

B.

	US Patients		Hungary Patients		Spain Patients		All Patients	
Total	191		220		367		778	
Total	Inpatient	Outpatient	Inpatient	Outpatient	Inpatient	Outpatient	Inpatient	Outpatient
	124	67	210	10	330	37	664	114
-173 G	115 (93%)	66 (98%)	204 (97%)	9 (90%)	315 (95%)	35 (95%)	634 (96%)	110 (96%)
-173 C	9 (7%)	1 (2%)	6 (3%)	1 (10%)	15 (5%)	2 (5%)	30 (4%)	4 (4%)
<i>p</i>	0.12		0.24		0.81		0.63	

Supplementary Table 2. Frequencies of the *MIF* -794 CATT₅₋₈ (A) and -173 G/C alleles (B) in inpatients and outpatients with COVID-19 in the three studied sites and in all patients. The -794 CATT₅₋₈ alleles are grouped into low-expresser (CATT_{5,6}) and high-expresser (CATT_{7,8}) variants.

Elixhauser comorbidities US Patients	-794 CATT _{5,6} n=137	-794 CATT _{7,8} n=26	<i>p</i>
HTN uncomplicated	75%	76%	0.79
HTN complicated	32%	26%	0.61
DM uncomplicated	43%	42%	0.94
DM complicated	35%	53%	0.09
Congestive heart failure	24%	19%	0.59
Cardiac arrhythmias	42%	39%	0.77
Valvular disease	28%	27%	0.93
Peripheral vascular disease	21%	27%	0.52
Chronic pulmonary disease	26%	31%	0.58
Pulmonary circulatory disorders	15%	23%	0.28
Coagulopathy	18%	23%	0.56
Deficiency anemia	19%	19%	0.97
Blood loss anemia	6%	8%	0.72
Peptic ulcer disease	5%	4%	0.79
Liver disease	16%	27%	0.18
Electrolyte disorder	46%	46%	0.99
Renal failure	26%	15%	0.27
hypothyroidism	17%	19%	0.76
Obesity	36%	27%	0.38
Weight loss	27%	23%	0.67
Solid tumor	24%	19%	0.59
Lymphoma	3%	0%	0.38
Metastatic cancer	23%	12%	0.15
Psychoses	9%	8%	0.86
Depression	32%	34%	0.81
Paralysis	5%	4%	0.79
Rheumatoid arthritis/ collagen vascular disease	10%	10%	0.15
HIV/ AIDS	2%	4%	0.41
Drug abuse	12%	15%	0.59
Alcohol abuse	7%	15%	0.17

Supplementary Table 3. Frequencies of Elixhauser comorbidities between patients with *MIF* -794 CATT_{5,6} and *MIF* -794 CATT_{5,6} alleles in the US cohort.

Comorbidities Hungary Patients	-794 CATT_{5,6} n=108	-794 CATT_{7,8} n=20	<i>p</i>
Chronic obstructive Respiratory disease	10%	5%	0.32
Respiratory Disorders	38%	44%	0.34
Cardiovascular Disorders	39%	42%	0.44

Supplementary Table 4. Frequencies of comorbidities between patients with *MIF* -794 CATT₅₋₆ and *MIF* -794 CATT₅₋₆ alleles in the Hungary cohort.