**EXTENDED RESPONSE 3 MUTATIONS AND GENE POOLS (Cystic Fibrosis)**

**IN CLASS EXTENDED ANSWER TOTAL 20M**

1. What is Cystic Fibrosis (CF) and what are the symptoms?

Cystic Fibrosis (CF) is an autosomal recessive genetic disorder of epithelial ion transport that affects a variety of organs and systems in the body. (1/2m)

It is highly lethal, with most afflicted dying in early childhood. (homozygous recessive) (1/2m)

Heterozygous CFTR function is important in regulation of the hydration of mucus secretions, and many of the symptoms of CF are associated with especially viscid mucous. In the lungs, this mucous impairs lung clearance, impedes air flow, and encourages an environment highly suitable for pathogenic microbes. Chronic lung infection is associated with recurrent lung inflammation and damage, and can eventually lead to respiratory failure. In the pancreas, duct function is impaired, and the consequent retention of digestive enzymes in the pancreas is associated both with poor digestion and with pancreatic damage, including both CF-related diabetes, and the pancreatic fibrosis from which the disorder derives its name (any one =1m)

2m

1. Where is the gene for CF found?

Gene located on human chromosome seven

More than 1400 alleles with diminished function

Most common CF disorder allele is D508 (any two) 1m

1. Is CF Autosomal dominant/recessive and state the phenotypes for: -

Autosomal recessive (1m)

1. Homozygous dominant Normal 1m
2. Heterozygous Suffers from lung/pancreatic problems 1m
3. Homozygous recessive Lethal 1m

4m

1. The incidence of CF in Europe is abnormally high in comparison with other parts of the world.

Describe the difference between Mutation, Migration, Natural Selection and Genetic Drift as mechanisms that might explain for this increase.

Mutation

**One is that it has a higher frequency in Europe than do other recessive lethal disorders. (1m) The other is that it has a higher frequency in Europe than elsewhere. (1m)** **Another possible explanation for a high frequency of deleterious alleles at a particular locus is that the gene in question has a particularly high mutation rate (1m) Any 2 2m**

Migration

The CF gene had mutated elseware (1m) and this small group migrated into Europe, therefore increasing the CF gene frequency within Europe (1m)

Natural Selection Any 2

Natural selection is another possibility is that in some way heterozygotes attain greater fertility than homozgyotes for the common fully-functional CFTR allele. (1m)

Indeed, this has been proposed for CF, and early studies suggested that CFTR heterozygotes had more children than ordinary homozygotes. (1m)

Heterozygotes may have an advantage leading to disease resistance or some other benefit (1m)

Genetic Drift

CF might simply be the rare case in which drift had been so extreme. (1m) Another way in which genetic drift might be involved is with a founder effect or bottleneck, in which European populations would have arisen from a small population that happened, by chance, to have a high incidence of the ∆F508 allele (1m)

Total 8m

1. Which of the above is most favoured and why?

Natural selection due to it being supported (1m) with mutation, migration and genetic drift being not supported (1m)

Total 2m

1. Does the Heterozygous form have any survival advantage and if so what is the advantage?

Heterozygote advantage leading to disease resistance as the most common mechanism (1/2m)

The major hypotheses for the selective agent for heterozygote advantage include:

1. Diarrheal diseases, including cholera
2. Tuberculosis
3. Typhoid fever ANY 2 = 1M

Explanation (1/2m) (any one)

1. Physiological studies should suggest a plausible basis by which the CFTR gene could be involved in resistance to that infectious disease
2. Clinical studies should show that heterozygotes do indeed have better outcomes when exposed to the infectious agent than homozygotes
3. There should be a good geographic match between areas with high historical incidence of the infectious disease, and those with a high incidence of CF alleles

Total 2m

1. What are the treatments for this disease?

Any 2 explained

Treatment of CF has traditionally been symptomatic, and includes a variety of modalities, including antibiotic therapy against lung pathogens, treatment of lung inflammation, a variety of techniques to encourage regular clearance of the lungs, pancreatic enzyme replacement, and nutritional management. 1/2m

1. What cures are there for this disease?

Any 2

More recently, various approaches have been tried to enhance CFTR function in CF patients. One set of approaches has utilized gene therapy to attempt to incorporate functional CFTR in lung epithelial cells.

Other approaches have used pharmacologic compounds to enhance the ability of mutant CFTR protein to incorporate into membranes and function effectively as an ion channel.

Total 1/2m

Total B 20m

Research component A 20m

Grand Total 40m