**Notch**

Dll4 shows up only with Notch4 (odd?, but consistent with other datasets)

Notch3 never appears alone as a receptor

Notch1 and Notch 2 can each appear alone

Rfng is fairly ubiquitous

Dll3 often has Lfng present (might be involved in helping to inhibit Notch)

Combining signals? Not too much of an issue

* Signal oscillates: can be receiver/sender at different times

Requiring cells to have at least 2 Notch genes—could enrich for cells that have both receptor/ligand in same cells

Ligands are usually expressed with receptors? – worried about making that statement given that we need 2 genes to be above a threshold

In final profile? Is it an endothelial profile?

* Dll4 is important in endothelium
* Notch4’s role is not understood 🡪 knockouts do nothing
* Competition between the ligands: Jags + Delta’s
  + Determines the fate, i.e. stalk vs tip

What about the second to last profile? All but Dll3 are on

* Is it a transitionary cell type?

Notch2 profiles are interesting:

* When it is co-expressed in the same cells as ligands, seems to be very *cis*-activated, especially with Dll ligands

Notch3 + Jag1: never the only expressed receptor, often co-expressed with Jag1

* Known to be a preferential ligand for Notch3, involved in development + cancer

Jag1 is also a preferential receptor for Notch2

Jag1 thought to be inhibitory for Notch1

The top profiles: Fringes + No ligands

* Fng

Motifs: almost all of these profiles have ≥ 3 genes expressed

* Lfng shows up with Notch 1 + Notch4
* Surprising that Lfng shows up with Notch 2
* Dll1 and Jag1 are pretty “promiscuous” in terms of the receptors they appear with
* Dll4 usually appears with predominantly Notch1 + Notch4
* Notch3? What’s the cut-off?
* Mfng seems to be particularly potent for Notch2
* Rfng doesn’t do a lot to Notch2 🡪 but Rfng is everywhere, what’s the point?
* What about combinations of the receptors:
  + All receptors + Jag 1: Notch1 + Jag1 is a combo
  + Jag1 always appear
* A bit puzzling that there are not profiles with only ligands
  + Check out Eph-Ephrin signaling
* Notch has a lot of important *cis* interactions between ligands and receptors
  + *Cis-inhibition* and *cis-activation:* This might explain why we don’t have profiles with only ligands
  + Reference cases where both ligands + receptors, but expression oscillates so the cell switches state between receiver/sender

Rachael to-do list:

Send the motif profiles figure + figure caption