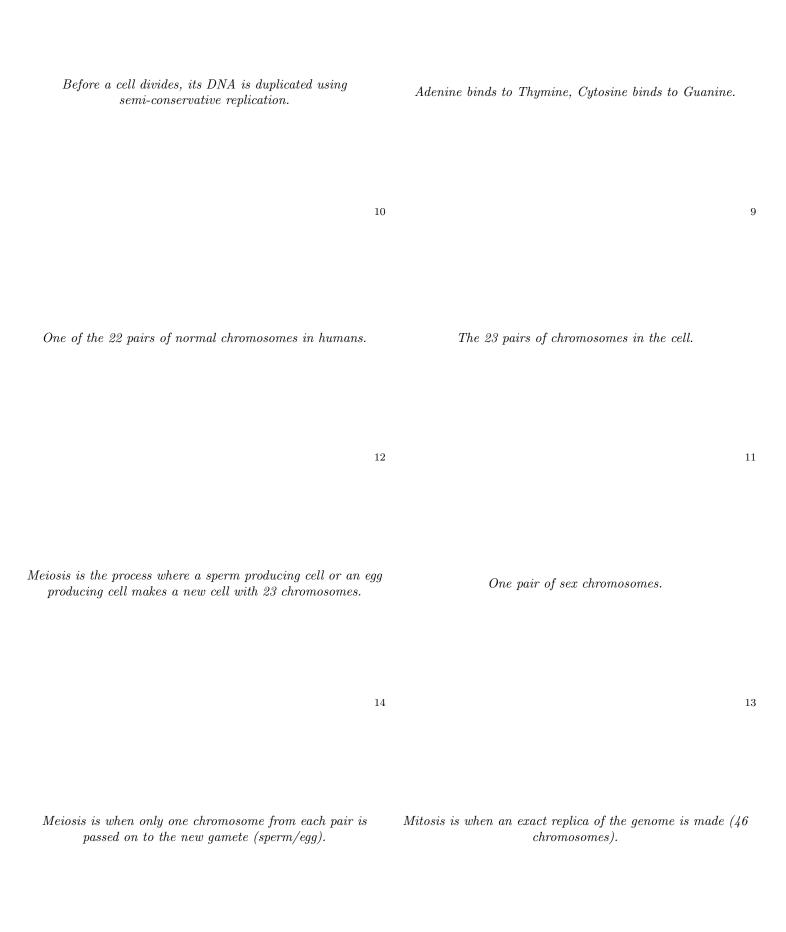
$Each\ DNA\ molecule\ is\ packed\ into\ a$.	$contain\ instructions\ for\ making$
The two strands of DNA twist to form a $oxedsymbol{1}$.	When replicating, the between the DNA strands break, and come to bind with the exposed ones on the separated strands to form new strands.
Proteins act alone or in functions. to perform many cellular	The four DNA bases are 6
A backbone provides structure for the DNA .	bonds hold the two strands of DNA together.

Genes contain instructions for making proteins.	Each DNA molecule is packed into a chromosome.
	2 1
When replicating, the hydrogen bonds between the DNA strands break, and new bases come to bind with the exposed ones on the separated strands to form new strands.	The two strands of DNA twist to form a double helix.
	4 3
Adenine, Thymine, Guanine, Cytosine	Proteins act alone or in complexes to perform many cellular functions.
	6 5
Hydrogen bonds hold the two strands of DNA together.	$A\ sugar-phosphate\ backbone\ provides\ structure\ for\ the\ DNA.$

binds to binds to	Before a cell divides, its DNA is duplicated using ${}^{\circ}$.
$What \ is \ the \ Karyotype?$	$What \ is \ an \ autosome?$
In addition to the autosomes, what other chromosomes are there?	is the process where a sperm producing cell or an egg producing cell makes a new cell with 23 chromosomes.
is when an exact replica of the genome is made (46 chromosomes).	is when only one chromosome from each pair is passed on to the new (sperm/egg).



$DNA \longrightarrow RNA \longrightarrow protein$	When a gene is, it forms many
molecules get into proteins.	Define an allele
Define polymorphism (in the context of DNA)	is when a person has two copies of one allele on a gene locus.
is when a person has two different alleles on a gene locus.	A gene is if the protein that it produces can be compensated for by the correct protein produced by



A gene is recessive if the mutated protein that it produces can

be compensated for by the correct protein produced by an

 $alternative \ allele.$

24

23

Heterozygous is when a person has two different alleles on a

gene locus.

If a mutated gene produces proteins that fulfil a new function, then it may be sometimes, since the original function will be fulfilled by .	Genes can be, or
Define genotype.	Define phenotype
The phenotype is controlled by derived from , and the	What bloodgroup is made from two co-dominant alleles?
Blood groups: $\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Allele frequency is linked to its in a given.

Genes can be recessive, dominant or co-dominant.

If a mutated gene produces proteins that fulfil a new function, then it may be co-dominant, since the original function will be fulfilled by the other allele.

26

25

The physical appearance of an individual, including its observable or measurable traits.

The genetic make-up of an individual, which includes the genes or alleles present in it.

28

27

AB

The phenotype is controlled by proteins derived from genes, and the environment.

30

29

Allele frequency is linked to the fitness it provides to its carriers in a given environment.

$$Blood\ groups: \begin{array}{c|cccc} & I^A & I^B & i \\ \hline I^A & A & AB & A \\ I^B & AB & B & B \\ i & A & B & O \\ \end{array}$$

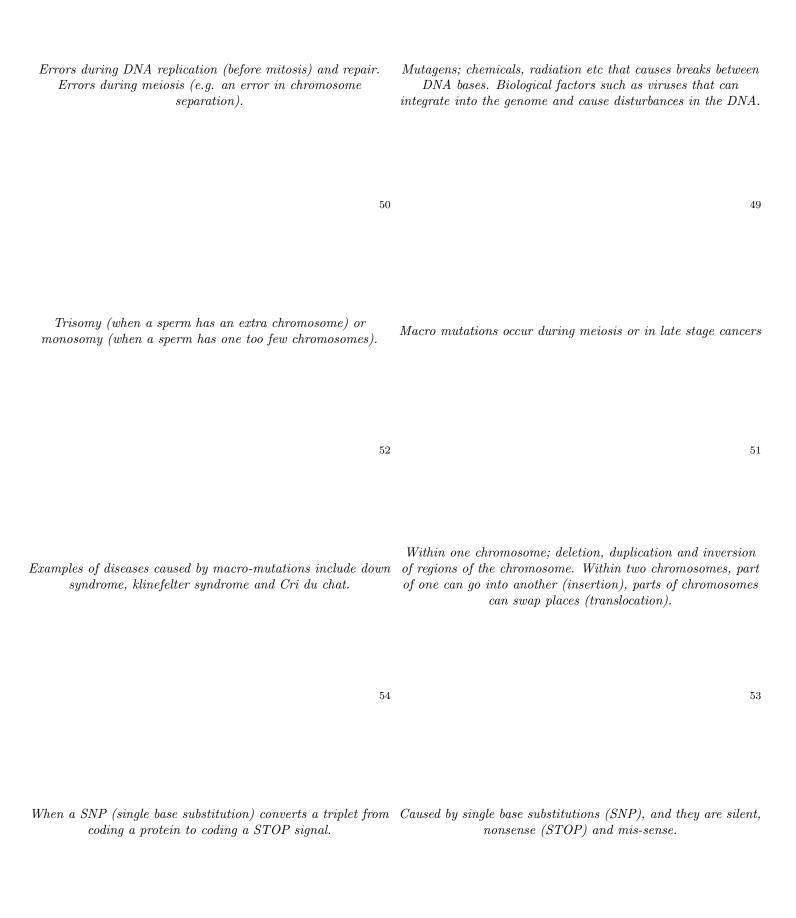
Define genetic fitness	If an allele provides , it is likely to and become in a given population.
Mutations have allowed us to our diet. This includes a mutation that lets us produce during adulthood (to drink milk) and another one that reduces the function of a allowing us to eat broccoli and sprouts! This is an example of .	Carriers of alleles are and get protection from malaria.
Carriers of alleles die if they are since their haemoglobin does not function well.	People for a mutation affecting are asymptomatic and immune to HIV. Probably because this gave protection against and in the past. This mutation is less effective against pathogens from .
Environment interaction can influence the genotype. and are sensitive to temperature, and change colour at different temperatures. This is caused by temperature sensitive.	The environment affects the phenotype; a can make a human twin grow to be smaller, and flowers have based on the soil.



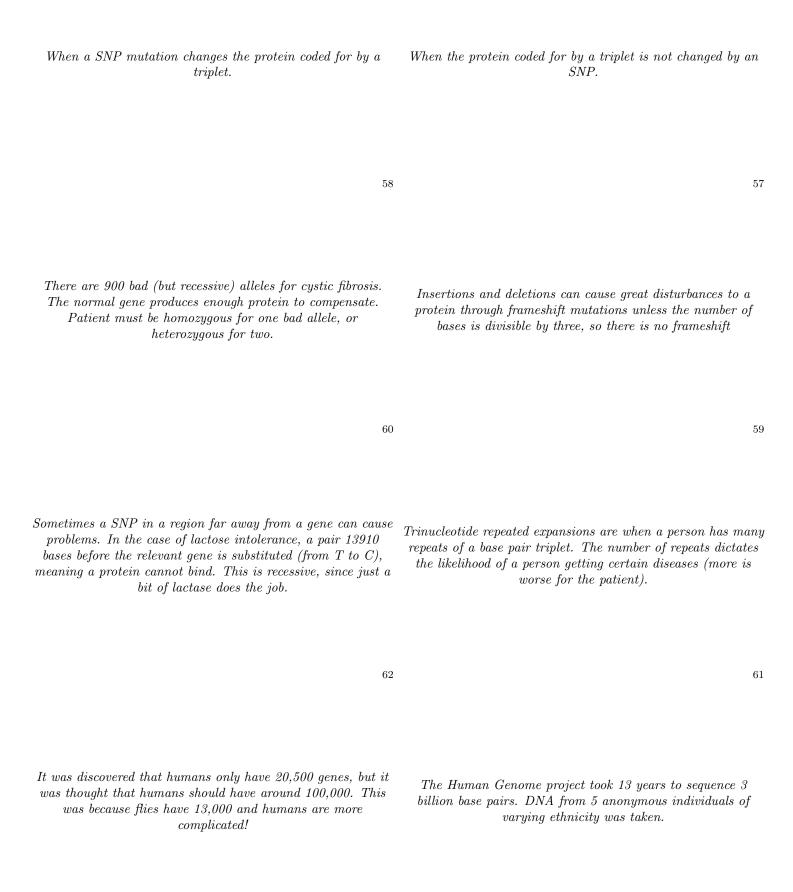
Most are due to several genes and the environment (e.g. , , , ,).	A greater similarity between for a particular compared to provides evidence that factors play a role.
twins share all their genes and their home environment. twins share their genes and a home environment.	Defineamutation
The size of mutations ranges from (- SNP) to	SNP mutations are, chromosome rearrangements are
Define a hereditary mutation.	Define an acquired (somatic) mutation.



$Environmental\ factors\ that\ cause\ mutations\ include$	Intrinsic factors causing mutations include
Macro mutations occur during or in	Mutations during meiosis include
$Single\ chromosome\ macro-mutations\ include$	Examples of diseases caused by macro-mutations include and .
33	04
What are the three types of substitution micro-mutations and what are they caused by?	How does a nonsense mutation occur?
55	56



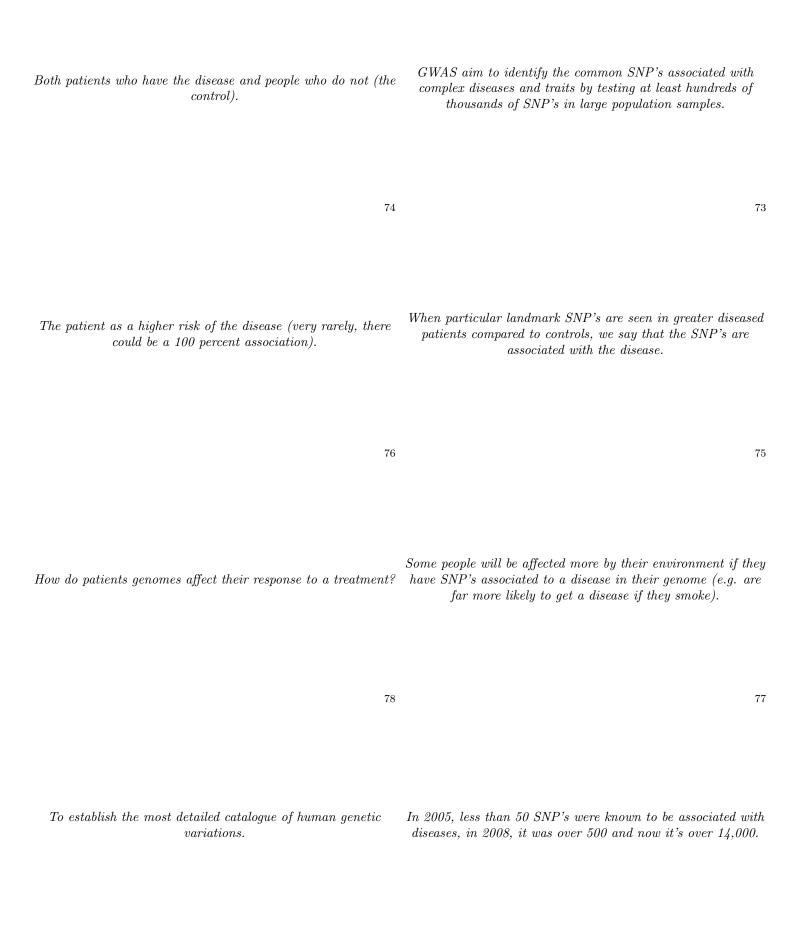
What is a silent mutation? 57	What is a mis-sense mutation? 58
can cause great disturbances to a protein through unless the number of bases , so there is no	There are bad (but) alleles for cystic fibrosis. The normal gene . Patient must be for one bad allele, or for two.
are when a person has many repeats of a base pair triplet. dictates the likelihood of a person getting certain diseases (more is worse for the patient).	Sometimes a SNP in a region far away from a gene can cause problems. In the case of lactose intolerance, a pair 13910 bases before the relevant gene is substituted (from T to C), meaning a protein cannot bind. This is recessive, since just a bit of lactase does the job.
The Human Genome project took to sequence base pairs. DNA from individuals of was taken.	It was discovered that humans only have genes, but it was thought that humans should have around . This was because flies have and humans are more complicated!



Humans share of their genes with flies, and only of the human DNA codes for genes.	Why can humans get by with so few genes?
Cells have the, but do not express the Where these are expressed determines the type of cell formed.	Humans genomes differ by about , which is about base pairs which are mostly
The frequency of SNP's is one in every base pairs. Most are and have	SNP's outside of genes are useful because
$GWAS\ stands\ for$	Most diseases result from , patients with have been found to be more at risk of developing some diseases.



GWAS aim to identify the common SNP's associated with by testing at least of SNP's in large population samples.	Where are the samples for GWAS taken from
73	74
When particular landmark SNP's are seen in greater diseased patients compared to controls, we say that the SNP's are with the disease.	If a patient has SNP's associated with a disease, what does it mean?
Some people will be affected more by if they have SNP's associated to a disease in their genome (e.g. are far more likely to get a disease if they smoke).	$What \ is \ pharmacogenomics?$
In 2005, SNP's were known to be associated with diseases, in 2008, it was and now it's over.	What was the aim of the 1000 genomes project?



On average, each person carries loss of function variants in annotated genes, and previously implicated in inherited disorders.	How many new disease causing mutations were identified in the 1000 genomes project?
In the 100,000 genomes project was started by It was split between helping and	The 100,000 genomes project sampled people including serious illness patients. cancer patient genomes (one cancer and one normal per patient), and rare disease genomes (three per patient;
and both let you get your genome sequenced. does not offer much advice or counselling, but does, and is therefore more expensive.	Immlumina tests healthy adults interested in learning about their risk for assessing their status and understanding their response to certain.
How many different types of cell are there in humans?	What is the first cell created by the fusion of the egg and sperm?



On average, each person carries 250-300 loss of function variants in annotated genes, and 50-100 previously implicated in inherited disorders.

82

81

The 100,000 genomes project sampled 75,000 people including 40,000 serious illness patients. 50,000 cancer patient genomes (one cancer and one normal per patient), and 50,000 rare disease genomes (three per patient; one patient genome and two blood relatives))

In 2014 the 100,000 genomes project was started by the NHS. It was split between helping cancer patients and patients with rare diseases.

84

83

Immlumina tests healthy adults interested in learning about their risk for a set of adult-onset conditions, assessing their carrier status and understanding their response to certain drugs.

23andMe and Illumina both let you get your genome sequenced. 23andMe does not offer much advice or counselling, but illumina does, and is therefore more expensive.

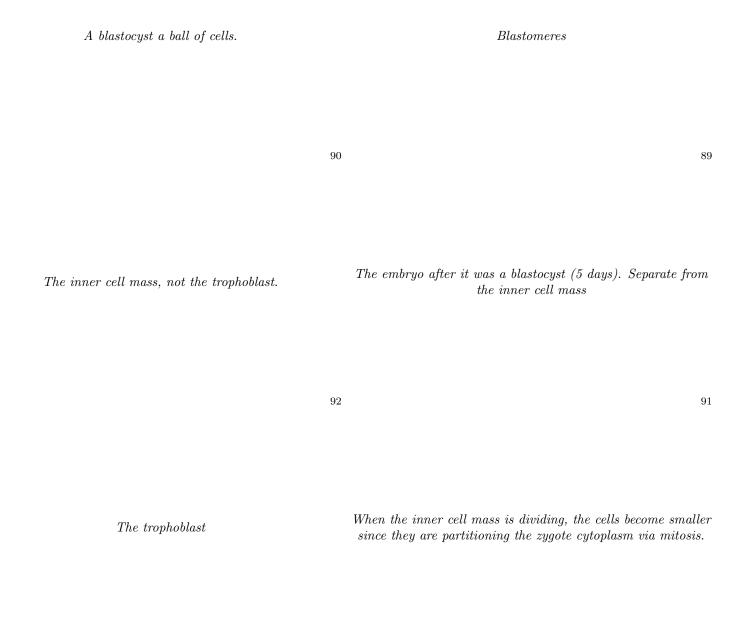
86

85

The zygote.

220 cell types.

What are the initial cells formed from the zygote called?	After there are more than 8 blastomeres, what is there?
$What \ is \ the \ trophoblast?$	Where does the embryo form from?
When the is dividing, the cells become smaller since they are partitioning the cytoplasm via mitosis.	What lets the embryo attach to the wall of the uterus?
is driven by the . The expands and changes shape and location, but is still .	Once attached to the uterus wall, the inner cell mass sets the is the axis.) The body is symmetrical along this.



Once attached to the uterus wall, the inner cell mass sets the axis of the body. The primitive streak is the anterior posterior (head to tail) axis.) The body is symmetrical along this.

uterine implantation is driven by the trophoblast. The Inner cell mass expands and changes shape and location, but is still only one type of cell.

After setting the axis, takes place. This is where cells migrate, along the bottom, endoderm form, in the middle at the top. will be the skin and nerves, forms and the forms the	What is a highly coordinated cell movement?	98
What structures become the vertebrae?	What do somites eventually form into?	100
Growing organs is called	By saying organogenesis is progressive, we mean	102
What is used as a reference for growing specialised cells in an embryo?	What is a differentiated cell?	104

After setting the axis, gastrulation takes place. This is where cells migrate, along the bottom, endoderm form, mesoderm in Gastrulationthe middle and ectoderm at the top. ectoderm will be the skin and nerves, mesoderm forms muscles, blood, skeleton, heart etc and the endoderm forms the digestive system, lungs etc 98 97 Muscles, vertebral column and dermis of the skin. They are Somites; they emit signals telling what organs to form where. landmarks for organ formation during development. 100 99 That the organs grow in stages, e.g. there is a little growth for Organogenesisthe arm first, then it gets longer, then it gets digits etc. 102 101

One where the shape, structure and function is well defined.

104

The head to tail framework.

The gurdon experiment was done on		The gurdon exp	eriment involves.	
105				106
Cells developmental potential (potency) changes how as it gets more specialised?	WI	hat is involved in	a grafting experi	ment?
107				108
	Source	Potential	Type of cell	Can develop into Whole organ-
The fate of a cell before differentiation. They	Zygote	$and \qquad self- \\ renewing$	Embryonic stem cell	Whole organism. Any cell type
can sometimes a new situation, up to	Adult	Multipotent,	multipotent	Some cell types
	Organ	Limited po- tential and renewal		Choice of be- tween types
	-	Limited divi-	committed pro-	1 type, locked
	-	sion No division	gentor Differentiated	fate. No division.
Once a cell is differentiated	Cells have	the same genes, genes that mak	but it's how they es them different	
111				112

Taking egg cells, removing the nuclei and inserting nuclei from either a small embryo or a developed intestine cell. The former usually develop into tadpoles, but the latter mostly stop developing before the tadpole stage.

Frogs

106

Cells from an early gastrula (early embryo) that would form an eye are taken and transplanted into an host embryo (oldest), as well as ones from an neurala (older embryo than gastrula). The ones from the younger embryo develop into anything depending where they are implanted, the ones from the older embryo develop into eyes.

It decreases.

108

Source	$oxed{Potential}$	Type of cell	$egin{array}{ccc} Can & develop \ into \end{array}$
Zygote	Totipotent	-	Whole organ-ism.
Blasocyst	Pluripotent and self-renewing	Embryonic stem cell	Any cell type
Adult	Multipotent, self-renewing	multipotent stem cells	Some cell types
Organ	Limited poten- tial and renewal	Progenitor	Choice of be- tween 2-6 types
-	Limited divi- sion	committed pro- gentor	1 type, locked fate.
-	No division	Differentiated	No division.

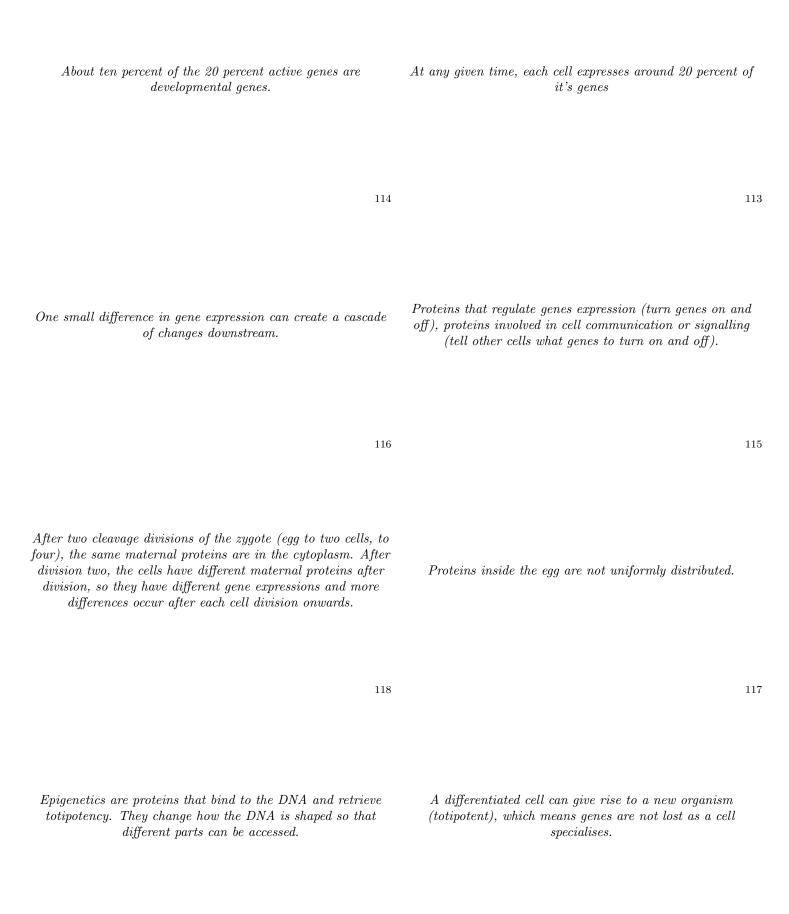
The fate of a cell can be locked before differentiation. They can sometimes not adapt to a new situation, up to 4 generations before.

110 109

Cells have the same genes, but it's how they express their genes that makes them different.

It has a clear cut identity and expresses specific proteins for morphology and function.

At any given time, each cell expresses around of it's genes	About of the active genes are developmental genes.
$Development al\ genes\ control:$	One small difference in gene expression can
Proteins inside the egg are .	After two of the zygote (egg to two cells, to four), the are in the cytoplasm. After division two, the cells have different maternal proteins after division, so they have different gene expressions and more differences occur after each cell division onwards.
A differentiated cell can give rise to a new organism (), which means genes are as a cell specialises.	are proteins that bind to the DNA and They change how the DNA is shaped so that different parts can be accessed.



The embryo starts with a zygote (It becomes a with a and and and and and are are an are are an are an are an are	stem cells can become any cell.
have the minimum level of specialisation, have the maximum level of specialisation.	cells are not stem cells, but cells are.
cell stage is the limit for totipotency in humans.	Stem cells in the ICM are
$Adult\ stem\ cells\ are$.	Adult stem cells are found in

The embryo starts with a zygote (totipotent.

It becomes a blastocyst with a trophoblast and ICM

(plurpiotent)

re full differentiation, cells become locked in their fat

Before full differentiation, cells become locked in their fate and are determined

At the gene level, cells become different by expressing different developmental genes

The initial differences come from the maternal developmental proteins being unevenly distributed in the egg cytoplasm. As blastomeres form from cleavage divisions, they end up not having the same developmental proteins.

122 121

Committed progenitor cells are not stem cells, but progenitor cells are.

Totipotent stem cells can become any cell.

totipotent stem cells have the minimum level of specialisation, differentiated cells have the maximum level of specialisation.

124 123

Stem cells in the ICM are pluripotent.

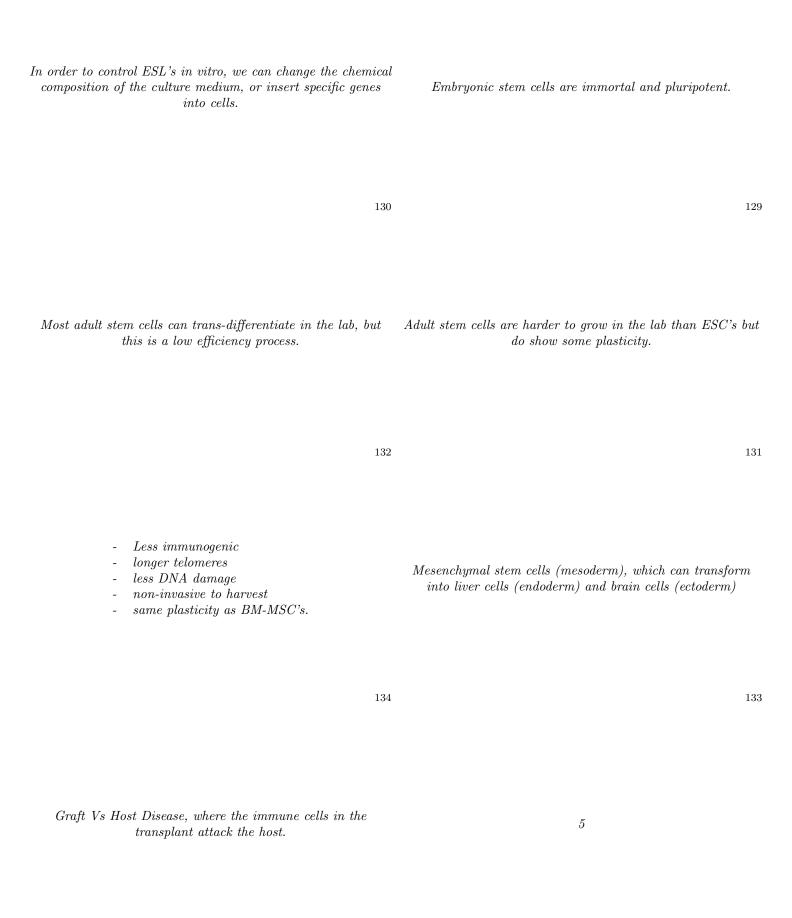
8 cell stage is the limit for totipotency in humans.

126 125

Brain, Skin, Bone Marrow, Skeletal muscle, Intestines (any cell that needs regrowth).

Adult stem cells are multipotent.

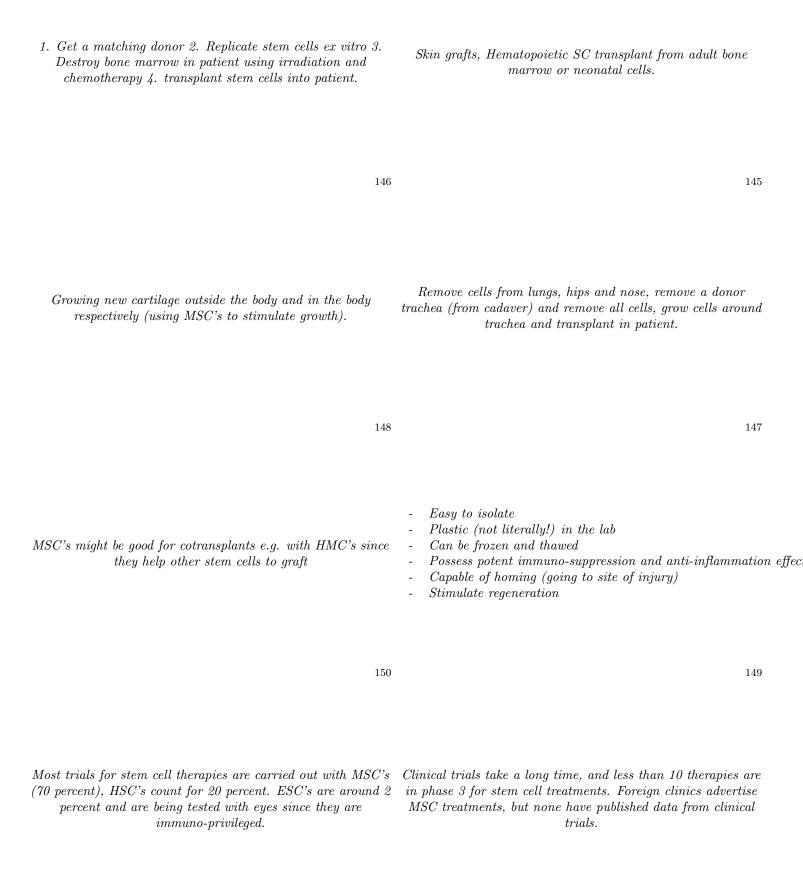
Embryonic stem cells are and .	In order to control ESL's in vitro, we can culture medium, or
Adult stem cells are to grow in the lab than but do show.	Describe the plasticity of ASC's
What are the most apparently plastic cells?	Why are UC-MSC's better than BM-MSC's?
How many proteins are usually considered for immuno-compatibility?	What is GVHD?



Why are neonatal (UC cells) less immunogenic?	Neonatal cells have longer (which), since they get shorter since they do not get replicated, and neonatal cells have not divided many times.
137	138
In ESC's what enzyme is expressed that stops a telomeres from getting shorter?	When is telomerase turned off?
What enzyme do most cancer cells produce and why?	What is a bank of ESC lines?
What are the three sources of human stem cells?	How could we make a stem cell with only some skin cells?
143	144



What are the currently approved stem cell based therapies?	How does a bone marrow transplant to cure leukaemia work?
Give an example of tissue engineering	What is ex-vivo and in-situ cartilage engineering
$List \ advantages \ of \ MSC's$	MSC's might be good for e.g. with HMC's since they help other stem cells to graft
Clinical trials take , and therapies are in phase 3 for stem cell treatments. Foreign clinics advertise MSC treatments, but none have published data from clinical trials.	Most trials for stem cell therapies are carried out with MSC's (), HSC's count for . ESC's are around and are being tested with . since they are .



SC's can be used for ,	For repairing and replacing cells, what type of cell should we use?
and	ust:
153	154
What is an induced pluripotent stem cell?	How to do Parkinson's in a dish?
155	156
The traditional approach to medicine is	The traditional approach to medicine does not take into account , which is successful for some, but not all patients.
$What\ is\ stratified\ medicine?$	Personalised medicine (aka) takes into account
159	160

The patients own cells (autologous transplants). This requires SC's can be used for replacing cells (e.g. transplants), adult stem cells that are reasonably plastic though, and its repairing cells (e.g. genetically modify SC's outside the body hard to isolate ASC's in the lab. Otherwise, use donor SC's and re-implant) and protecting via MSC immunosupression. with low immunogenicity. 154 153 Collect skin cells Re-program them into stem cells When you reprogram a normal (e.g. skin) cell by inserting Grow brain cells from them (induce brain genes (via viruses or otherwise). Only 3-4 gene insertions cell differentiation) required.Stress out the brain cells with toxins Observe Parkinson's-like features 156 155 The traditional approach to medicine does not take into account individual differences between patients, which is The traditional approach to medicine is one size fits all. successful for some, but not all patients. 158 157

Personalised medicine (aka precision medicine) takes into

account

160 159

Targeting different types of specific diseases made up of lots of

different genes e.g. maturity onset diabetes

Examples of historical personalised medicine include	When the human genome project started, drugs had pharmacogenetic information. After it ended, drugs had this information and ten years later, there drugs. Now the and examined.
Genetic changes of interest include, and These all change how much of the proteins coded for by an affected gene is produced.	What are the advantages of personalised medicine (6 things)?
What genes increase your risk of breast and ovarian cancer and how much by?	There are over predictive tests looking at genes. They can of treating patients.
Even if a predictive test for a gene doesn't have an associated drug to lower risk, you can Sergey Brin does this for Alzheimer's!	It's easy to take biopsy of cancer tumours (because they're by definition, not needed), so they can have their genome sequenced to see what genes the cancers have.

When the human genome project started, 4 drugs had pharmacogenetic information. After it ended, 46 drugs had this information and ten years later, there 104 drugs. Now the genome, proteome, metabolome and epigenome are examined.

Inheritance of alkaptunoria, blood transfusions using blood capability testing, genetic basis of selective toxicity of an antimalarial drug.

162 161

- Shift reaction to prevention
- Predict susceptibility of developing a disease

Genetic changes of interest include SNP's, base insertions,

- Improve dosing of drugs (increase efficiency, reduce side effects) copy-number variations and variable number tandem repeats.

 Reduce cost, time and attrition rate in drug development.
- Reduce cost, time and attrition rate in drug development

Decrease adverse affects of drugs, increase diagnostic and detection power for disease gene is produced.

164 163

There are over 15000 predictive tests looking at 2800 genes. They can save the cost of treating patients.

BRAC1, BRAC2; 85 percent higher lifetime chance of breast cancer and 60 percent chance of ovarian cancer.

166 165

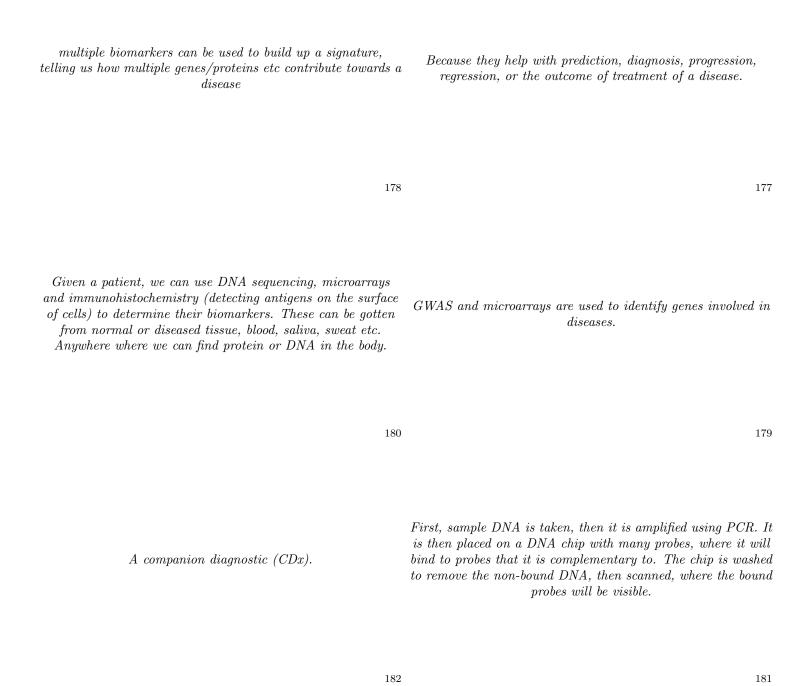
It's easy to take biopsy of cancer tumours (because they're by definition, not needed), so they can have their genome sequenced to see what genes the cancers have.

Even if a predictive test for a gene doesn't have an associated drug to lower risk, you can change environmental factors (e.g. eat better, stop smoking etc). Sergey Brin does this for Alzheimer's!

There are drugs (Ivacaftor) that target the of diseases rather than just treating symptoms.	What does metastatic cancer mean?
109	170
Enzymes metabolise drugs, and metabolise over percent of drugs. There are in genes that code for these enzymes. Some people metabolise fast (and are at risk of), or even ultra-fast metabolisers (meaning the drugs).	After a stent has been put into an artery, the body recognises it as foreign and blood will clot around it. A drug is given to stop clotting, but one enzyme (CYP 2C19) converts the drug from inactive to active. Variations in this enzyme mean not as much is converted, meaning the blood can clot possibly causing a heart attack or stroke.
What are some problems with personalised medicine?	What are the ethical problems with personalised medicine (5 things)?
mutations can be involve with genes. Drugs need to target driver mutations in order to be effective.	Define biomarker
1/0	170



Why are biomarkers helpful?	can be used to build up a signature, telling us how multiple towards a disease
and are used to identify genes involved in diseases.	Given a patient, we can use and and (detecting antigens on the surface of cells) to determine their biomarkers. These can be gotten from , , , , , , , , , , , , , , , , , , ,
How do DNA chips work?	What is the name for a test that goes with a drug?
Oncotype Dx identifies genes associated with and housekeeping genes (used as a control). These are used to give a score of 1-100 giving the likely reoccurrence of within the next years. It also predicts the response to . This costs .	determines how aggressive a tumor is (i.e. whether there is a high or low risk of). It measures the mRNA of genes. A biopsy is taken and determined to make sure that or more cells are cancerous, then the tissue is used for a 184



MammaPrint determines how aggressive a breast cancer tumor is (i.e. whether there is a high or low risk of metastasis). It measures the mRNA of 1900 genes. A biopsy is taken and determined to make sure that thirty percent or more cells are cancerous, then the tissue is used for a microarray.

Oncotype Dx identifies 16 genes associated with breast cancer and 5 housekeeping genes (used as a control). These are used to give a score of 1-100 giving the likely reoccurrence of the tumor within the next ten years. It also predicts the response to chemotherapy. This costs \$4175.