

6. Asymmetries & cellular differentiation

Thursday, 9 September 2021

Remember to turn on zoom



confusions / clarifications / questions?

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Evolving clonal multicellularity

Predation and defense appear to be important drivers of evolutionary innovation. As an example, the origin of eukaryotes appears to have involve at least one "phagotrophic" event, involving the ingestion, but not the digestion of a bacterial cell that evolved into mitochondria.

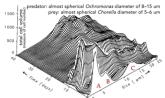
We can explore the effects of predation experimentally. [Borass et al](#) (see also [Herron et al 2019](#)) found that when the unicellular predator

Ochromonas vallescia was introduced into cultures of the unicellular alga *Chorella vulgaris* multicellular forms of *Chorella* appeared. Over time, eight cell forms of *Chorella* became dominant.

Borass et al argued that this was an evolutionary rather than a signaling event.

Q: Propose experiments that would reveal whether the multicellular phenotype was due to evolutionary change rather than an adaptive response to the presence of the predator? (1)

How do the data support their conclusion



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The last common ancestor of metazoans

A number of lines of evidence suggest that choanoflagellates are the closest unicellular relatives of the metazoa.

Homologs of choanoflagellate genes play roles essential to metazoan development, processes not obviously present in choanoflagellates. Propose (1) a model for the presence of these genes in choanoflagellates.



Where they generated in anticipation of the evolution of metazoans? do the data support their conclusion

[Paps & Holland \(2018\)](#) concluded that the last common ancestor of the metazoans shared 25 unique genes. With evolved clonal multicellularity, it appears that all of the cells are similar - they are more like a colony of cells rather than a true multicellular organism. Describe (in general terms) how you might identify metazoan-specific genes?

What are the characteristics of homologous genes?

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One of the simplest organisms that can be termed truly multicellular is the colonial algae Volvox. A mature Volvox consists of two cell types: gonidial (germ) cells and surface (somatic) cells.

The somatic cells have flagella, they are embedded in a clear extracellular matrix and evenly arranged in the organism's surface. They are involved in organic movement. The gonidial cells lie with the surface layer, and they give rise to new organisms.

Once formed, the somatic cells are terminally differentiated and no longer can divide. The 16 gonidial cells are asymmetrically distributed within the interior. During organic reproduction the gonidial cells divide to form new organisms that hatch out of the original organism, which dies.

Q: What advantages (to the organism) could be associated with having certain (somatic) cells become terminally differentiated?

your thoughts

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In Volvox, a new organism begins when a gonidial cell begins to divide. The first ~5 divisions are symmetric. After that divisions become asymmetric; one daughter is larger than the other. A number of mutations have been identified that influence cell differentiation in Volvox. As an example, a mutation in *glsA*, a gene that encodes a chaperone, leads to loss of asymmetric divisions and the loss of gonidial cells.

Q: What is your understanding of what a chaperone does (1)?

Gonidium → symmetric divisions → 32-cell embryo → *glsA*, *hsp70A* → asymmetric divisions → Small cells (rep4 ON) → Repress gonidial genes → Somatic cells → Senescence
G. Martí, J. Umer / Developmental Biology 419 (2016) 99–113

how might a chaperone influence the activity of a transcription factor?

Based on this (1) pathway, propose a simple model by which the absence of chaperone activity would lead to somatic cell only differentiation? (-)

consider factors that influence protein activity

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A clarification (based on a dossier comment):

An evolutionary relationship does not mean that animals "came out of" or "came from" choanoflagellates, but rather that animals and choanoflagellates share a common ancestor (some billion or so years ago), an ancestor that has the distinctive trait (e.g. the collared flagellum).

Such a trait is known as a **synapomorphy**

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How would you define the difference between a somatic cell and a germ line cell (↓)?

in general terms

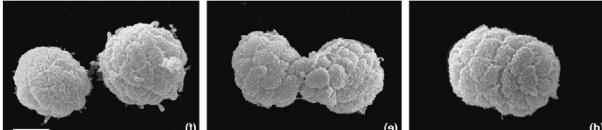
Why might somatic cells accumulate mutations at a higher rate than germ line cells, particularly in a large multicellular metazoan? (-)

what factors might play a role?

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Finishing up from last time: One cell, two cell, red cell, blue cell: the persistence of a unicellular stage in multicellular life histories

R.K. Grosberg
R.R. Strathmann



Are the cells in these structures genetically identical?

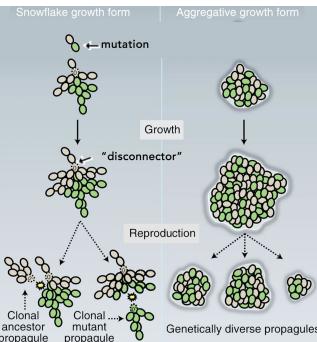
Q: Why would animals go through a single celled stage?

Suppress potential conflicts between clones
Remove deleterious alleles (no "rescue" by wild type cells)

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Genetic bottleneck during reproduction (in snowflake yeast)

- Cell death through apoptosis generates "weak links" between chains of cells in a cluster.
- As cells within the cluster divide, they grow into one another, putting a strain on the connection between cells.
- Dead cells break more easily, resulting in earlier cell separation and the production of smaller propagules.
- Resulting colonies are clonal and genetically similar (to start)
- Germ line:** Self sacrificing behavior (in somatic cells) easier to understand in a clone



Ratcliff, W. C., Fankhauser, J. D., Rogers, D. W., Greig, D., & Travisano, M. (2015). Origins of multicellular evolvability in snowflake yeast. *Nature communications*, 6(1), 1-9.

- consider the establishment of molecular, cellular, and gametic asymmetries

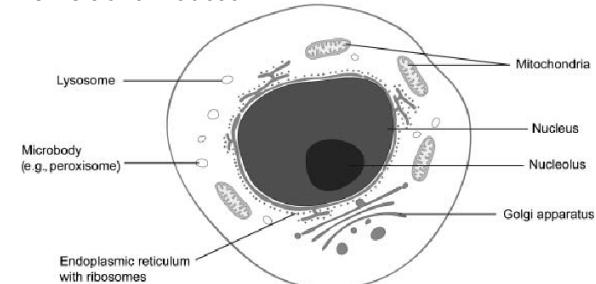
Reminder: gametes - egg and sperm
– Haploid - Products of meiosis

Oocytes and spermatogonia are diploid

- produced by mitosis
- asymmetries develop during extended meiotic prophase and post-meiotic processes (which haploid)

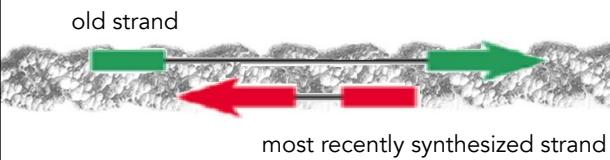
How asymmetries arises between cells?

Intrinsic and induced



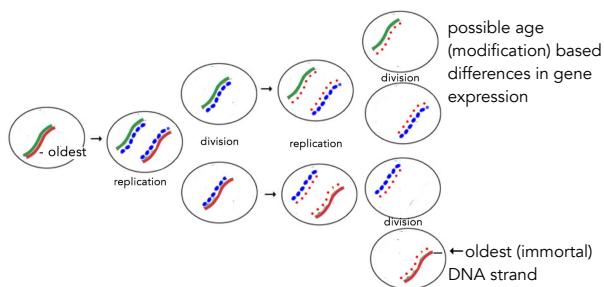
Q: What inherent polarity axes/asymmetries are present?

DNA-based asymmetries



Q: If there is a point mutation during DNA replication, how does the cell "know" which strand to repair? How does "repair accuracy" change with time?

DNA strand age (different genes on anti-parallel strands)

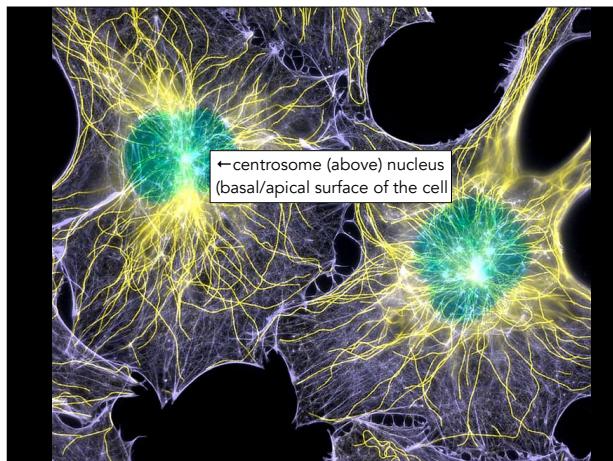


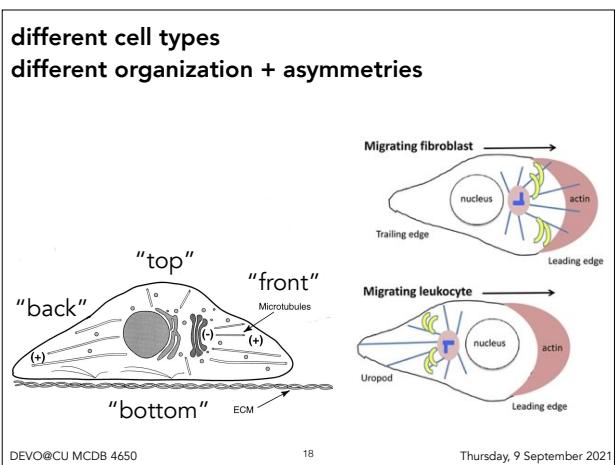
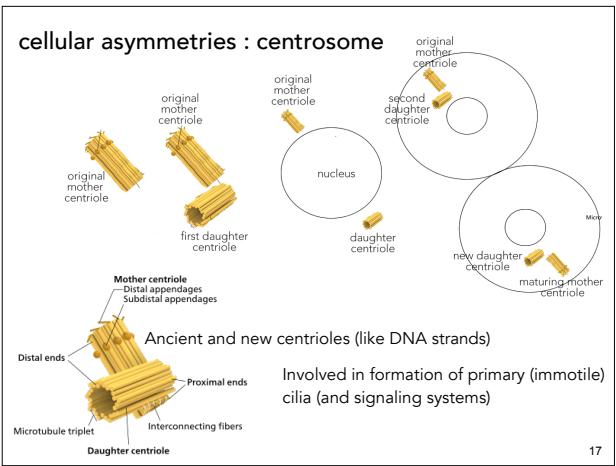
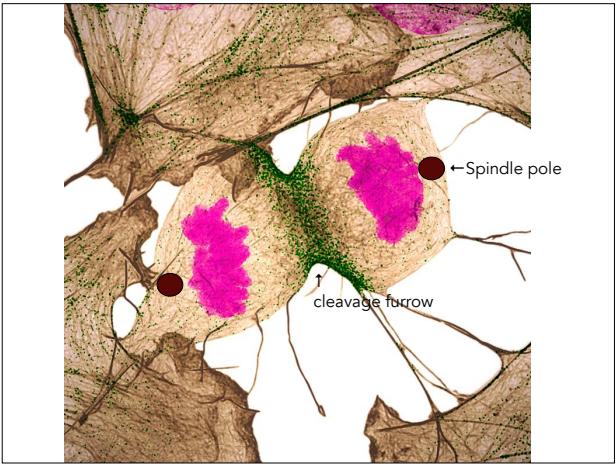
groupQ: How might asymmetries in gene expression arise based on the age of the DNA strand?

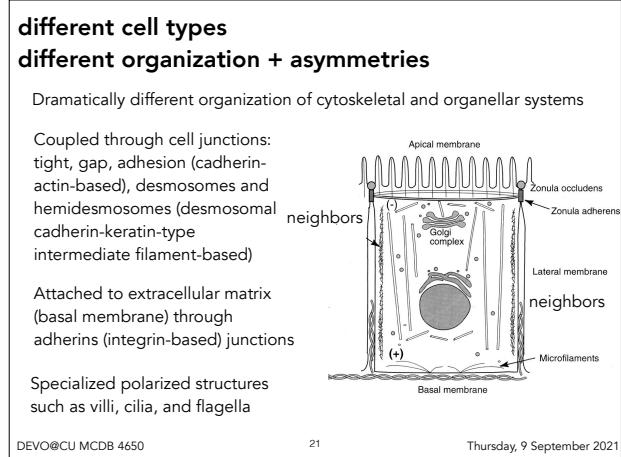
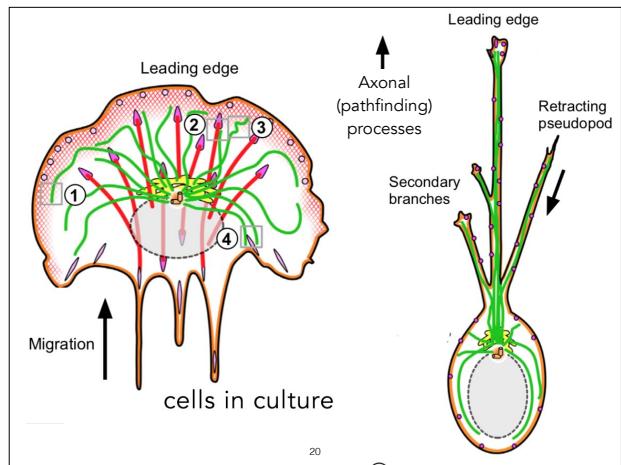
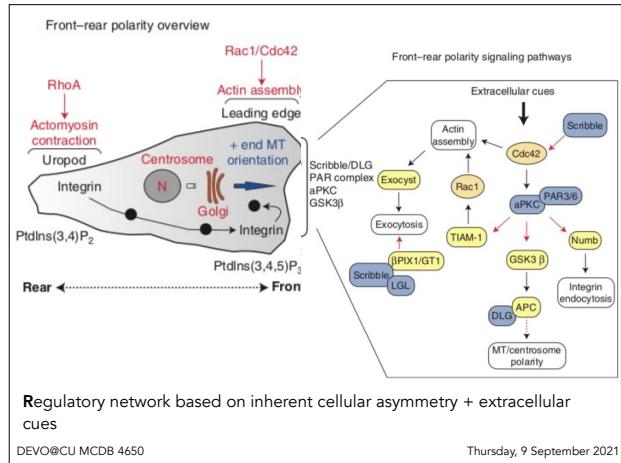
cellular polarities

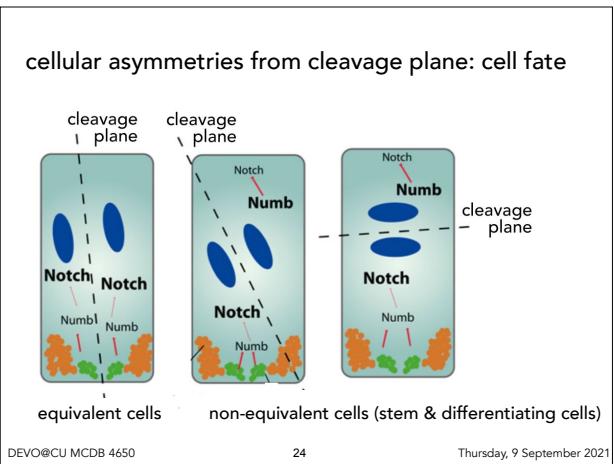
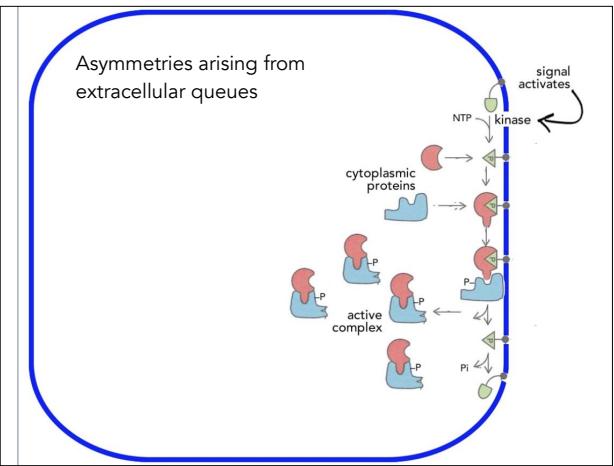
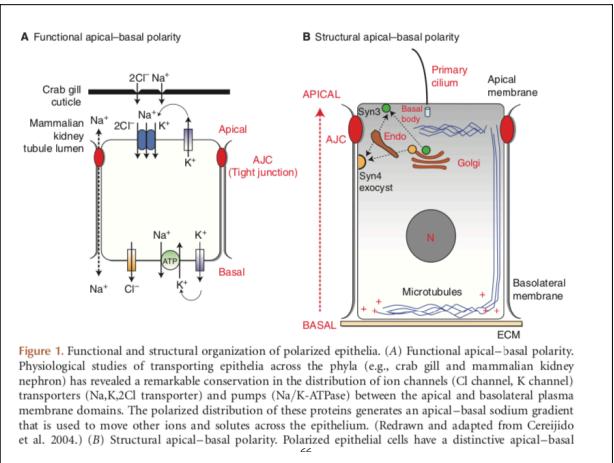
- directionality of cytoskeletal polymers
 - microtubules microfilaments +/- ends
 - motors (kinesin/dynein + myosin)
- cytoplasmic organization (Golgi/ER - secretion, etc)
- regional asymmetries
 - cell-cell/cell-matrix junctions
 - signaling receptors / response components

leading to changes in gene expression, cell morphology, migration, tissue organization, and other behaviors



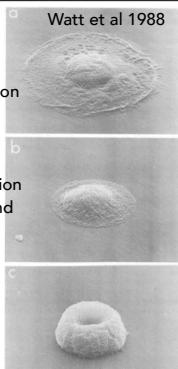






Cell shape / movement: cytoskeletal bases

changing shape - changing gene expression



Shape controlled by controlling area of adhesion to substrate; leads to changes in cell shape and patterns of gene expression.

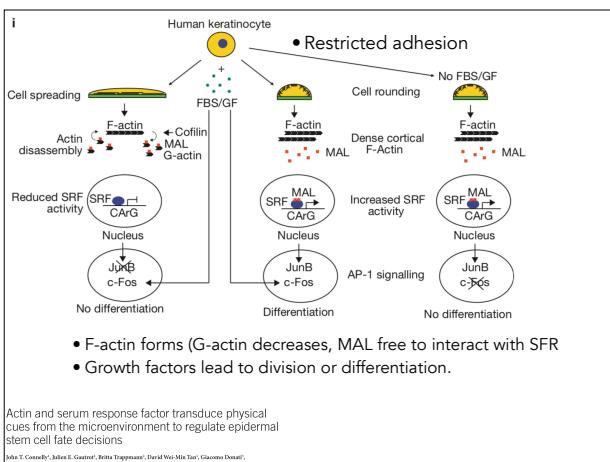
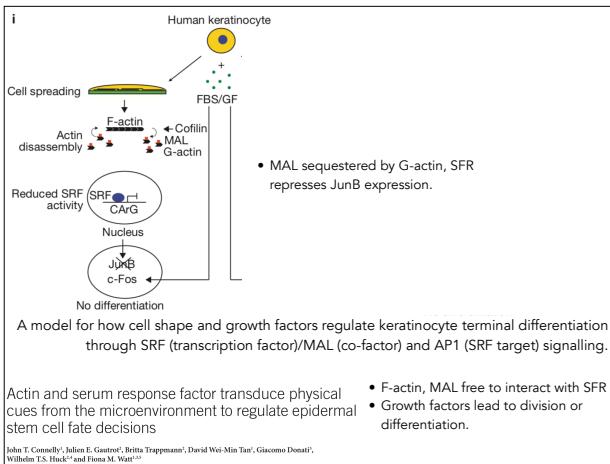
Cell shape controls terminal differentiation of human epidermal keratinocytes

(cell adhesion/proliferation/terminal expression)

FIONA M. WATT¹*, PETER W. JORDAN¹, AND CHARLES H. O'NEILL¹

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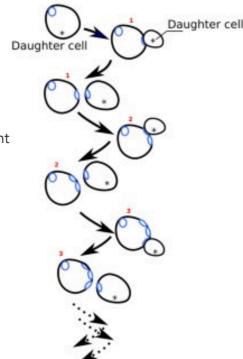
Fig. 1. Scanning electron micrographs of keratinocytes seeded on different sizes of islands: 2000 μm² island (a); 400 μm² islands (b) and (c). The doughnut-shaped cell in (c) has enlarged, collapsed, and developed a roughened surface, indicating the development of a cornified envelope and marking the end stage of terminal differentiation. (bar = 10 μm.)



Review

Creating Age Asymmetry: Consequences of Inheriting Damaged Goods in Mammalian Cells

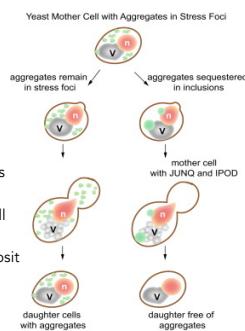
Darcie L. Moore^{1,*} and Sebastian Jessberger^{2,*}



Yeast cell division cycles result in the formation of the mother cells with different numbers of chitin enriched bud scars.

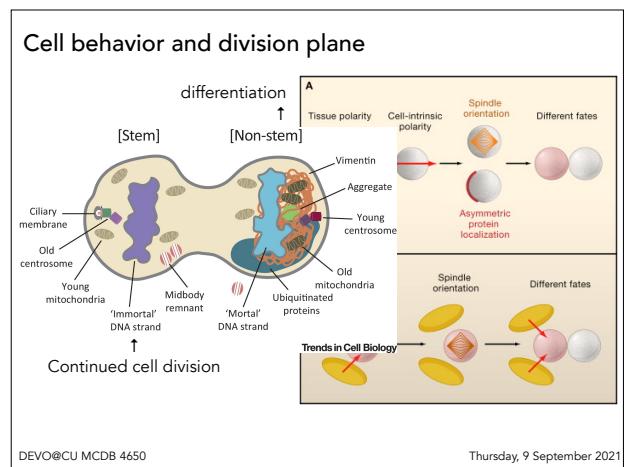
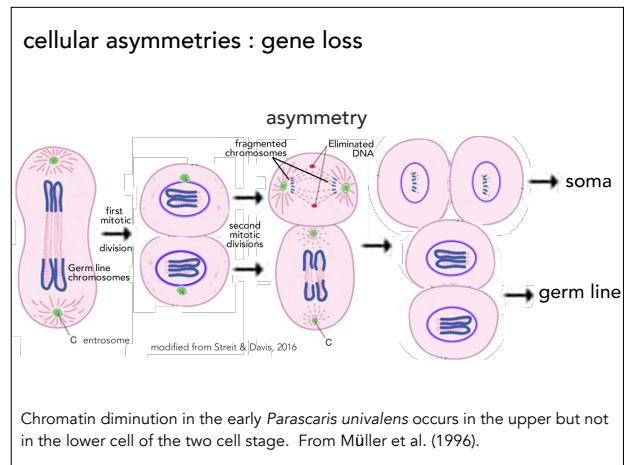
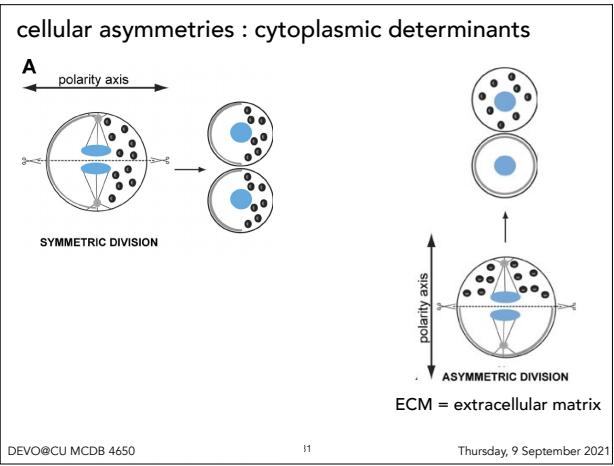
Azbarova et al., (2017). The contribution of *Saccharomyces cerevisiae* replicative age to the variations in the levels of Trx2p, Pdr5p, Can1p and Idh isoforms. *Scientific reports*, 7, 1-10.

- Mother and daughter cells are asymmetric with respect to age; asymmetry coincides with inheritance of damaged and aggregated proteins by the mother cell.
 - Misfolded proteins are retained in the mother cell (sequestered in juxtanuclear quality control compartment (JUNQ) and insoluble protein deposits (IPOD) inclusions).



Confinement to Organelle-Associated Inclusion Structures Mediates Asymmetric Inheritance of Aggregated Protein in Budding Yeast

Rachel Spokoini,¹ Ofer Moldavski,² Yaakov Nahmias,¹ Jeremy L. England,³ Maya Schuldiner,² and Daniel Kaganovich^{1,*}



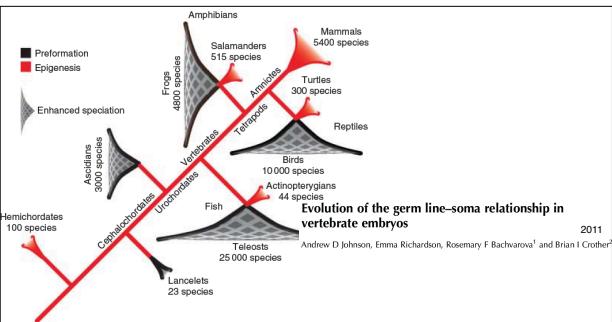
Germ line development

- Two basic mechanisms:
 - Germ line formation specified by the presence of inherited cytoplasmic "determinants"
 - Arising through inductive interactions with neighboring cells.

Q: How might germ line determinants work?

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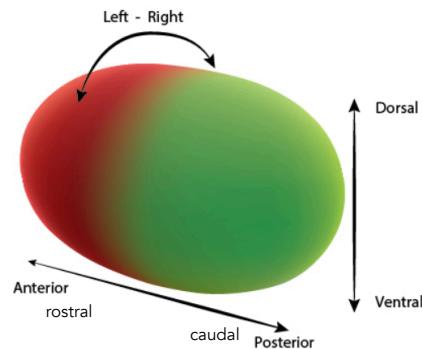


Intrinsic specification of the germ line allows for greater flexibility, since it is easier for the germ line to "ignore" what is going on around it.

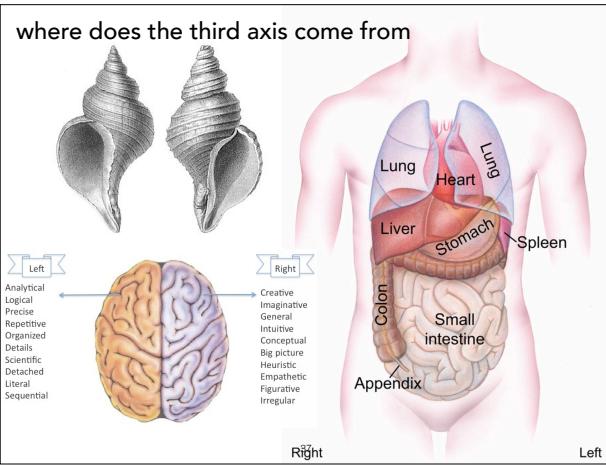
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Macroscopic (embryonic) axes



Developmental polarity is observed along three axes; anterior-posterior, dorsal-ventral and left-right. This polarity can be established by concentration gradients of secreted proteins, or by asymmetric organisation of cellular components, such as the cytoskeleton.



Effects of asymmetry reversal

<https://www.theguardian.com/science/blog/2016/sep/08/situs-inversus-and-my-through-the-looking-glass-body>

Situs inversus and my 'through the looking glass' body
 My body's organs are placed in mirror image to the norm. It's a rare condition, and has left me curious about its history and wider cultural implications Saskia Solomon Thu 8 Sep 2016

Q: 1 in 10,000 liver births: complete versus partial – why is partial more severe than complete?

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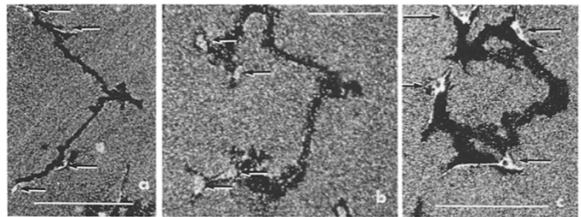
left-right handedness in cells

DAUGHTER 3T3 CELLS
 Are They Mirror Images of Each Other?
 GUENTER ALBRECHT-BUEHLER
 From the Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 117

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How to study cellular handedness

- Cover cell substrate with removable objects (small colloidal gold particles)
- Add cells at low density (look at motility of individual cells) after cell division



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How to study cellular handedness

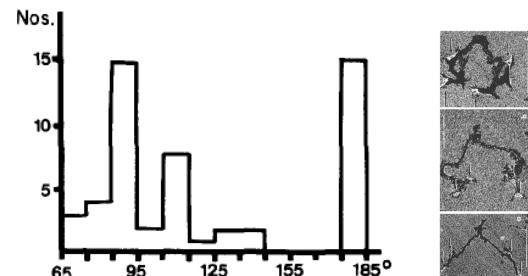


FIGURE 5 Histogram of the angles of separation between daughter 3T3 cells based on 53 measurements on branching phagokinetic tracks.

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DEVELOPMENTAL BIOLOGY

Molecular to organismal chirality is induced by the conserved myosin 1D

G. Lebreton^{1*}, C. Géminard^{1††}, F. Lapraz^{1‡‡}, S. Pyrpassopoulos^{2‡‡}, D. Cerezo¹, P. Spéder^{3§}, E. M. Ostap³, S. Noselli^{1¶}

we will be reasonably superficial

What did they know before they started?

- myo1D is a situs inversus gene
 - its absence leads to the full reversal of organ positioning along the LR axis, with organs adopting a mirror-image orientation (sinistral) – as opposed to dextral.

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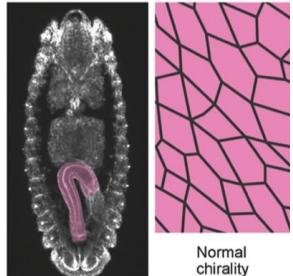
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Cell Chirality Drives Left-Right Asymmetric Morphogenesis

Mikiko Inaki, Takeshi Sasamura and Kenji Matsuno*

Department of Biological Sciences, Graduate School of Science, Osaka University, Osaka, Japan

Wild type



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Portfolio questions:

- 6.1 How might molecular asymmetries (in both DNA and cellular components) influence gene expression and cellular behavior?
- 6.2 How might left-right asymmetries arise at the cellular level and what is the evidence that they can be "flipped"?
- 6.3 How might asymmetries during stem cell division lead to changes in cellular behavior (and survival)?

M2

I will send an email explaining later today

MCDB-DevoChat-2021

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Ended here