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Supplemental Information

Movement Directionality

in Collective Migration

of Germ Layer Progenitors

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Supplemental Experimental Procedures

Numerical Simulations of Cell Migration

Numerical simulations of cell migration were performed as follows. Cells of unit diameter are modeled as soft spheres. The tendency of cells to aggregate is modeled by a short ranged spring force, with an equilibrium cell-cell separation of $\alpha = 0.8$. For two cells i and j separated by a center to center distance r_{ij} the spring force f_S on cell i due to cell j is

$$f_S = \kappa_{ij}(r_{ij}-\alpha)\Theta(1- r_{ij})\, r_{ij}.$$

Here r_{ij} is the unit vector pointing from i to j, and $\Theta(u)$ is the Heaviside step function which satisfies $\Theta(u) = 0$ for $u < 0$ and $\Theta(u) = 1$ for $u \geq 0$. The spring force is thus repulsive at short range ($r_{ij} < \alpha$), which prevents the cells from overlapping too much, attractive for ($\alpha < r_{ij} \leq 1$), and 0 for cells which are not in contact ($r_{ij} > 1$). Here κ_{ij} is the spring constant between cells i and j, which takes the value K for wild-type control – wild-type control contacts, and value k for wild-type control – morphant or morphant – morphant contacts.

In addition to the spring force, each cell experiences a chemotactic force which depends on the cell position $\mathbf{r_i} = (x_i,y_i)$. In a rectangular domain of height y = h and length x = L the chemotactic force on cell i is

$$\mathbf{f_C} = f_C \exp(-(L- x_i)/\lambda)\, \mathbf{x}.$$

Here x is a unit vector in the x-direction, f_C is the magnitude of the force, and λ is the decay length which measures how quickly the chemotactic gradient falls off as one moves away from the source located at x = L. The model also contains a collective migration term [1]. Namely, in each time step a cell i attempts to move in the average direction of motion $\langle\Phi_i\rangle$ of its neighbors during the previous step. Here neighboring cells j are defined as all cells for which $r_{ij} < R$. The "Vicsek" force on each cell is then

$$\mathbf{f_V} = f_V (\cos\langle\Phi_i\rangle\, \mathbf{x} + \sin\langle\Phi_i\rangle\, \mathbf{y}).$$

Here f_V measures the magnitude of the "Vicsek" force. There is also a force $\mathbf{f_n}$ on each cell due to random noise. For a system of N cells we have numerically integrated the system of N coupled Langevin equations,

$$b^{-1} (d\mathbf{r_i}/dt) = \Sigma_{j \neq i} \mathbf{f_S} + \mathbf{f_C} + \mathbf{f_V} + \mathbf{f_n}.$$

Here b is the cell mobility. The simulations are performed with periodic boundary conditions in the y direction. A total of N = 100 cells of which $N_m = 10$ are morphant cells are initially placed in a random cluster located at x = 0 which spans the vertical extent of the domain h. Averaging over many simulations we obtain statistics for the mean squared displacement for the normal and morphant cells (see Figure S4).

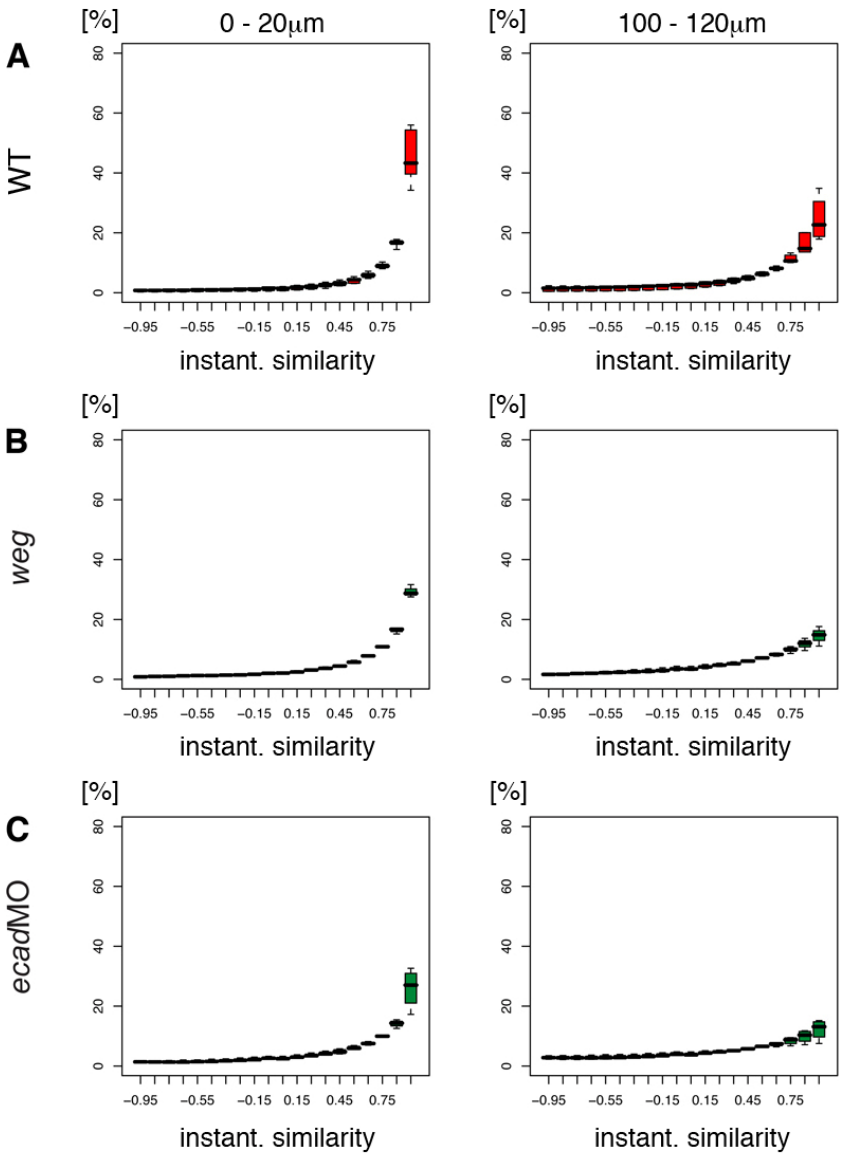

Figure S1. Mesendoderm Movement Similarity as a Function of Distance
Instantaneous similarity of mesendoderm progenitor movements for different cell-cell distances in wild-type (WT; A), *e-cadherin* morphant (*ecad*MO; B; 4 ng/ embryo) and mutant embryos (*weg*; C). Values range from -1.0 (opposite direction of movement) over 0 (movement vectors are orthogonal) to +1 (parallel movement). Box plots show the distribution of the bin heights among the embryos.

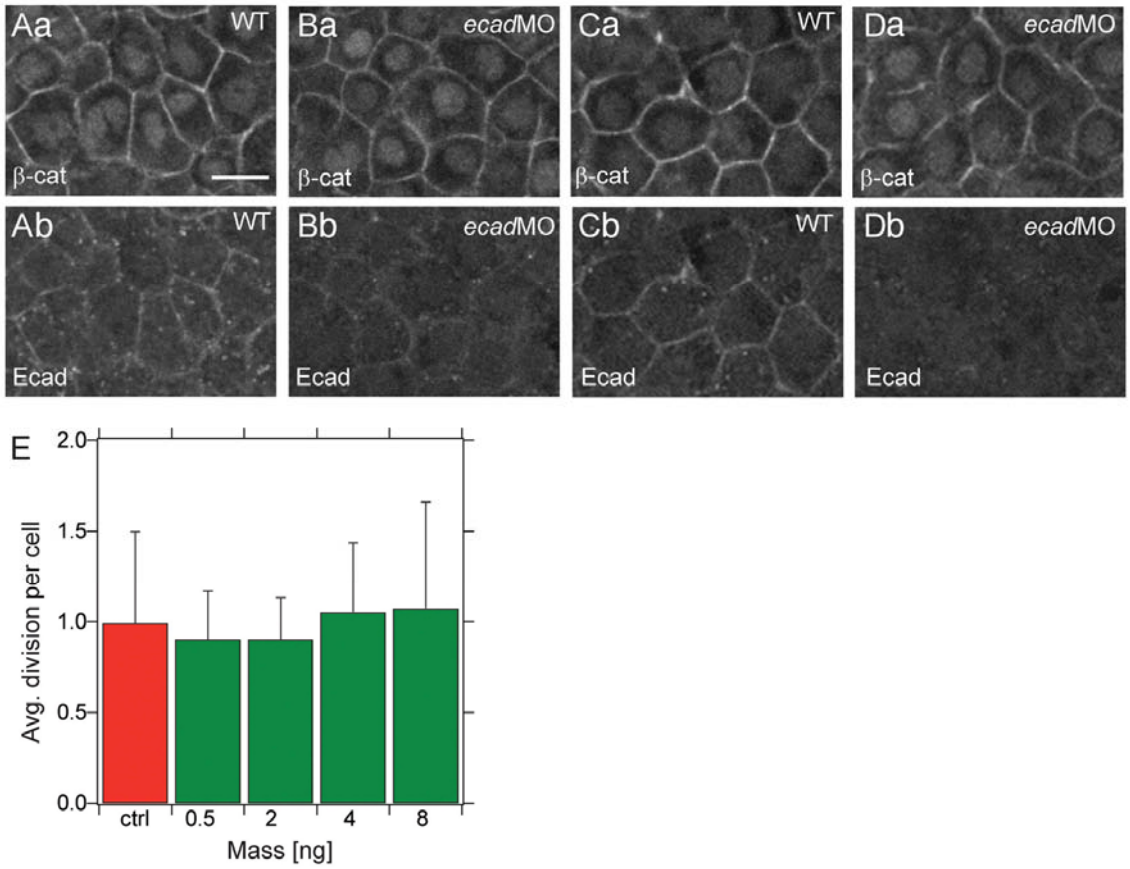

Figure S2. Antibody Staining Against β-Catenin and E-Cadherin in Wild-Type and *e-cadherin* Morphant Embryos

(Aa-Db) Epiblast (ectoderm) cells (Aa-Bb) and hypoblast (mesendoderm) cells (Ca-Db) expressing β-catenin (Aa-Da) and E-cadherin (Ab-Db) in wild-type (WT; Aa, Ab, Ca, and Cb) and *e-cadherin* morphant embryo (*ecad*MO; Ba, Bb, Da, and Db) at 7 hpf. Scale bar in (A) represents 12.5 μm.

(E) Average number of cell divisions of transplanted control and *e-cadherin* morphant cells (4 ng MO/embryo) during gastrulation (from 6 hpf to 10 hpf).

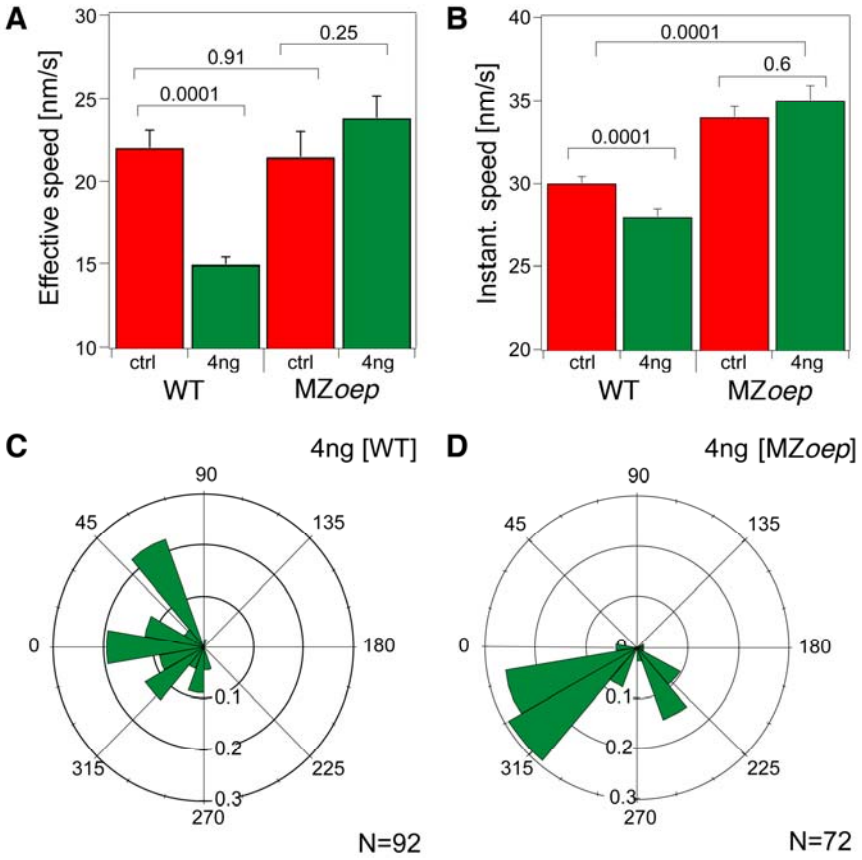

Figure S3. Movement of Individual Mesendoderm Cells with Reduced Cell-Cell Adhesion in Wild-Type and MZ*oep* Mutant Embryos

(A) Effective displacement speed (mean ± SEM) of individual wild-type control (ctrl; red) and *e-cadherin* morphant donor cells (green; 4 ng/ embryo) transplanted into wild-type (WT) or *MZoep* mutant host embryos.

(B) Instantaneous movement speed (mean ± SEM) of individual wild-type control (ctrl; red) and *e-cadherin* morphant donor cells (green; 4 ng/ embryo) transplanted into wild-type (WT) and *MZoep* mutant host embryos.

(C and D) Angular histogram of the movement orientation of individual *e-cadherin* morphant donor cells (green; 4 ng/ embryo) transplanted into wild-type (WT; C) or *MZoep* mutant host embryos (D). Error bars represent standard error of the mean. p values determined by t test are shown above the brackets. N represents number of analyzed cells.

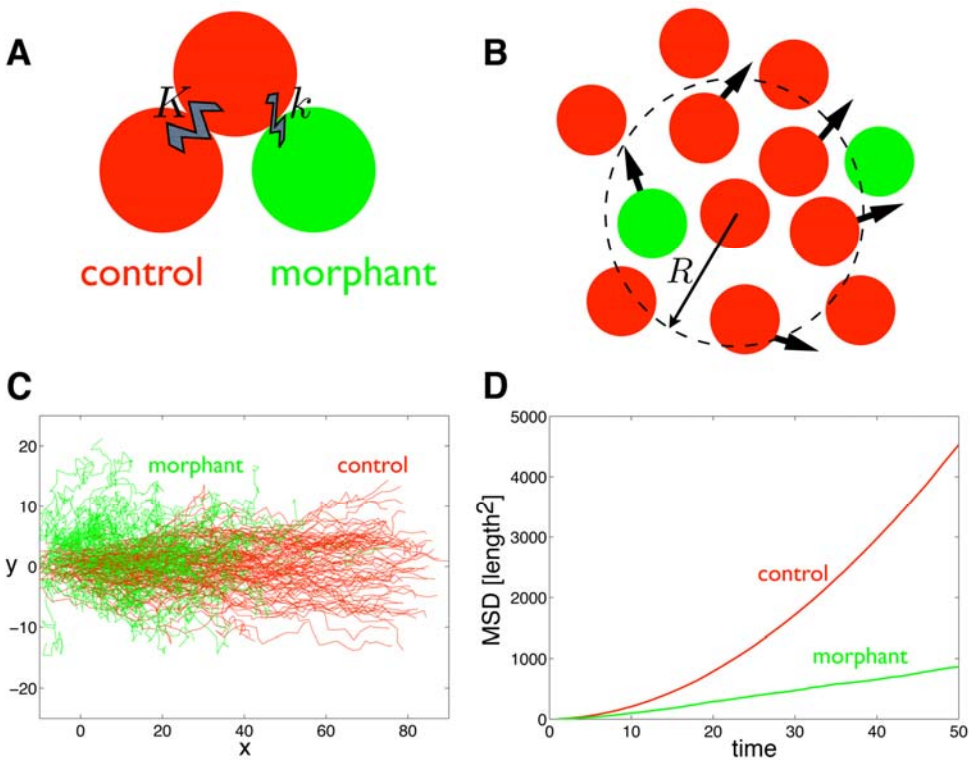

Figure S4. Numerical Simulations of Cell Migration
(A) Cells are modeled as soft spheres connected by short-range springs. The spring constant K for the adhesive force between wild-type control cells is larger than the spring constant k for the heterotypic contacts (wild-type control - morphant).
(B) Explanation of the "Vicsek" force for collective cell migration. At each time step, a cell looks in its neighborhood of radius R, and determines the average direction of motion of its neighbors during the previous step. The cell takes a step in this average direction with some random perturbation added.
(C) A sample of 100 wild-type control (red) and 100 morphant (green) cell tracks from the simulation. In the figure, the units are chosen so that the cell diameter has a length of 1.
(D) Mean-squared displacement of wild-type control (red) and morphant (green) cells obtained from the simulation.

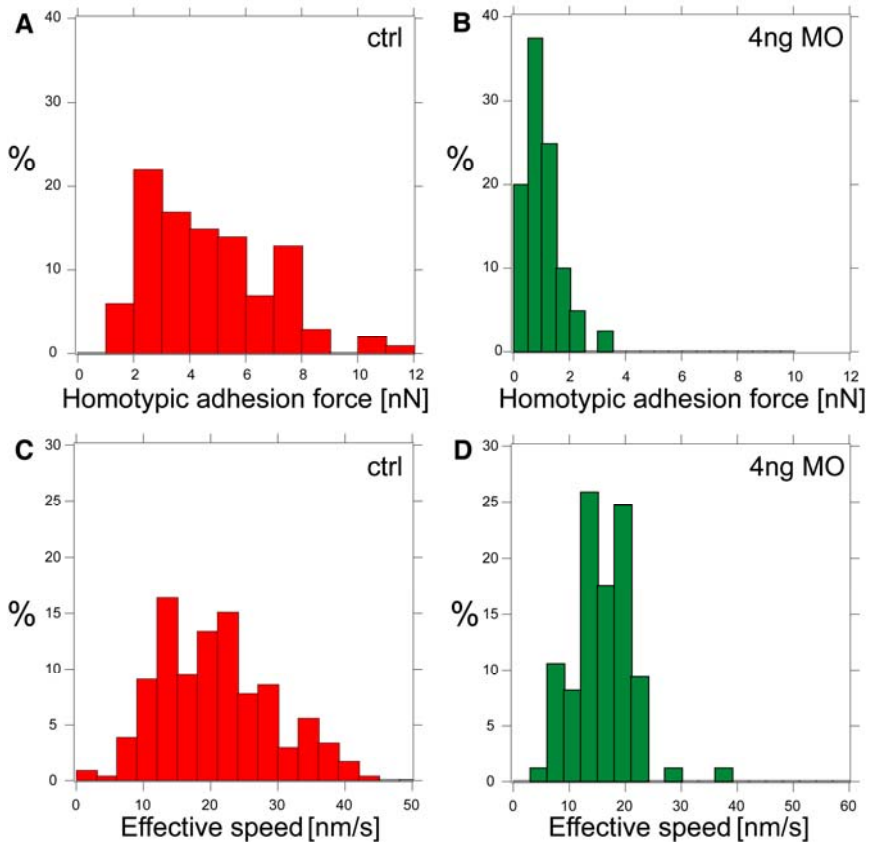

Figure S5. Probability Distribution in Adhesion and Movement Measurements
(A and B) Probability distribution of adhesion force for homotypic contacts acquired with wild-type control cells (ctrl; red; A) and cells from *e-cadherin* morphant embryos (MO; 4 ng/embryo; green; B).
(C and D) Probability distribution of effective movement speed measured for wild-type control cells (red; C) and *e-cadherin* morphant cells (4 ng MO/embryo; green; D) transplanted into wild-type host embryos.

Supplemental Reference

1. Vicsek, T., Czirok, A., Ben-Jacob, E., Cohen, I.I., and Shochet, O. (1995). Novel type of phase transition in a system of self-driven particles. Phys Rev Lett *75*, 1226-1229.