Each DNA molecule is packed into a [redacted].

1

[redacted] *contain instructions for making* [redacted].

2

The two strands of DNA twist to form a [redacted].

3

When replicating, the [redacted] *between the DNA strands break, and* [redacted] *come to bind with the exposed ones on the separated strands to form new strands.*

4

Proteins act alone or in [redacted] *to perform many cellular functions.*

5

The four DNA bases are...

6

A [redacted] *backbone provides structure for the DNA.*

7

[redacted] *bonds hold the two strands of DNA together.*

8

Genes contain instructions for making proteins.

2

Each DNA molecule is packed into a chromosome.

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.

4

The two strands of DNA twist to form a double helix.

3

Adenine, Thymine, Guanine, Cytosine

6

Proteins act alone or in complexes to perform many cellular functions.

5

Hydrogen bonds hold the two strands of DNA together.

8

A sugar-phosphate backbone provides structure for the DNA.

7

binds to , *binds to* .

9

Before a cell divides, its DNA is duplicated using .

10

What is the Karyotype?

11

What is an autosome?

12

In addition to the autosomes, what other chromosomes are there?

13

is the process where a sperm producing cell or an egg producing cell makes a new cell with 23 chromosomes.

14

is when an exact replica of the genome is made (46 chromosomes).

15

is when only one chromosome from each pair is passed on to the new (sperm/egg).

16

Before a cell divides, its DNA is duplicated using semi-conservative replication.

10

Adenine binds to Thymine, Cytosine binds to Guanine.

9

One of the 22 pairs of normal chromosomes in humans.

12

The 23 pairs of chromosomes in the cell.

11

Meiosis is the process where a sperm producing cell or an egg producing cell makes a new cell with 23 chromosomes.

14

One pair of sex chromosomes.

13

Meiosis is when only one chromosome from each pair is passed on to the new gamete (sperm/egg).

16

Mitosis is when an exact replica of the genome is made (46 chromosomes).

15

DNA [redacted] *RNA* [redacted] *protein*

17

When a gene is [redacted]*, it forms many* [redacted] *molecules.*

18

[redacted] *molecules get* [redacted] *into proteins.*

19

Define an allele

20

Define polymorphism (in the context of DNA)

21

[redacted] *is when a person has two copies of one allele on a gene locus.*

22

[redacted] *is when a person has two different alleles on a gene locus.*

23

A gene is [redacted] *if the* [redacted] *protein that it produces can be compensated for by the correct protein produced by* [redacted]*.*

24

When a gene is transcribed, it forms many RNA molecules.

18

$DNA \xrightarrow{transcription} RNA \xrightarrow{translation} protein$

17

Any of several forms of a gene, usually arising through mutation. Alleles are responsible for hereditary variation.

20

RNA molecules get translated into proteins.

19

Homozygous is when a person has two copies of one allele on a gene locus.

22

The existence of several alleles for one gene locus. Individuals have one or two alleles per locus.

21

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

Heterozygous is when a person has two different alleles on a gene locus.

23

If a mutated gene produces proteins that fulfil a new function, then it may be [redacted]*, since the original function will be fulfilled by* [redacted].

25

Genes can be [redacted]*,* [redacted] *or* [redacted].

26

Define genotype.

27

Define phenotype

28

The phenotype is controlled by [redacted] *derived from* [redacted]*, and the* [redacted].

29

What bloodgroup is made from two co-dominant alleles?

30

Blood groups:

	I^A	I^B	i
I^A	[redacted]	[redacted]	[redacted]
I^B	[redacted]	[redacted]	[redacted]
i	[redacted]	[redacted]	[redacted]

31

Allele frequency is linked to [redacted] *to its* [redacted] *in a given* [redacted].

32

Genes can be recessive, dominant or co-dominant.

26

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.

25

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

28

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

27

AB

30

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

29

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

32

Blood groups:

	I^A	I^B	i
I^A	A	AB	A
I^B	AB	B	B
i	A	B	O

31

Define genetic fitness

33

If an allele provides [redacted] *, it is likely to* [redacted] *and become* [redacted] *in a given population.*

34

Mutations have allowed us to [redacted] *our diet. This includes a mutation that lets us produce* [redacted] *during adulthood (to drink milk) and another one that reduces the function of a* [redacted] *allowing us to eat broccoli and sprouts! This is an example of* [redacted] *.*

35

Carriers of [redacted] *alleles are* [redacted] *and get protection from malaria.*

36

Carriers of [redacted] *alleles die if they are* [redacted] *since their haemoglobin does not function well.*

37

People [redacted] *for a mutation affecting* [redacted] *are asymptomatic and immune to HIV. Probably because this gave protection against* [redacted] *and* [redacted] *in the past. This mutation is less effective against pathogens from* [redacted] *.*

38

Environment interaction can influence the genotype. [redacted] *and* [redacted] *are sensitive to temperature, and change colour at different temperatures. This is caused by temperature sensitive* [redacted] *.*

39

The environment affects the phenotype; a [redacted] *can make a human twin grow to be smaller, and flowers have* [redacted] *based on the soil* [redacted] *.*

40

If an allele provides an advantage, it is likely to persist and become more prominent in a given population.

34

The reproductive success of a genotype, measured as the number of offspring produced by and individual that survive to a reproductive age relative to the average age for the population.

33

Carriers of sickle cell anaemia alleles are asymptomatic and get protection from malaria.

36

Mutations have allowed us to diversify our diet. This includes a mutation that lets us produce lactase during adulthood (to drink milk) and another one that reduces the function of a bitter substance taste receptor allowing us to eat broccoli and sprouts! This is an example of natural selection.

35

People homozygous for a mutation affecting CCR5 are asymptomatic and immune to HIV. Probably because this gave protection against the plague and smallpox in the past. This mutation is less effective against pathogens from developing countries.

38

Carriers of sickle cell anaemia alleles die if they are homozygous since their haemoglobin does not function well.

37

The environment affects the phenotype; a worse diet can make a human twin grow to be smaller, and flowers have different colours based on the soil pH.

40

Environment interaction can influence the genotype. Himalayan rabbits and arctic foxes are sensitive to temperature, and change colour at different temperatures. This is caused by temperature sensitive tyrosine.

39

Most [redacted] *are due to several genes and the environment (e.g.* [redacted]*,* [redacted]*,* [redacted]*).*

41

A greater similarity between [redacted] *for a particular* [redacted] *compared to* [redacted] *provides evidence that* [redacted] *factors play a role.*

42

[redacted] *twins share all their genes and their home environment.* [redacted] *twins share* [redacted] *their genes and a home environment.*

43

Define a mutation

44

The size of mutations ranges from [redacted] *(*[redacted] *- SNP) to* [redacted] *(*[redacted]*)*

45

SNP mutations are [redacted]*, chromosome rearrangements are* [redacted]

46

Define a hereditary mutation.

47

Define an acquired (somatic) mutation.

48

A greater similarity between identical twins for a particular trait compared to fraternal twins provides evidence that genetic factors play a role.

42

Most phenotypes are due to several genes and the environment (e.g. skin colour, height, weight).

41

*A **permanent** alteration in the DNA sequence passed on into daughter cells (and sometimes gametes).*

44

Identical twins share all their genes and their home environment. Fraternal twins share half their genes and a home environment.

43

SNP mutations are micro-mutations, chromosome rearrangements are macro-mutations

46

The size of mutations ranges from a single base pair (single nucleotide polymorphism - SNP) to large segments of a chromosome (chromosome rearrangement)

45

When a mutation occurs at some point in a person's life, and is present only in the cell that it occurred and it's daughter cells (through mitosis).

48

A mutation inherited from a parent gamete and present throughout a person's life and in every cell in their body. This can be passed on to progeny through meiosis.

47

Environmental factors that cause mutations include...

49

Intrinsic factors causing mutations include...

50

Macro mutations occur during [redacted] *or in* [redacted]

51

Mutations during meiosis include...

52

Single chromosome macro-mutations include...

53

Examples of diseases caused by macro-mutations include [redacted], [redacted] *and* [redacted].

54

What are the three types of substitution micro-mutations and what are they caused by?

55

How does a nonsense mutation occur?

56

Errors during DNA replication (before mitosis) and repair. Errors during meiosis (e.g. an error in chromosome separation).

50

Mutagens; chemicals, radiation etc that causes breaks between DNA bases. Biological factors such as viruses that can integrate into the genome and cause disturbances in the DNA.

49

Trisomy (when a sperm has an extra chromosome) or monosomy (when a sperm has one too few chromosomes).

52

Macro mutations occur during meiosis or in late stage cancers

51

Examples of diseases caused by macro-mutations include down syndrome, klinefelter syndrome and Cri du chat.

54

Within one chromosome; deletion, duplication and inversion of regions of the chromosome. Within two chromosomes, part of one can go into another (insertion), parts of chromosomes can swap places (translocation).

53

When a SNP (single base substitution) converts a triplet from coding a protein to coding a STOP signal.

56

Caused by single base substitutions (SNP), and they are silent, nonsense (STOP) and mis-sense.

55

What is a silent mutation?

57

What is a mis-sense mutation?

58

[redacted] *can cause great disturbances to a protein through* [redacted] *unless the number of bases* [redacted]*, so there is no* [redacted]

59

There are [redacted] *bad (but* [redacted]*) alleles for cystic fibrosis. The normal gene* [redacted]*. Patient must be* [redacted] *for one bad allele, or* [redacted] *for two.*

60

[redacted] *are when a person has many repeats of a base pair triplet.* [redacted] *dictates the likelihood of a person getting certain diseases (more is worse for the patient).*

61

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.

62

The Human Genome project took [redacted] *to sequence* [redacted] *base pairs. DNA from* [redacted] *individuals of* [redacted] *was taken.*

63

It was discovered that humans only have [redacted] *genes, but it was thought that humans should have around* [redacted]*. This was because flies have* [redacted] *and humans are more complicated!*

64

When a SNP mutation changes the protein coded for by a triplet.

58

When the protein coded for by a triplet is not changed by an SNP.

57

There are 900 bad (but recessive) alleles for cystic fibrosis. The normal gene produces enough protein to compensate. Patient must be homozygous for one bad allele, or heterozygous for two.

60

Insertions and deletions can cause great disturbances to a protein through frameshift mutations unless the number of bases is divisible by three, so there is no frameshift

59

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.

62

Trinucleotide repeated expansions are when a person has many repeats of a base pair triplet. The number of repeats dictates the likelihood of a person getting certain diseases (more is worse for the patient).

61

It was discovered that humans only have 20,500 genes, but it was thought that humans should have around 100,000. This was because flies have 13,000 and humans are more complicated!

64

The Human Genome project took 13 years to sequence 3 billion base pairs. DNA from 5 anonymous individuals of varying ethnicity was taken.

63

Humans share [redacted] *of their genes with flies, and only* [redacted] *of the human DNA codes for genes.*

65

Why can humans get by with so few genes?

66

Cells have the [redacted]*, but do not express the* [redacted]*. Where these* [redacted] *are expressed determines the type of cell formed.*

67

Humans genomes differ by about [redacted]*, which is about* [redacted] *base pairs which are mostly* [redacted]

68

The frequency of SNP's is one in every [redacted] *base pairs. Most are* [redacted] *and have* [redacted]*.*

69

SNP's outside of genes are useful because...

70

GWAS stands for...

71

Most diseases result from [redacted]*, patients with* [redacted] *have been found to be more at risk of developing some diseases.*

72

Humans share sixty percent of their genes with flies, and only two percent of the human DNA codes for genes.

65

Alternative splicing; the same gene can produce different proteins when it is shaped differently (isoforms). This means that we can make 100k proteins with 23k genes.

66

Cells have the same genome, but do not express the same genes and isoforms. Where these proteins are expressed determines the type of cell formed.

67

Humans genomes differ by about 0.01 percent, which is about 3 million base pairs which are mostly SNP's

68

The frequency of SNP's is one in every 300 base pairs. Most are outside genes and have no effect on the phenotype.

69

They act as landmarks for us as scientists!

70

Genome wide association studies

71

Most diseases result from polygenic and environmental interactions, patients with particular groups of landmark SNP's have been found to be more at risk of developing some diseases.

72

GWAS aim to identify the common SNP's associated with [redacted] *by testing at least* [redacted] *of SNP's in large population samples.*

73

Where are the samples for GWAS taken from

74

When particular landmark SNP's are seen in greater diseased patients compared to controls, we say that the SNP's are [redacted] *with the disease.*

75

If a patient has SNP's associated with a disease, what does it mean?

76

Some people will be affected more by [redacted] *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).*

77

What is pharmacogenomics?

78

In 2005, [redacted] *SNP's were known to be associated with diseases, in 2008, it was* [redacted] *and now it's over* [redacted].

79

What was the aim of the 1000 genomes project?

80

GWAS aim to identify the common SNP's associated with complex diseases and traits by testing at least hundreds of thousands of SNP's in large population samples.

73

Both patients who have the disease and people who do not (the control).

74

When particular landmark SNP's are seen in greater diseased patients compared to controls, we say that the SNP's are associated with the disease.

75

The patient as a higher risk of the disease (very rarely, there could be a 100 percent association).

76

Some people will be affected more by their environment 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).

77

How do patients genomes affect their response to a treatment?

78

In 2005, less than 50 SNP's were known to be associated with diseases, in 2008, it was over 500 and now it's over 14,000.

79

To establish the most detailed catalogue of human genetic variations.

80

On average, each person carries [redacted] *loss of function variants in annotated genes, and* [redacted] *previously implicated in inherited disorders.*

81

How many new disease causing mutations were identified in the 1000 genomes project?

82

In [redacted] *the 100,000 genomes project was started by* [redacted]*. It was split between helping* [redacted] *and* [redacted]*.*

83

The 100,000 genomes project sampled [redacted] *people including* [redacted] *serious illness patients.* [redacted] *cancer patient genomes (one cancer and one normal per patient), and* [redacted] *rare disease genomes (three per patient;* [redacted]*)*

84

[redacted] *and* [redacted] *both let you get your genome sequenced.* [redacted] *does not offer much advice or counselling, but* [redacted] *does, and is therefore more expensive.*

85

Immlumina tests healthy adults interested in learning about their risk for [redacted]*, assessing their* [redacted] *status and understanding their response to certain* [redacted]*.*

86

How many different types of cell are there in humans?

87

What is the first cell created by the fusion of the egg and sperm?

88

671

82

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

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))

84

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

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.

86

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.

85

The zygote.

88

220 cell types.

87

What are the initial cells formed from the zygote called?

89

After there are more than 8 blastomeres, what is there?

90

What is the trophoblast?

91

Where does the embryo form from?

92

When the [redacted] *is dividing, the cells become smaller since they are partitioning the* [redacted] *cytoplasm via mitosis.*

93

What lets the embryo attach to the wall of the uterus?

94

[redacted] *is driven by the* [redacted]*. The* [redacted] *expands and changes shape and location, but is still* [redacted]*.*

95

Once attached to the uterus wall, the inner cell mass sets the [redacted]*. The* [redacted] *is the* [redacted] *axis.) The body is symmetrical along this.*

96

A blastocyst a ball of cells.

90

Blastomeres

89

The inner cell mass, not the trophoblast.

92

The embryo after it was a blastocyst (5 days). Separate from the inner cell mass

91

The trophoblast

94

When the inner cell mass is dividing, the cells become smaller since they are partitioning the zygote cytoplasm via mitosis.

93

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.

96

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.

95

After setting the axis, [redacted] takes place. This is where cells migrate, along the bottom, endoderm form, [redacted] in the middle [redacted] at the top. [redacted] will be the skin and nerves, [redacted] forms [redacted] and the [redacted] forms the [redacted]

97

What is a highly coordinated cell movement?

98

What structures become the vertebrae?

99

What do somites eventually form into?

100

Growing organs is called...

101

By saying organogenesis is progressive, we mean

102

What is used as a reference for growing specialised cells in an embryo?

103

What is a differentiated cell?

104

Gastrulation

98

After setting the axis, gastrulation takes place. This is where cells migrate, along the bottom, endoderm form, mesoderm in the 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

97

Muscles, vertebral column and dermis of the skin. They are landmarks for organ formation during development.

100

Somites; they emit signals telling what organs to form where.

99

That the organs grow in stages, e.g. there is a little growth for the arm first, then it gets longer, then it gets digits etc.

102

Organogenesis

101

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

104

The head to tail framework.

103

The gurdon experiment was done on...

105

The gurdon experiment involves...

106

Cells developmental potential (potency) changes how as it gets more specialised?

107

What is involved in a grafting experiment?

108

The fate of a cell [redacted] *before differentiation. They can sometimes* [redacted] *a new situation, up to* [redacted].

109

Source	***Potential***	***Type of cell***	***Can develop into***
Zygote	[redacted]	-	*Whole organism.*
[redacted]	[redacted] *and self-renewing*	*Embryonic stem cell*	*Any cell type*
Adult	*Multipotent,* [redacted]	*multipotent*	*Some cell types*
Organ	*Limited potential and renewal*	[redacted]	*Choice of between* [redacted] *types*
-	*Limited division*	*committed progentor*	*1 type, locked fate.*
-	*No division*	*Differentiated*	*No division.*

110

Once a cell is differentiated...

111

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

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.

106

Frogs

105

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.

108

It decreases.

107

Source	***Potential***	***Type of cell***	***Can develop into***
Zygote	*Totipotent*	*-*	*Whole organism.*
Blasocyst	*Pluripotent and self-renewing*	*Embryonic stem cell*	*Any cell type*
Adult	*Multipotent, self-renewing*	*multipotent stem cells*	*Some cell types*
Organ	*Limited potential and renewal*	*Progenitor*	*Choice of between 2-6 types*
-	*Limited division*	*committed progentor*	*1 type, locked fate.*
-	*No division*	*Differentiated*	*No division.*

110

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

109

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

112

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

111

At any given time, each cell expresses around [redacted] *of it's genes*

113

About [redacted] *of the* [redacted] *active genes are developmental genes.*

114

Developmental genes control:

115

One small difference in gene expression can [redacted].

116

Proteins inside the egg are [redacted].

117

After two [redacted] *of the zygote (egg to two cells, to four), the* [redacted] *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.*

118

A differentiated cell can give rise to a new organism ([redacted]*), which means genes are* [redacted] *as a cell specialises.*

119

[redacted] *are proteins that bind to the DNA and* [redacted]*. They change how the DNA is shaped so that different parts can be accessed.*

120

About ten percent of the 20 percent active genes are developmental genes.

114

At any given time, each cell expresses around 20 percent of it's genes

113

One small difference in gene expression can create a cascade of changes downstream.

116

Proteins that regulate genes expression (turn genes on and off), proteins involved in cell communication or signalling (tell other cells what genes to turn on and off).

115

After two cleavage divisions of the zygote (egg to two cells, to four), the same maternal proteins 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.

118

Proteins inside the egg are not uniformly distributed.

117

Epigenetics are proteins that bind to the DNA and retrieve totipotency. They change how the DNA is shaped so that different parts can be accessed.

120

A differentiated cell can give rise to a new organism (totipotent), which means genes are not lost as a cell specialises.

119

The embryo starts with a zygote (.
It becomes a *with a* *and*
( )
Before full differentiation, cells
and are
At the gene level, cells become different by
The initial differences come from the
being unevenly distributed
in the *. As* *form from*
, they end up not having the same
.

121

stem cells can become any cell.

122

have the minimum level of
specialisation, *have the maximum level*
of specialisation.

123

cells are not stem cells, but
cells are.

124

cell stage is the limit for totipotency in humans.

125

Stem cells in the ICM are .

126

Adult stem cells are .

127

Adult stem cells are found in...

128

Totipotent stem cells can become any cell.

122

The embryo starts with a zygote (totipotent.
It becomes a blastocyst with a trophoblast and ICM (plurpiotent)
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.

121

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

124

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

123

Stem cells in the ICM are pluripotent.

126

8 cell stage is the limit for totipotency in humans.

125

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

128

Adult stem cells are multipotent.

127

Embryonic stem cells are [redacted] *and* [redacted].

129

In order to control ESL's in vitro, we can [redacted] *culture medium, or* [redacted].

130

Adult stem cells are [redacted] *to grow in the lab than* [redacted] *but do show* [redacted].

131

Describe the plasticity of ASC's

132

What are the most apparently plastic cells?

133

Why are UC-MSC's better than BM-MSC's?

134

How many proteins are usually considered for immuno-compatibility?

135

What is GVHD?

136

In order to control ESL's in vitro, we can change the chemical composition of the culture medium, or insert specific genes into cells.

130

Embryonic stem cells are immortal and pluripotent.

129

Most adult stem cells can trans-differentiate in the lab, but this is a low efficiency process.

132

Adult stem cells are harder to grow in the lab than ESC's but do show some plasticity.

131

- *Less immunogenic*
- *longer telomeres*
- *less DNA damage*
- *non-invasive to harvest*
- *same plasticity as BM-MSC's.*

134

Mesenchymal stem cells (mesoderm), which can transform into liver cells (endoderm) and brain cells (ectoderm)

133

Graft Vs Host Disease, where the immune cells in the transplant attack the host.

136

135

Why are neonatal (UC cells) less immunogenic?

137

Neonatal cells have longer [redacted] *(which* [redacted]*), since they get shorter* [redacted] *since they do not get replicated, and neonatal cells have not divided many times.*

138

In ESC's what enzyme is expressed that stops a telomeres from getting shorter?

139

When is telomerase turned off?

140

What enzyme do most cancer cells produce and why?

141

What is a bank of ESC lines?

142

What are the three sources of human stem cells?

143

How could we make a stem cell with only some skin cells?

144

Neonatal cells have longer telomeres (which indicate the age of the cell), since they get shorter at each cell division since they do not get replicated, and neonatal cells have not divided many times.

138

Embryos and foetuses have to evade the mother's immune system, so there are less surface markers on cells. Also, newly born babies have no/little immune system so there is less chance of GVHD.

137

Before the baby is born

140

Telomerase

139

A bank of embryonic stem cells, where each 'line' of cells is derived from a single embryo.

142

Telomerase so that the cells are immortal and divide indefinitely.

141

Make it into an induced pluripotent stem cell in the lab.

144

Embryonic SC's, Neonatal SC's, adult SC's (bone marrow, fat tissue (liposuction), skin).

143

What are the currently approved stem cell based therapies?

145

How does a bone marrow transplant to cure leukaemia work?

146

Give an example of tissue engineering

147

What is ex-vivo and in-situ cartilage engineering

148

List advantages of MSC's

149

MSC's might be good for [redacted] *e.g. with HMC's since they help other stem cells to graft*

150

Clinical trials take [redacted]*, and* [redacted] *therapies are in phase 3 for stem cell treatments. Foreign clinics advertise MSC treatments, but none have published data from clinical trials.*

151

Most trials for stem cell therapies are carried out with MSC's ([redacted]*), HSC's count for* [redacted]*. ESC's are around* [redacted] *and are being tested with* [redacted] *since they are* [redacted]*.*

152

1. Get a matching donor 2. Replicate stem cells ex vitro 3. Destroy bone marrow in patient using irradiation and chemotherapy 4. transplant stem cells into patient.

146

Skin grafts, Hematopoietic SC transplant from adult bone marrow or neonatal cells.

145

Growing new cartilage outside the body and in the body respectively (using MSC's to stimulate growth).

148

Remove cells from lungs, hips and nose, remove a donor trachea (from cadaver) and remove all cells, grow cells around trachea and transplant in patient.

147

MSC's might be good for cotransplants e.g. with HMC's since they help other stem cells to graft

150

- *Easy to isolate*
- *Plastic (not literally!) in the lab*
- *Can be frozen and thawed*
- *Possess potent immuno-suppression and anti-inflammation effec*
- *Capable of homing (going to site of injury)*
- *Stimulate regeneration*

149

Most trials for stem cell therapies are carried out with MSC's (70 percent), HSC's count for 20 percent. ESC's are around 2 percent and are being tested with eyes since they are immuno-privileged.

152

Clinical trials take a long time, and less than 10 therapies are in phase 3 for stem cell treatments. Foreign clinics advertise MSC treatments, but none have published data from clinical trials.

151

SC's can be used for [redacted], [redacted] *and* [redacted].

153

For repairing and replacing cells, what type of cell should we use?

154

What is an induced pluripotent stem cell?

155

How to do Parkinson's in a dish?

156

The traditional approach to medicine is [redacted].

157

The traditional approach to medicine does not take into account [redacted]*, which is successful for some, but not all patients.*

158

What is stratified medicine?

159

Personalised medicine (aka [redacted]*) takes into account*

160

The patients own cells (autologous transplants). This requires adult stem cells that are reasonably plastic though, and its hard to isolate ASC's in the lab. Otherwise, use donor SC's with low immunogenicity.

154

SC's can be used for replacing cells (e.g. transplants), repairing cells (e.g. genetically modify SC's outside the body and re-implant) and protecting via MSC immunosupression.

153

- *Collect skin cells*
- *Re-program them into stem cells*
- *Grow brain cells from them (induce brain cell differentiation)*
- *Stress out the brain cells with toxins*
- *Observe Parkinson's-like features*

156

When you reprogram a normal (e.g. skin) cell by inserting genes (via viruses or otherwise). Only 3-4 gene insertions required.

155

The traditional approach to medicine does not take into account individual differences between patients, which is successful for some, but not all patients.

158

The traditional approach to medicine is one size fits all.

157

Personalised medicine (aka precision medicine) takes into account

160

Targeting different types of specific diseases made up of lots of different genes e.g. maturity onset diabetes

159

Examples of historical personalised medicine include...

161

When the human genome project started, [redacted] drugs had pharmacogenetic information. After it ended, [redacted] drugs had this information and ten years later, there [redacted] drugs. Now the [redacted], [redacted], [redacted] and [redacted] are examined.

162

Genetic changes of interest include [redacted], [redacted], [redacted] and [redacted]. These all change how much of the proteins coded for by an affected gene is produced.

163

What are the advantages of personalised medicine (6 things)?

164

What genes increase your risk of breast and ovarian cancer and how much by?

165

There are over [redacted] predictive tests looking at [redacted] genes. They can [redacted] of treating patients.

166

Even if a predictive test for a gene doesn't have an associated drug to lower risk, you can [redacted].
Sergey Brin does this for Alzheimer's!

167

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.

168

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.

162

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

161

- *Shift reaction to prevention*
- *Predict susceptibility of developing a disease*
- *Improve dosing of drugs (increase efficiency, reduce side effects)*
- *Reduce cost, time and attrition rate in drug development*
- *Decrease adverse affects of drugs, increase diagnostic and detection power for disease*

164

Genetic changes of interest include SNP's, base insertions, copy-number variations and variable number tandem repeats. These all change how much of the proteins coded for by an affected gene is produced.

163

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

166

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

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.

168

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!

167

There are drugs (Ivacaftor) that target the [redacted] *of diseases rather than just treating symptoms.*

169

What does metastatic cancer mean?

170

Enzymes metabolise drugs, and [redacted] *metabolise over* [redacted] *percent of drugs. There are* [redacted] *in genes that code for these enzymes. Some people metabolise fast (and are at risk of* [redacted]*), or even ultra-fast metabolisers (meaning the drugs* [redacted]*).*

171

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.

172

What are some problems with personalised medicine?

173

What are the ethical problems with personalised medicine (5 things)?

174

[redacted] *mutations can be involve with genes. Drugs need to target driver mutations in order to be effective.*

175

Define biomarker

176

When the cancer has moved from the original site to other areas of the body.

170

There are drugs (Ivacaftor) that target the gene underlying cause of diseases rather than just treating symptoms.

169

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.

172

Enzymes metabolise drugs, and one family of enzymes metabolise over 90 percent of drugs. There are thousands of mutations in genes that code for these enzymes. Some people metabolise fast (and are at risk of overdose toxicity), or even ultra-fast metabolisers (meaning the drugs are broken down before they have an effect).

171

Who sees the data? How will it be stored? How will it be used? Could it be used against us? What legal protection do we have?

174

Ethics, multiple gene variations per disease, quantity of data

173

A naturally occurring molecule, gene or characteristic by which a particular pathological or physiological process, disease etc can be identified.

176

Driver and passenger mutations can be involve with genes. Drugs need to target driver mutations in order to be effective.

175

Why are biomarkers helpful?

177

can be used to build up a signature, telling us how multiple etc contribute towards a disease

178

and are used to identify genes involved in diseases.

179

Given a patient, we can use , and (detecting antigens on the surface of cells) to determine their biomarkers. These can be gotten from , , , etc. Anywhere where we in the body.

180

How do DNA chips work?

181

What is the name for a test that goes with a drug?

182

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 .

183

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

multiple biomarkers can be used to build up a signature, telling us how multiple genes/proteins etc contribute towards a disease

178

Because they help with prediction, diagnosis, progression, regression, or the outcome of treatment of a disease.

177

Given a patient, we can use DNA sequencing, microarrays and immunohistochemistry (detecting antigens on the surface of cells) to determine their biomarkers. These can be gotten from normal or diseased tissue, blood, saliva, sweat etc. Anywhere where we can find protein or DNA in the body.

180

GWAS and microarrays are used to identify genes involved in diseases.

179

A companion diagnostic (CDx).

182

First, sample DNA is taken, then it is amplified using PCR. It is then placed on a DNA chip with many probes, where it will bind to probes that it is complementary to. The chip is washed to remove the non-bound DNA, then scanned, where the bound probes will be visible.

181

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.

184

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.

183