群馬大学

'12

受験番号	

前期日程

医学部医学科小論文問題2

注　意　事　項

1. 試験開始の合図があるまで問題冊子を開いてはいけません。
2. この問題冊子のページ数は9ページです。問題冊子，答案用紙及び下書き用紙に落丁，乱丁，印刷不鮮明などがある場合には申し出てください。
3. 解答は指定の答案用紙に記入してください。
   (1) 文字はわかりやすく，横書きで，はっきりと記入してください。
   (2) 解答の字数に制限がある場合には，それを守ってください。
   (3) 訂正，挿入の語句は余白に記入してください。
   (4) ローマ字，数字を使用するときは，ます目にとらわれなくてもかまいません。
4. 試験時間は90分です。
5. 答案用紙は持ち帰ってはいけません。
6. 問題冊子と下書き用紙は持ち帰ってください。

次の文章を読んで設問A～Iに答えなさい。文末に，＊のついた単語の訳注があります。

Cystic fibrosis* is one of the commonest of genetic* diseases, affecting roughly one in 2, 500 children born in the UK and one in 4, 000 of those born in the USA, with a similar incidence in Australia and Canada. (A) Although less common in Asia and African populations, —for example, the incidence in US-born Caucasian* children is the same as in the UK, while the incidence in Asian Americans is roughly one in 30, 000 —the disease is actually global in its distribution, affecting boys and girls with equal frequency. In 1989 an international team of scientists discovered the genetic cause, which proved to be mutations affecting a single gene*, known as the cystic fibrosis transmembrane* regulator* gene, or *CFTR*, which is located on human chromosome* 7, and which codes for the transport of salt and water across membranes* in glands* that produce mucus* and sweat in several different organs of the body. The worst-affected organs are the lungs, the digestive* organs known as the pancreas*, the liver, intestines*, sinuses* and the sex organs. Normally the mucus produced by these organs is thin and oily*, so that it flows easily and smoothly, but in people affected by cystic fibrosis the mucus is thick and sticky, causing local build-ups* and obstructions within the organs. For example, in the lungs this can block the airways, which in turn allows bacteria to invade the stagnant* parts of the lungs. This means that sufferers are very susceptible to* chest infections, including pneumonia*, which threatens health, and even life. Similar stagnation* damages the pancreas, which is a major digestive organ. This shows up as failure to thrive in infancy, or as malnutrition* through failure to digest food, and particularly fat, in older children and adults. The same genetic malfunction* causes excessive amounts of salt to be lost in sweat —this is the basis of the diagnostic test for the condition, known as the "sweat test". Cystic fibrosis shows a wide range of severity*, from the very severe form that manifests at or soon after birth, to mild forms that may be diagnosed in late adolescence* or even adult life.

Although there is currently no cure, sufferers can be helped by a number of measures, such as physiotherapy* to help keep the lungs clear, and replacement therapies* for the defective digestive enzymes*. Cystic fibrosis is also one of the frontline* illness in modern medical research aimed at curing the condition by correcting the genetic cause of the disease. To understand what this means, we need to know a little more about genes and how a malfunction of their normal operation can help in understanding the underlying causes of many important diseases. In fact the basis of genetics is quite simple, and logical so that anybody can grasp the essential details.

One way of looking at genes is to regard each gene as a very long word written in a code we call DNA. The code itself is made up from an alphabet of just four letters. These letters are chemicals known as nucleotides*, containing the nucleic acids* guanine*, adenine*, cytosine* and thymine*, which are conveniently referred to using the letters G, A, C and T. It might appear a very limited alphabet but if you imagine the many different permutations* of just those four letters that are possible in a word that is anything from hundreds to thousands of letters long, you appreciate how the DNA code offers virtually an unlimited variety of words.

(B) The 20,000 human genes are grouped together into 46 chromosomes — following the word analogy, the chromosomes might be seen as 46 chapters, which make up the book of our nuclear genome*. In the formation of eggs and sperm* inside the human ovaries* and testes*, the *CFTR* must be copied. Each of these germ* cells will then contribute a single copy of *CFTR* to the offspring*, so that every baby will be born with one gene from the father and another from the mother.

If, during the copying process, an error is made, so that the spelling of *CFTR* is defective, the code will be altered. This is what we mean by a mutation. But if you think it through, a mutation such as this will only affect one of the two copies of *CFTR*. Thus if the baby gets one defective copy and one normal copy, the normal copy might still be enough to prevent disease.

Here we turn to another strand of the synthesis — Mendelian genetics. (C) In Mendel's day, naturalists* assumed that heredity* arose through a process of blending of the parental characters, which was adopted by Darwin as the basis for hereditary* change in his evolutionary theory. Mendel, the abbot* of an Augustinian monastery* in Czechoslovakia, happened to be a farmer's son, and he studied the effects of cross-fertilizing* different varieties of peas*, which he grew in the monastery's vegetable garden. When, for example, he took the pollen* from yellow peas and used it to fertilize the female parts of the flowers of green peas, the offspring were not yellowish green, as one might have expected if parental characteristics blended. Instead they were all yellow. Even more intriguingly*, when Mendel crossbred* this new all-yellow generation, the next generation reverted* to a mixture of yellow and green, like the original parents. Even stranger still, the ratio of yellow to green in the new generation was not equal: there were three times as many as yellow as green peas. By analyzing his results, Mendel realized that the inheritance* of pea color could not be based on blending, but rather some "discrete*" factors must be responsible for the two different colors. He had discovered that the coding of heredity comes in small packages, which we inherit from either parents and which we now call genes. But this was not all that Mendel had discovered. What was the meaning of the curious ratios he had observed in the color experiments?

In fact what he had discovered was that when the offspring inherited two different variations of a gene, sometimes one of the two variations dominated over the other. In the case of the peas, the gene for yellow was dominant*. Thus when he blended green and yellow, the offspring, although some only had a single gene for yellow, all appeared yellow. When he further crossbred generations that had one yellow and one green gene, on the law of averages the offspring had a one-in-four chance of having two yellow genes, a two-in-four chance of having one yellow and one green, and a one-in-four chance of having two green genes. Not only does this explain Mendel's finding, it also proves helpful when we go back (D) consider the genetics of cystic fibrosis.

Medical geneticists* have indeed confirmed that when a child inherits* one normal copy of the gene *CFTR* from one parent and mutated version of the gene from the other parent, the coding for the normal copy dominates over that of the mutated gene. From the coding perspective, the mutated gene is essentially passive in the presence of the second normal gene. And this, in turn, implies that only if he or she inherits a mutated gene from both parents will a child suffer from cystic fibrosis. In medical genetics, this is known as a recessive* pattern of inheritance. From this level of understanding, we see that (E) there are two aspects of the recessive inheritance of cystic fibrosis that make it particularly amenable to* gene therapy. The disease is the result of a malfunction of single gene, *CFTR*. Moreover, the two defective copies of the *CFTR* in the sufferer's chromosomes are passive and can be ignored. All that the sufferer needs to correct the condition is the introduction of a single copy of the normal *CFTR* gene.

I have no doubt that, in time it will become possible to correct the genetic cause of cystic fibrosis through the introduction of a single copy of *CFTR* into the chromosomes of sufferers, though there will be problems, both ethical and technical, to be overcome before we reach this stage. For the moment, scientists have restricted their efforts to gene therapy directed exclusively at stem cells* within the lungs, which, to date, have had a limited success.

(F) Other single gene disorders may be the result of dominantly* inherited mutations, for example achondroplasia*, which causes a profound shortening* of the limbs, leading to a common form of dwarfism*, and Huntington's disease*, which causes jerky* involuntary* movements of the body and limbs and a decline in mental abilities. When a mutation affects a gene on the sex chromosomes, the genetics becomes a little more complex. For example, hemophilia*, which causes excessive bleeding through defects in the blood-clotting* factor VIII, is a recessive condition arising from mutations of a gene carried on the X chromosome. But since males only have a single X chromosome, inherited from their mothers, the single copy of the recessive gene will still give rise to the disease. This is why females,

G . Thus we see that hemophilia is not only sex-linked*, it is also a Mendelian recessive condition. Other mutations affecting genes on the sex chromosomes can be dominant, for example the condition known as Vitamin D resistant rickets*, so that mutated gene on just a single X chromosome will cause the disease in either sex.

To date, geneticists have found causative* mutations for more than 5,000 single-gene disorders. Other mutations can change the number of chromosomes, as in Down's syndrome*, where the individual has an additional copy of chromosome 21, or delete, duplicate* fragment, or otherwise damage the structure of chromosomes, giving rise to a variety of medical conditions. While specific gene therapy is at an early stage in the treatment of such conditions, a number of approaches to family screening, advice and prevention are already established and available to assist families known to have an increased risk of mutation and hereditary disease.

The medical approach includes prevention, through genetic counseling, public education about the risks of increasing maternal age, avoidance* of risk factors such as radiation of the germ cells and fetus*, caution over drug and chemical exposure, such as thalidomide*, and vaccination* against the rubella virus*, which is known to damage the developing fetus. Newer genetic measures, such as *in vitro* fertilization* of the sperm and egg, followed by genetic screening of the resultant* fetus when it is at the stage of a ball of cells, can be offered to high-risk families. Known as pre-implantation* genetic diagnosis, or PGD (H), this may be helpful in variety of diseases, including sex-linked disorders, single gene defects and chromosomal disorders. The potentially amenable sex-linked disorders include hemophilia, fragile X syndrome*, most of the neuromuscular* disorders (currently there are more than 900 recognized neuromuscular dystrophies*) and hundreds of other diseases. Indeed, the potentially amenable single gene defects also include cystic fibrosis, Tay-Sachs disease*, sickle-cell anemia* and Huntington's disease.

As a general rule, we can see that genetic abnormality* is more likely to respond to PGD if it is predictable, because the genetic inheritance is known, and if its effects can be demonstrated in isolated embryological cells*. Some people will have ethical objections to such manipulations of the human embryo*(I), but for governments and the groups who monitor the ethics of medicine, the advantages to families will usually outweigh* the ethical worries. It is also important to grasp that pre-implantation genetic diagnosis, with selection for healthy embryos, not only removes the risk of serious disease in an affected offspring but in some cases also eliminates the risk to future generations of the family.

(Frank Ryan 著, "Virolution" Collins 社より, 一部改変)

訳　注

cystic fibrosis：嚢胞性線維症
Caucasian：白人の
transmembrane：膜貫通型の
chromosome：染色体
gland：腺組織
digestive：消化の
intestine：腸
oily：油状の
stagnant/stagnation：よどんだ/よどみ
pneumonia：肺炎
malfunction：機能不全
adolescence：思春期
therapy：治療
frontline：最前線
nucleic acid：核酸
adenine：アデニン
thymine：チミン
genetic/genetics：遺伝の/遺伝学
gene：遺伝子
regulator：調節性の
membrane：細胞膜
mucus：粘液
pancreas：膵臓
sinus：副鼻腔
build-up：堆積物
susceptible to：かかりやすい
malnutrition：栄養失調
severity：重症度
physiotherapy：理学療法
enzyme：酵素
nucleotide：ヌクレオチド
guanine：グアニン
cytosine：シトシン
permutation：順列

genome：ゲノム
ovary：卵巣
germ：胚
naturalist：自然学者
abbot：修道長
Augustinian monastery：アウグスチン修道会
cross-fertilize：交雑受精する
pollen：花粉
crossbreed：異種交配させる
inheritance/inherit：遺伝/遺伝で受継ぐ
dominant：優性の
recessive：劣性の
stem cell：幹細胞
achondroplasia：軟骨無形成症
dwarfism：小人症，低身長症
jerky：ギクシャクした
hemophilia：血友病
sex-linked：伴性の
causative：原因となる
duplicate：二重の
fetus：胎児
vaccination：ワクチンを受けること
in vitro fertilization：体外受精
pre-implantation：移植前，着床前
neuromuscular：神経筋の
Tay-Sachs disease：テイ・サックス病
abnormality：異常
embryo：胚
sperm：精子
testis：精巣
offspring：子，子孫
heredity/hereditary：遺伝/遺伝的な
pea：エンドウマメ
intriguingly：興味深い
revert：もとに戻す
discrete：別個の
geneticist：遺伝学者
amenable to：受けることができる
dominantly：優性に
shortening：短縮
Huntington's disease：ハンチントン病
involuntary：不随意の
blood-clotting：血液凝固
rickets：くる病
Down's syndrome：ダウン症候群
avoidance：避けること，回避
thalidomide：サリドマイド
the rubella virus：風疹ウイルス
resultant：結果として生じた
fragile X syndrome：脆弱X症候群
dystrophy：ジストロフィー
sickle-cell anemia：鎌状赤血球貧血
embryological cell：胚細胞
outweigh：より重要である

設　問

A．下線部(A)に関して，アメリカ合衆国において，CFTR 遺伝子に変異を持つ健常児（細胞の中にある 2 個の CFTR 遺伝子のうち，1 個の CFTR 遺伝子に変異をもつ）は新生児何人に一人と推定できるか。計算の過程，根拠も合わせて推定値を答案用紙 2—1 のA欄に記入しなさい。

B．下線部(B)に関して，15 個の塩基からなる遺伝子はどれほどの異なる塩基配列（多様性）を生じうるか。2^{10} を 1000 とし，計算の過程及び概算した値を答案用紙 2—1 のB欄に記入しなさい。

C．下線部（C）に関して，メンデルが行ったエンドウ豆の実験とその観察結果について，黄色の遺伝子をⓎ，緑の遺伝子をⓖ とし，答案用紙 2－2 のC欄に図示し，日本語で説明しなさい。

D．下線部(D)に関して，嚢胞性線維症患者の遺伝学的背景をメンデルの観察をもとに答案用紙 2—2 のD欄に日本語 120 字以内（句読点を含めて）で説明しなさい。

E．下線部(E)に関して，嚢胞性線維症の遺伝子治療が可能である 2 つの根拠を，答案用紙 2—3 のE—1，2 欄に日本語 50 字以内（句読点も含む）で記入しなさい。また，遺伝子治療の方策を答案用紙 2—3 のE—3 欄に日本語 40 字以内（句読点も含む）で記入しなさい。

F．Eで挙げた遺伝子治療の方策は下線部(F)の疾患に適応できるか。根拠も合わせてその適否を答案用紙 2—3 のF欄に日本語 50 字以内（句読点も含む）で記入しなさい。

G．空欄 G には女性では血友病が稀である理由が述べられている。考えられる理由を答案用紙 2—4 のG欄に日本語 100 字以内（句読点も含む）で記入しなさい。

H．下線部(H)に関して，PGD とはどのようなことをするのか。答案用紙 2—4 のH—1 欄に 60 字以内で記入しなさい。また，これまでの出生前診断より優れていることは何か。答案用紙 2—4 のH—2 欄に日本語 80 字以内（句読点も含む）で記入しなさい。

I．下線部(I)に関して，どのような倫理的問題を含んでいると思うか答案用紙 2—4 のI欄に日本語 120 字以内（句読点も含む）で記入しなさい。