

Description of Additional Supplementary Files:

Supplementary Dataset 1: Output from SpatialDM, SpatialCorr, Giotto, CellChat (Trimean & Truncated-mean) and SpaTalk (in separated sheets) in the melanoma dataset.

Supplementary Dataset 2: Output from SpatialDM, SpatialCorr, Giotto, CellChat (Trimean & Truncated-mean) and SpaTalk in the melanoma dataset with 663 unique shuffled pairs to reflect false positive selections.

Supplementary Dataset 3: Full lists of interactions belonging to the 3 clusters in the melanoma dataset (Fig 2b)

Supplementary Dataset 4: GO analysis result for FCER-upregulated spots in the melanoma dataset (Supplementary Figure 3e)

Supplementary Dataset 5: SpatialDM identified results (FDR<0.05) for pairs discussed by Corbett, et al.

Supplementary Dataset 6: SpatialDM results for the 8 samples from the intestine dataset.

Supplementary Dataset 7: Full lists of interactions belonging to the 4 clusters in the intestine dataset (Fig 3d & Supplementary Figure 7a)

Supplementary Dataset 8: Differential analysis for the interactions in the intestine dataset with differential p-values computed by the likelihood-ratio test of global zscores.