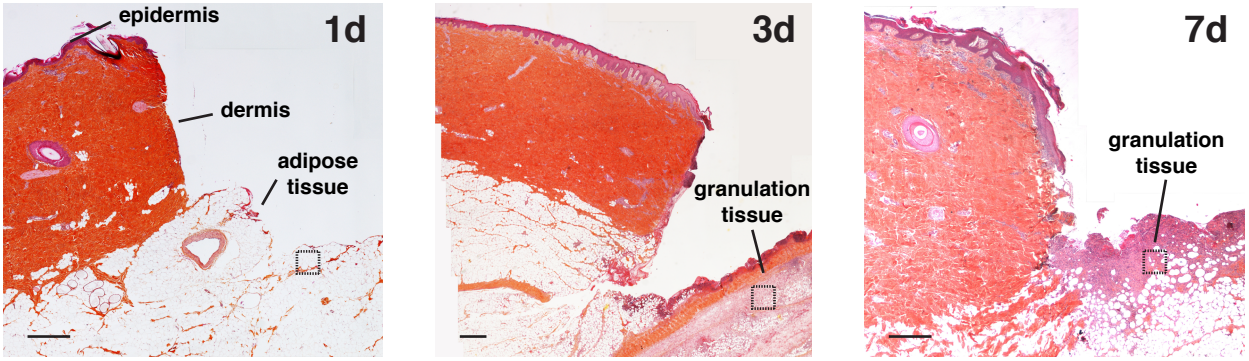

Figure S1 Histologies of wound edges at 1, 3 and 7 days after wounding. Tissue slides were prepared from wounds upon removal of polyurethane foams and stained with hematoxylin/eosin. Dashed squares indicate regions magnified in Figure 1B. Scale bars represent 1 mm.

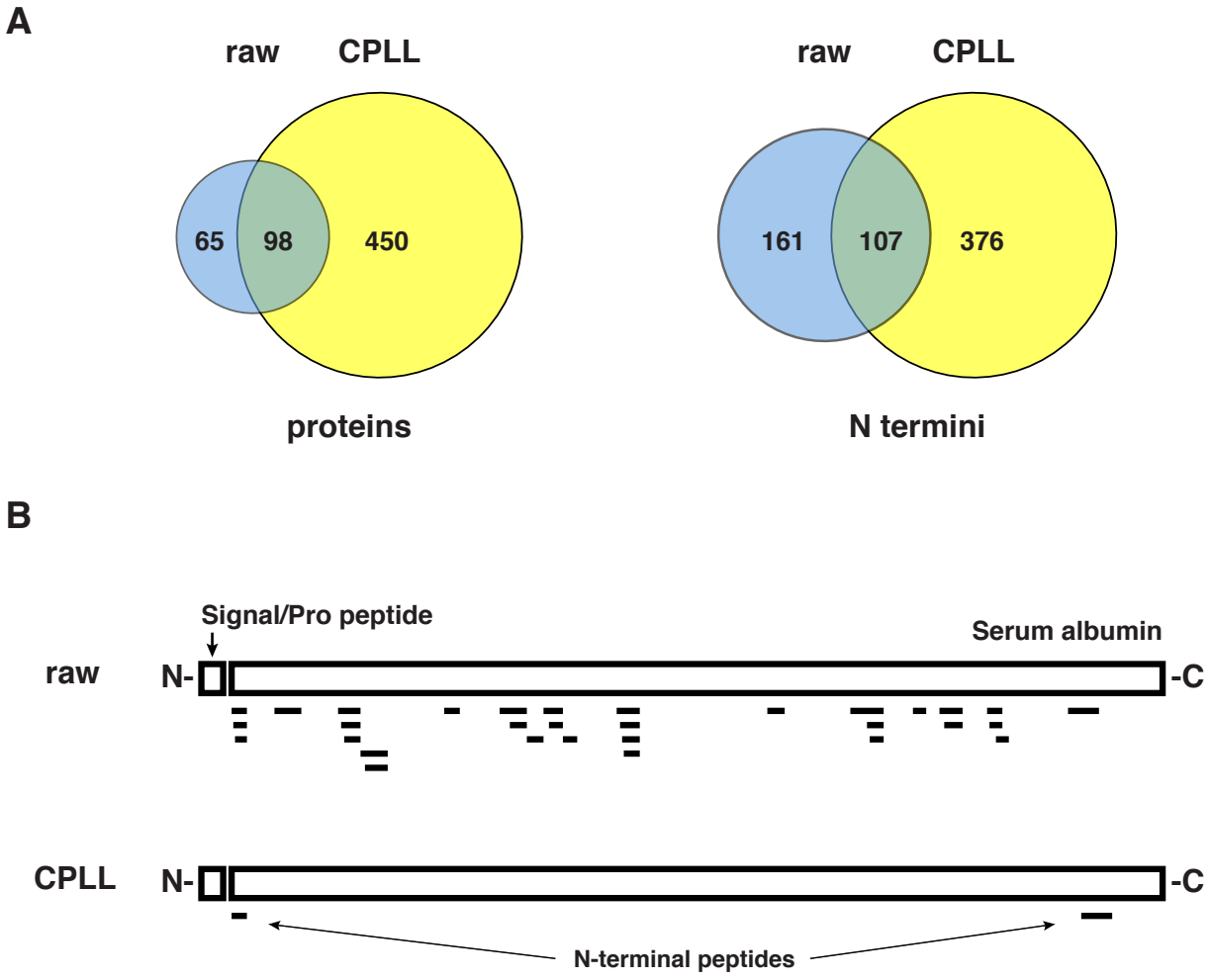

Figure S2 Effect of protein equalization by combinatorial peptide ligand libraries (CPLL) on number of identified proteins and N termini. For optimal results wound fluids extracted from polyurethane foams were buffer exchanged by ultrafiltration (5 kDa cutoff) to 50 mM HEPES, pH 7.8 and adjusted to a concentration of 50-70 mg/ml. Samples (1 ml) were loaded onto CPLL (ProteoMiner, BioRad, Hercules, CA) columns, washed and proteins eluted in 300 µl elution buffer (8 M urea, 2% CHAPS). For iTRAQ-TAILS analysis the buffer was exchanged to 250 mM HEPES, pH 7.8 and 2.5 M GuHCl by ultrafiltration, and protein concentrations were adjusted to 1 mg/ml. (**A**) Proportional Venn diagrams of proteins and N termini identified in raw wound fluids and after treatment with CPLL. CPLL treatment increased the total number of detected proteins from 163 to 548 and of N termini from 268 to 483. (**B**) N-terminal peptides assigned to serum albumin identified without and with CPLL treatment of wound fluids. CPLL treatment significantly reduced the number of N termini derived from multiply processed highly abundant proteins, allowing detection of a higher number of N termini from proteins with lower abundances.

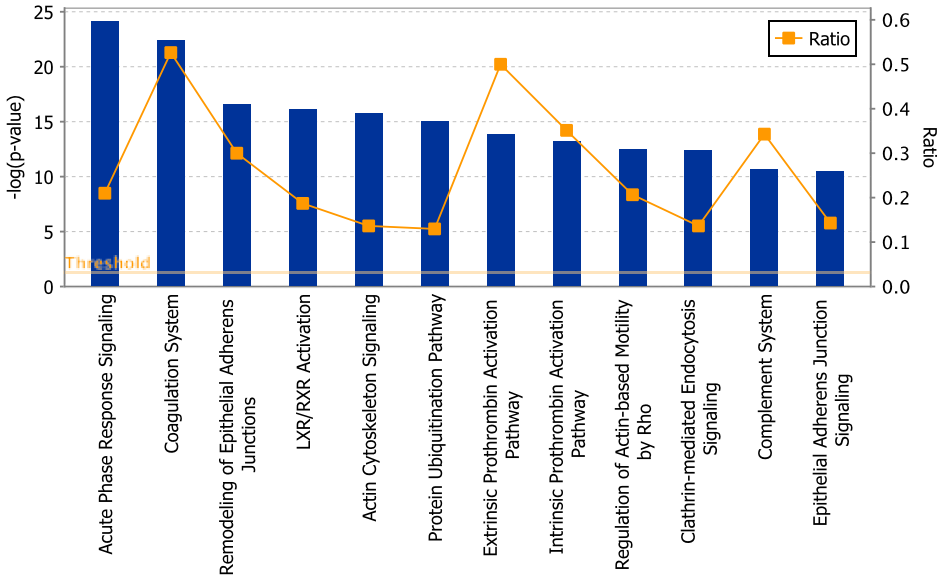

Figure S3 Ingenuity pathway enrichment analysis of proteins identified in pig wound exudates. Six hundred and six (606) human orthologs were determined from all 664 identified proteins using the InParanoid Version 8.0 ortholog table for H.sapiens-S. Scrofa and subjected to pathway enrichment analysis using Ingenuity® Pathway Analysis (IPA®, QIAGEN Redwood City, CA). The 12 top enriched canonical pathways are shown. Left y-axis indicates statistical significance of enrichment based on p-values from Fisher's exact test and right y-axis ratios of numbers of pathway elements identified and all elements of the respective canonical pathway (i.e. a ratio of 0.5 means that 50% of all pathway elements have been identified). Threshold marks a p-value of 0.05 for statistical significance of pathway enrichment.

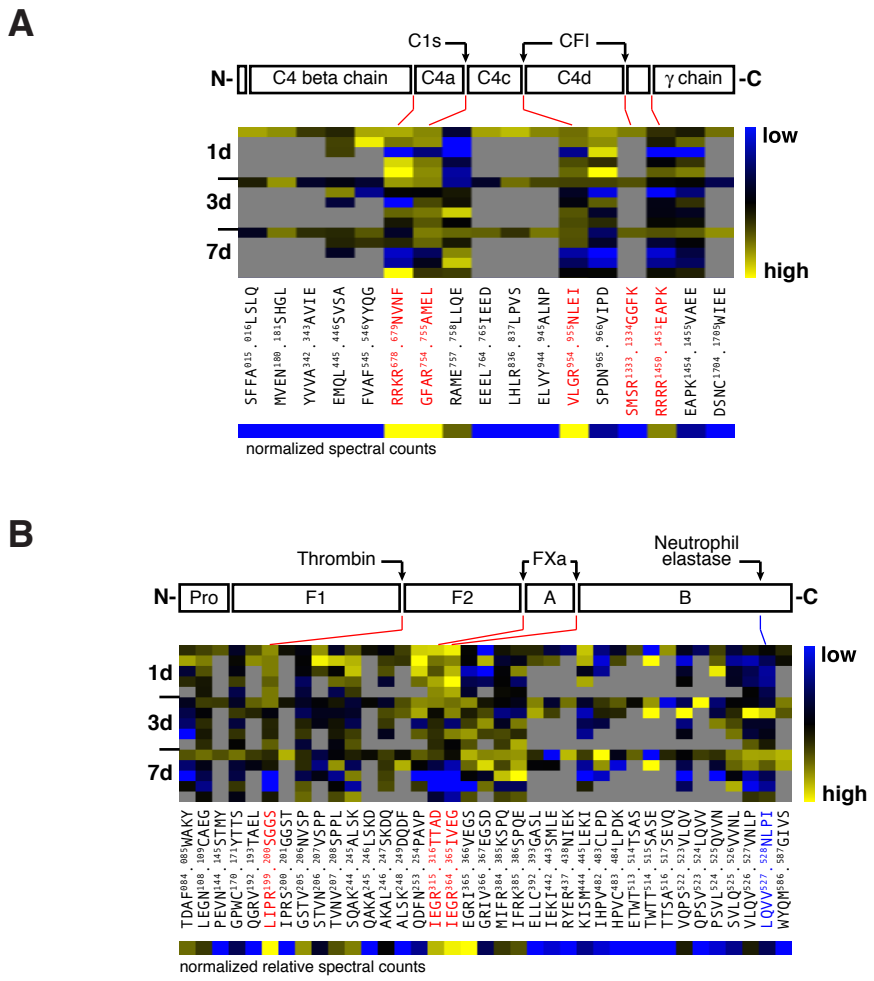

Figure S4 Domain structures of complement C4 and prothrombin with heatmaps of assigned N termini and their relative abundances in wound fluids at distinct time points after wounding. N-terminal peptides are indicated by their related cleavage motifs, known major cleavages are in red. Normalized relative spectral counts reflect relative intensities of N termini that correlate with major known processing events. (**A**) Complement C4. High normalized spectral counts were recorded for neo-N termini resulting from cleavages by complement C1s, complement factor I (CFI) as well as for the N termini of the alpha and gamma chains. (**B**) Prothrombin. Highest abundances were assigned to neo-N termini resulting from cleavages by activated coagulation factor Xa (FXa) at positions Arg^{315} and Arg^{364} and by active Thrombin at position Arg^{199} between fragment 1 (F1) and fragment 2 (F2). A known neutrophil elastase cleavage site is highlighted in blue. Pro: Propeptide; A, B: A and B chains of α-thrombin.

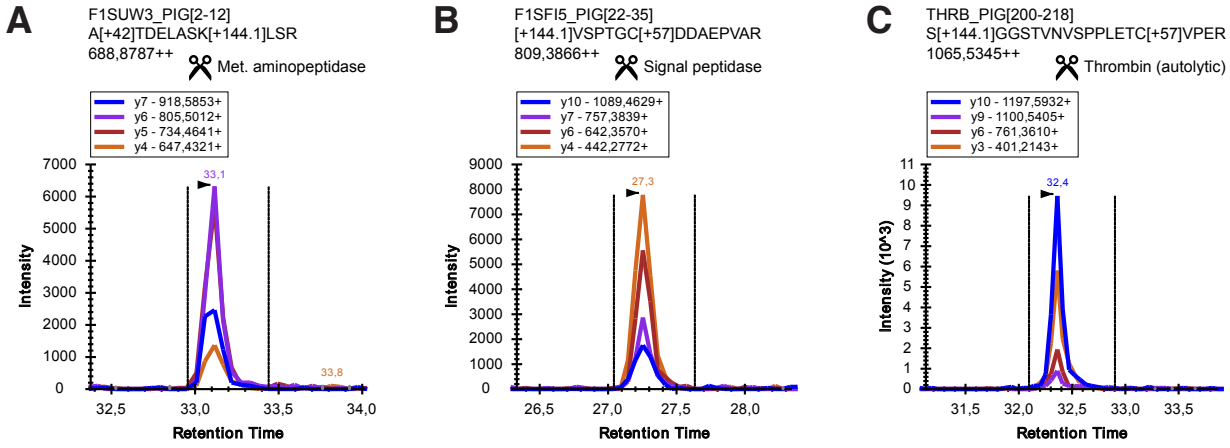

Figure S5 Examples of TAILS N-terminal peptides monitored by SRM in pig wound exudates. All panels show fragment ion traces recorded on a QQQ MS in SRM mode. Samples were processed following the iTRAQ-TAILS procedure including HPG-ALD polymer pullout. [+144.1] indicates mass shift in Da corresponding to iTRAQ 4plex modification on peptide N terminus or lysine; [+42] N-terminal acetylation; [+57] Carbamidomethyl. Data were generated using Skyline (version 2.6) and are avaliable as supplemental material. (**A**) Acetylated natural protein N terminus upon removal of initiator methionine (EF-hand domain-containing protein D2; F1SUW3). (**B**) Natural protein N-terminal peptide upon signal peptide removal (Histidine-rich glycoprotein; F1SFI5). (**C**) Protein neo-N terminus upon endoproteolytic processing (Prothrombin; Q19AZ8; autolytic cleavage).

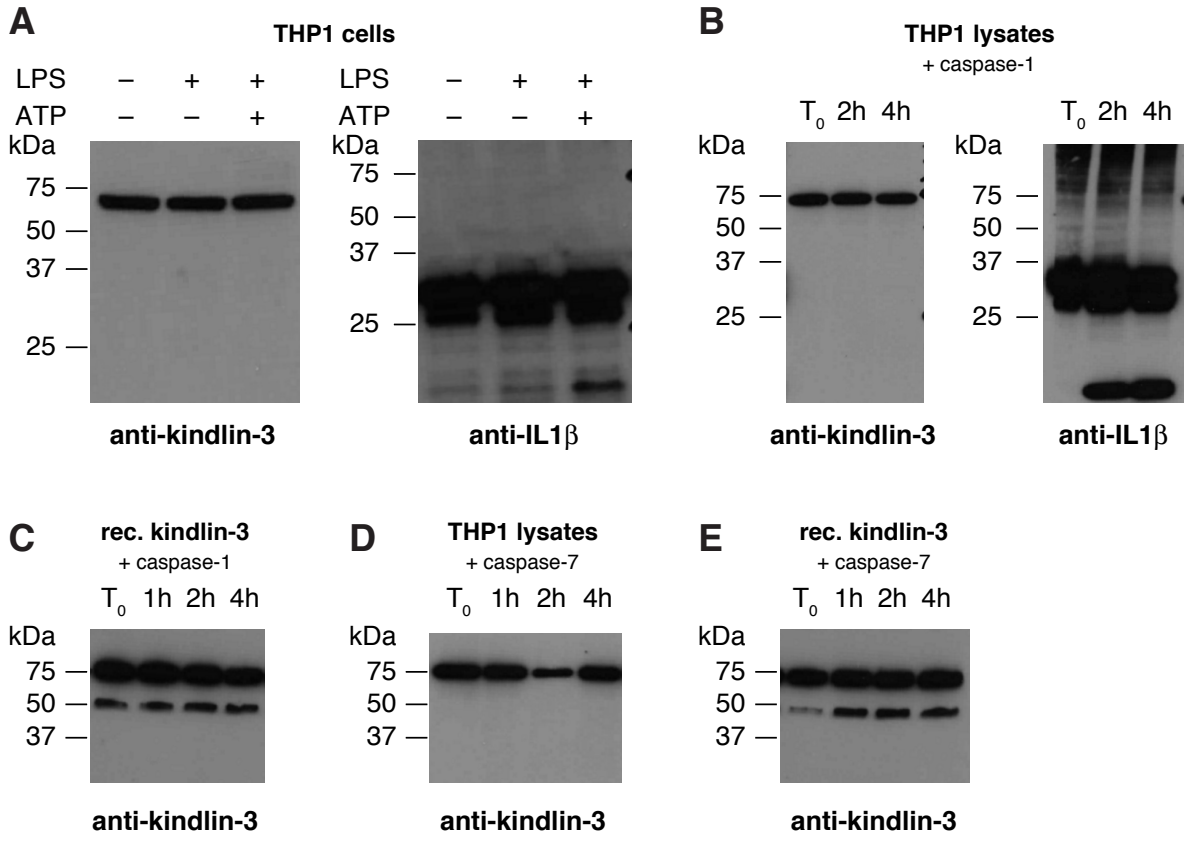

Figure S6 Lack of processing of kindlin-3 by caspase-1 and caspase-7. (**A**) THP1 cells were differentiated by incubation with TPA, primed with LPS and the inflammasome activated with ATP. Immunoblot analysis showed no cleavage of kindlin-3, while IL1β was efficiently processed only upon inflammasome activation. (**B**) Lysates from differentiated THP1 cells were incubated with recombinant active caspase-1 for indicated time points and tested for cleavage of kindlin-3 or interleukin (IL)1β by immunoblot analysis. IL1β was processed, whereby no cleavage product was observed for kindlin-3. (**C**) Recombinant human kindlin-3 was incubated with active caspase-1 and processing monitored by immunoblot analysis. No cleavage of kindlin-3 was detected. A second band at 50 kDa was observed in the commercial kindlin-3 preparation irrespective of protease incubation. (**D**) Lysates from differentiated THP1 cells were treated with recombinant active caspase-7 and analyzed for kindlin-3 processing by immunoblot. No cleavage fragment was observed. (**E**) Recombinant kindlin-3 was incubated with active caspase-7. Immunoblot analysis showed no specific processing of the protein.