**Supplementary Table S1**. **Summary of biomarker genes identified and used in this study.** Data-driven markers consist of the top 9 representative DE genes for each cell type, identified using differential expression analysis. Prior knowledge-based gene markers represent gene sets curated from the published literature.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Marker type** | **Cell type** | | | | | | | |
|  | Cycling SC | DCS (types 1 and 2) | EC | EEC | Goblet (types 1 and 2) | Noncycling SC | TA | Tuft cell |
| Data driven | Csrp2  Hspd1  Mgst1  Ran  Ppia  Stmn1  Rack1  C1qbp  Ybx1 | Hsd11b2  Ramp1  Spink4  Reg4  Fcgbp  Ly6e  Best2  Atoh1  Mptx1 | Krt19  Krt8  Lgals3  Lypd8  Selenbp1  Lgals4  Ethe1  Fth1  Gsdmc4 | Cpe  Chga  Pcsk1n  Map1b  Neurod1  Scg5  Insm1  Ddc  Resp18 | Agr2  Muc2  Smim14  Gfpt1  Txndc5  Tspan13  Spdef  Tpd52  Stard10 | Gas5  Eef1b2  Gm6368  Sdc4  Zfas1  Eef1a1  Rps3a1  Snhg1  Rack1 | Ptma  Atp5g2  Hmgb1  Wdr89  Aldh1b1  Hsp90ab1  Grh42418  Ubb  Gpx2 | Tuba1a  St18  Kctd12  Rgs13  Ltc4s  Trpm5  Sh2d6  Fyb  Avil |
| Prior knowledge | Kcnq1  Mki67  PCNA  Smoc2  Stmn1  Tifa  Tuba1b  Tubb5  Aqp1  Lgr5  Ascl2  Ube2c | Clec2h  Fhl1  Spink1  Zg16  Tff3  Copz2  Reg4  Dll4  Dll1 | Maob  Ces2a  Ces2c  Ces2e  Chp2  Coro2a  Cyp2c65  Cyp2c68  Dgkq  Dpep1  Emp1  Krt20  Cdkn1a  Lgals3  Mxd1  Sprr2a3  Fam3b  Clec2h  Fhl1  Gde1  Guca2a  Il18 | Chgb  Bex2  Pcsk1  Marcksl1 | Syt7  Ang  MUC2  Agr2  Ccl9  Anxa3  Bcas1  Fcgbp  Mlph  Rab27b  Rep15  Sytl2  Cbfa2t3  Etv5  Galnt5  Galnt10  Kcnh3  Kcnk6  Mon1a  Mt3  Sec24d  Sidt1  Stk38l  Tpd52l1  Ccl6  Fam103a1  Foxa3  Guca2b  Rassf6  Spink4  Guca2a  Tff3 | Ung  Acot1  Lgr5  Birc5  Top2a  Gjb3  Ascl2  Ccdc34  Soat1 | Nrarp  Ifngr2  Sfn | Lrmp  Dclk1  Alox5ap |

**Supplementary Table S2. Results of Kolmogorov-Smirnov tests associated with the velocity length of WT and Ahr KO samples.** The K-S test was used to decide whether the velocity length from the KO and WT samples comes from the same distribution. The K-S statistics and P-values show that across all cell types, the distribution of the velocity length of the KO sample is different from that of the WT sample. In all cases, the mean of the velocity length of the KO sample is greater than that of the WT sample.

|  |  |  |
| --- | --- | --- |
| **Cell type** | **KS statistic** | **P-value** |
| Cycling SC | 0.57 | 2.80e-154 |
| DCS (type 1) | 0.33 | 3.40e-29 |
| DCS (type 2) | 0.11 | 1.20e-05 |
| EC | 0.49 | 7.40e-149 |
| EEC | 0.81 | 2.50e-114 |
| Goblet (type 1) | 0.68 | 2.10e-167 |
| Goblet (type 2) | 0.59 | 2.60e-89 |
| Noncycling SC | 0.74 | 2.50e-132 |
| TA | 0.69 | 2.10e-160 |
| Tuft cell | 0.89 | 2.90e-63 |

**Supplementary Table S3**. **CellChat-identified significant ligand-receptor pairs in WT crypt cells.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Source** | **Target** | **Ligand** | **Receptor** | **Prob** | **P-value** | **Interaction\_ name** | **Pathway\_ name** |
| 1 | Noncycling SC | EEC | Hbegf | Egfr | 4.22E-09 | 0 | HBEGF\_EGFR | EGF |
| 2 | Noncycling SC | Goblet (type 1) | Hbegf | Egfr | 4.22E-09 | 0 | HBEGF\_EGFR | EGF |
| 3 | EEC | EEC | Pyy | Npy1r | 3.84E-07 | 0 | PYY\_NPY1R | NPY |
| 4 | Cycling SC | DCS (type 1) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 5 | EC | DCS (type 1) | Kitl | Kit | 5.06E-08 | 0 | KITL\_KIT | KIT |
| 6 | Noncycling SC | DCS (type 1) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 7 | TA | DCS (type 1) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 8 | Cycling SC | DCS (type 2) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 9 | EC | DCS (type 2) | Kitl | Kit | 5.06E-08 | 0 | KITL\_KIT | KIT |
| 10 | Noncycling SC | DCS (type 2) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 11 | TA | DCS (type 2) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 12 | Cycling SC | Goblet (type 1) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 13 | EC | Goblet (type 1) | Kitl | Kit | 5.06E-08 | 0 | KITL\_KIT | KIT |
| 14 | Noncycling SC | Goblet (type 1) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 15 | TA | Goblet (type 1) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 16 | Cycling SC | Goblet (type 2) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 17 | EC | Goblet (type 2) | Kitl | Kit | 5.06E-08 | 0 | KITL\_KIT | KIT |
| 18 | Noncycling SC | Goblet (type 2) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 19 | TA | Goblet (type 2) | Kitl | Kit | 6.75E-08 | 0 | KITL\_KIT | KIT |
| 20 | Cycling SC | Tuft cell | Kitl | Kit | 1.69E-08 | 0 | KITL\_KIT | KIT |
| 21 | EC | Tuft cell | Kitl | Kit | 1.27E-08 | 0 | KITL\_KIT | KIT |
| 22 | Noncycling SC | Tuft cell | Kitl | Kit | 1.69E-08 | 0 | KITL\_KIT | KIT |
| 23 | TA | Tuft cell | Kitl | Kit | 1.69E-08 | 0 | KITL\_KIT | KIT |
| 24 | DCS (type 2) | DCS (type 1) | Grn | Sort1 | 3.80E-08 | 0.01 | GRN\_SORT1 | GRN |
| 25 | Noncycling SC | DCS (type 1) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 26 | Cycling SC | DCS (type 2) | Grn | Sort1 | 1.69E-08 | 0 | GRN\_SORT1 | GRN |
| 27 | DCS (type 2) | DCS (type 2) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 28 | EC | DCS (type 2) | Grn | Sort1 | 1.69E-08 | 0.01 | GRN\_SORT1 | GRN |
| 29 | Goblet (type 1) | DCS (type 2) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 30 | Goblet (type 2) | DCS (type 2) | Grn | Sort1 | 1.69E-08 | 0.04 | GRN\_SORT1 | GRN |
| 31 | Noncycling SC | DCS (type 2) | Grn | Sort1 | 6.75E-08 | 0 | GRN\_SORT1 | GRN |
| 32 | TA | DCS (type 2) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 33 | Cycling SC | Goblet (type 1) | Grn | Sort1 | 1.69E-08 | 0.01 | GRN\_SORT1 | GRN |
| 34 | DCS (type 1) | Goblet (type 1) | Grn | Sort1 | 1.69E-08 | 0.05 | GRN\_SORT1 | GRN |
| 35 | DCS (type 2) | Goblet (type 1) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 36 | EC | Goblet (type 1) | Grn | Sort1 | 1.69E-08 | 0.01 | GRN\_SORT1 | GRN |
| 37 | Goblet (type 1) | Goblet (type 1) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 38 | Noncycling SC | Goblet (type 1) | Grn | Sort1 | 6.75E-08 | 0 | GRN\_SORT1 | GRN |
| 39 | TA | Goblet (type 1) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 40 | DCS (type 2) | Goblet (type 2) | Grn | Sort1 | 3.80E-08 | 0.02 | GRN\_SORT1 | GRN |
| 41 | Noncycling SC | Goblet (type 2) | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 42 | DCS (type 2) | Noncycling SC | Grn | Sort1 | 3.80E-08 | 0.03 | GRN\_SORT1 | GRN |
| 43 | Goblet (type 1) | Noncycling SC | Grn | Sort1 | 3.80E-08 | 0.05 | GRN\_SORT1 | GRN |
| 44 | Noncycling SC | Noncycling SC | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 45 | DCS (type 2) | TA | Grn | Sort1 | 3.80E-08 | 0.01 | GRN\_SORT1 | GRN |
| 46 | Goblet (type 1) | TA | Grn | Sort1 | 3.80E-08 | 0.04 | GRN\_SORT1 | GRN |
| 47 | Noncycling SC | TA | Grn | Sort1 | 5.06E-08 | 0 | GRN\_SORT1 | GRN |
| 48 | Noncycling SC | Tuft cell | Grn | Sort1 | 1.69E-08 | 0.05 | GRN\_SORT1 | GRN |
| 49 | DCS (type 1) | Cycling SC | Guca2a | Gucy2c | 4.81E-07 | 0.04 | GUCA2A\_GUCY2C | GUCA |
| 50 | DCS (type 2) | Cycling SC | Guca2a | Gucy2c | 7.47E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 51 | EC | Cycling SC | Guca2a | Gucy2c | 5.57E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 52 | Goblet (type 1) | Cycling SC | Guca2a | Gucy2c | 1.14E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 53 | Goblet (type 2) | Cycling SC | Guca2a | Gucy2c | 8.35E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 54 | DCS (type 1) | EC | Guca2a | Gucy2c | 6.41E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 55 | DCS (type 2) | EC | Guca2a | Gucy2c | 9.96E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 56 | EC | EC | Guca2a | Gucy2c | 7.43E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 57 | Goblet (type 1) | EC | Guca2a | Gucy2c | 1.52E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 58 | Goblet (type 2) | EC | Guca2a | Gucy2c | 1.11E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 59 | DCS (type 1) | EEC | Guca2a | Gucy2c | 6.41E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 60 | DCS (type 2) | EEC | Guca2a | Gucy2c | 9.96E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 61 | EC | EEC | Guca2a | Gucy2c | 7.43E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 62 | Goblet (type 1) | EEC | Guca2a | Gucy2c | 1.52E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 63 | Goblet (type 2) | EEC | Guca2a | Gucy2c | 1.11E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 64 | DCS (type 1) | Goblet (type 1) | Guca2a | Gucy2c | 1.28E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 65 | DCS (type 2) | Goblet (type 1) | Guca2a | Gucy2c | 1.99E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 66 | EC | Goblet (type 1) | Guca2a | Gucy2c | 1.49E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 67 | Goblet (type 1) | Goblet (type 1) | Guca2a | Gucy2c | 3.04E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 68 | Goblet (type 2) | Goblet (type 1) | Guca2a | Gucy2c | 2.23E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 69 | DCS (type 1) | Goblet (type 2) | Guca2a | Gucy2c | 6.41E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 70 | DCS (type 2) | Goblet (type 2) | Guca2a | Gucy2c | 9.96E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 71 | EC | Goblet (type 2) | Guca2a | Gucy2c | 7.43E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 72 | Goblet (type 1) | Goblet (type 2) | Guca2a | Gucy2c | 1.52E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 73 | Goblet (type 2) | Goblet (type 2) | Guca2a | Gucy2c | 1.11E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 74 | DCS (type 1) | Noncycling SC | Guca2a | Gucy2c | 8.02E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 75 | DCS (type 2) | Noncycling SC | Guca2a | Gucy2c | 1.24E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 76 | EC | Noncycling SC | Guca2a | Gucy2c | 9.28E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 77 | Goblet (type 1) | Noncycling SC | Guca2a | Gucy2c | 1.90E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 78 | Goblet (type 2) | Noncycling SC | Guca2a | Gucy2c | 1.39E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 79 | DCS (type 1) | TA | Guca2a | Gucy2c | 6.41E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 80 | DCS (type 2) | TA | Guca2a | Gucy2c | 9.96E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 81 | EC | TA | Guca2a | Gucy2c | 7.43E-07 | 0 | GUCA2A\_GUCY2C | GUCA |
| 82 | Goblet (type 1) | TA | Guca2a | Gucy2c | 1.52E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 83 | Goblet (type 2) | TA | Guca2a | Gucy2c | 1.11E-06 | 0 | GUCA2A\_GUCY2C | GUCA |
| 84 | DCS (type 1) | Cycling SC | Guca2b | Gucy2c | 6.33E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 85 | DCS (type 2) | Cycling SC | Guca2b | Gucy2c | 1.52E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 86 | Goblet (type 1) | Cycling SC | Guca2b | Gucy2c | 7.59E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 87 | Goblet (type 2) | Cycling SC | Guca2b | Gucy2c | 5.06E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 88 | DCS (type 1) | DCS (type 1) | Guca2b | Gucy2c | 2.11E-08 | 0.04 | GUCA2B\_GUCY2C | GUCA |
| 89 | DCS (type 2) | DCS (type 1) | Guca2b | Gucy2c | 5.06E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 90 | Goblet (type 1) | DCS (type 1) | Guca2b | Gucy2c | 2.53E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 91 | DCS (type 1) | DCS (type 2) | Guca2b | Gucy2c | 2.11E-08 | 0.04 | GUCA2B\_GUCY2C | GUCA |
| 92 | DCS (type 2) | DCS (type 2) | Guca2b | Gucy2c | 5.06E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 93 | Goblet (type 1) | DCS (type 2) | Guca2b | Gucy2c | 2.53E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 94 | DCS (type 1) | EC | Guca2b | Gucy2c | 8.44E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 95 | DCS (type 2) | EC | Guca2b | Gucy2c | 2.03E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 96 | Goblet (type 1) | EC | Guca2b | Gucy2c | 1.01E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 97 | Goblet (type 2) | EC | Guca2b | Gucy2c | 6.75E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 98 | DCS (type 1) | EEC | Guca2b | Gucy2c | 8.44E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 99 | DCS (type 2) | EEC | Guca2b | Gucy2c | 2.03E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 100 | Goblet (type 1) | EEC | Guca2b | Gucy2c | 1.01E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 101 | Goblet (type 2) | EEC | Guca2b | Gucy2c | 6.75E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 102 | DCS (type 1) | Goblet (type 1) | Guca2b | Gucy2c | 1.69E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 103 | DCS (type 2) | Goblet (type 1) | Guca2b | Gucy2c | 4.05E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 104 | EC | Goblet (type 1) | Guca2b | Gucy2c | 3.38E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 105 | Goblet (type 1) | Goblet (type 1) | Guca2b | Gucy2c | 2.03E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 106 | Goblet (type 2) | Goblet (type 1) | Guca2b | Gucy2c | 1.35E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 107 | DCS (type 1) | Goblet (type 2) | Guca2b | Gucy2c | 8.44E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 108 | DCS (type 2) | Goblet (type 2) | Guca2b | Gucy2c | 2.03E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 109 | Goblet (type 1) | Goblet (type 2) | Guca2b | Gucy2c | 1.01E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 110 | Goblet (type 2) | Goblet (type 2) | Guca2b | Gucy2c | 6.75E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 111 | DCS (type 1) | Noncycling SC | Guca2b | Gucy2c | 1.05E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 112 | DCS (type 2) | Noncycling SC | Guca2b | Gucy2c | 2.53E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 113 | EC | Noncycling SC | Guca2b | Gucy2c | 2.11E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 114 | Goblet (type 1) | Noncycling SC | Guca2b | Gucy2c | 1.27E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 115 | Goblet (type 2) | Noncycling SC | Guca2b | Gucy2c | 8.44E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 116 | DCS (type 1) | TA | Guca2b | Gucy2c | 8.44E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 117 | DCS (type 2) | TA | Guca2b | Gucy2c | 2.03E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 118 | Goblet (type 1) | TA | Guca2b | Gucy2c | 1.01E-07 | 0 | GUCA2B\_GUCY2C | GUCA |
| 119 | Goblet (type 2) | TA | Guca2b | Gucy2c | 6.75E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 120 | DCS (type 1) | Tuft cell | Guca2b | Gucy2c | 2.11E-08 | 0.04 | GUCA2B\_GUCY2C | GUCA |
| 121 | DCS (type 2) | Tuft cell | Guca2b | Gucy2c | 5.06E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 122 | Goblet (type 1) | Tuft cell | Guca2b | Gucy2c | 2.53E-08 | 0 | GUCA2B\_GUCY2C | GUCA |
| 123 | Cycling SC | Cycling SC | Lgals9 | Cd44 | 8.44E-09 | 0 | LGALS9\_CD44 | GALECTIN |
| 124 | Goblet (type 1) | Cycling SC | Lgals9 | Cd44 | 8.44E-09 | 0 | LGALS9\_CD44 | GALECTIN |
| 125 | Goblet (type 2) | Cycling SC | Lgals9 | Cd44 | 8.44E-09 | 0 | LGALS9\_CD44 | GALECTIN |
| 126 | Noncycling SC | Cycling SC | Lgals9 | Cd44 | 8.44E-09 | 0 | LGALS9\_CD44 | GALECTIN |
| 127 | TA | Cycling SC | Lgals9 | Cd44 | 8.44E-09 | 0 | LGALS9\_CD44 | GALECTIN |
| 128 | Cycling SC | Noncycling SC | Lgals9 | Cd44 | 3.80E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 129 | Goblet (type 1) | Noncycling SC | Lgals9 | Cd44 | 3.80E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 130 | Goblet (type 2) | Noncycling SC | Lgals9 | Cd44 | 3.80E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 131 | Noncycling SC | Noncycling SC | Lgals9 | Cd44 | 3.80E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 132 | TA | Noncycling SC | Lgals9 | Cd44 | 3.80E-08 | 0 | LGALS9\_CD44 | GALECTIN |

**Supplementary Table S4**. **CellChat-identified significant ligand-receptor pairs in Ahr KO crypt cells.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Source** | **Target** | **Ligand** | **Receptor** | **Prob** | **P-value** | **Interaction\_ Name** | **Pathway\_ name** |
| 1 | EC | Cycling SC | Hbegf | Egfr | 8.41E-09 | 0 | HBEGF\_EGFR | EGF |
| 2 | Noncycling SC | Cycling SC | Hbegf | Egfr | 1.68E-08 | 0 | HBEGF\_EGFR | EGF |
| 3 | EC | EC | Hbegf | Egfr | 8.41E-09 | 0 | HBEGF\_EGFR | EGF |
| 4 | Noncycling SC | EC | Hbegf | Egfr | 1.68E-08 | 0 | HBEGF\_EGFR | EGF |
| 5 | EC | EEC | Hbegf | Egfr | 8.41E-09 | 0 | HBEGF\_EGFR | EGF |
| 6 | Noncycling SC | EEC | Hbegf | Egfr | 1.68E-08 | 0 | HBEGF\_EGFR | EGF |
| 7 | EC | Goblet (type 1) | Hbegf | Egfr | 8.41E-09 | 0 | HBEGF\_EGFR | EGF |
| 8 | Noncycling SC | Goblet (type 1) | Hbegf | Egfr | 1.68E-08 | 0 | HBEGF\_EGFR | EGF |
| 9 | EC | Goblet (type 2) | Hbegf | Egfr | 8.41E-09 | 0 | HBEGF\_EGFR | EGF |
| 10 | Noncycling SC | Goblet (type 2) | Hbegf | Egfr | 1.68E-08 | 0 | HBEGF\_EGFR | EGF |
| 11 | Cycling SC | Noncycling SC | Mif | CD74\_CD44 | 4.20E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 12 | DCS (type 1) | Noncycling SC | Mif | CD74\_CD44 | 1.35E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 13 | DCS (type 2) | Noncycling SC | Mif | CD74\_CD44 | 1.35E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 14 | EC | Noncycling SC | Mif | CD74\_CD44 | 1.51E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 15 | EEC | Noncycling SC | Mif | CD74\_CD44 | 6.73E-08 | 0 | MIF\_CD74\_CD44 | MIF |
| 16 | Goblet (type 1) | Noncycling SC | Mif | CD74\_CD44 | 1.35E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 17 | Goblet (type 2) | Noncycling SC | Mif | CD74\_CD44 | 1.51E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 18 | Noncycling SC | Noncycling SC | Mif | CD74\_CD44 | 5.72E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 19 | TA | Noncycling SC | Mif | CD74\_CD44 | 3.70E-07 | 0 | MIF\_CD74\_CD44 | MIF |
| 20 | Tuft cell | Noncycling SC | Mif | CD74\_CD44 | 1.68E-08 | 0 | MIF\_CD74\_CD44 | MIF |
| 21 | Cycling SC | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 22 | DCS (type 1) | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 23 | DCS (type 2) | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 24 | EC | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 25 | EEC | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 26 | Goblet (type 1) | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 27 | Goblet (type 2) | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 28 | Noncycling SC | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 29 | TA | EC | Nampt | Insr | 2.52E-08 | 0 | NAMPT\_INSR | VISFATIN |
| 30 | EEC | EEC | Pyy | Npy1r | 8.41E-09 | 0 | PYY\_NPY1R | NPY |
| 31 | Cycling SC | DCS (type 1) | Kitl | Kit | 5.38E-07 | 0 | KITL\_KIT | KIT |
| 32 | EC | DCS (type 1) | Kitl | Kit | 5.38E-07 | 0 | KITL\_KIT | KIT |
| 33 | Noncycling SC | DCS (type 1) | Kitl | Kit | 5.38E-07 | 0 | KITL\_KIT | KIT |
| 34 | TA | DCS (type 1) | Kitl | Kit | 2.69E-07 | 0 | KITL\_KIT | KIT |
| 35 | Cycling SC | DCS (type 2) | Kitl | Kit | 2.69E-07 | 0 | KITL\_KIT | KIT |
| 36 | EC | DCS (type 2) | Kitl | Kit | 2.69E-07 | 0 | KITL\_KIT | KIT |
| 37 | Noncycling SC | DCS (type 2) | Kitl | Kit | 2.69E-07 | 0 | KITL\_KIT | KIT |
| 38 | TA | DCS (type 2) | Kitl | Kit | 1.35E-07 | 0 | KITL\_KIT | KIT |
| 39 | Cycling SC | Goblet (type 1) | Kitl | Kit | 4.04E-07 | 0 | KITL\_KIT | KIT |
| 40 | EC | Goblet (type 1) | Kitl | Kit | 4.04E-07 | 0 | KITL\_KIT | KIT |
| 41 | Noncycling SC | Goblet (type 1) | Kitl | Kit | 4.04E-07 | 0 | KITL\_KIT | KIT |
| 42 | TA | Goblet (type 1) | Kitl | Kit | 2.02E-07 | 0 | KITL\_KIT | KIT |
| 43 | Cycling SC | Goblet (type 2) | Kitl | Kit | 7.40E-07 | 0 | KITL\_KIT | KIT |
| 44 | EC | Goblet (type 2) | Kitl | Kit | 7.40E-07 | 0 | KITL\_KIT | KIT |
| 45 | Noncycling SC | Goblet (type 2) | Kitl | Kit | 7.40E-07 | 0 | KITL\_KIT | KIT |
| 46 | TA | Goblet (type 2) | Kitl | Kit | 3.70E-07 | 0 | KITL\_KIT | KIT |
| 47 | Cycling SC | Goblet (type 2) | Sema3b | NRP2\_PLXNA2 | 1.19E-08 | 0 | SEMA3B\_NRP2\_PLXNA2 | SEMA3 |
| 48 | DCS (type 1) | Goblet (type 2) | Sema3b | NRP2\_PLXNA2 | 1.19E-08 | 0 | SEMA3B\_NRP2\_PLXNA2 | SEMA3 |
| 49 | EC | Goblet (type 2) | Sema3b | NRP2\_PLXNA2 | 3.57E-08 | 0 | SEMA3B\_NRP2\_PLXNA2 | SEMA3 |
| 50 | Goblet (type 1) | Goblet (type 2) | Sema3b | NRP2\_PLXNA2 | 1.19E-08 | 0 | SEMA3B\_NRP2\_PLXNA2 | SEMA3 |
| 51 | Goblet (type 2) | Goblet (type 2) | Sema3b | NRP2\_PLXNA2 | 3.57E-08 | 0 | SEMA3B\_NRP2\_PLXNA2 | SEMA3 |
| 52 | TA | Goblet (type 2) | Sema3b | NRP2\_PLXNA2 | 1.19E-08 | 0 | SEMA3B\_NRP2\_PLXNA2 | SEMA3 |
| 53 | Cycling SC | Goblet (type 2) | Sema3c | NRP2\_PLXNA2 | 1.19E-08 | 0 | SEMA3C\_NRP2\_PLXNA2 | SEMA3 |
| 54 | EC | Goblet (type 2) | Sema3c | NRP2\_PLXNA2 | 4.76E-08 | 0 | SEMA3C\_NRP2\_PLXNA2 | SEMA3 |
| 55 | Noncycling SC | Goblet (type 2) | Sema3c | NRP2\_PLXNA2 | 3.57E-08 | 0 | SEMA3C\_NRP2\_PLXNA2 | SEMA3 |
| 56 | TA | Goblet (type 2) | Sema3c | NRP2\_PLXNA2 | 1.19E-08 | 0 | SEMA3C\_NRP2\_PLXNA2 | SEMA3 |
| 57 | Cycling SC | Goblet (type 2) | Sema3c | Plxnd1 | 8.41E-09 | 0 | SEMA3C\_PLXND1 | SEMA3 |
| 58 | EC | Goblet (type 2) | Sema3c | Plxnd1 | 3.36E-08 | 0 | SEMA3C\_PLXND1 | SEMA3 |
| 59 | Noncycling SC | Goblet (type 2) | Sema3c | Plxnd1 | 2.52E-08 | 0 | SEMA3C\_PLXND1 | SEMA3 |
| 60 | TA | Goblet (type 2) | Sema3c | Plxnd1 | 8.41E-09 | 0 | SEMA3C\_PLXND1 | SEMA3 |
| 61 | Cycling SC | Cycling SC | Grn | Sort1 | 1.68E-07 | 0.01 | GRN\_SORT1 | GRN |
| 62 | DCS (type 1) | Cycling SC | Grn | Sort1 | 1.68E-07 | 0.01 | GRN\_SORT1 | GRN |
| 63 | EC | Cycling SC | Grn | Sort1 | 2.10E-07 | 0 | GRN\_SORT1 | GRN |
| 64 | Noncycling SC | Cycling SC | Grn | Sort1 | 1.68E-07 | 0.01 | GRN\_SORT1 | GRN |
| 65 | Cycling SC | DCS (type 1) | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 66 | DCS (type 1) | DCS (type 1) | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 67 | DCS (type 2) | DCS (type 1) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 68 | EC | DCS (type 1) | Grn | Sort1 | 3.36E-07 | 0 | GRN\_SORT1 | GRN |
| 69 | Goblet (type 1) | DCS (type 1) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 70 | Goblet (type 2) | DCS (type 1) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 71 | Noncycling SC | DCS (type 1) | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 72 | TA | DCS (type 1) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 73 | EC | DCS (type 2) | Grn | Sort1 | 1.68E-07 | 0.01 | GRN\_SORT1 | GRN |
| 74 | Cycling SC | EC | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 75 | DCS (type 1) | EC | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 76 | DCS (type 2) | EC | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 77 | EC | EC | Grn | Sort1 | 3.36E-07 | 0 | GRN\_SORT1 | GRN |
| 78 | Goblet (type 1) | EC | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 79 | Goblet (type 2) | EC | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 80 | Noncycling SC | EC | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 81 | TA | EC | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 82 | EC | Goblet (type 1) | Grn | Sort1 | 1.68E-07 | 0.02 | GRN\_SORT1 | GRN |
| 83 | Cycling SC | Goblet (type 2) | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 84 | DCS (type 1) | Goblet (type 2) | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 85 | DCS (type 2) | Goblet (type 2) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 86 | EC | Goblet (type 2) | Grn | Sort1 | 3.36E-07 | 0 | GRN\_SORT1 | GRN |
| 87 | Goblet (type 1) | Goblet (type 2) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 88 | Goblet (type 2) | Goblet (type 2) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 89 | Noncycling SC | Goblet (type 2) | Grn | Sort1 | 2.69E-07 | 0 | GRN\_SORT1 | GRN |
| 90 | TA | Goblet (type 2) | Grn | Sort1 | 2.02E-07 | 0 | GRN\_SORT1 | GRN |
| 91 | Cycling SC | Cycling SC | Lgals9 | Cd44 | 5.04E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 92 | DCS (type 2) | Cycling SC | Lgals9 | Cd44 | 5.04E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 93 | EC | Cycling SC | Lgals9 | Cd44 | 5.04E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 94 | Goblet (type 1) | Cycling SC | Lgals9 | Cd44 | 2.02E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 95 | Goblet (type 2) | Cycling SC | Lgals9 | Cd44 | 2.02E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 96 | Noncycling SC | Cycling SC | Lgals9 | Cd44 | 5.04E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 97 | TA | Cycling SC | Lgals9 | Cd44 | 5.04E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 98 | Goblet (type 1) | Goblet (type 1) | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 99 | Goblet (type 2) | Goblet (type 1) | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 100 | Cycling SC | Goblet (type 2) | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 101 | DCS (type 2) | Goblet (type 2) | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 102 | EC | Goblet (type 2) | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 103 | Goblet (type 1) | Goblet (type 2) | Lgals9 | Cd44 | 1.35E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 104 | Goblet (type 2) | Goblet (type 2) | Lgals9 | Cd44 | 1.35E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 105 | Noncycling SC | Goblet (type 2) | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 106 | TA | Goblet (type 2) | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 107 | Cycling SC | Noncycling SC | Lgals9 | Cd44 | 1.43E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 108 | DCS (type 2) | Noncycling SC | Lgals9 | Cd44 | 1.43E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 109 | EC | Noncycling SC | Lgals9 | Cd44 | 1.43E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 110 | Goblet (type 1) | Noncycling SC | Lgals9 | Cd44 | 5.72E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 111 | Goblet (type 2) | Noncycling SC | Lgals9 | Cd44 | 5.72E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 112 | Noncycling SC | Noncycling SC | Lgals9 | Cd44 | 1.43E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 113 | TA | Noncycling SC | Lgals9 | Cd44 | 1.43E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 114 | Cycling SC | TA | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 115 | DCS (type 2) | TA | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 116 | EC | TA | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 117 | Goblet (type 1) | TA | Lgals9 | Cd44 | 1.35E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 118 | Goblet (type 2) | TA | Lgals9 | Cd44 | 1.35E-07 | 0 | LGALS9\_CD44 | GALECTIN |
| 119 | Noncycling SC | TA | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 120 | TA | TA | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 121 | Goblet (type 1) | Tuft cell | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |
| 122 | Goblet (type 2) | Tuft cell | Lgals9 | Cd44 | 3.36E-08 | 0 | LGALS9\_CD44 | GALECTIN |