<u>S1 Movie.</u> An example of an individual vascular network generated by wild type ECs during simulation of our model with uniform VEGF = 50 ng/ml.

The leftmost panel shows the concentration of Delta, \mathbf{D} . The colour bar indicates level of Delta, \mathbf{D} , (green colour corresponds to tip cells, red—to stalk cells). Arrows indicate the configuration of the orientation landscape, \mathbf{I} . The central panel indicates the concentration of the ECM, \mathbf{c} . The rightmost panel—the polarity angle, $\mathbf{\mu}$, variable. A circular colour bar indicates the value of $\mathbf{\mu}$. The simulation was performed using **Setup 1** from <u>S4 Table</u> with final simulation time, $T_{max} = 2.5$. Parameter values are listed in <u>S1</u> and <u>S2</u> Tables for subcellular and cellular/tissue scales, respectively.

https://doi.org/10.1371/journal.pcbi.1008055.s015

<u>S2 Movie.</u> Cell migration from a cell bead in substrates of different collagen density.

Single realisations of angiogenic sprouting from a cell bead in substrates of different collagen densities (reproducing the results of the polarisation experiment in [38]). Maximum collagen density (A) $c_{max} = 0.1$, (B) $c_{max} = 1.0$, (C) $c_{max} = 1.7$, (D) $c_{max} = 3.0$. The VEGF linear gradient starts with 0 ng/ml at y = 0 and increases up to 5 ng/ml at $y = 125 \, \mu m$. Central bead initial and basement membrane conditions, $\mathcal{I}_{BM} = \mathcal{I}_{init}$, are outlined by a black thick line on each plot. Colour bars indicate the level of Delta ligand. The simulations were performed using **Setup 3** from <u>S4 Table</u>. Parameter values are listed in <u>S1</u> and <u>S2</u> Tables for subcellular and cellular/tissue scales, respectively.

https://doi.org/10.1371/journal.pcbi.1008055.s016

<u>S3 Movie.</u> Single realisations of cells shuffling within a linear sprout when two given cell lines are mixed 1:1 (50% to 50%).

The cell lines used in each realization are indicated in the titles. In the top row, no treatment with DAPT inhibitor was applied to cells; in the bottom row, all ECs were treated with DAPT. The leading edge corresponds to two rightmost voxels of each sprout. The colour bar for Delta level of the WT goes from red colour (stalk cell) to green (tip cell), whereas for the mutant cells the bar goes from purple colour (stalk cell) to yellow (tip cell). The simulations were performed using **Setup 4** from $\underline{S4 \text{ Table}}$. Parameter values are listed in $\underline{S1}$ and $\underline{S2}$ Tables for subcellular and cellular/tissue scales, respectively, except for the changed parameters for the mutant cells listed in $\underline{S1}$ Appendix. Final simulation time, $T_{max} = 50.0$.

https://doi.org/10.1371/journal.pcbi.1008055.s017

<u>S4 Movie.</u> Examples of an individual vascular networks generated by wild type and mutant (VEGFR2 $^{+/-}$ and VEGFR1 $^{+/-}$) ECs during simulation of our model with uniform VEGF = 5 ng/ml.

The cell line is indicated in the title of each panel. The colour bar indicates level of Delta, \mathbf{D} , (green colour corresponds to tip cells, red—to stalk cells). Arrows indicate the configuration of the orientation landscape, \mathbf{I} . Numerical simulation was performed using **Setup 1** from $\underline{S4 \text{ Table}}$ with final simulation time, $T_{max} = 2.5$. Parameter values are listed in $\underline{S1}$ and $\underline{S2}$ Tables for subcellular and cellular/tissue scales, respectively, except for the changed parameters for the mutant cells listed in $\underline{S1 \text{ Appendix}}$.

https://doi.org/10.1371/journal.pcbi.1008055.s018