Figure S1

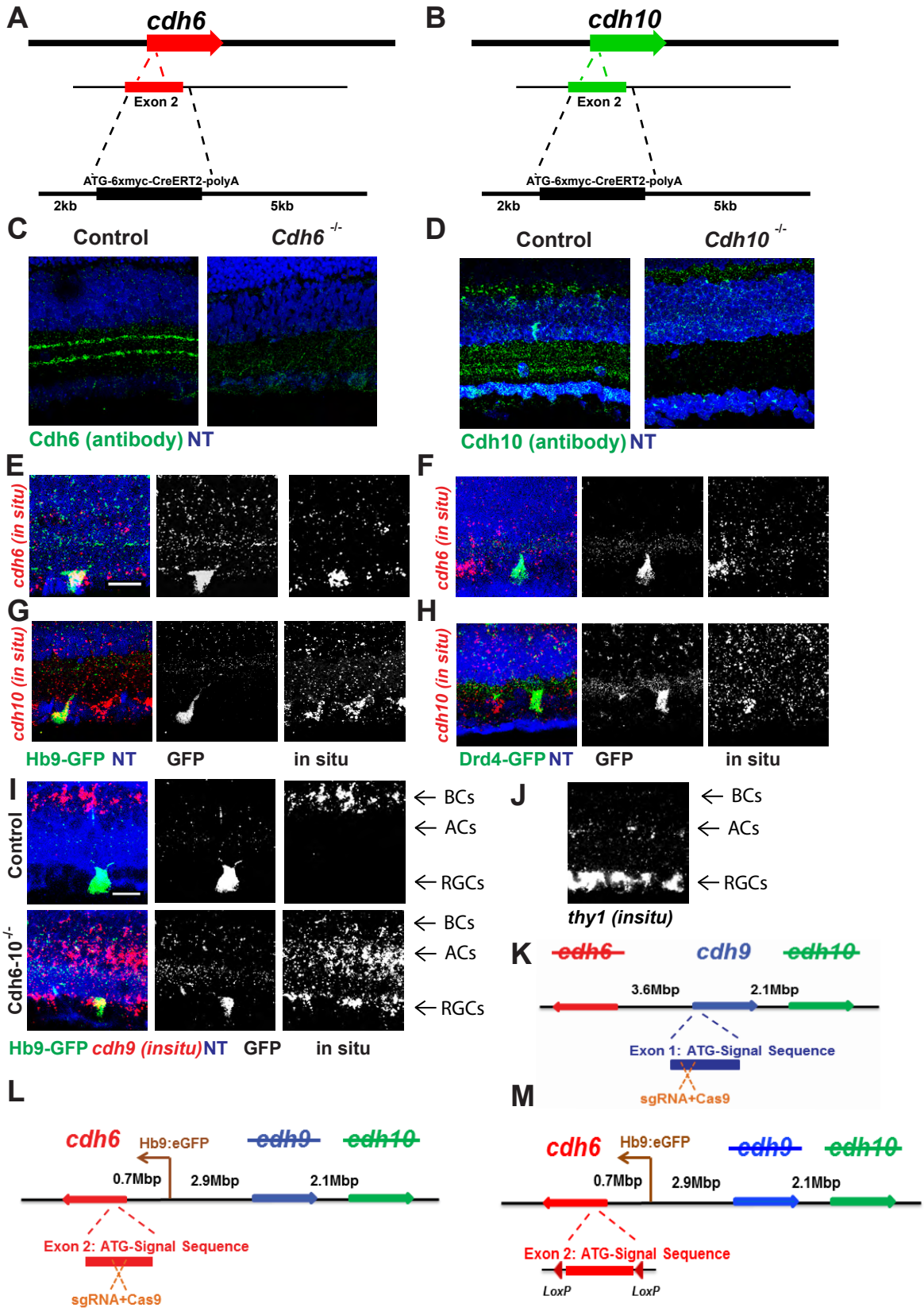

A
cdh6
Exon 2
ATG-6xmyc-CreERT2-polyA
2kb
5kb
B
cdh10
Exon 2
ATG-6xmyc-CreERT2-polyA
2kb
5kb
C
Control
Cdh6 -/-
Cdh6 (antibody) NT
D
Control
Cdh10 -/-
Cdh10 (antibody) NT
E
cdh6 (in situ)
F
cdh6 (in situ)
G
cdh10 (in situ)
Hb9-GFP NT
GFP
in situ
H
cdh10 (in situ)
Drd4-GFP NT
GFP
in situ
I
Control
Cdh6-10 -/-
BCs
ACs
RGCs
Hb9-GFP cdh9 (insitu) NT
GFP
in situ
J
BCs
ACs
RGCs
thy1 (insitu)
K
edh6
cdh9
edh10
3.6Mbp
2.1Mbp
Exon 1: ATG-Signal Sequence
sgRNA+Cas9
L
cdh6
Hb9:eGFP
edh9
edh10
0.7Mbp
2.9Mbp
2.1Mbp
Exon 2: ATG-Signal Sequence
sgRNA+Cas9
M
cdh6
Hb9:eGFP
edh9
edh10
0.7Mbp
2.9Mbp
2.1Mbp
Exon 2: ATG-Signal Sequence
LoxP
LoxP

Figure S2

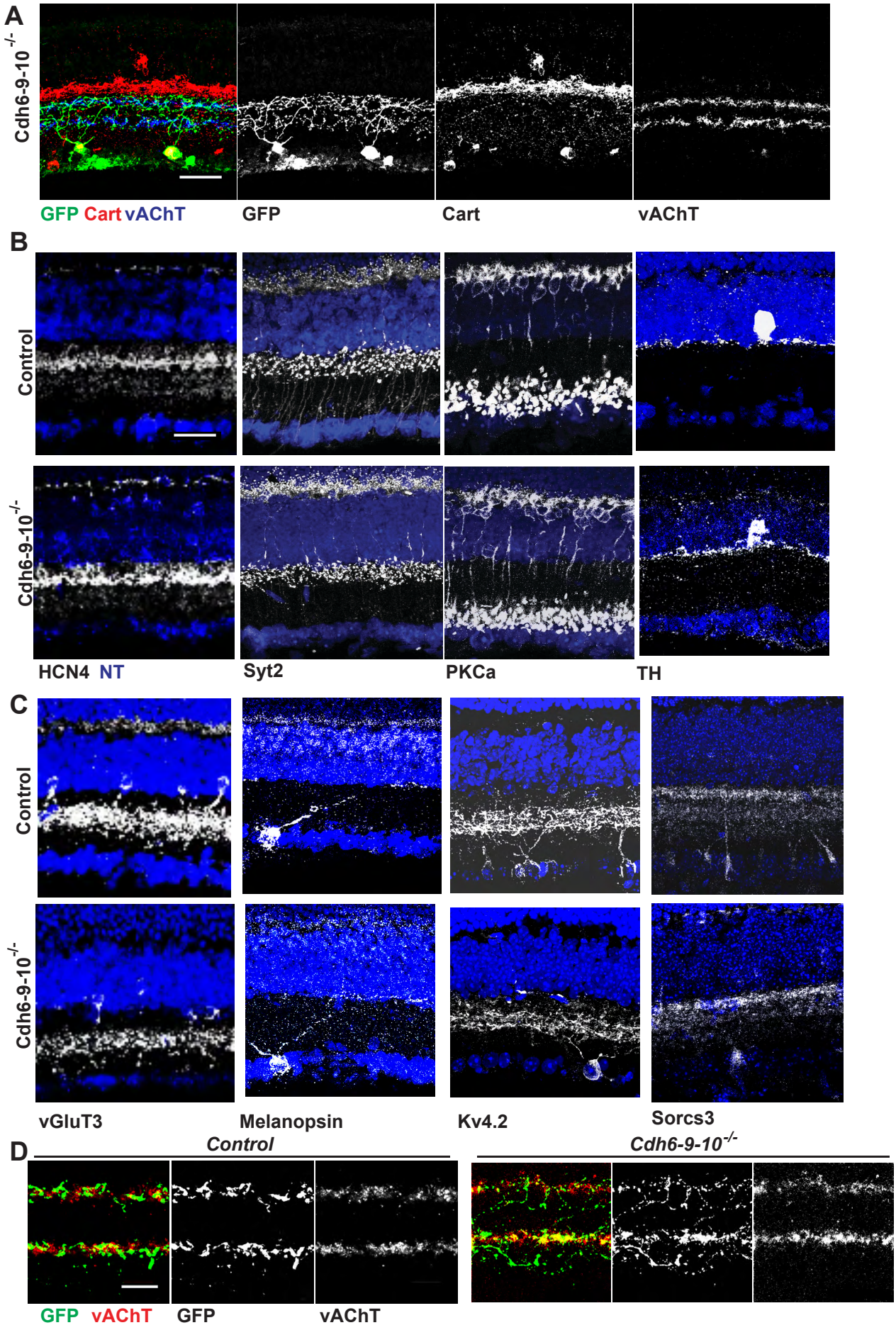

A
Cdh6-9-10 -/-
GFP Cart vAChT
GFP
Cart
vAChT
B
Control
Cdh6-9-10 -/-
HCN4 NT
Syt2
PKCa
TH
C
Control
Cdh6-9-10 -/-
vGluT3
Melanopsin
Kv4.2
Sorcs3
D
Control
Cdh6-9-10 -/-
GFP vAChT
GFP
vAChT

Figure S3

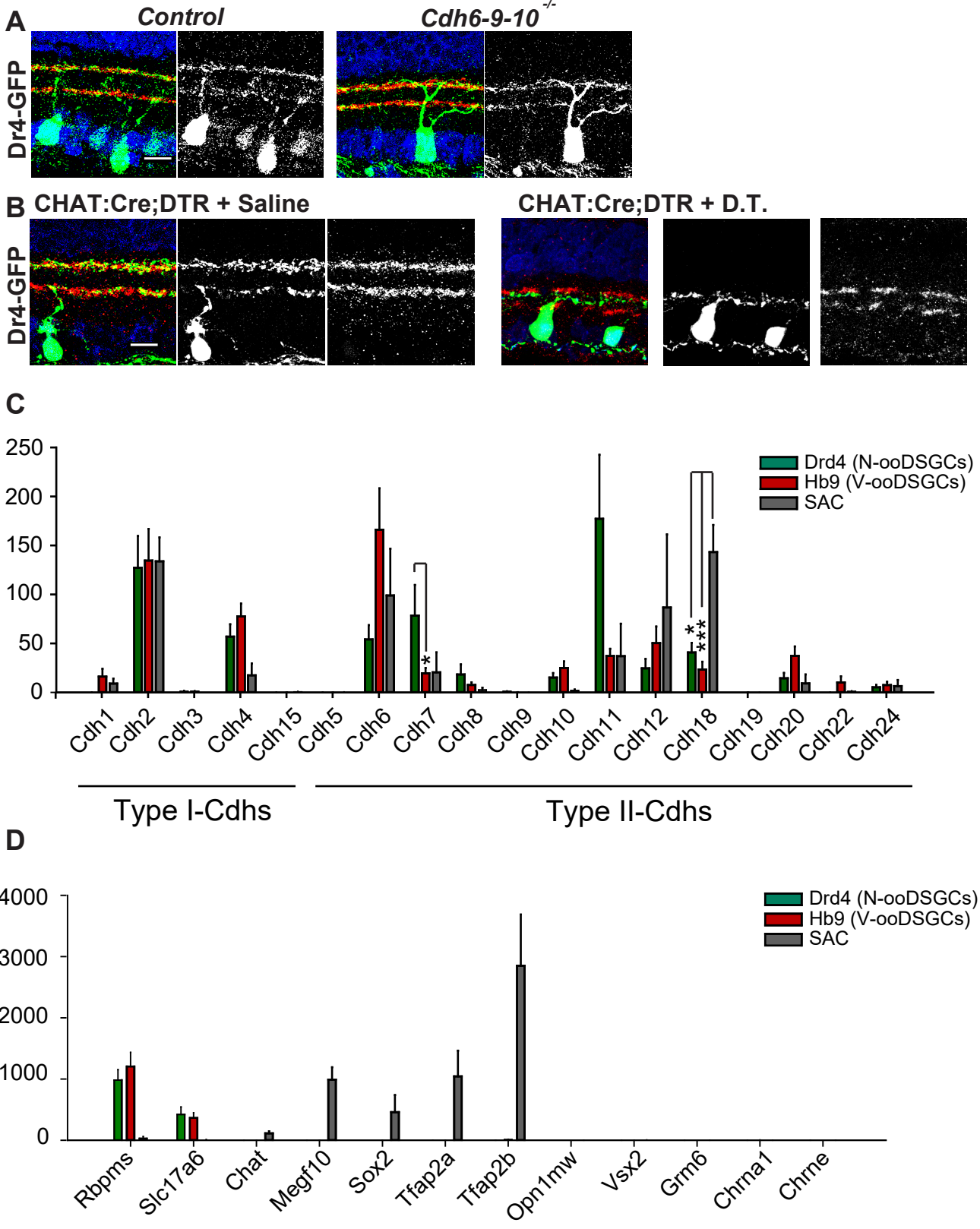
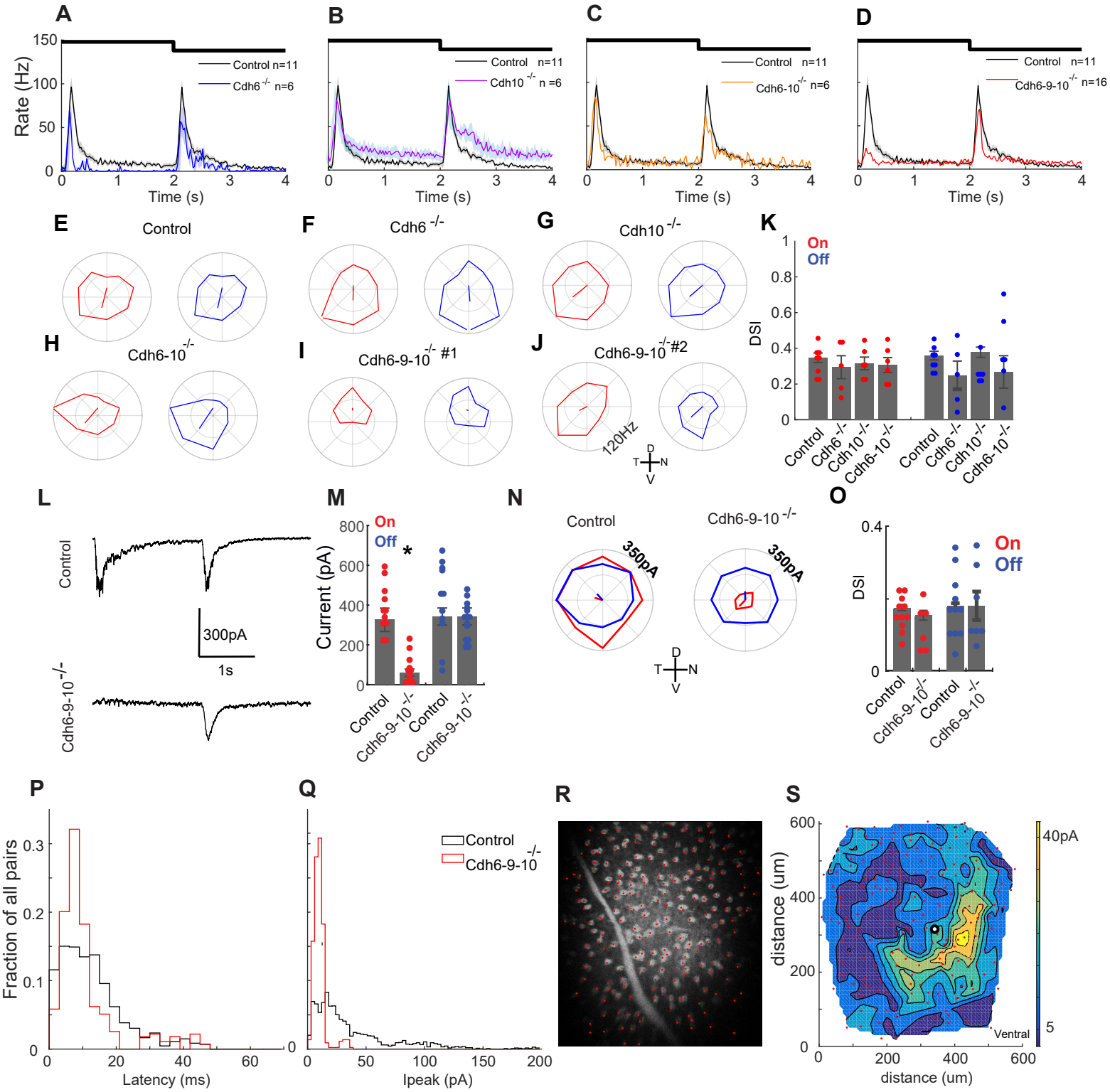

A
Control
Cdh6-9-10 -/-
Dr4-GFP
B
CHAT:Cre;DTR + Saline
CHAT:Cre;DTR + D.T.
Dr4-GFP
C
TPM
250
200
150
100
50
0
Drd4 (N-ooDSGCs)
Hb9 (V-ooDSGCs)
SAC
*
***
Cdh1
Cdh2
Cdh3
Cdh4
Cdh15
Cdh5
Cdh6
Cdh7
Cdh8
Cdh9
Cdh10
Cdh11
Cdh12
Cdh18
Cdh19
Cdh20
Cdh22
Cdh24
Type I-Cdhs
Type II-Cdhs
D
TPM
4000
3000
2000
1000
0
Drd4 (N-ooDSGCs)
Hb9 (V-ooDSGCs)
SAC
Rbpms
Slc17a6
Chat
Megf10
Sox2
Tfap2a
Tfap2b
Opn1mw
Vsx2
Grm6
Chrna1
Chrne

Figure S4


A
B
C
D
Rate (Hz)
Time (s)
Control n=11
Cdh6 -/- n=6
Cdh10 -/- n =6
Cdh6-10 -/- n=6
Cdh6-9-10 -/- n=16
E
Control
F
Cdh6 -/-
G
Cdh10 -/-
H
Cdh6-10 -/-
I
Cdh6-9-10 -/- #1
J
Cdh6-9-10 -/-#2
120HZ
K
On
Off
DSI
L
Control
300pA
1s
Cdh6-9-10 -/-
M
Current (pA)
*
N
Control
Cdh6-9-10 -/-
350pA
O
P
Fraction of all pairs
Latency (ms)
Q
Control
Cdh6-9-10 -/-
Ipeak (pA)
R
S
distance (um)
Ventral
40pA
5

CADHERIN COMBINATIONS RECRUIT DENDRITES OF DISTINCT RETINAL NEURONS TO A SHARED INTERNEURONAL SCAFFOLD

SUPPLEMENTARY FIGURE LEGENDS

Figure S1. Generation and validation of cadherin mutants. (Related to Figure 1)

(A, B) Recombineering strategy to replace the first coding exon of *cdh6* (A) and *cdh10* (B) with CreER.

(C, D) Loss of Cdh6 and Cdh10 immunoreactivity in *Cdh6* (C) and *Cdh10* (D) mutants. Bar is 20μm.

(E, F) Expression of *cdh6* mRNAs in V-ooDSGCs (Hb9-GFP, E) and N-ooDSGCs (Drd4-GFP, F). 84±3% of V-ooDSGCs and 3±2% of N-ooDSGCs are *cdh6*-positive (n=55 and 58 cells each).

(G, H) Expression of *cdh10* mRNAs in V-ooDSGCs (Hb9-GFP) (G) and N-ooDSGCs (Drd4-GFP) (H). 72±4% of V-ooDSGCs and 6±4% of N-ooDSGCs are *cdh10*-positive (n=35 and 52 cells each).

(I, J) Increased *cdh9* expression in V-ooDSGCs and other retinal cells in *Cdh6-10* mutant retinas compared to controls. In E-I, gene expression was assayed in P14 retinal sections by in situ hybridization using TSA detection. Sections were counterstained with anti-GFP and Neurotrace. BCs, bipolar cells; ACs, amacrine cells; RGCs, retinal ganglion cells. Top panel in (I) shows expression of *cdh9* in bipolar cells as shown previously (Duan et al., 2014) and (J) shows enrichment of *thy1* in RGCs. Cdh9 is expressed in 76% (83/109) of cells in the inner part of the INL (mostly amacrine cells) and in 24% (26/109) of cells in the ganglion cell layer (RGCs and amacrine cells); <2% (1/75) of cells in either layer were detectable cdh9-positive in wild-type mice. Scale bars, 10μm.

(K, L) CRISPR/Cas9-mediated genome-engineering strategy to introduce indels into the first coding exon of *cdh9* on the *Cdh6-10* (J) or *Cdh9-10;Hb9-GFP* (K) background.

(M) CRISPR/Cas9-mediated genome-engineering strategy to generate a conditional *Cdh6* allele ($Cdh6^{Flx}$), with its Exon 2 floxed by two LoxP sites, on the *Cdh9-10;Hb9-GFP* background.

Figure S2. Deletion of *cdh6, cdh9 and cd10* has no detectable effect on lamination of several types of bipolar, amacrine and retinal ganglion cells. (Related to Figure 1)

(A) D/V-ooDSGCs (YFP) in control and *Cdh6-9-10* mutants retain CART, a specific marker for ooDSGCs amongst RGCs (Kay et al., 2011). A subset of amacrines is also labeled.

(B) Cdh6, 9 and 10 are not required for formation of lamina specific arbors of Type 3a bipolar cells (HCN4), Type 2 bipolar cells (Syt2), Rod bipolar cells (PKCα), or dopaminergic amacrine cells (Tyrosine Hydroxylase).

(C) Cdh6, 9 and 10 are not required for formation of lamina specific arbors of VG3-ACs (VGlut3), Type 1 and 2 ipRGCs (melanopsin), S3-projecting RGCs (Kv4.2) or S1-projecting RGCs (Sorcs3; see (Liu et al., 2018)).

Scale bars, 20 μm.

(D) High magnification images of ooDSGC dendrites in control (top) and *Cdh6-9-10* mutant (bottom) retinas. Note that ooDSGC dendrites lose co-fasciculation with SACs in the mutants. Scale bar, 10 μm.

Figure S3. Differential roles and expression of Cdhs in V-ooDSGCs and N-ooDSGCs.

(Related to Figure 3)

(A) N-ooDSGC (Drd4-GFP, green) and SAC dendrites (vAChT, red) in control and *Cdh6-9-10* mutants. NT, Neurotrace, blue.

(B) N-ooDSGC (Drd4-GFP, green) and SAC dendrites (vAChT, red) in control (+saline) and SAC-depleted retinas (+ D.T.). Bars are 20μm.

(C-D) RNA-seq analysis showing expression levels of classical (Types I and II) Cdhs (C) and other genes (D) in developing V-ooDSGCs (Hb9-GFP, n=8), N-ooDSGCs (Drd4-GFP, n=4) and SACs (n=3) at P5-7. D includes genes known to be expressed selectively in RGCs (Rbpms, Slc17a6), SACs (ChAT, Megf10, Sox2), amacrines generally (Tfap2a,b), cones (Opn1mw), or bipolars (vsx2, grm6), or in no retinal cells (Chrna1, Chrne) TPM, Transcripts Per Kilobase Million. Error bars represent SEM among replicates. *** indicates $p<0.005$ and * indicates $p<0.05$

Figure S4. Recordings from ooDSGCs in mice lacking Cdh6, Cdh9 and Cdh10, alone and in combination. (Related to Figure 4)

(A-D) Histogram of spike responses to a small spot (200μm diameter) flashed for 2 seconds on Hb9-RGCs recorded in (A) *Cdh6*, (B) *Cdh10*, (C) *Cdh6-10*, and (D) *Cdh6-9-10* mutants. Rates were calculated using a bin width of 25ms and spike histogram recorded in control ($Cdh6^{CreER/+}$ Heterozygotes) is shown for comparison. ON responses are severely reduced in the absence of *Cdh9*. Solid lines are average firing rate and shading is (± SEM). Sample numbers for each condition are indicated in the legend.

(E-J) Sample polar plots of spike responses and associated DSI vector to a bright bar moving in 8 different directions in V-ooDSGCs recorded in (E) control, (F) *Cdh6* mutants, (G) *Cdh10* mutants, (H) *Cdh6-10* mutants, and (I-J) *Cdh6-9-10* mutants. The examples in (I) and (J) show rarely encountered response variants that are ON-OFF direction non-selective (2 out of 14 cells), and ON-OFF weakly direction-selective (1 out of 14 cells). The common pattern is shown in

Figure 4D. Control sample (E) replotted from Figure 4D for comparison. Firing rates and DSI indicated on outer radius.

(K) Average DSI for experiments shown in E-J. Bars show average ± SEM.

(L) Inward currents recorded from V-ooDSGCs in control (top) and *Cdh6-9-10* mutant (bottom) retinae to a ~200μm flashing spot.

(M) Average peak inward current recorded from V-ooDSGCs in control (n=11) and *Cdh6-9-10* mutant (n=15) in response to the onset (red) and offset (blue) of a flashing spot. ON inward currents are strongly reduced in *Cdh6-9-10* mutant retinae. * indicated $p<0.05$.

(N) Polar plot of excitatory currents on V-ooDSGCs evoked by a bar moving in 8 directions in control (top) and *Cdh6-9-10* mutant (bottom) retinas. Leading (On, red) and trailing (Off, blue) edge responses are shown separately. On inward currents are reduced in *Cdh6-9-10* mutant retina.

(O) Average DSI computed from experiments in (n) for control (n = 11 cells) and *Cdh6-9-10* mutant (n = 7 cells) V-ooDSGCs.

(P) Histogram of synaptic latencies recorded for all SAC to V-ooDSGC pairs in control and *Cdh6-9-10* mutant retinae. Counts are expressed as a fraction of all recorded pairs.

(Q) Histogram of peak synaptic current amplitude recorded for all SAC to V-ooDSGC pairs in control and *Cdh6-9-10* mutant retinas. Counts are expressed as a fraction of all recorded pairs. SAC to V-ooDSGC connections are substantially weaker in *Cdh6-9-10* mutant retinae.

(R) Field of ChR2-positive SACs marked for stimulation.

(S) Contour map of peak current amplitude on a control V-ooDSGC (white circle in the center) in evoked by stimulating ChR2-positive SACs (red dots) shown in (R). Color-bar denotes peak amplitude of evoked currents.