**Q1.**

(a)     250 000;

**1**

(b)     (i)      Loss of 3 bases / triplet = 2 marks;;

*‘Stop codon / code formed’ = 1 mark max unless related to the last amino acid*

Loss of base(s) = 1 mark;

*eg triplet for last amino acid is changed to a stop codon / code = 2 marks*

*3 bases / triplet forms an intron = 2 marks*

*Accept: descriptions for ‘intron’ eg non-coding DNA*

*‘Loss of codon’ = 2 marks*

**2**

(ii)     1.      Change in tertiary structure / active site;

*Neutral: change in 3D shape / structure*

2.      (So) faulty / non-functional protein / enzyme;

*Accept: reference to examples of loss of function eg fewer E-S complexes formed*

**2**

**[5]**

**Q2.**

(a)  1.   Change in (sequence of) amino acid(s)/primary structure;

*Reject amino acids are formed.*

*Reject amino acids code.*

2.   Change in hydrogen/ionic/disulfide bonds;

3.   Alters tertiary/30 structure;

*Reject active site.*

*Ignore quaternary.*

*Ignore 3D.*

**3**

(b)  1.   Produce healthy (red blood) cells

**OR**

Produce (normal) polypeptide/haemoglobin;

*Produce only healthy (red blood) cells is only equivalent to mark point 1.*

*Accept produce ‘normal’/non-SCD cells.*

*Ignore type of stem cell e.g. pluripotent.*

2.   No sickle/faulty/SCD (red blood) cells (produced)

**OR**

No defective polypeptide/haemoglobin;

3.   Stem/marrow cells (continuously) divide/replicate

**OR**

Less chance of rejection (from brother/sister);

*Differentiate is not equivalent to divide/replicate.*

*Ignore type of stem cell e.g. pluripotent.*

**3**

(c)

***Max 2 marks*** *for marking points 1, 2 and 3*

(For gene therapy)

1.   No destruction of bone marrow

**OR**

No destruction of stem cells;

*Accept no destruction of faulty bone marrow unless context indicates this is against gene therapy.*

2.   Donors are not required;

*Stating ‘only own cells used’ is* ***not*** *equivalent.*

3.   Less/no chance of rejection (own stem cells);

(Against gene therapy)

4.   Sickle/faulty (red blood) cells still produced

5.   Immune response against genetically modified cells/virus

**OR**

Long-term effect not known (as is new treatment)

**OR**

Virus could cause side effects;

*Accept ‘virus could cause problems’ or ‘risk(s) with virus’.*

**3 max**

**[9]**

**Q3.**

(a)     Correlation coefficient **and** because looking for correlation / relationship / association between two variables / between B cells destroyed and CD20;

*Accept Pearson and Spearman*

*Accept factor for variable*

***Wrong test or wrong reason = 0 marks***

**1**

(b)     1.      The more CD20 (on B cells), higher the percentage of / more B cells destroyed / more effective it is;

*Ignore ref. to ‘positive correlation’ unqualified*

*Ignore ref. to correlation vs. causation*

*Ignore ref. to effects on the immune system*

2.      (At best) only destroys (about) 80% of B cells

**OR**

In no cases are all B cells killed;

3.      Don’t know % / proportion of cancer cells killed;

4.      Won’t cure CLL / cancer / slows but doesn’t stop CLL / cancer;

5.      Little effect below (about) 5 CD20 on cells;

*Ignore ref. to little effect where little CD20*

**3 max**

(c)     1.8 x 108;;

If correct difference but expressed in non-standard form, award 1 mark;

*Award 1 mark if answer given as 1.8 x 10–8*

**2**

(d)     1.      Mutation changes the tertiary structure / amino acid sequence of transcription factor;

*Do not accept unqualified statements about non-functional transcription factor – this is in stem of question*

*Answers must be in context of transcription factor, not CD20, or generic statements*

2.      Transcription factor not complementary to / cannot bind to CD20 gene / CD20 DNA;

*Do not accept unqualified statements about non-functional transcription factor – this is in stem of question*

*Answers must be in context of transcription factor, not CD20, or generic statements*

*Accept TF cannot bind to promoter (on DNA)*

3.      Little / less / not enough / no mRNA for CD20 produced

**OR**

Little / less / not enough / no (mRNA for) CD20 translated / produced;

4.      (Not enough CD20 so) nothing / little for Rituximab to bind to, so few / no B cells destroyed;

*Accept converse for cells with a lot of CD20*

*Accept lower median percentage for fewer cells destroyed*

**3 max**

**[9]**

**Q4.**

(a)     1.      Heritable changes in gene function;

2.      Without changes to the base sequence of DNA;

**2**

(b)

|  |  |  |
| --- | --- | --- |
| **Control element** | **Binds with DNA** | **Binds with protein** |
| Oestrogen |   | ✔ |
| Methyl groups | ✔ |   |
| Acetyl groups |   | ✔ |

*1 mark for each correct column.*

*Accept both boxes ticked in oestrogen row.*

**2**

(c)     1.      Methyl groups (could be) added to (both copies of) a tumour suppressor gene;

2.      The transcription of tumour suppressor genes is inhibited;

3.      Leading to uncontrolled cell division.

**3**

(d)     Cells of benign tumours cannot spread to other parts of the body / metastasise;

**OR**

Cells of benign tumours cannot invade neighbouring tissues.

*Accept answers clearly in the context of malignant tumours.*

**1**

**[8]**

**Q5.**

(a)     1.      Produce healthy (blood) cells;

*Accept produce ‘normal’ /non-MDS cells.*

2.      No MDS/faulty/cancerous (blood) cells;

*Produce only healthy/normal (blood) cells =* ***two marks.***

*Accept no (cancerous) tumour.*

3.      Stem cells divide/replicate;

*Ignore reference to totipotent/pluripotent/ multipotent/unipotent*

*Accept ‘clone’ for divide.*

**3**

(b)     1.      (AZA) reduces methylation (of DNA/cytosine/gene);

*Reject any reference to mutation.*

2.      (Tumour suppressor) gene is transcribed/expressed;

*Accept mRNA produced for transcription/transcribed.*

*Ignore gene is ‘switched on’ or activated but allow protein is formed.*

3.      Prevents rapid/uncontrollable cell division

**OR**

Cell division can be controlled/stopped/slowed;

*Ignore growth.*

**3**

(c)     1.      Effect of AZA can be compared;

*Comparison on its own is not enough for a mark.*

2.      Unethical not to treat (control group);

**2**

(d)     1.      Correct answer of 29/28.8 = **2 marks**;;

2.      Working shows 0.74 **and** 0.58 = **1 mark**

**OR**

58/57.6 = **1 mark**

**OR**

28 = **1 mark**;

**2**

**[10]**

**Q6.**

(a)     1.      Correct answer of 625 = **2 marks**;;

2.      Shows 625 but decimal point incorrect = **1 mark**

**OR**

Working shows 40 = **1 mark**

**OR**

1600/1.6 = **1 mark**

**OR**

667/666.6 = **1 mark**;

**2**

(b)     (Cell/membrane has a) phospholipid bilayer

**OR**

No channel/carrier protein (for uptake)

**OR**

No need for channel/carrier protein (for uptake);

**1**

(c)     1.      Both are more effective than the control;

***Mark points 4 to 10 = 4 max.***

*Accept both (results) are below the control.*

2.      Differences in the means not (likely to be) due to chance

**OR**

Significant difference (in effectiveness between both types);

*Reject ‘results are significant’.*

*Accept significantly higher or significantly lower in correct context.*

3.      (As) SDs do not overlap;

*Accept error bars do not overlap.*

4.      HBsAg (reduced), not zero

**OR**

Replication (reduced), not zero;

5.      Not (investigated in) humans

**OR**

(Investigated in) mice;

6.      shRNA (more effective as) 7.5% (of control) compared with 50% for lhRNA;

*Accept 42.5% difference.*

*Accept (mean) concentration for %.*

7.      No indication of sample size/number;

8.      Long term effects not known

**OR**

Side effects not known;

*Accept ‘could be toxic’ for side effects not known.*

9.      No statistical test to determine significance;

10.      (Investigated) in vitro

**OR**

Not (investigated) in vivo;

*Accept not done inside an organism or not done in liver (organ) but ‘only tested in liver cells’ is insufficient unless qualified.*

*Ignore only ‘one study’ or ‘no repeats’.*

**5 max**

**[8]**

**Q7.**

(a)     665 (people per month);;

Allow one mark for 7980/7981 in working (number of deaths from throat cancer per year)

*Accept answers not rounded*

**2**

(b)     1.      (EGCG) binds to active site of DNMT;

*Ignore active site changes shape*

*Ignore ‘forms enzyme-substrate’ complex*

2.      (DNMT) cannot methylate (promoter region of tumour suppressor gene);

3.      Transcription(al) factor(s) can bind (to promoter region);

4.      RNA polymerase (stimulated/activated);

*Accept less methylation (of promoter region/tumour suppressor gene)*

**3 max**

(c)     1.      Only investigated in throat cancer

**OR**

Might not work for other types of cancer;

2.      Not all cancers are caused by (increased) methylation (of a tumour suppressor gene)

**OR**

There are other causes of cancer;

3.      Only a significant reduction with 20/50/above 10 (µmol)

*Allow converse, ie no significant effect with 5/10 (µmol)*

4.      Do not know how much EGCG is in green tea;

5.      Only reduces growth rate (of cancer cells)

**OR**

No evidence of cancer being cured;

6.      *In vivo* cells/cells in the body might respond (to EGCG) differently (from those grown *in vitro*);

**3 max**

**[8]**

**Q8.**

(a)     Box 2.

An inversion will result in a change in the number of DNA bases.

*Reject if more than one box with tick. Ignore crossed-out ticks*

**1**

(b)     1.      (Increased) methylation (of tumour suppressor genes);

*Accept abnormal methylation or hypermethylation*

*Ignore decreased acetylation of histones*

2.      Mutation (in tumour suppressor genes);

3.      Tumour suppressor genes are not transcribed/expressed

**OR**

Amino acid sequence/primary structure altered;

*Accept mRNA for transcription/transcribed*

*Accept tertiary structure altered*

*Accept different amino acid*

*Ignore reference to protein not being formed*

4.      (Results in) rapid/uncontrollable cell division;

*Accept cell division cannot be regulated*

*Ignore growth*

**3 max**

(c)     1.      Correct answer of 1.9/1.93 × 1025 = **2 marks**;;

*Accept 2 × 1025 = 2 marks*

*Ignore any numbers after 1.93*

2.      Incorrect answer but shows 84 = **1 mark**

**OR**

28 × 3 = **1 mark**

**OR**

Incorrect answer but shows 672 divided by 8 = **1 mark**;

**2**

**[6]**

Examiner reports

**Q1.**

(a)     Nearly all students gave the correct answer of **250,000**.

(b)     (i)      One-third of students gained at least one mark. This question required students to apply the principle that three bases code for one amino acid to an unfamiliar context. However, other creditworthy approaches were used to explain why the faulty protein has one amino acid missing. This said, many students simply defined the term ‘mutation’ or repeated information given in the question stem. Consequently, there were many references to a *change* in the base sequence or amino acid sequence. Only the best responses mentioned a loss of bases. Students who took a different approach fell into one of two camps. Some suggested that a stop codon had formed for one mark. However, it was rare to see this related to the final amino acid of the protein. Similarly,others were clearly aware of introns but rarely mentioned that three bases may form an intron. Unfortunately, a minority of students provided a good response to (c) (ii) for this question part.

(ii)     One-third of students gained full marks. Many were aware that the protein produced could be faulty or non-functional. However, the ability to explain this in terms of a change in tertiary structure or active site discriminated well. Unfortunately, some students went no further than to state that the protein would have a different primary structure. This was given in the question stem and therefore not credited.

**Q2.**

(a)  This question proved to be a very effective discriminator. Around 90% of students gained at least one mark and around 30% gained full marks. Many students appreciated that there would be a change in the polypeptide’s primary structure. However, a number of these responses were not credited as they suggested that a new amino acid would be formed or produced. Similarly, although to a lesser extent, the mark for a change in tertiary structure was negated by stating that there would be a change in ‘the active site’. Other common errors included confusion between amino acids and bases, ‘amino acids coding for proteins’ and a base substitution causing a ‘frame shift’. Students gaining full marks referred to changes in specified bonds rather than general statements on bonds being altered.

(b)  Although almost 90% of students gained at least one mark, only about 12% obtained full marks. The most common response to gain credit was related to ‘healthy’ or ‘normal’ red blood cells being produced. Some responses only referred to ‘healthy’ or ‘faulty’ bone marrow cells rather than the red blood cells produced by them. Students gaining two marks often referred to a lower chance of rejection when using a sibling as a donor. Students often understood that the bone marrow cells were able to renew themselves and differentiate into other cells, but did not explain that they replicated or divided. Relatively few students referred to no SCD cells or defective polypeptide/haemoglobin being produced.

(c)  This proved more difficult than expected, with less than two-thirds of students gaining one mark and only 5% obtaining all three marks. The most commonly awarded marks supporting gene therapy were for the idea of a reduced chance of rejection and that donors are not required. Arguments against gene therapy usually referred to the ‘side effects’ of using a viral vector, unknown long-term effects and the possibility of an immune response to the virus. However, correct responses often only included one of these points. Surprisingly, very few students appreciated that there was no destruction of bone marrow with gene therapy or that SCD cells would still be produced using this procedure. Some answers failed to evaluate the information and simply provided the method of carrying out gene therapy. Other students confused the procedures and it was difficult to assess the points they made.

**Q3.**

Question (a) related to the figure, a scatter graph. 41% of students correctly suggested some form of correlation coefficient and the reason that some form of correlation between two variables was being considered. The question discriminated well.

Question (b) started with an instruction to consider the data in the figure. This question tested AO3, the ability to draw conclusions from information and data provided. The data concern the use of Rituximab to treat CLL, a ‘real life’ context. Many students (57%) obtained onemark, usually for noting that the more CD20 on B cells, the more B cells Rituximab destroys. A further 28% obtained two marks, usually for either noting that in no case are all B cells killed, or that the data do not show the proportion of cancerous and normal B cells killed. Only 5% of students made both points to score three marks. Very few students noted that Rituximab cannot cure CLL. There was a mark available for noting that Rituximab has little effect below 5 arbitrary units of CD20, but few students accurately noted this point in the trend of the data. Many students who failed to score simply described the data, quite often point to point. Others drifted away from these data and speculated on the possible lethal effects of damage to the immune system by Rituximab, meaning that it should not be used. This question was based on a treatment that is used, for a real cancer. Students should assume that doctors and scientists follow proper, ethical scientific and medical procedures and do not set out to kill patients.

In question (c), 54% of students calculated the correct difference and expressed it in standard form. One mark was obtained by 6% of students who calculated the correct difference but did not put it into standard form. The question discriminated well.

Question (d) discriminated very well. One mark was obtained by 20% of students, usually for either deducing that less CD20 would be produced in people with the *NOTCH1* mutation, or that there would be little for Rituximab to bind to and so few B cells destroyed. 24% of students obtained two marks, usually by making both linked points. Some obtained two marks by noting that the mutation would lead to a change in the tertiary structure of the transcription factor, leading to it not binding to the gene for CD20. Some 14% of students gave the whole story and obtained all three marks. This left 20% who failed to score. Many appeared not to know what a transcription factor is and often wrongly suggested that the mutation would affect the gene for CD20, or the structure of CD20, making it the wrong shape to bind to Rituximab.

**Q5.**

Almost 84% of students gained at least one mark and 40% at least two marks for part (a). The most common response to gain credit was related to ‘healthy’ or ‘normal’ (blood) cells being produced. Students gaining two marks often referred to no MDS/faulty/cancerous (blood) cells being produced, or that only healthy cells were produced. Students often understood that stem cells were able to renew or regenerate themselves and differentiate into other cells, but did not explain that they replicated or divided. Consequently only 10% of students obtained maximum marks.

Part (b) proved to be an excellent discriminator. Approximately 73% of students gained at least one mark and 42% at least two marks. Most students obtained mark point 1 by stating that AZA would reduce methylation (of DNA/cytosine/gene). Fewer students obtained mark point 2 by referring to the transcription/expression of the tumour suppressor gene. Often this was due to poor terminology such as ‘switched on’, but also due to clear errors such as ‘translated’. More students had success in explaining the role of the tumour suppressor gene in controlling cell division and obtained mark point 3. Approximately 23% of students obtained all three mark points.

29% of students obtained both marks and 55% one mark for (c). The most frequently credited mark was that using conventional drugs enabled the effect of AZA to be compared. Students who referred to AZT but did not gain the mark failed to include the idea of a comparison. Conversely some responses simply stated ‘for comparison’ without any reference to AZT. A significant number of students appreciated that it would be unethical not to supply conventional drug treatment to cancer patients. Incorrect responses included reference to ‘placebos’, ‘double-blind experiments’ and ‘side effects’.

Part (d), assessing mathematical skills, was a poor discriminator. Approximately 34% obtained two marks and 52% one mark. Students obtaining a single mark often did so for correct readings from the graph or for a final answer of 28 due to incorrect rounding of 28.8.

**Q6.**

Approximately 40% correctly performed the calculation in (a) for two marks. Approximately 24% of students obtained one mark, usually for showing ’40’ in the working. However, a significant number of students gained a mark for a final answer showing 625 but with the decimal point in the incorrect place, e.g. 6.25, 62.5, 6250. These students had often made an error when converting units of measurement. Common incorrect answers were 2400 (60 000 divided by 25), 240 and 2.4.

Approximately 39% of students obtained the mark for (b), almost invariably by referring to the phospholipid bilayer. Only a handful of students gained the mark for suggesting that no carrier/channel proteins would be available for uptake of the RNAi molecules. Many of the responses which were not credited lacked sufficient detail, for example by stating that the cell-surface membrane has ‘phospholipids’, ‘a lipid bilayer’ or ‘a lipid layer’, or that the molecule was now ‘lipid soluble’. More fanciful explanations involved the lipids acting as receptors and carrying the RNAi across the membrane. Others suggested that the RNAi had lipid receptors to which the lipid could bind.

(c) was an excellent discriminator, the most effective on the paper. Approximately 80% of students gained at least one mark, and almost 14% obtained the maximum five marks. Although mark points 1, 4 and 10 were rarely awarded, all the points on the mark scheme were credited at some stage of marking. The most frequent mark awarded related to the investigation being on mice rather than on humans. Students who gained a mark by referring to the overlap in standard deviations often obtained another mark by stating that there was a significant difference in the effectiveness of the two types of RNAi. It was pleasing to note that few students referred to the ‘results being significant’. However, a substantial number of students omitted any reference to the overlap in standard deviations but instead compared the spread of this data around the mean in terms of reliability of the results. Almost 47% of students gained at least three marks. There was some variation in how higher marks were achieved. The most frequent additional points related to long-term or side-effects not being known and the fact that sample size was unknown. However, a significant number of students did use the data in **Figure 2** to compare the effectiveness of the types of RNA. Less frequent were responses which referred to the lack of a statistical test to determine significance or references to the investigation being *in vitro* rather than *in vivo*.

**Q7.**

(a) tested similar maths skills to (c) and nearly 72% of students scored both marks.

(b) discriminated well, however only 14% scored 3 marks. There was confusion about what is the enzyme and what is the substrate. Students stated that EGCG binds to the promotor region instead of DNMT and also that ECGC and DNMT have similar shapes so bind to the same thing, despite being told that ECGC is a competitive inhibitor.

(c) was fairly well answered, with only 11% failing to score a mark. There were many rotelearned responses in evidence, such as ‘no statistical tests,’ despite being told on the graph that two of the amounts of ECGC had a significant effect. Students also stated there was no control; there was. ‘May be other factors’, ‘need to see long-term effects’, ‘small sample size’ and ‘correlation doesn’t mean causation’ were also often seen.

**Q8.**

(a)     The vast majority of students (94%) realised that an inversion would not result in a change in the number of DNA bases.

(b)     This question proved to be a very effective discriminator with one in three students gaining maximum marks. Nearly all students (91%) gained at least one mark, often for referring to mutation or methylation of tumour suppressor genes. Mutation was the most frequently credited marking point, although a significant number of students mentioned both alterations for two marks. Weaker students who provided further details on mutations often limited their descriptions to a non-functional protein being produced. Better answers included changes in primary or tertiary structure. Many students describing methylation did appreciate that this could prevent transcription of tumour suppressor genes. A significant minority of students referred to uncontrollable cell growth rather than uncontrollable or rapid cell division. There were also irrelevant, and often incorrect, references to oncogenes.

(c)     Over 83% of students gained at least one mark, almost invariably for showing 84 cell divisions. Slightly more than half of these students provided further calculations leading to a correct answer for two marks. Common errors included 842 and 283.