Experiment	EXPERIMENT
Wilhem Roux' embryos  Week 1: Intro	Hans Drierich Sea Urchins  Week 1: Intro
Definition  Pattern formation	Types of regulatory signalling and their range
Week 1: Intro	Week 1: Intro
DEFINITION	DEFINITION
Maternal factors	Mosaic vs regulatory development
Week 1: Intro	Week 1: Intro
Definition  Cell fate, specification and determination	Definition  Gastrulation
Week 1: Intro	Week 1: Intro
Definition  Cleavage	Definition  Blastula and blastocyst
Week 1: Intro	Week 1: Intro

Hans Drierich showed that 4 Sea Urchin embryo cells could grow into separate organisms IF they were separated, contradicting Roux' experiment where he punctured one of two cells.	Wilhem Roux showed that if one of two embryonic frog cells were killed, the result would be a half-complete frog. However, he did not detach the dead cell, which would have resulted in a normal frog.
Gap junctions, only between adjacent cells Surface protein interactions, adjacent cells Diffusion of ligands, any two cells	One or multi-dimensional gradients of extracellular ligands, that cause cell differentiation depending on concentration.
Mosaic: two cells contain different growth factors (proteins, RNA) and thus take different paths Regulatory: two cells are identical, but receive different extracellular signalling and thus take different paths	Proteins and mRNA supplied by the mother to the zygote.
The process in which germ layers are formed.  Organism starts to resemble itself.	Fate: normal developmental path for cell, either differentiation or apoptosis  Specification: a specified cell has been given instructions, but can change path unless determined Determination: a determined cell cannot change its fate
Occurs after cleavage, and consists of a single, hollowed layer of cells. Called blastocysts in vertebrates.	When the zygote divides without increasing the size of cells, resulting in a blastula.

Germ Layers	Germ layers
Ectoderm  Week 1: Intro	Mesoderm  Week 1: Intro
Germ Layers	CELL LINEAGES
Endoderm	Number of somatic and germ cells
Week 1: Intro	Week 2: C. elegans
Cell lineages	Cell lineages
Number of C, D and E cells, PCD count	Number of AB and MS cells, PCD count
Week 2: C. elegans	Week 2: C. elegans
Cell lineages	CELL LINEAGES
$AB_a$ cells form	$AB_p$ cells form
Week 2: C. elegans	Week 2: C. elegans
Cell lineages	CELL LINEAGES
$m{MS}$ cells form	<b>E</b> cells form
Week 2: C. elegans	Week 2: C. elegans

Middle layer - muscle, heart, blood. In vertebrates also skeleton and kidney	Outer layer - skin (or cuticle in insects) and nervous system
959 somatic cells, around 2000 germ cells; invariant	Inner layer - epithelial layer of gut. In vertebrates also liver and lungs
606 AB cells, an additional 116 undergo PCD. 252 MS cells, additional 14 undergo PCD.	47 C-cells, 20 D-cells, 34 E-cells. 1 C-cell undergoes PCD.
Neurons, skin, specialised cells.	Neurons, skin, anterior mesodermal pharynx.
Gut cells (only one cell type)	Muscle cells, nerve cells, posterior mesodermal pharynx

Cell lineages	Cell lineages
$oldsymbol{C}$ cells form	$oldsymbol{D}$ cells form
Week 2: C. elegans	Week 2: C. elegans
Cell lineages	DEFINITION
$m{P}$ cells form due to the presence of	Use $P_1$ and $AB$ as examples of autonomous and conditional modes of specification
Week 2: C. elegans	Week 2: C. elegans
EARLY CELL FATES	Maternal genes
SKN-1 does is inhibited by	Role of PIE-1
Week 2: C. elegans	Week 2: C. elegans
MATERNAL GENES	Induction events
Role of MEX-1	The role of APX-1 and GLP-1
Week 2: C. elegans	Week 2: C. elegans
Induction events	Induction events
Equivalents of APX-1 and GLP-1 in Drosophila	Descendants of ABa are specified as pharyngeal precursor cells through
Week 2: C. elegans	Week 2: C. elegans

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Muscle cells (only one cell type)	Skin cells, nerve cells and muscle cells
The AB cell requires the $P_1$ to develop, and is therefore undergoes conditional specification. $P_1$ cell can develop on its own, autonomous.	Germ line cells, presence of P-granules
Pharynx and Intestinal Excess. Inhibits the activity of SKN-1 in the P2-cell, preventing it from adopting EMS fate.	SKN-1 specifies the EMS cell. If not present, the EMS cell becomes a P2-like cell. Inhibited by PIE-1.
Required to give ABp its cell identity. GLP-1 is activated in ABp because the cell is in contact with P2; if ABp and ABa are swapped, ABa will be induced instead.	Muscle Excess. Prevents SKN-1 from entering ABa and ABp, which prevents them adopting the EMS fate. If mutated, they develop into muscle cells.
Activation of the transcription factor PHA-4. The receptor is GLP-1, but the ligand is <i>not</i> APX-1	Delta (ligand) and Notch (receptor)

Induction events	Induction events
Activation of PHA-4 is caused by	The specification of gut (E) cells is induced through
Week 2: C. elegans	Week 2: C. elegans
Induction events	Genes
Consequences of high vs low amounts of pop-1	The molecules involved in inhibiting POP-1 are
Week 2: C. elegans	Week 2: C. elegans
Vulva formation	Vulva formation
Vulva cell names,, ancestor cell, total cells in developed vulva	Determinant for primary cell fate, fate if mutated
Week 2: C. elegans	Week 2: C. elegans
Vulva formation	Vulva formation
Determinant for secondary cell fate, fate if mutated	Determinant for tertiary cell fate
Week 2: C. elegans	Week 2: C. elegans
Partition genes	Partition genes
Par-1 mutant distribution of SKN-1, MEX-3 and GLP-1 at four cell stage	Par-2 mutant distribution of SKN-1, MEX-3 and GLP-1 at four cell stage
Week 2: C. elegans	Week 2: C. elegans

Cell-cell interactions between EMS and P2. The molecule mom-2 is released from P2 and activates the mom-5 receptor in EMS, which downregulates pop-1 so that the E cell is formed.	GLP-1 is the receptor, but the ligand in this case is not APX-1
mom-2, mom-5, mom-4, wrm-1, lit-1	Active: MS cells, as pop-1 specifies MS fate Inactive: E cells
LIN-3 from the anchor cell, which binds to LET-23 receptor. Results in repressing the LIN-12 receptor, which determines secondary cell fate. If mutated, all cells become tertiary, vulvaless.	Anchor cell, P3-P8 (not the same as germ line), descends from the ABp cell. Mature vulva contains 22 cells.
LIN-15 from the epidermis inhibits the formation of primary cell fates if the signal is weak. Thus P3, P4 and P8 adopts tertiary cell fate. If mutated, all cells become secondary or primary, multivulva.	LIN-12 activated by ligands from the primary cell. Signal represses primary fate. If mutated, the two secondary cells become primary, multivulva?
GLP-1 is found in all four cells.	All three determinants are found in all four cells.

Partition genes	Apoptosis
Par-3 mutant distribution of SKN-1, MEX-3 and GLP-1 at four cell stage	How many cells undergo programmed cell death? How many of them are in the nervous sytem?
Week 2: C. elegans	Week 3: C. elegans
Background strains used by Horvitz et al	Background strains used by Horvitz et al
nuc-1 mutants	ced-1/ced-2 mutants
Week 3: C. elegans	Week 3: C. elegans
Background strains used by Horvitz et al	Background strains used by Horvitz et al
eg11 (gof) mutants	Wild type
Week 3: C. elegans	Week 3: C. elegans
C. ELEGANS PCD PATHWAY	C. ELEGANS PCD PATHWAY
ced-9	egl-1
Week 3: C. elegans	Week 3: C. elegans
C. ELEGANS PCD PATHWAY	C. ELEGANS PCD PATHWAY
ced-4	ced-3
Week 3: C. elegans	Week 3: C. elegans

131/105	SKN-1 and GLP-1 are found in all four cells.
No phagocytosis; apoptotic cells do not disappear. Discovered the killer gene ced3 (less cell death in mutants)	$\it Nuc$ lease abnormal; no DNA destruction during apoptosis. Unsuccesful
Genes discovered:  • ced-9 (gof) - NSM sister cell which usually dies survives. ced-9 functions unlike ced-3 and ced-4 in that it protects against cell death  • nuc-1  • ced-1  • egl1 (gof)	Cannot lay eggs becuase nerve cell (HSN neuron) connected to vulva dies. Discovered a new killer gene, ced4 (can lay eggs because cell death suppressed, meaning HSN neuron does not die)
Egg laying deficient. Hermaphrodite specifying neuron (HSN) dies if egl-1 has gof mutation. Cell death activator. Repressers the PCD repressor ced-9, by forcing it to release ced-4 and starting PCD.	Cell death repressor. Binds $ced$ -4, preventing it from cleaving $ced$ -3 which initiates PCD. Repressed by $egl$ -1
Cell death activator. Last part of the central pathway, activated by ced-4	Cell death activator. Prepares $ced$ -3 by cleaving it, initiating PCD. Released from $ced$ -9 after binding $egl$ -1

FLY FACTS	Oogenesis
No. of genes in Drosophila and C. elegans, no. lethal genes in Drosophila	Oogenesis, follicle cells, oocyte
Week 4: Drosophila melanogaster	Week 4: Drosophila melanogaster
Oogenesis	Oogenesis
Nurse cells	Syncytial specification
Week 4: Drosophila melanogaster	Week 4: Drosophila melanogaster
Embryo structures	Embryo structures
Cephalic furrow, ventral furrow	Segment names (head, thorax, abdomen)
Week 4: Drosophila melanogaster	Week 4: Drosophila melanogaster
MATERNAL FACTORS	MATERNAL FACTORS
Anterior posterior axis specification	Bicoid is a and is assisted to the anterior by
Week 4: Drosophila melanogaster	Week 4: Drosophila melanogaster
Maternal factors	MATERNAL FACTORS
Nanos is a and is assisted to the posterior by	Bicoid/nanos effects on hunchback/caudal
Week 4: Drosophila melanogaster	Week 4: Drosophila melanogaster

Oogenesis is the creation of the oocyte, the unfertilized, haploid egg cell. Follicle cells are somatic cells - the "shell" of the oocyte.	13600 genes in Drosophila vs 19000 in C. elegans. 5000 lethal genes.
Syn-cytial, same-cell. Control of individual cell specification in a cell with many nuclei, but no membranes. Occurs varying concentrations of maternal factors (e.g. bicoid) throughout the cytoplasm.	Nurse cells are <b>germ line</b> cells. 15 nurse cells are created from one stem cell after 4 divisions, in addition to oocyte.
Mx, Ma, Lb, T1-T3, A1-A8.	Cephalic furrow is ridge in embryo that separates head from thorax. Ventral furrow eventually invaginates and creates mesoderm layer.
Transcription factor, assisted by exuperantia, swallow	First, nucleus localizes to posterior and releases Gurken mRNA close to the posterior follicle cells. Gurken protein binds to the torpedo receptor. Now bicoid and nanos can separate.
Nanos-pumilio complex — hunchback Bicoid — caudal Bicoid — ¿ hunchback	Translational repressor (hunchback). Assisted by Oskar, tudor, vasa and valois

MATERNAL FACTORS	MATERNAL FACTORS
Torso does and is activated by	Hunchback mRNA stems from
Week 4: Drosophila melanogaster	Week 4: Drosophila melanogaster
MATERNAL FACTORS	MATERNAL FACTORS
Overexpressed bicoid results in No bicoid results in Inserted bicoid results in	No nanos results in No torso results in
Week 4: Drosophila melanogaster	Week 4: Drosophila melanogaster
GAP GENES, ANTERIOR-POSTERIOR	GAP GENES, ANTERIOR-POSTERIOR
The three important anterior-posterior gap genes are, and they are repressed by	If an anterior-posterior gap gene is deleted
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
Gap genes, anterior-posterior	Gap genes, dorsal-ventral
Gap genes of type are required for acron and activated by	The dorsal side is initially specified by
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
GAP GENES, DORSAL-VENTRAL	Gap genes, dorsal-ventral
The ventral side reaction chain involves the proteins	A fly is ventralised in the case of a LOF in proteins
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes

Both a maternal factor and transcription/translation in the zygote.	Torso represses groucho, a repressor of acron/telson proteins huckebein (hkb) and tailless (tll). Activated by trunk, which is activated by torso-like protein.  Torso-like only located on extremities.
No abdomen. No acron or telson.	Larger head and thorax region.  No head, thorax or acron.  Head, thorax and maybe acron region at insertion.
The region normally specified is deleted.	Krüppel, repressed by all except bicoid (knirps, giant, hunchback, tailless, etc.) knirps, repressed by all except bicoid giant, repressed by all except bicoid and hunchback All transcription factors.
After anterior-posterior specification, nucleus releases Gurken mRNA at random side - dorsal side. Gurken activates torpedo, which inhibits pipe, which is used in the ventral side.	Bicoid actiavtes otd, ems and btd, <b>only</b> required for acron, while tailless and huckebein from torso are required for acron and telson. They are all <b>transcription factors</b>
Cactus, as it inhibits dorsal. Gurken and torpedo, as they inhibit pipe	Nudel and pipe activate proteases Gd –; Snake –; Easter. Easter activates ligand Spätzle, which binds to membrane receptor Toll. Toll releases Cactus from Dorsal, allowing Dorsal into the nucleus, specifying ventral side.

Gap genes, dorsal-ventral	Dorsal concentration gradient
A fly is dorsalised in the case of a LOF in proteins	Highest concentrations of dorsal activate which specify the
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
DORSAL CONCENTRATION GRADIENT	Dorsal concentration gradient
Low concentrations of dorsal activate (top to bottom)	Dorsal represses (top to bottom)
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
DORSAL CONCENTRATION GRADIENT	SEGMENT POLARITY GENES
Snail and twist are not activated at low dorsal concentrations due to	Segment polarity genes are activated by and the involved genes are
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
Pair rule genes	RNAI VS GENETIC SCREENING
The pair rule genes are initially in the and move to the in the segments	The benefits of RNAi over genetic screening and vice versa are
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
Pair rule genes	Homeotic genes
Even-skipped stripe two is activated by and repressed by	Homeotic genes and segment polarity genes appear after
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes

Proteins twist and snail, specifies the mesoderm (e.g. gut)	Pipe, Nudel, Gd, Snake, Easter, Spätzle, Toll and Dorsal.
zerknüllt, tolloid, decapentaplegic.	rhomboid, short gastrulation and single-minded (lowest affinity for dorsal of the three)
Engrailed activated by even skipped and fushi taratzu. Involved genes: Engrailed —; hedgehog — patched — smoothened —; Cubitus Interruptus —; wingless —; frizzled — zeste white 3 — armadillo —; engrailed Engrailed and cubitus interruptus are TFs.	Low activator site affinity for dorsal. Harder to bind long enough for transcription to start.
Genetic screening: Can discover tissue-specific promotorers by non-coding DNA mutations. Can discover gain of function mutations, though lethal genes hard to mutate RNAi Much cheaper, bypasses lethal gene limits, discovers redundant genes.	anterior –; posterior.
The cellular blastoderm (individual cells) has formed.	Activated by hunchback and bicoid. Repressed to the anterior by giant, to the posterior by Krüppel.

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HOMEOTIC GENES	HOMEOTIC GENES
Homeotic genes do	Antennapedia LOF causes GOF causes
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
HOMEOTIC GENES	HOMEOTIC GENES
Homeotic genes resemble the genes in humans	In homeotic genes, LOF causes while GOF causes
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
HOMEOTIC GENES	HOMEOTIC GENES
Antennapedia GOF replaces antennae with legs due to	The three last homeotic genes are and they are each necessary for
Week 5: Drosophila melanogaster II, gap genes	Week 5: Drosophila melanogaster II, gap genes
Experiment	General terms
Hans Spemanns experiments	Blastula, blastocoel, blastomere
Week 6: Xenopus	Week 6: Xenopus
General terms	General terms
Gastrula(tion), Neurula(tion)	Invagination, involution, epiboly
Week 6: Xenopus	Week 6: Xenopus

LOF causes antennae to appear at 2nd legs, along with other thorax modifications GOF causes antennae to be replaced by legs.	Homeotic genes are localized genes that activate realizator genes, leading to the local development of appendages, etc.
LOF causes anteriorizations, GOF causes posteriorizations due to posterior dominance.  Posterization = anterior part gets posterior elements, e.g. legs instead of antennae.	HOX-genes.
Ultrabitthorax, abdominal A and abdominal B. Ubx controls T3-A1, abdA A2-A4 and abdB A5-A8. Each required for their part, posterior genes take precedence.	Antennapedia represses the antennae-related genes and activates leg-related genes.
Blastula is the embryo after cleavage, but before gastrulation. Blastocoel is the empty area inside the embryo on the animal side. Blastomere is a cell in a blastula.	Hans Spemann showed that by transplanting the organizer region from a frog embryo to another, a second body w. spinal column and CNS formed.
Invagination is the creation of a slit (dorsal lip), involution is the movement of cells through the slit (endoderm/mesoderm layer), epiboly is the spreading of the ectoderm (skin) around the embryo as the rest of the cells move inside.	Gastrulation means that the germ layers have started to form (cells move inside). Neurulation means that the spinal column has started to form.

General terms	General terms
No knock-out in Xenopus due to but an alternative is	Put the elements in order: Grey crescent Corsical rotation Gastrulation Organizer Nieuwkoop center Fertilization
Week 6: Xenopus	Week 6: Xenopus
EARLY DEVELOPMENT	EARLY DEVELOPMENT
Mid-blastula transition (MBT) is and occurs at	First three cell divisions, axis
Week 6: Xenopus	Week 6: Xenopus
GASTRULATION	The dorso-ventral axis
Archenteron	How is the dorsal region specified?
Week 6: Xenopus	Week 6: Xenopus
The dorso-ventral axis	The dorso-ventral axis
Cortical rotation can be inhibited through	How to rescue a dorsalized embryo?
Week 6: Xenopus	Week 6: Xenopus
The dorso-ventral axis	The dorso-ventral axis
Belly pieces are the result of	The Nieuwkoop center eventually becomes
Week 6: Xenopus	Week 6: Xenopus

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Fertilization, corsical rotation, grey crescent, Nieuwkoop center, Organizer, gastrulation.	Tetraploid genes makes it very difficult. Antisense oligos can be injected instead in case of mRNA.
First division divides left/right (both halves can form embryo) second division divides dorsal/ventral, third is animal/vegetal.	Zygotic genes are expressed. 12th cell cycle division.
Point of sperm entry specifies the ventral side. Dsh protein moves to the opposite side by cortical rotation. This becomes the Nieuwkoop center.	Empty space inside the embryo created during gastrulation. Eventually becomes gut.
Injection of any of the molecules found on the dorsal side: Dsh, betacatenin, simois, noggin, chordin, goosecoid or lithium, which will inhibit GSK-3, just like Dsh.  Centrifugation experiments can also work.	The chemical nocodazole, or UV-radiation, which inhibits the actin filaments. Both give a dorsalized embryo/'belly piece'.
Endoderm tissue.	A ventralized embryo, which is missing the organizer.

The dorso-ventral axis	The dorso-ventral axis
The organizer can not form at the bottom due to	Name the proteins in the pathway resulting in the organizer, along with their function.
Week 6: Xenopus	Week 6: Xenopus
The dorso-ventral axis	INDUCTION OF THE MESODERM
Goosecoid protein causes	Mesoderm cells are the result of
Week 6: Xenopus	Week 6: Xenopus
INDUCTION OF THE MESODERM	INDUCTION OF THE MESODERM
Maternal factors in the vegetal pole	$VegT\ activates$
Week 6: Xenopus	Week 6: Xenopus
INDUCTION OF THE MESODERM	Organiser
Function of Vg-1, Derriere, Xnrf	What's required for siamois to activate goosecoid and form the organiser?
Week 6: Xenopus	Week 6: Xenopus
Organiser	Organiser
Which gene indicates the presence of the organiser?	For dorsal mesoderm specification, you need
Week 6: Xenopus	Week 6: Xenopus

Dsh -I GSK-3 -I B-catenin -¿ siamois (TF) -¿ goosecoid	The organizer is made from marginal zone ectoderm cells.
Endoderm cells inducing ectoderm cells at the marginal zone by releasing Vg-1.	Movement of dorsal lip cells, induces dorsal mesodermal fate in cells, recruits nearby cells to lip
Derriere, Xnrf, Vg-1	VegT, Vg1.
High levels of Xnrf released from the Nieuwkoop center, meaning only ectodermal cells can form dorsal mesoderm/organiser.	Transforms ectoderm cells to mesoderm cells when received, by activating Xbra in mesoderm cells, determining their fate.
B-catenin. Usually depleted by GSK-3, but Dsh protein, which is found in the dorsal region, inhibits GSK-3, allowing Betacatenin to bind to Tcf-3 and transform it from a repressor to an activator of simois.	Goosecoid.

BMP-4 in mesodermal differentiation	BMP-4 IN MESODERMAL DIFFERENTIAION
High levels of BMP specify	Intermediate levels of BMP specify
Week 6: Xenopus	Week 6: Xenopus
BMP4 IN MESODERMAL DIFFERENTIAION	BMP4 IN MESODERMAL DIFFERENTIAION
Low levels of BMP4 specify	BMP4 is inhibited by
Week 6: Xenopus	Week 6: Xenopus
NEURULATION	NEURULATION
Paraxial mesoderm essentially means	The notochord is responsible for
Week 7: Xenopus	Week 7: Xenopus
NEURULATION	NEURULATION
The neural plate becomes the neural tube by	The part of the ectoderm that forms neurons is
Week 7: Xenopus	Week 7: Xenopus
Neurulation	General
Ectodermic cells isolated form due to	Embryos look similar at the stage
Week 7: Xenopus	Week 7: Xenopus

Kidneys, muscle, heart.	Blood.
Noggin, chordin (and frizzzzzzbee) from the organiser.	Notochord.
Forming the neural plate, eventually becomes spine, brain and CNS.	Cells that form somites, which forms trunk and limb muscles, and ribcage.
The part closest to the organizer after gastrulation.	Neural folds folding over, "zipping" the neural plate up.
Phylotypic stage, late part of organogenesis.	Neurons, as the community effect with BMP is necessary for epidermis to form.

AP AXIS IN NEURULATION	AP AXIS IN NEURULATION
Neural tissue is induced by and differentiated by	Posterior ectoderm is induced by high amounts of
Week 7: Xenopus	Week 7: Xenopus
AP AXIS IN NEURULATION	AP AXIS IN NEURULATION
Trunk is induced by high amounts of	Head is induced by high amounts of
Week 7: Xenopus	Week 7: Xenopus
AP AXIS IN NEURULATION	General terms
High amounts of retinoic acid causes	Morula, Zona Pellucida, Trophoblast
Week 7: Xenopus	Week 8: Stem cells
General terms	General terms
When cells move through the primitive streak/node	Totipotent, pluripotent, multipotent, unipotent
Week 8: Stem cells	Week 8: Stem cells
Experiment	
John B. Gurdon and Yamanaka showed that	
Week 8: Stem cells	

Wnt, FGF, retinoic acid (RA).	planar signals (along the surface), lateral signals (from the notochord).
Wnt inhibitors Cerberus, frizzbee, dickkopf plus IGF (insulin growth factor).	Inhibitors of BMP chordin, noggin and follistatin
The morula is a solid ball opposed to the blastula, which is hollowed. The morula is inside the zona pellucida until blastulation occurs. Trophoblast is the extraembryonic tissue in the blastula.	Posteriorization of embryo.
Cells that can make respectively all cells (including extraembryonic), all cells (excluding extraembryonic), some types of cells, one type of cell.	When cells move through the primitive streak in a mouse, they develop into mesoderm cells. Notochord if moving through node.
	Normal cells can be induced to become pluripotent stem cells by subjecting them to specific transcription factors. Impossible with mechanical or chemical stress.