SUPPLEMENTAL FIGURES

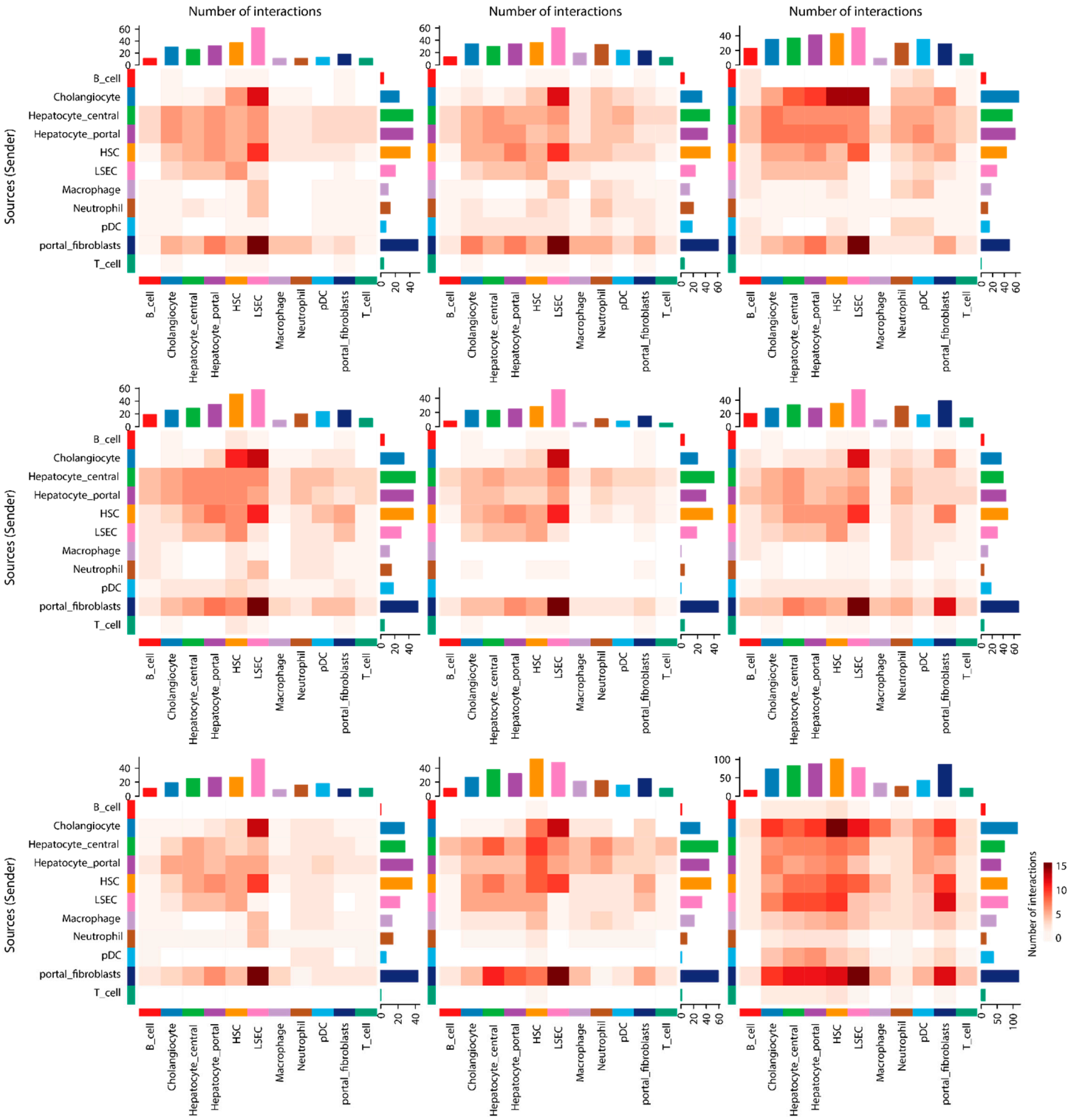

Figure S1. The number of incoming and outgoing inferred interactions across cell types following TCDD treatment. Hepatic snRNAseq data from male mice gavaged with sesame oil or 0.01 – 30 ug/kg TCDD every 4 days for 28 days was analyzed for cell-cell interactions via secreted factors using CellChat. The number of inferred interactions is shown as outgoing and incoming across all cell types.

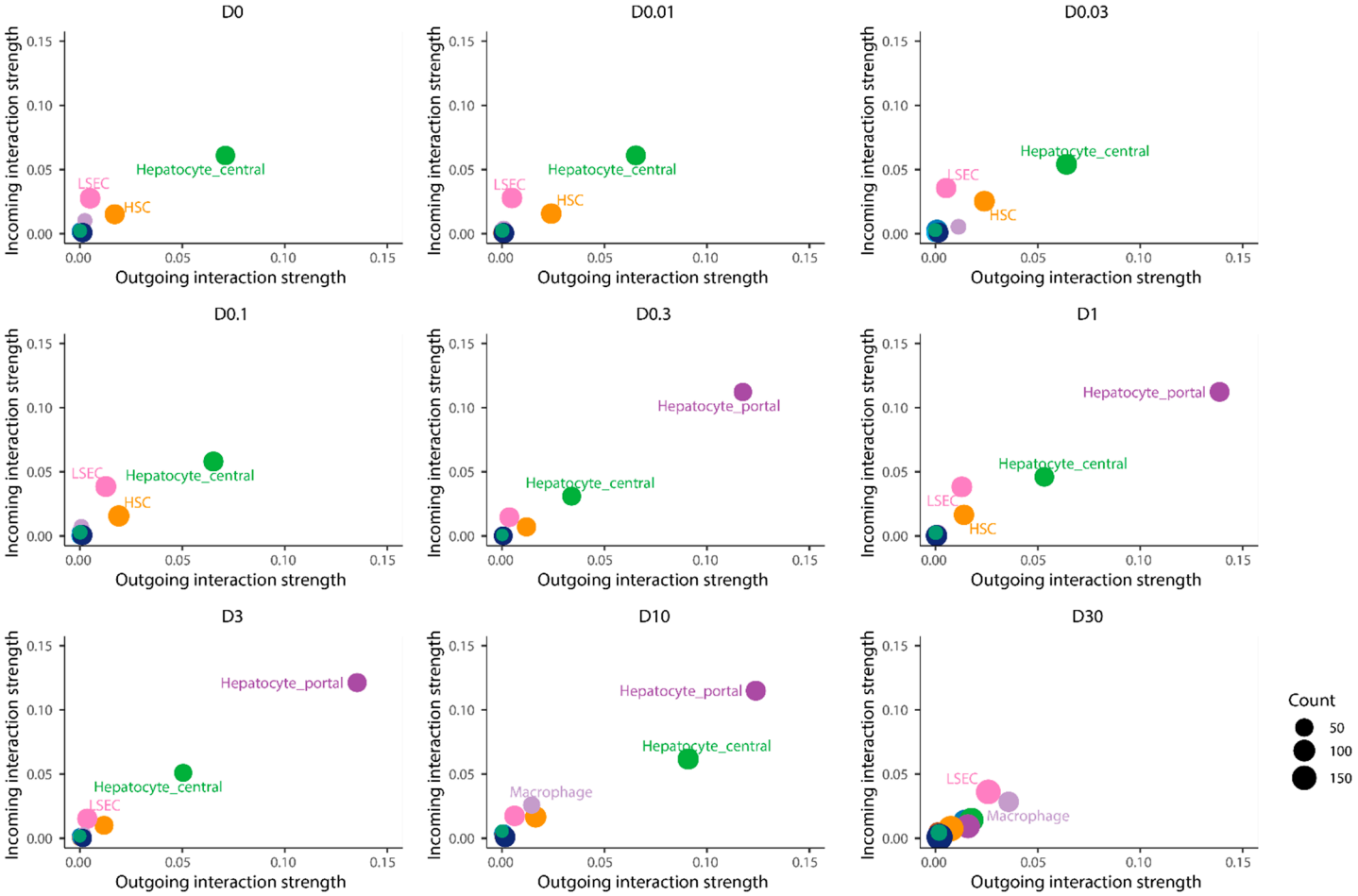

Figure S2. Incoming and outgoing interaction strength across cell types and TCDD dose. Hepatic snRNAseq data from male mice gavaged with sesame oil or 0.01 – 30 μg/kg TCDD every 4 days for 28 days was analyzed for cell-cell interactions using CellChat. Interaction strengths were estimated for outgoing and incoming inferred interactions across all cell types and are shown for each dose group showing dose-dependent changes in contributions of cell types to cell-cell interactions following treatment with TCDD.

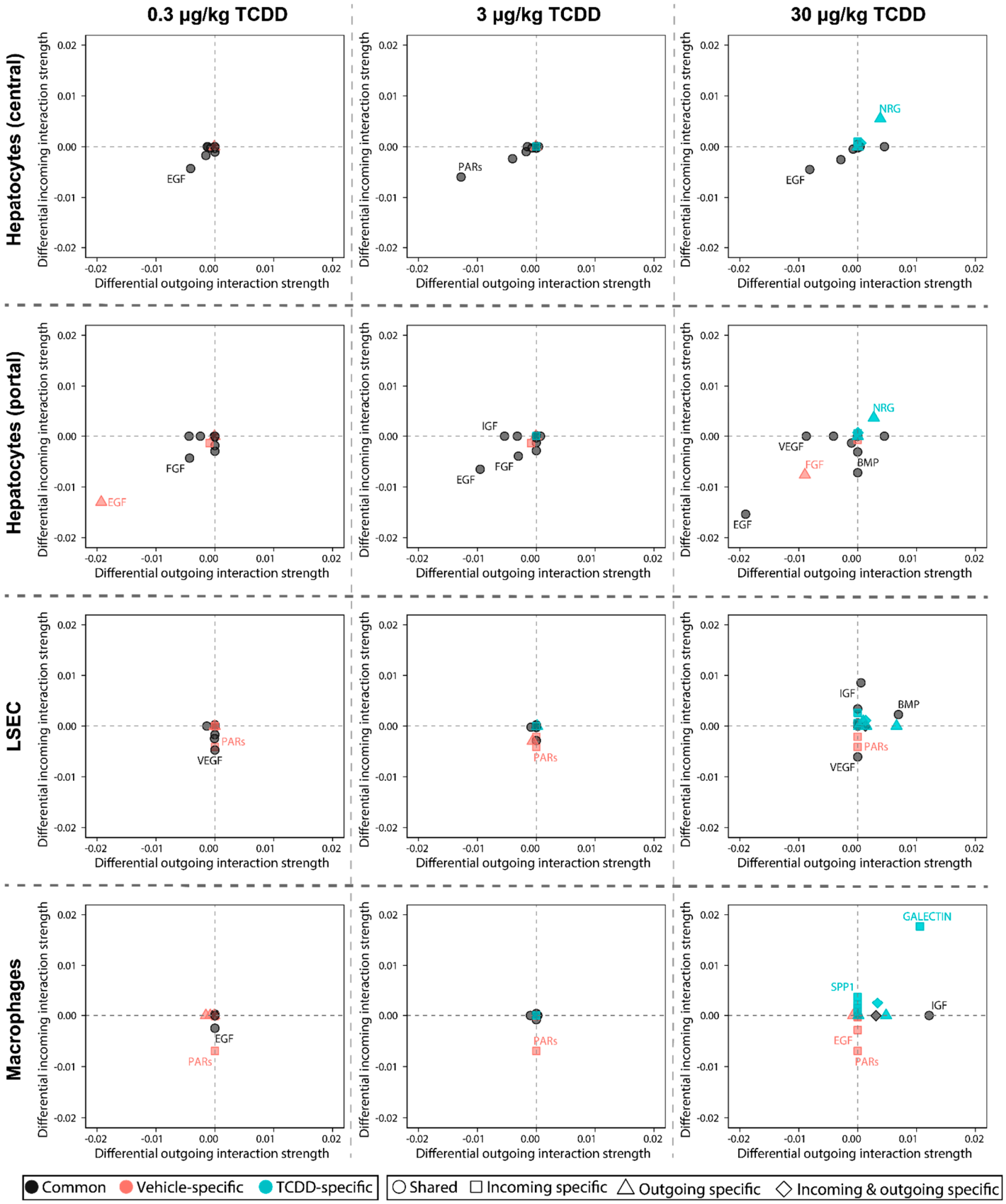

Figure S3. Changes in incoming and outgoing signaling across portal and central hepatocytes, LESCs and macrophages. The interaction strength between vehicle and 30 µg/kg TCDD dose groups were compared for each signaling pathway in each cell type.

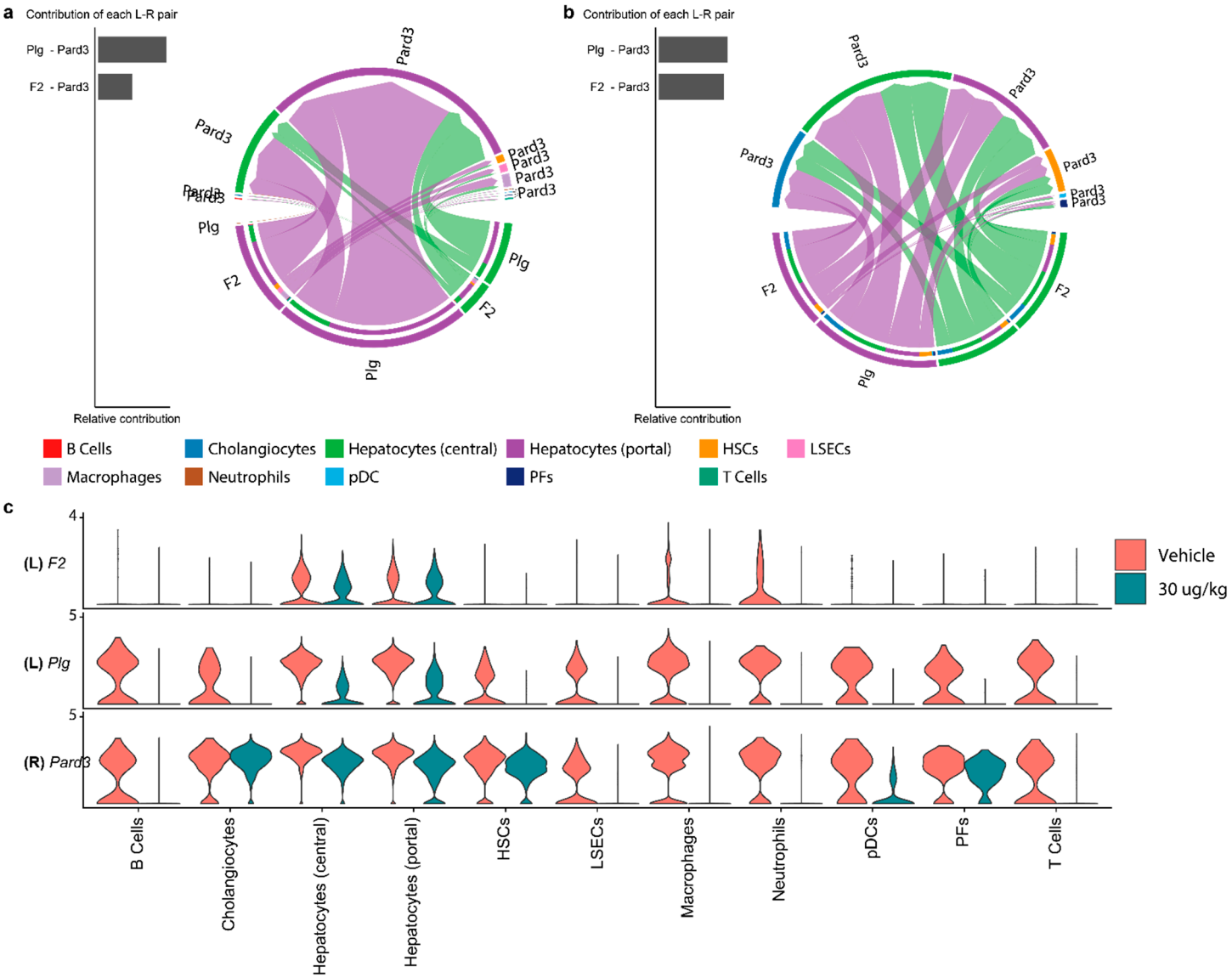

Figure S4. Contributions of individual PARs ligand-receptor pairs. Inferred PARs signaling interactions between cells were examined for specific ligand-receptor (L-R) pair interactions in (a) vehicle and (b) 30 μg/kg TCDD treated groups. Chord plots show the ligand expressed by a specific cell type (outer lower ring), the cell type receiving the L (inner lower ring), and the cell type expressing the R (outer upper ring). Color represents the L-R pair interactions by cell type. (c) Expression levels of contributing ligands (L) and receptors (R) in the snRNAseq dataset are shown for each cell type in the vehicle and 30 μg/kg TCDD dose groups.

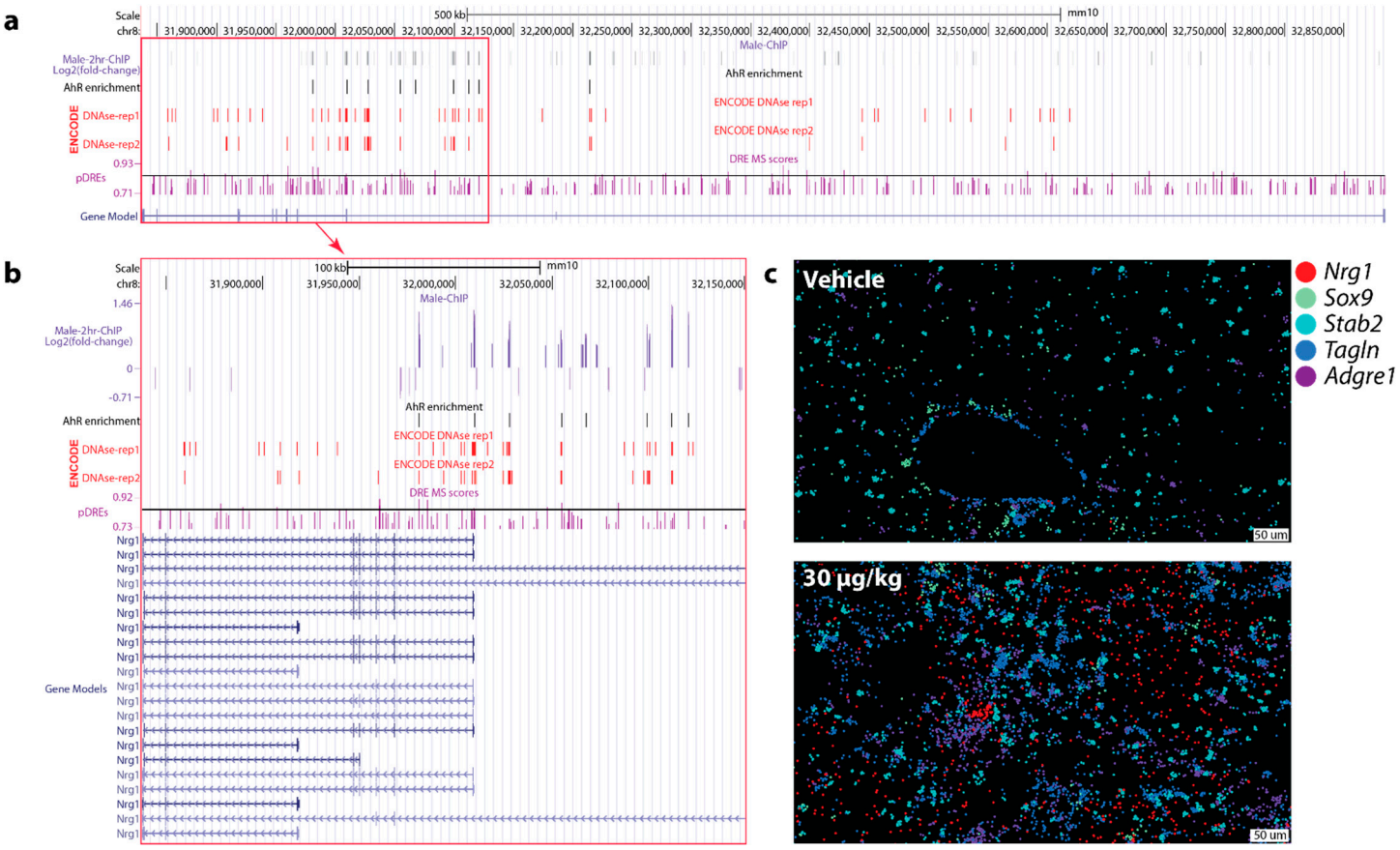

Figure S5. *Nrg1* induction by TCDD-mediated AHR activation. (a) *Nrg1* region of the mm10 mouse genome shown in UCSC Genome Browser (https://genome.ucsc.edu/) and (b) magnification of the *Nrg1* region showing the most binding of AHR by ChIP-seq and multiple *Nrg1* isoform start sites. Tracks from top to bottom show AHR enrichment compared to IgG control determined by ChIP-seq (GSE109865); Regions demonstrating significant AHR enrichment (adjusted p-value ≤ 0.05); two replicates for DNAse hypersensitivity data showing accessible chromatin regions determined by the Encyclopedia of DNA elements (ENCODE) for livers of adult (8 weeks) male mice (GSM1014195); calculated matrix similarity scores (MSS) for putative dioxin response elements (pDREs; https://doi.org/10.7910/DVN/JASCVZ/HX9XWZ) with a line delineating a significance threshold of 0.856; and *Nrg1* gene models. (c) Spatially resolved *Nrg1* expression (red) as well as cell types markers *Sox9* (green, cholangiocytes), *Stab2* (aqua, LSEC), *Tagln* (blue, HSC), and *Adgre1* (purple, macrophages) was determined using the Resolve Biosciences Molecular Cartography platform as previously described (GSE206294; SCP1875) [19].