

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                                                                                                                                                                                                                                                                                      |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The exact sample size ( <i>n</i> ) for each experimental group/condition, given as a discrete number and unit of measurement                                                                                                                               |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly                                                                                                                                    |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided<br><i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>                                                               |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> A description of all covariates tested                                                                                                                                                                                                                                |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons                                                                                                                                        |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> 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) |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted<br><i>Give P values as exact values whenever suitable.</i>                     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings                                                                                                                                                                      |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes                                                                                                                                                |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i> ), 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 | FACS Aria Fusion sorter (BD), Chromium™ Controller (10x genomics). Biolayer interferometry (BLI) data were acquired using Octet R2 (Sartorius). The cryo-EM data was collected by using EPU software on Titan Krios, equipment with Falcon IV detector in electron counting mode. |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Data analysis

BLI data analysis was performed using the Octet software and GraphPad Prism (Version 10).  
 Fluorescence microscopy of stained cells was automated using a high-performance EVOS M7000 imaging system.  
 CryoEM analysis was done with cryoSPARC (Version 4.4), Coot (V0.9.8.8) and Phenix (Version 1.21).  
 Structure display ChimeraX Version 1.5 and Pymol (Version 4.6).  
 FACS:BD FACSDiva (version .9.0) software, FlowJo (v.10.7.1).  
 Cellranger (v10.0) for the preprocessing of the raw 10X V(D)J data.  
 V(D)J annotation was performed using cellranger vdj (v10.0) on each sample individually, after which sequences and annotations were pooled into a single filtered\_contig.fasta and filtered\_contig\_annotations.csv file for downstream processing within the Immcantation framework (<http://immcantation.org>; Change-O v1.3.0). Sequences were subsequently annotated using IgBLAST v1.22 against the IMGT database (accessed 8 December 2025).  
 The associated scripts are available on <https://github.com/MathildeFogPerez/manuscript-iglon5-D1>. Raw sequencing data files for single-cell VDJ sequencing are available at ENA database: PRJEB109754. Processed data files (BCR repertoires) are available at Zenodo: <https://doi.org/10.5281/zenodo.18925481>.  
 Statistical analysis were performed with R Statistical Software (v4.4.2)

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](#)

The associated scripts are available on <https://github.com/MathildeFogPerez/manuscript-iglon5-D1>.  
 Raw sequencing data files for single-cell VDJ sequencing are available at ENA database: PRJEB109754.  
 Processed data files (BCR repertoires) are available at Zenodo: <https://doi.org/10.5281/zenodo.18925481>.  
 Cryo-EM map and PDB Model were deposited on EMDb: and PDB with the following accession numbers EMD-57080 and EMD-57198 with PDB-ID:29CP and PDB-ID: 29IN

## 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

Blood samples were collected from one adult male individual.

Reporting on race, ethnicity, or other socially relevant groupings

Race and ethnicity information were not collected.

Population characteristics

PBMCs were obtained from a 60-year-old male diagnosed with anti-IgLN5 disease.

Recruitment

PBMCs were obtained from a 60-year-old male diagnosed with anti-IgLN5 disease. The patient presented a 7-year history of sleep disturbances characterized by abnormal nocturnal movements and behaviors, mild sleep-onset and maintenance insomnia, and severe daytime somnolence with episodes of unintended sleep.

Ethics oversight

The study was approved by the ethics committee of Hospital Clínic (2018-0336 ER-01), Barcelona, Spain.

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](https://www.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

Only one human donor.

Data exclusions

No data are excluded.

|               |                                           |
|---------------|-------------------------------------------|
| Replication   | Experiments were at least repeated twice. |
| Randomization | No randomization was performed.           |
| Blinding      | No blinding.                              |

## 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                                     |
|--------------------------|-----------------------------------------------------------|
| <input type="checkbox"/> | <input checked="" type="checkbox"/> Antibodies            |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> Eukaryotic cell lines |
| <input type="checkbox"/> | <input type="checkbox"/> Palaeontology and archaeology    |
| <input type="checkbox"/> | <input type="checkbox"/> Animals and other organisms      |
| <input type="checkbox"/> | <input type="checkbox"/> Clinical data                    |
| <input type="checkbox"/> | <input type="checkbox"/> Dual use research of concern     |
| <input type="checkbox"/> | <input type="checkbox"/> Plants                           |

### Methods

| n/a                      | Involved in the study                              |
|--------------------------|----------------------------------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> ChIP-seq                  |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> Flow cytometry |
| <input type="checkbox"/> | <input type="checkbox"/> MRI-based neuroimaging    |

### Antibodies

|                 |                                                                                                                                                                                        |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Antibodies used | CD3-APC/Cy7 (clone HIT3a, Cat No#300317, BioLegend), CD20-PE-Cy7 (clone L27, Cat No#335793, BD Biosciences), and anti-human IgD PE-CF594 (BD Biosciences; Cat No#562540; Clone IA6-2). |
| Validation      | Validation is available on the manufacturer's website.                                                                                                                                 |

### Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

|                                                                   |                                                                                    |
|-------------------------------------------------------------------|------------------------------------------------------------------------------------|
| Cell line source(s)                                               | Expi293F cells (ThermoFisher, Cat No# A14527) and SH-SY5Y cells, (ATCC # CRL-2266) |
| Authentication                                                    | Done by the manufacturer's.                                                        |
| Mycoplasma contamination                                          | Cells were regularly tested negative for mycoplasma.                               |
| Commonly misidentified lines (See <a href="#">ICLAC</a> register) | No commonly misidentified cell line have been used in this study.                  |

### Palaeontology and Archaeology

|                          |                                                                                                                        |
|--------------------------|------------------------------------------------------------------------------------------------------------------------|
| Specimen provenance      | NA                                                                                                                     |
| Specimen deposition      | NA                                                                                                                     |
| Dating methods           | NA                                                                                                                     |
| <input type="checkbox"/> | Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information. |
| Ethics oversight         | NA                                                                                                                     |

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

### Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

|                    |    |
|--------------------|----|
| Laboratory animals | NA |
| Wild animals       | NA |

|                         |    |
|-------------------------|----|
| Reporting on sex        | NA |
| Field-collected samples | NA |
| Ethics oversight        | NA |

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

## Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

|                             |    |
|-----------------------------|----|
| Clinical trial registration | NA |
| Study protocol              | NA |
| Data collection             | NA |
| Outcomes                    | NA |

## Dual use research of concern

Policy information about [dual use research of concern](#)

### Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

| No                                  | Yes                      |                            |
|-------------------------------------|--------------------------|----------------------------|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Public health              |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | National security          |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Crops and/or livestock     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Ecosystems                 |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Any other significant area |

### Experiments of concern

Does the work involve any of these experiments of concern:

| No                                  | Yes                      |                                                                             |
|-------------------------------------|--------------------------|-----------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Demonstrate how to render a vaccine ineffective                             |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Confer resistance to therapeutically useful antibiotics or antiviral agents |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enhance the virulence of a pathogen or render a nonpathogen virulent        |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Increase transmissibility of a pathogen                                     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Alter the host range of a pathogen                                          |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enable evasion of diagnostic/detection modalities                           |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enable the weaponization of a biological agent or toxin                     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Any other potentially harmful combination of experiments and agents         |

## Plants

|                       |    |
|-----------------------|----|
| Seed stocks           | NA |
| Novel plant genotypes | NA |
| Authentication        | NA |

## ChIP-seq

### Data deposition

- ☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- ☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

|                                                                    |    |
|--------------------------------------------------------------------|----|
| Data access links<br><i>May remain private before publication.</i> | NA |
| Files in database submission                                       | NA |
| Genome browser session<br>(e.g. <a href="#">UCSC</a> )             | NA |

### Methodology

|                         |    |
|-------------------------|----|
| Replicates              | NA |
| Sequencing depth        | NA |
| Antibodies              | NA |
| Peak calling parameters | NA |
| Data quality            | NA |
| Software                | NA |

## Flow Cytometry

### Plots

Confirm that:

- ☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- ☒ All plots are contour plots with outliers or pseudocolor plots.
- ☐ A numerical value for number of cells or percentage (with statistics) is provided.

### Methodology

|                           |                                                                                                                                              |
|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Sample preparation        | PBMCs were stained on ice with the specified fluorochrome-labelled antibodies. SH-SY5Y cells were incubated on ice with biotinylated IgLON5. |
| Instrument                | BD FACSDiva and FACS Aria III                                                                                                                |
| Software                  | FlowJo (v.10.7.1) and GraphPad Prism (Version 10).                                                                                           |
| Cell population abundance | NA                                                                                                                                           |
| Gating strategy           | NA                                                                                                                                           |

- ☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

## Magnetic resonance imaging

### Experimental design

|                                 |    |
|---------------------------------|----|
| Design type                     | NA |
| Design specifications           | NA |
| Behavioral performance measures | NA |

### Acquisition

|                               |                                                                 |
|-------------------------------|-----------------------------------------------------------------|
| Imaging type(s)               | NA                                                              |
| Field strength                | NA                                                              |
| Sequence & imaging parameters | NA                                                              |
| Area of acquisition           | NA                                                              |
| Diffusion MRI                 | <input type="checkbox"/> Used <input type="checkbox"/> Not used |

### Preprocessing

|                            |    |
|----------------------------|----|
| Preprocessing software     | NA |
| Normalization              | NA |
| Normalization template     | NA |
| Noise and artifact removal | NA |
| Volume censoring           | NA |

### Statistical modeling & inference

|                                           |                                                                                                       |
|-------------------------------------------|-------------------------------------------------------------------------------------------------------|
| Model type and settings                   | NA                                                                                                    |
| Effect(s) tested                          | NA                                                                                                    |
| Specify type of analysis:                 | <input type="checkbox"/> Whole brain <input type="checkbox"/> ROI-based <input type="checkbox"/> Both |
| Statistic type for inference              | NA                                                                                                    |
| (See <a href="#">Eklund et al. 2016</a> ) |                                                                                                       |
| Correction                                | NA                                                                                                    |

### Models & analysis

|                                     |                                                                       |
|-------------------------------------|-----------------------------------------------------------------------|
| n/a                                 | Involved in the study                                                 |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Functional and/or effective connectivity     |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Graph analysis                               |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> Multivariate modeling or predictive analysis |