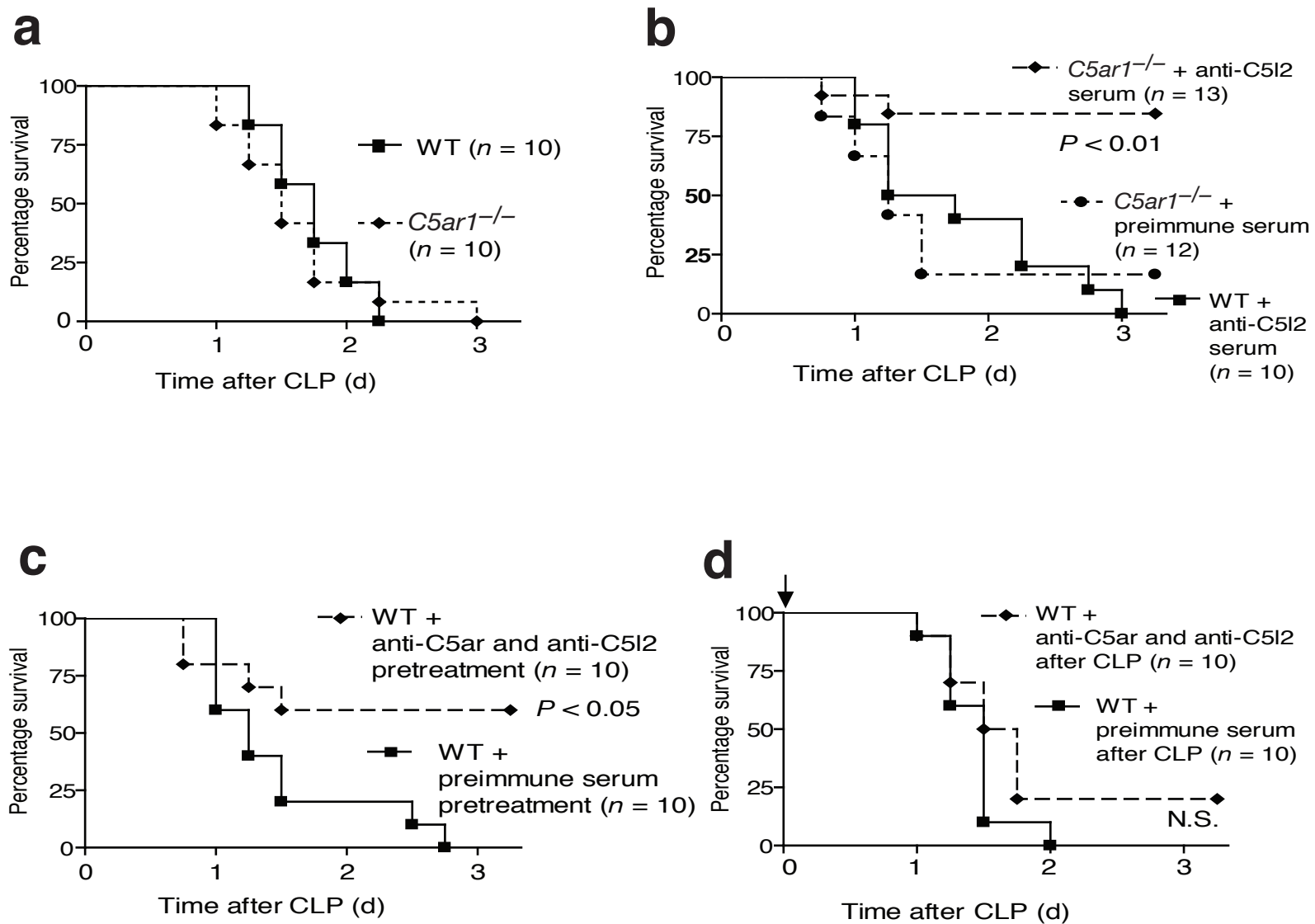


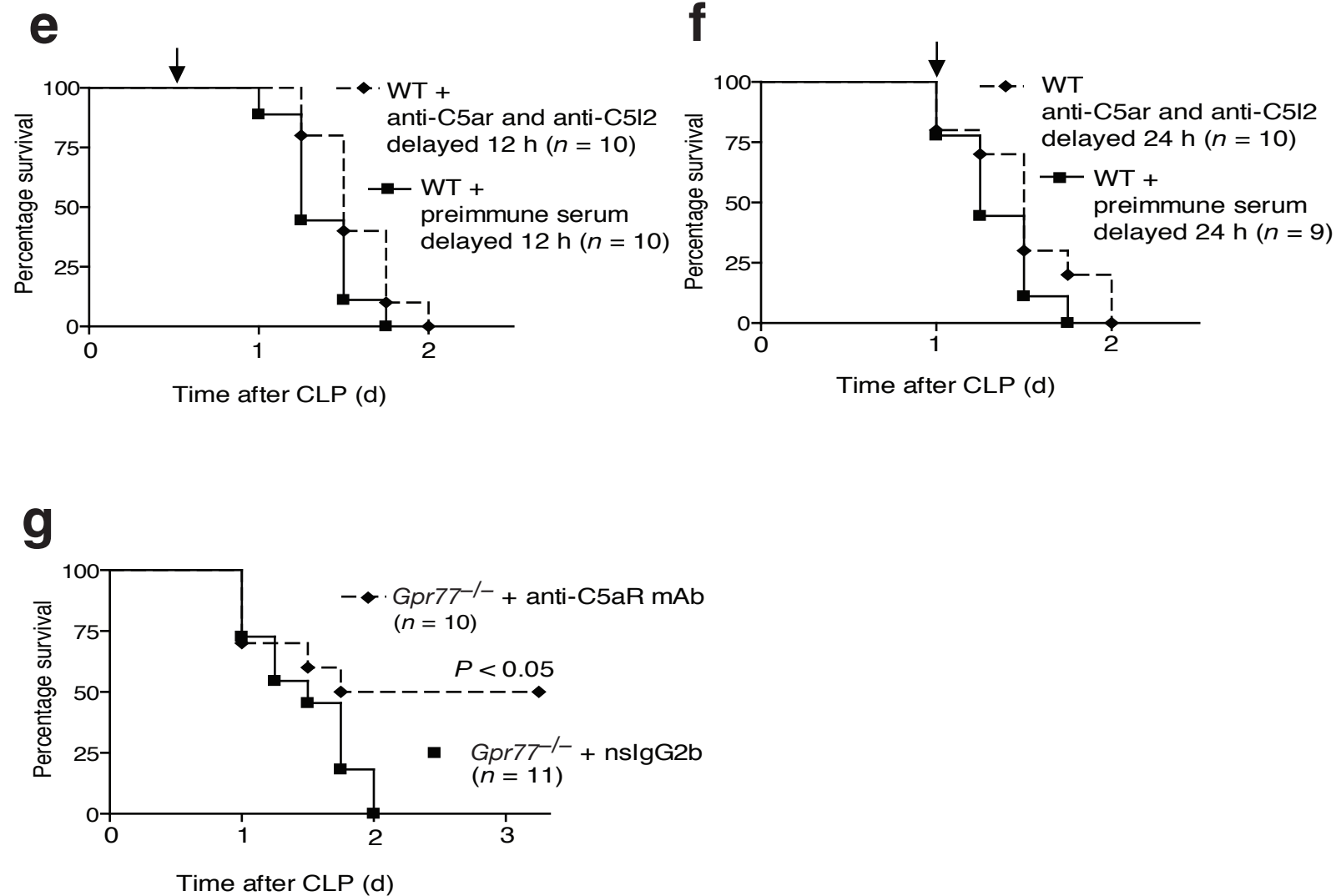
# Functional Roles for C5a Receptors in Sepsis

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## Supplementary Figure 1



## Supplementary Figure 1



**Supplementary Figure 1** Additional survival curves for high-grade CLP. (a) Survival for severe sepsis in *C5ar1*-deficient mice. (b-g) Effect of combined blockade of C5ar and C5I2 on survival in severe sepsis. (b) Survival of *C5ar1*<sup>-/-</sup> mice treated with antiserum to C5I2 or preimmune serum or wild-type (WT) mice treated with C5I2-specific antiserum. (c) High-grade sepsis in wild-type mice pretreated with antiserum to C5ar and C5I2 or with preimmune serum. Mice received 1 ml C5ar- and C5I2-specific antiserum or preimmune serum by subcutaneous (s.c.) injection 12 h prior to CLP. (d) Dual blockade of C5a receptors in wild-type mice by treatment with combined antiserum to C5ar and C5I2 (1 ml s.c.) immediately post CLP. (e) Combined antibody-induced blockade of C5ar and C5I2 12 h after CLP (1 ml antiserum to C5ar and C5I2 s.c.). (f) Delayed treatment of wild-type mice with antiserum to C5ar and C5I2 (1 ml s.c.) 24 hr after CLP. Arrows indicate the time point of injection. (g) Survival in severe sepsis of *Gpr77*<sup>-/-</sup> mice treated with 100  $\mu$ g (200  $\mu$ l i.v.) mouse C5ar-specific monoclonal antibody (clone 20/70) or non-specific IgG (nslgG2b) immediately after sepsis induction by CLP. For each curve, the  $n$  value is given as are the corresponding  $P$  values.

**Supplementary Table 1.** Dose-response effects of MAPK / Akt inhibitors on C5a-induced HMGB1 release by *C5ar1*<sup>-/-</sup> macrophages

Inhibitor	Dose [ $\mu$ M]	% inhibition of HMGB1 release
UO126 (MEK1/2)	50	2.2 ( $\pm$ 0.9) <sup>NS</sup>
	100	65.0 ( $\pm$ 23.9) *
	200	100.0 ( $\pm$ 0.0) *
SP600125 (JNK1/2)	1	0.2 ( $\pm$ 0.2) <sup>NS</sup>
	5	72.1 ( $\pm$ 15.0) *
	10	92.4 ( $\pm$ 4.6) *
SB203580 (p38)	10	1.1 ( $\pm$ 1.1) <sup>NS</sup>
	50	1.5 ( $\pm$ 1.4) <sup>NS</sup>
	100	1.0 ( $\pm$ 1.0) <sup>NS</sup>
Wortmannin (Akt/PI3K)	0.1	68.9 ( $\pm$ 5.1) *
	0.5	58.8 ( $\pm$ 3.7) *
	1	81.3 ( $\pm$ 0.0) *

$n \geq 2$  for each group.

All *P* values are based on comparison to DMSO + C5a (50nM) positive controls.

\*  $P < 0.05$

NS = not significant