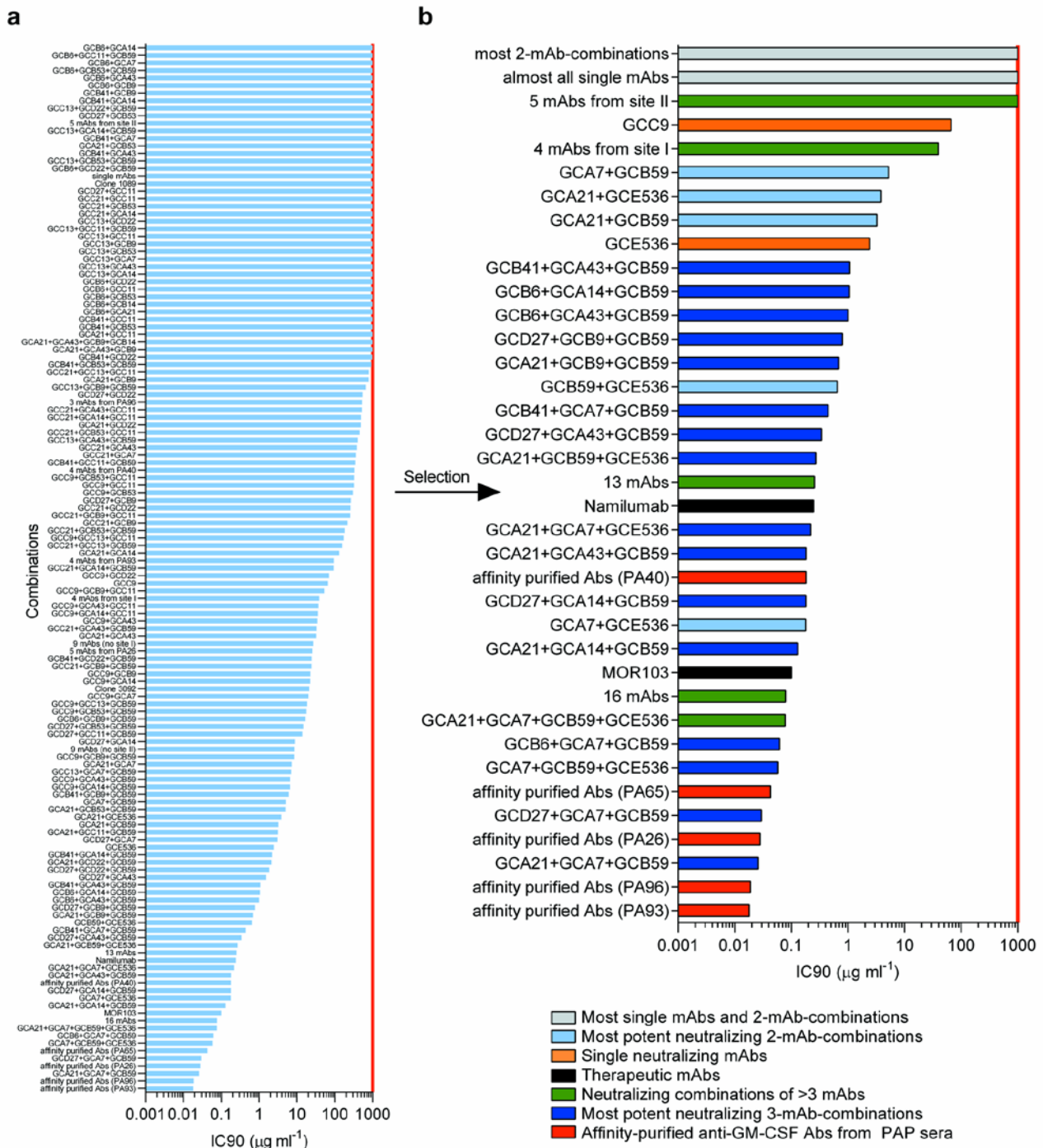


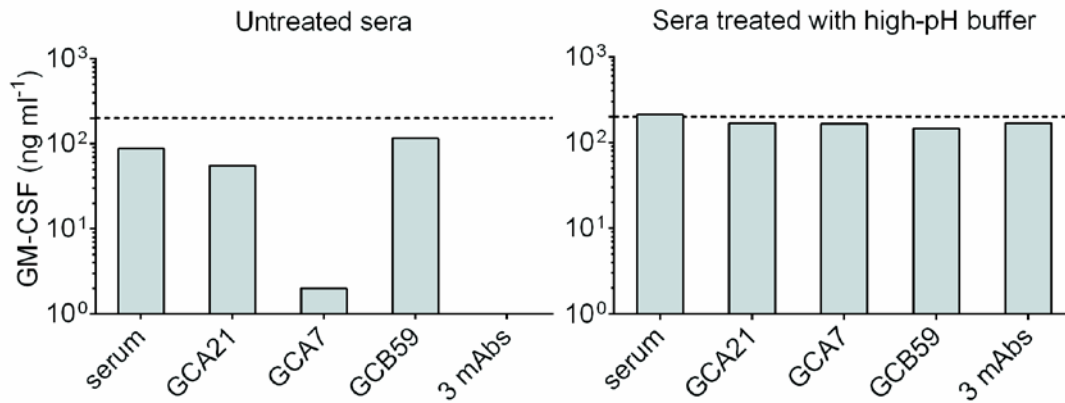
# SUPPLEMENTARY INFORMATION



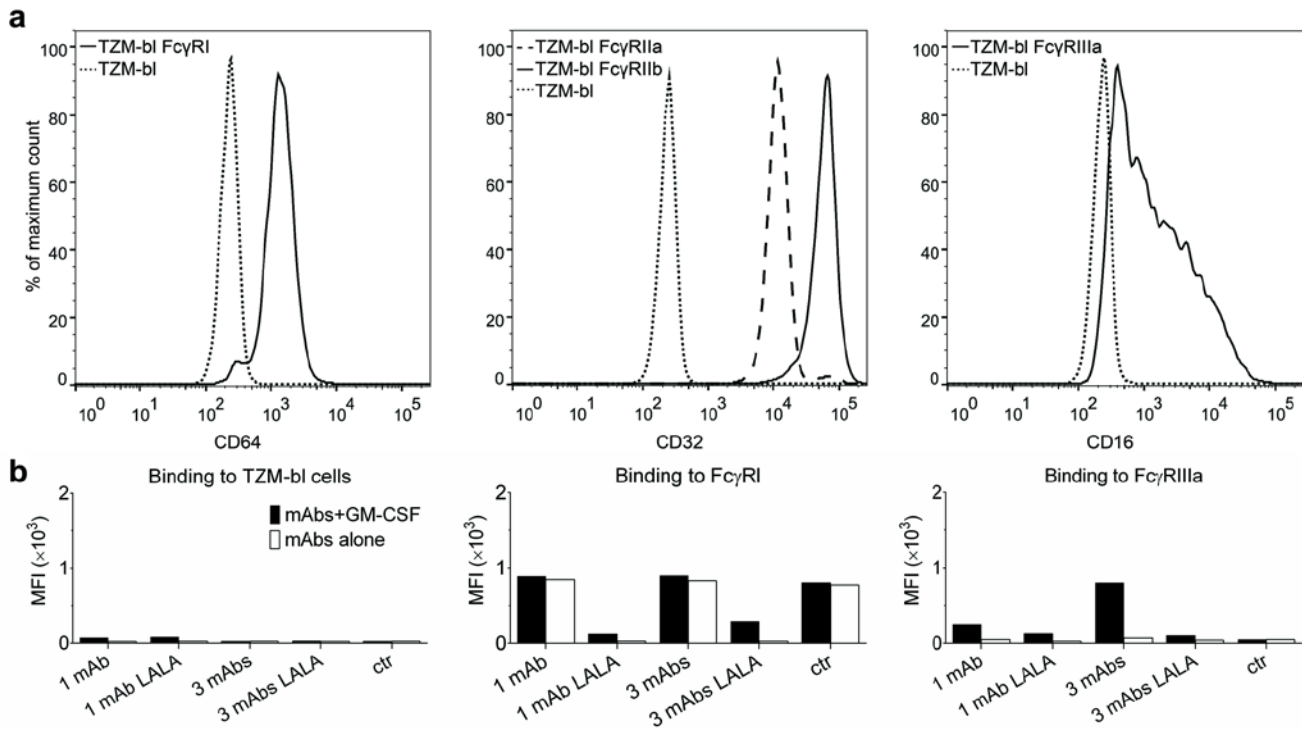
**Supplementary Figure 1. *In vitro* neutralization of GM-CSF by single or multiple antibodies.**

**(a)** Rank of neutralizing activity (IC90 values) of 140 different combinations of GM-CSF mAbs. **(b)**

A selection of the most potent neutralizing combinations is shown and compared to therapeutic anti-GM-CSF antibodies (MOR103 and Namilumab) and to autoantibodies purified from PAP sera.



**Supplementary Figure 2. A sandwich ELISA to detect GM-CSF in the presence of specific antibodies.** A fixed amount of GM-CSF was added to mouse serum together with three monoclonal antibodies (GCA21, GCA7, GCB59) added separately or in combination. The quantification of GM-CSF was performed by a sandwich ELISA using an antibody specific for site II for capture and site I for detection. Serial dilutions of serum in neutral (left) or alkaline buffer (right) were added and GM-CSF concentration was determined with reference to a GM-CSF standard. The dotted line represents the concentration of GM-CSF measured in the absence of antibodies.



**Supplementary Figure 3. Binding of immune complexes to TzM-bl cells expressing different FcγRs.** (a) Expression of FcγRs on TzM-bl cells transfected with FcγRI, FcγRIIa/b and FcγRIIIa, as detected by antibodies to CD64, CD32 and CD16, respectively. Untransfected TzM-bl cells were used as negative control. (b) Shown is also the binding of GM-CSF immune complexes containing one or three antibodies to TzM-bl cells expressing FcγRI or FcγRIIIa or to untransfected TzM-bl cells.

**Supplementary Table 1**  
Features of 5 PAP patients

<b>ID</b>	<b>Code</b>	<b>Gender</b>	<b>Birth year</b>	<b>Diagnosis year</b>	<b>Therapy</b>	<b>Follow up (years)</b>	<b>DSS</b>	<b>Serum GM-CSF abs (<math>\mu\text{g ml}^{-1}</math>)</b>
PA93	GCA	M	1943	2010	-	2	3	804.5
PA26	GCB	F	1966	2005	-	7	3	454.9
PA40	GCC	F	1954	2005	WLL	7	1	100.6
PA96	GCD	M	1980	2010	-	2	1	741.2
PA65	GCE	F	1959	2005	WLL	7	1	46.0

WLL = whole lung lavage; DSS = Disease Severity Score calculated at the time of sample collection; abs = antibodies

**Supplementary Table 2**

Somatic mutations in the V segment critically contribute to the specificity of GM-CSF autoantibodies

<b>mAb</b>	<b>Version</b>	<b>EC50 (ng ml<sup>-1</sup>)</b>	<b>Ka (M s<sup>-1</sup>)</b>	<b>Kd (s<sup>-1</sup>)</b>	<b>KD (M)</b>
<b>GCA21</b>	<i>WT</i>	33.3	1.3E+06	5.5E-04	5.7E-10
	<i>VK UCA</i>	77.3	3.1E+06	2.6E-02	1.1E-08
	<i>VH UCA</i>	nc	nc	nc	nc
	<i>UCA</i>	nc	nc	nc	nc
	<i>UCA - HCDR3 WT</i>	nc	nc	nc	nc
<b>GCA7</b>	<i>WT</i>	52.4	1.8E+05	3.1E-05	2.3E-10
	<i>VK UCA</i>	64.8	4.9E+04	1.7E-05	3.5E-10
	<i>VH UCA</i>	nc	nc	nc	nc
	<i>UCA</i>	7724	nc	nc	nc
	<i>UCA - HCDR3 WT</i>	354.2	3.4E+04	2.1E-03	6.3E-08
<b>GCB59</b>	<i>WT</i>	428.7	1.0E+06	1.7E-03	1.8E-09
	<i>VL UCA</i>	24039	1.3E+06	1.0E-02	8.4E-09
	<i>VH UCA</i>	nc	nc	nc	nc
	<i>UCA</i>	nc	nc	nc	nc
	<i>UCA - HCDR3 WT</i>	nc	nc	nc	nc
<b>GCB9</b>	<i>WT</i>	322	3.1E+05	7.5E-04	2.5E-09
	<i>VK UCA</i>	258.3	4.8E+05	2.8E-03	6.2E-09
	<i>VH UCA</i>	956	4.2E+05	3.9E-03	1.5E-08
	<i>UCA</i>	6765	1.7E+05	1.2E-02	8.2E-08
	<i>UCA - HCDR3 WT</i>	3664	5.9E+04	8.5E-03	1.5E-07
<b>GCA43</b>	<i>WT</i>	258	2.5E+05	1.5E-04	6.2E-10
	<i>VK UCA</i>	286.7	3.0E+05	1.7E-04	6.5E-10
	<i>VH UCA</i>	nc	nc	nc	nc
	<i>UCA</i>	nc	nc	nc	nc
	<i>UCA - HCDR3 WT</i>	nc	nc	nc	nc
<b>GCB6</b>	<i>WT</i>	31.1	5.2E+05	4.4E-04	1.0E-09
	<i>VK UCA</i>	35.1	6.5E+05	1.0E-02	1.9E-08
	<i>VH UCA</i>	nc	nc	nc	nc
	<i>UCA</i>	nc	nc	nc	nc
	<i>UCA - HCDR3 WT</i>	nc	nc	nc	nc
<b>GCE536</b>	<i>WT</i>	54.3	5.8E+05	1.4E-04	2.5E-10
	<i>VK UCA</i>	37.5	7.3E+05	9.5E-04	1.3E-09
	<i>VH UCA</i>	56.3	4.7E+04	5.4E-05	1.1E-09
	<i>UCA</i>	19773	2.4E+03	8.7E-05	9.0E-08
	<i>UCA - HCDR3 WT</i>	13.7	5.5E+05	6.0E-03	1.0E-08

Binding of WT, UCA, UCA-HCDR3 WT and shuffled variants VK/VL UCA and VH UCA to GM-CSF as measured by ELISA and SPR. nc = not calculable