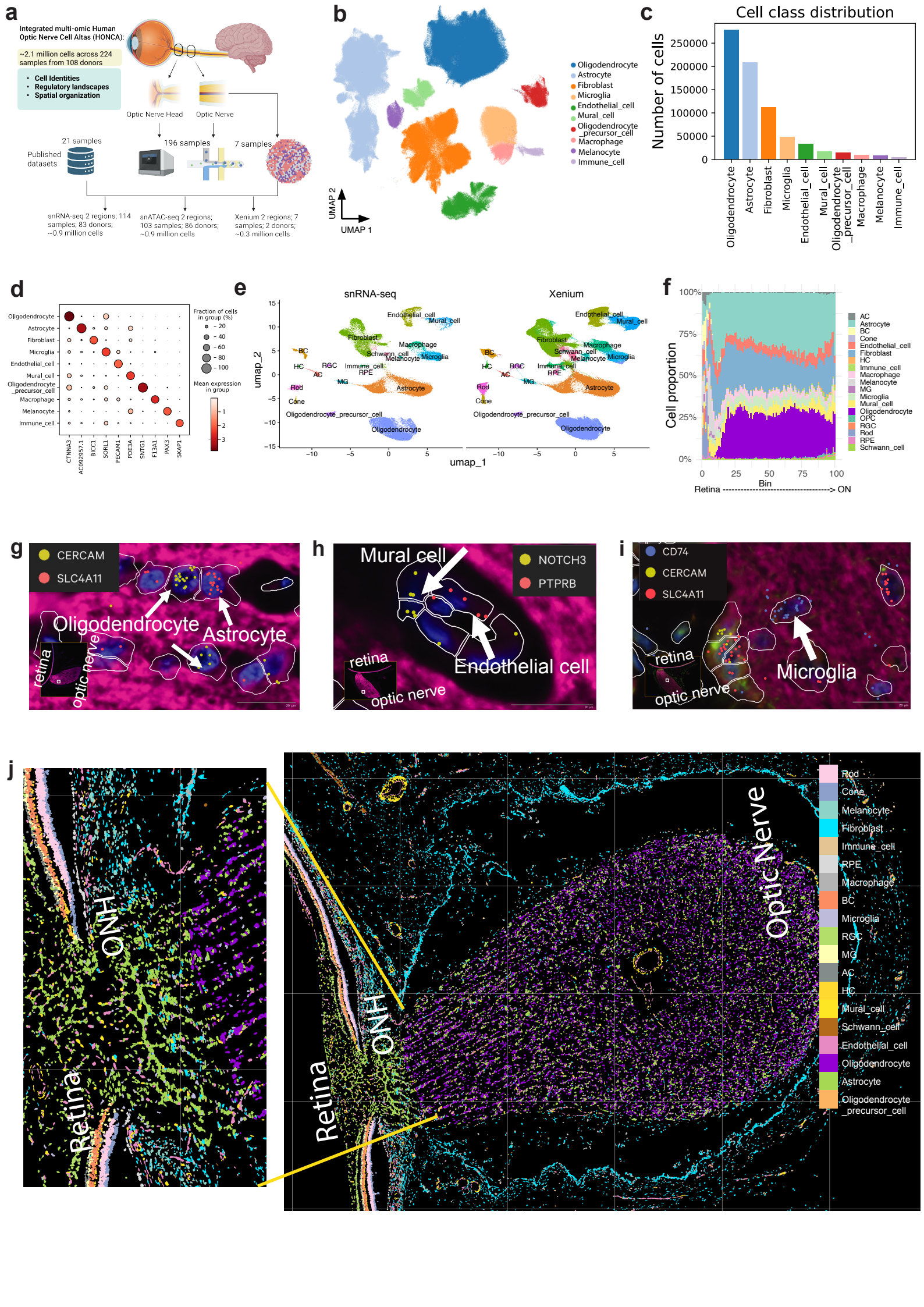
a
Integrated multi-omic Human Optic Nerve Cell Altas (HONCA):
~2.1 million cells across 224 samples from 108 donors
Cell Identities
Regulatory landscapes
Spatial organization
Optic Nerve Head
Optic Nerve
21 samples
Published datasets
196 samples
7 samples
snRNA-seq 2 regions; 114 samples; 83 donors; ~0.9 million cells
snATAC-seq 2 regions; 103 samples; 86 donors; ~0.9 million cells
Xenium 2 regions; 7 samples; 2 donors; ~0.3 million cells
b
UMAP 2
UMAP 1
Oligodendrocyte
Astrocyte
Fibroblast
Microglia
Endothelial_cell
Mural_cell
Oligodendrocyte_precursor_cell
Macrophage
Melanocyte
Immune_cell
c
Cell class distribution
Number of cells
250000
200000
150000
100000
50000
0
Oligodendrocyte
Astrocyte
Fibroblast
Microglia
Endothelial_cell
Mural_cell
Oligodendrocyte_precursor_cell
Macrophage
Melanocyte
Immune_cell
d
Oligodendrocyte
Astrocyte
Fibroblast
Microglia
Endothelial_cell
Mural_cell
Oligodendrocyte_precursor_cell
Macrophage
Melanocyte
Immune_cell
CTNNA3
AC092957.1
BICC1
SORL1
PECAM1
PDE3A
SNTG1
F13A1
PAX3
SKAP1
Fraction of cells in group (%)
20
40
60
80
100
Mean expression in group
1
2
3
e
snRNA-seq
Xenium
umap_2
umap_1
Endothelial_cell
Mural_cell
Fibroblast
Macrophage
Schwann_cell
Melanocyte
Microglia
BC
HC
RGC
Immune_cell
RPE
AC
MG
Astrocyte
Rod
Cone
Oligodendrocyte_precursor_cell
Oligodendrocyte
f
Cell proportion
100%
75%
50%
25%
0%
0
25
50
75
100
Bin
Retina ----------> ON
AC
Astrocyte
BC
Cone
Endothelial_cell
Fibroblast
HC
Immune_cell
Macrophage
Melanocyte
MG
Microglia
Mural_cell
Oligodendrocyte
OPC
RGC
Rod
RPE
Schwann_cell
g
CERCAM
SLC4A11
Oligodendrocyte
Astrocyte
retina
optic nerve
h
Mural cell
NOTCH3
PTPRB
Endothelial cell
retina
optic nerve
i
CD74
CERCAM
SLC4A11
Microglia
retina
optic nerve
j
Retina
ONH
Optic Nerve
Rod
Cone
Melanocyte
Fibroblast
Immune_cell
RPE
Macrophage
BC
Microglia
RGC
MG
AC
HC
Mural_cell
Schwann_cell
Endothelial_cell
Oligodendrocyte
Astrocyte
Oligodendrocyte_precursor_cell

Figure 1. Integrated transcriptomic and spatial cell atlases of the human optic nerve. **a,** Schematic overview of sample collection for the human optic nerve multi-omic single cell atlases. **b,** UMAP of the transcriptomic cell atlas derived from snRNA-seq data, with cells colored by major cell classes. **c**, Bar plot summarizing the cell abundance of each major cell class. **d**, Dot plot showing expression of marker genes across major cell classes in the snRNA-seq data. **e**, UMAP showing the co-embedding snRNA-seq (left) and Xenium (right) cells, with cells colored by major cell classes. **f,** Bar plot displaying cell proportional composition of major cell classes across the optic nerve head and optic nerve in situ derived from Xenium spatial transcriptomic data. **g,** Validation of oligodendrocytes (labeled by *CERCAM* transcripts) and astrocytes (labeled by *SLC4A11* transcripts) in situ with Xenium explorer browser. **h,** Validation of mural cells (labeled by *NOTCH3* transcripts) and endothelial cells (labeled by *PTPRB* transcripts) in situ with Xenium explorer browser. **i,** Validation of microglia (labeled by *CD74* transcripts). **j,** ImageDimPlot showing the spatial distribution of major cell classes cross the optic nerve head (left) and the optic nerve (right) in situ through Xenium spatial transcriptomics.