Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

| Item | Confirmed |
|------|-----------|
| The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement | ✓ |
| An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly | ✓ |
| The statistical test(s) used AND whether they are one- or two-sided | ✓ |
| Only common tests should be described solely by name; describe more complex techniques in the Methods section. |
| A description of all covariates tested | ✓ |
| A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons | ✓ |
| A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals) | ✓ |
| For null hypothesis testing, the test statistic (e.g. $F$, $t$, $r$) with confidence intervals, effect sizes, degrees of freedom and $P$ value noted | ✓ |
| Give $P$ values as exact values whenever suitable. |
| For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings | ✓ |
| For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes | ✓ |
| Estimates of effect sizes (e.g. Cohen's $d$, Pearson's $r$), indicating how they were calculated | ✓ |
| Clearly defined error bars | ✓ |
| State explicitly what error bars represent (e.g. SD, SE, CI) | ✓ |

Software and code

Policy information about availability of computer code

Data collection

| Software |
|----------|
| LI-COR image Studio 4.0, Compass Hystar 3.2 SR4 (Bruker), otofControl 4.0 (Bruker) |

Data analysis

| Software |
|----------|
| R software (version 3.4.3) and RStudio (version 1.1.383), Prism 7.0(v7a, GraphPad), ImageJ 1.49V, ProteinScape 4.0.3.315 and Bruker Compass DataAnalysis 4.3(x64) (Bruker Daltonics), Mascot Search Engine (Matrix Science), lme4 package (version 1.1-15) in R, emmeans (version 1.1) package in R, Microsoft Excel for Mac v14.3.6 |

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.
Data

Policy information about availability of data
All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:
- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support the findings of this study are available in the extended Supplementary Information. Proteomics data are available in the Proteomics IDENTifications (PRIDE) database. Dataset identifier is provided in the Data availability statement section. The link will be made public once the paper is online.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

| Sample size | No sample size calculations were performed. The sample size was determined by material available. The sample size was sufficient. All analyses indicated either clear dramatic differences (highly significant) or clear lack of difference (no significance and no observable trends in the data). |
| Data exclusions | No data were excluded from the analysis. |
| Replication | For all analyses, three technical replicates were gathered for each sample and for most analyses assays were repeated across two or three batches. Statistical analyses used all replicates in a mixed model to appropriately account for all sources of variance. All replications were successful. |
| Randomization | This was not a randomized study. For comparisons between IgG and C3, we used an observational design. For all other experiments, we compared treatment conditions to untreated measurements within the same subject. |
| Blinding | Blinding was not done for this experiment or analysis. The blinding was not possible due to nature of sample collection and processing in this study. |

Reporting for specific materials, systems and methods

Materials & experimental systems

| Method | n/a |
|--------|-----|
| Involved in the study | n/a |
| ☒ ☐ Unique biological materials |
| ☒ ☐ Antibodies |
| ☒ ☐ Eukaryotic cell lines |
| ☒ ☐ Palaeontology |
| ☒ ☐ Animals and other organisms |
| ☒ ☐ Human research participants |

Methods

| Method | n/a |
|--------|-----|
| Involved in the study | n/a |
| ☒ ☐ ChiP-seq |
| ☒ ☐ Flow cytometry |
| ☒ ☐ MRI-based neuroimaging |

Unique biological materials

Policy information about availability of materials

Obtaining unique materials

Plasma of breast cancer patients cannot be shared due to the COMIRB protocol limitations. Plasma and sera of healthy donors can be obtained from authors upon request.
## Antibodies

| Antibodies used | All antibodies with the respective catalog numbers and lot numbers are listed in Methods section |
|-----------------|------------------------------------------------------------------------------------------------|
| Validation      | The antibodies were validated by the respective manufacturers (www.quidel.com, www.complementtech.com, licor.com, www.jacksonimmuno.com). All the information including list of references is available on the respective websites. Anti-C3 and anti-C1q antibodies were validated in this paper, either via complement inhibition by EDTA, or use of C1 depleted sera. |

## Human research participants

Policy information about studies involving human research participants

| Population characteristics | For normal serum/plasma, both females and males were recruited. Age 18+. The patients were metastatic breast cancer positive, females, age 18+. All ethnicities/races were included in the sample enrollment. |
|----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Recruitment                | Plasma and sera were collected from anonymous consented healthy donors at the University of Colorado blood bank. Both genders were enrolled under standard Institutional Review Board protocol using the consent forms available at the University of Colorado blood bank. Plasma from cancer patients were collected from anonymous deidentified patients undergoing exploratory sample collection trial at the University of Colorado (trial 16-0610). All ethnicities/races were included in the sample enrollment. |