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

**Notes (3Pgs) to be surrendered when Extended Answer is written**

1. What is Cystic Fibrosis (CF) and what are the symptoms? 3m

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

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

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)

1. Where is the Gene for Cystic Fibrosis located? 2m

Gene located on human chromosome seven

More than 1400 alleles with diminished function

Most common CF disorder allele is D508 (any two)

1. Is CF Autosomal dominant/recessive and describe the Phenotype of: -

Autosomal recessive (1m)

1. Homozygous dominant Normal 1m
2. Heterozygous Suffers from lung/pancreatic problems 1m
3. Homozygous recessive Lethal 1m 4m
4. The incidence of CF in Europe is abnormally high in comparison with other parts of the world.
5. In terms of mutation describe how this increase in the CF gene may have occurred

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

1. In terms of migration describe how this increase in the CF gene may have occurred

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

1. In terms of natural selection describe how this increase in the CF gene may have occurred

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) Any 2 2m

1. In terms of genetic drift describe how this increase in the CF gene may have occurred

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)

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 10m

1. Does the heterozygous genotype contribute to ant survival advantage and if so how?

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

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

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

Explanation (1m) (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 4m
4. What are the treatments for CF?

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.

Total 2m

1. Describe any possible cures for this condition 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 2m

Bibliography 3m

Total 30m

Reduced to (A) 20m

Validation Test (B) 20m

Grand Total A +B 40m