

Supplemental Figures

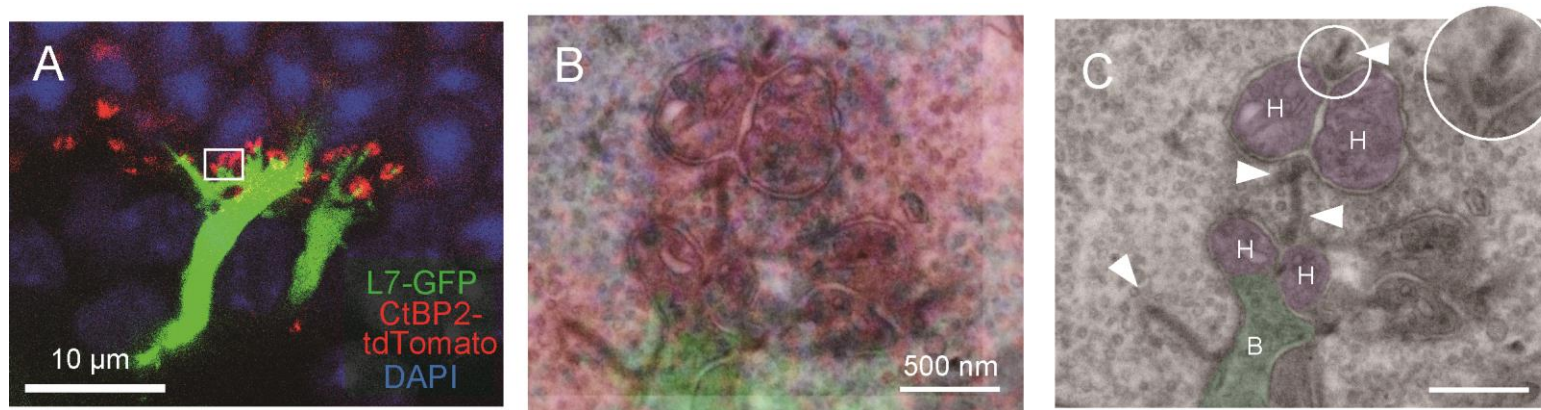


Figure S1. Correlative array tomography images of host-graft synapse after retinal organoid transplantation.

(A) Fluorescent image obtained by confocal microscopy of the host-graft synapse (Green; L7-GFP, Red; CtBP2-tdTomato, Blue; DAPI).

(B) High magnification overlaid image of confocal and Field emission scanning electron microscopy (FE-SEM) image of host-graft synapse. (Green; L7-GFP, Red; CtBP2-tdTomato, Blue; DAPI).

(C) FE-SEM image corresponding to (D) and (E) respectively. Cell types of each process are labelled as follows: H; horizontal cell (colored by purple), B; bipolar cells (colored by green). White arrowheads indicate synaptic ribbons, the yellow arrows indicate the fluffy density and the white circle indicate the arciform density. The arciform density is magnified without pseudocolor as inset in the (C).

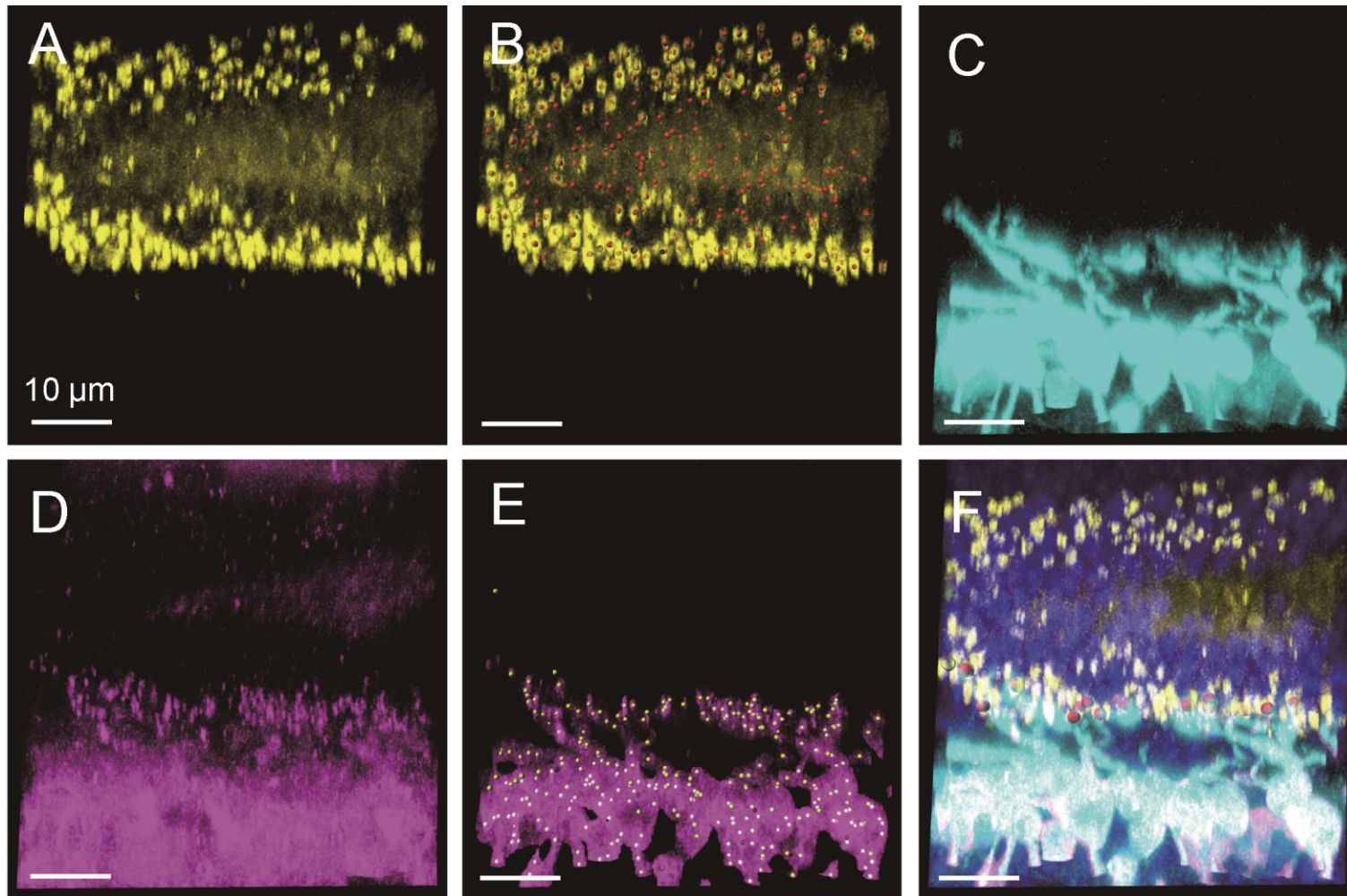


Figure S2. Steps for Semi-automated 3D quantification of host-graft synapse by Imaris software.

(A) Confocal image of post-transplantation retina was masked for the CtBP2-tdTomato signal with auto-threshold.

(B) “spot” detection function of Imaris software was used to detect the center coordinates of the presynaptic CtBP2. Detected spots were indicated by red dots.

(C) Host rod bipolar cells were masked with L7-GFP signal with auto-threshold.

(D) Postsynaptic mGluR6 immunostaining signal was masked with the mask for L7-GFP in order to eliminate the non-specific staining outside the host rod bipolar cell.

(E) “spot” detection function of Imaris software was used to detect the center coordinates of the postsynaptic mGluR6. Detected spots were indicated by yellow dots.

(F) “coloc” function was used to identify the pairs of pre-and postsynaptic markers that are within the 1 μm as host-graft synapses. Detected synapses are indicated by red spheres.

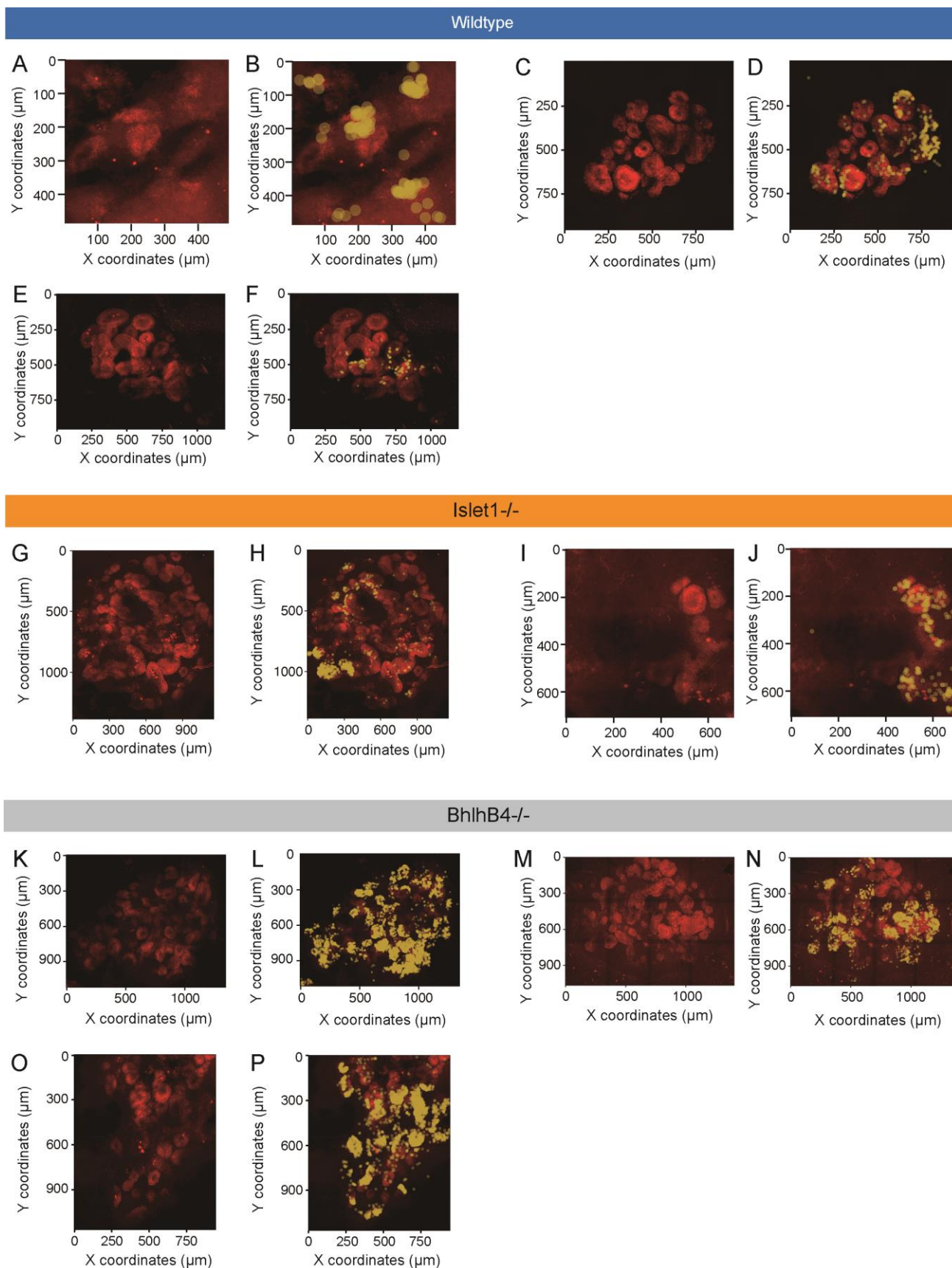


Figure S3. Semi-automated 3D quantification of host-graft synapse after wildtype, *isl*^{-/-} and

bhlhb4-/- graft transplantation from all samples.

(A) 1st sample of whole-mount confocal image of CtBP2 channel of rd1 retina after wildtype graft transplantation.

(B) Detected host-graft synapse coordinates overlaid to (A).

(C-D) 2nd sample of wildtype graft transplantation.

(E-F) 3rd sample of wildtype graft transplantation.

(G-H) 1st sample of Islet1-/- graft transplantation.

(I-K) 2nd sample of Islet1-/- graft transplantation.

(K-L) 1st sample of Bhlhb4-/- graft transplantation.

(M-N) 2nd sample of Bhlhb4-/- graft transplantation.

(O-P) 3rd sample of Bhlhb4-/- graft transplantation.

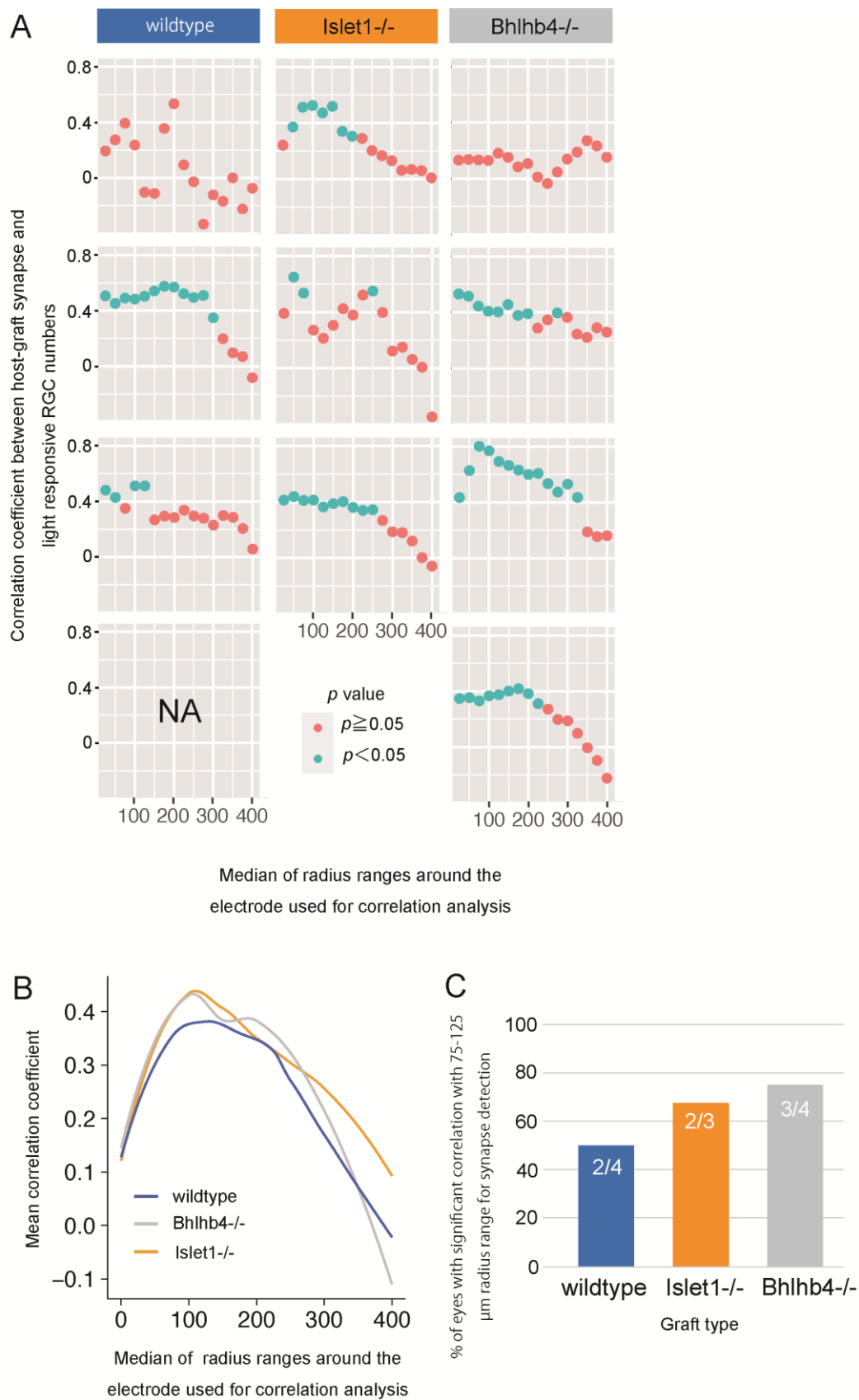


Figure S4. Correlation analysis between host-graft synapse number and light responsive

retinal ganglion cells (RGCs).

(A) Correlation coefficient of Pearson's rank correlation test between host-graft synapses detected within each 50- μm radial bin with a 25- μm step size from each individual electrode, and the number of detected light responsive RGCs from the corresponding electrode. For example, the correlation coefficients at 100- μm radius are calculated using the numbers of host-graft synapses within the distance of 75-125 μm from each individual electrode. Each panel represent data from single eye.

(B) Regression line of the mean correlation was calculated using "locally estimated scattered smoothing" method for all three graft types.

(C) The percentage of samples with statistically significant positive correlation ($p < 0.05$) between the number of synapses within $100 \pm 25 \mu\text{m}$ radial bin and the number of light responsive RGCs detected by the corresponding electrodes.

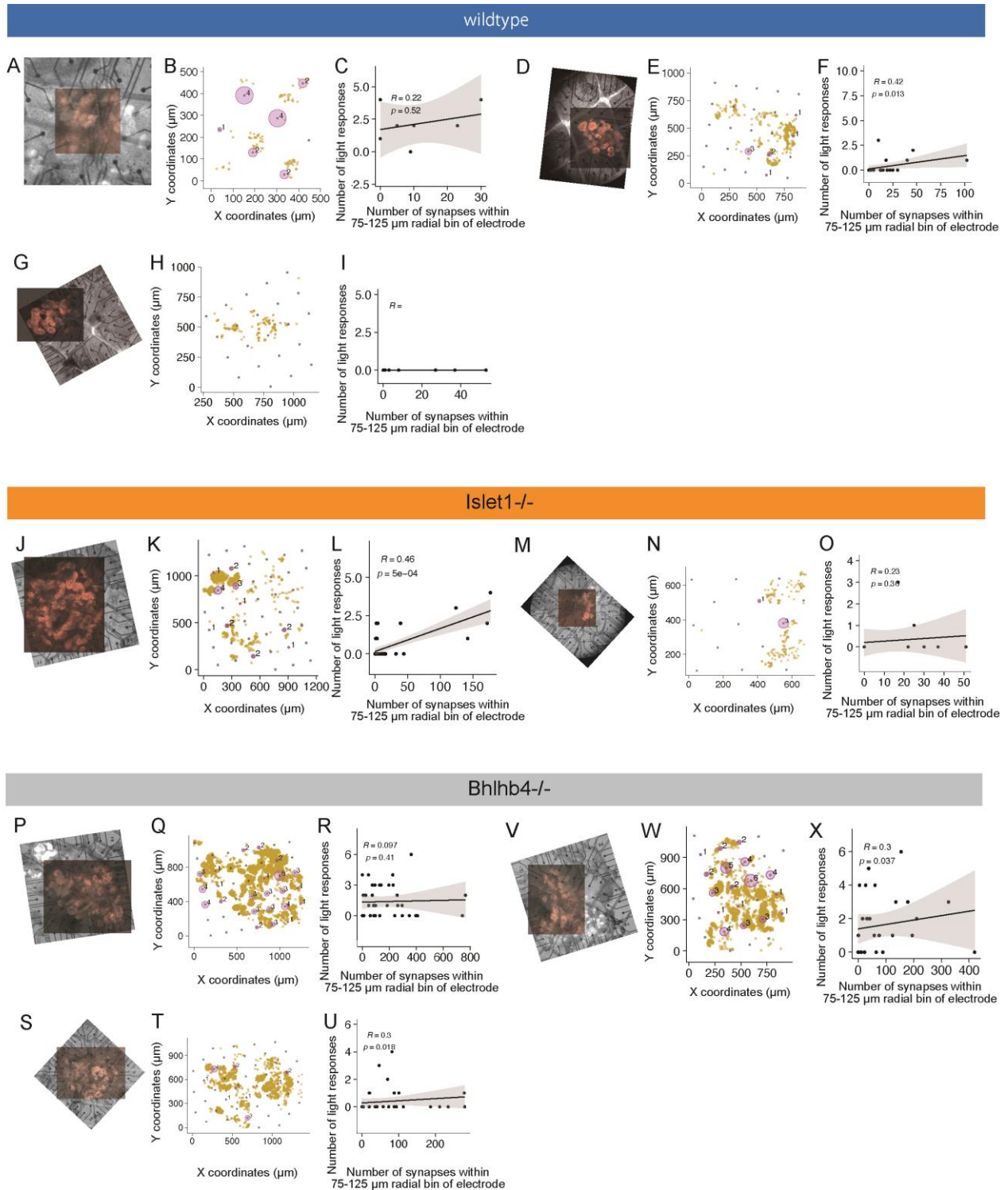


Figure S5 Correlation of host-graft synapse coordinates and multielectrode array (MEA) results from all samples.

(A) 1st sample of whole-mount confocal image of retina after wildtype graft transplantation

aligned and overlaid to infrared image taken during MEA recording.

(B) Coordinates of host-graft synapse (yellow dots) and the number of light-responsive host retinal ganglion cell (RGC) numbers (Purple circle and the numbers) from 1st sample of wildtype graft transplantation.

(C) Result of Spearman's rank correlation test between host-graft synapse numbers within $100 \pm 25 \mu\text{m}$ radial bin of MEA electrode and the number of light responsive RGC numbers detected by that electrode obtained from 1st sample after wildtype graft transplantation.

(D-F) Equivalent results obtained from 2nd wildtype graft transplantation.

(G-I) Equivalent results obtained from 3rd wildtype graft transplantation.

(J-L) Equivalent results obtained from 1st *Isl1*^{-/-} graft transplantation.

(M-O) Equivalent results obtained from 2nd *Isl1*^{-/-} graft transplantation.

(P-R) Equivalent results obtained from 1st *Bhlhb4*^{-/-} graft transplantation.

(S-U) Equivalent results obtained from 2nd *Bhlhb4*^{-/-} graft transplantation.

(V-X) Equivalent results obtained from 3rd *Bhlhb4*^{-/-} graft transplantation.