nature portfolio

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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on 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 statistical parameters 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

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Initial h5ad anndata objects for analysis were created using tileDB 0.21.6 (CosMx), spatial data 0.2.3, spatialdata-io 0.1.5 (Xenium) together with squidpy 1.2.3 and scanpy 1.9.3.
Data analysis	All code is available at: https://github.com/Woopsydaisy/Spatial-Human-Kidney-Map scvi tool 1.1.5 Python 3.10 squidpy 1.2.3 Nichecompass 0.2.1 GSEApy 1.0.6 CellphoneDB v5 scenvi 0.3.7 Hotspot 1.1.1 sklearn 1.1.2

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Raw data, processed data, and metadata from snRNA seq have been deposited previously (https://zenodo.org/records/15007208) as well as bulk sequencing (GSE115098). The single-cell B cell sequencing atlas has been published previously (https://zenodo.org/records/11468564). The full spatial data will be made available upon publication https://zenodo.org/records/18674907?token=eyJhbGciOiJIUzUxMiJ9.eyJpZCI6ImE1Nzk5MWJkLWFjZjEtNDc0OC1iOTk3LTUwMmNkODUwZGNiNSIsImRhdGEiOnt9LCJyYW5kb20iOiIxNTgxYWVmYzIwNDIxYjJiMGY1Y2RkZDc5MmUyMTI1ZSJ9.xZ70qKUdO0wvpeM3GQrzm_UrO8a4qCn7pYy3uhIDP9Ccwu-WMqRwiZxhvNopzmWmpEITmDc3UI4l3H3eGLKPxQ and the data can be viewed on www.susztaklab.com browser.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	We report on sex on all individuals included in the study.
Reporting on race, ethnicity, or other socially relevant groupings	We report on race on all individuals included in the study.
Population characteristics	A full description of each individual human patient is provided in the sample metadata information in supplementary table 1. 58 patients (26% female, with a mean age of 57.3 years) were included. Mean kidney function (eGFR) was 58 with a minimum of 12 and maximum of 112 mL/min/1.73m². Dataset included 29 DKD samples and 15 Control samples.
Recruitment	N/a
Ethics oversight	The University of Pennsylvania institutional review board (IRB) approved the collection of human kidney tissue for this study. Left-over kidney samples were irreversibly de-identified, and no personal identifiers were gathered. Therefore, they were exempt from IRB review (category 4). We engaged an external, honest broker who was responsible for clinical data collection without disclosing personally identifiable information. Participants were not compensated. Some samples were collected as part of the Transformative Research in Diabetic Nephropathy (TRIDENT) study, a multicenter observational cohort study that enrolls, follows, and performs multiomics characterization of subjects with DKD. This study was approved by the University of Pennsylvania IRB and by the TRIDENT Steering Committee. Informed consent was obtained from each participant. The present research using the UKBB Resource was approved under Application Number 273810. Participants from the UKBB provided written informed consent allowing the use of their samples and data for medical research purposes.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is 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/documents/nr-reporting-summary-flat.pdf

Life sciences study design

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

Sample size	We aimed to generate a population-scale atlas representative for the sample heterogeneity expected in diabetic kidney disease patients. No sample size calculation was performed. 29 samples from patients with DKD and 15 control samples were included, which is consistent with current large-scale human spatial profiling studies given the technical complexity of the assay. Key findings were validated in an independent observational DKD cohort (TRIDENT study, n = 280 patients).
Data exclusions	No data was excluded.
Replication	3 samples were replicated on CosMx and Xenium platform, 3 samples were replicated on CosMx platform.
Randomization	No randomization was performed. This study analyzed observational, patient-derived kidney tissue samples, and no experimental group allocation was conducted.

Blinding	Blinding was not performed. Samples were assigned to groups based on established clinical diagnoses, and spatial transcriptomics analyses were conducted using standardized, automated computational pipelines, minimizing investigator bias.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	CD11c EP1347Y ab216655 abcam CD20 H1 3161029D Fluidigm CD27 EPR8569 3171024D Fluidigm CD4 EPR6855 3156033D Fluidigm CD45 CD45-2B11 3152016D Fluidigm CD8 C8/144B 3162034D Fluidigm Ki67 B56 3168022D Fluidigm CD38 EPR4106 ab226034 abcam Bcl-6 K112-91 3147020D Fluidigm
Validation	n/a

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*