1. A person shows symptoms of tyrosinemia 1, with a high level of 4-fumarylacetoacetate in the blood. Please answer the following questions:

i) What enzyme is likely missing or defective in people with tyrosinemia 1?

ii) What medical conditions arise due to this disease (please use the web)?

i) They are missing 4-fumarylacetoacetase, the enzyme that splits 4-fumarylacetoacetate to fumarate and acetoacetate.doxil

ii) Fever, diarrhea, vomiting, jaundice, severe liver disease, cirrhosis, hepatocarcinoma (https://rarediseases.org/rare-diseases/tyrosinemia-type-1/)

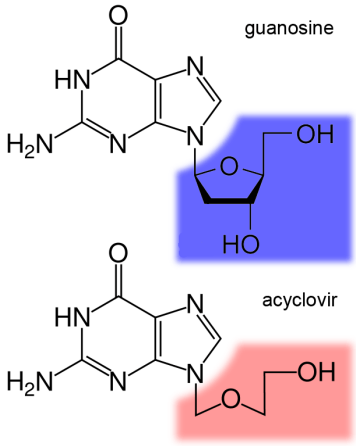
2. What is the drug doxil and what is it used to treat (please use the web)?

It is the drug doxorubicin encapsulated in liposomes, used to treat cancer (https://www.baxter.com/doxil-doxorubicin-hcl-liposome-injection-hospital-care)

3. An individual has a high cholesterol levels. You sequence the LDL receptor and find that the central part of the protein now contains polar amino acids instead of non-polar ones. Suggest a reason why the person has high cholesterol levels.

The LDL receptor probably cannot insert in to the membrane, consequently the LDL particles cannot be internalized and degraded. This will prevent the cell from sensing the amount of cholesterol in the blood to regulate the production of cholesterol.

4. Acyclovir is an antiviral agent. The structure of acyclovir and guanosine (deoxy) are shown on the right. Note that Acyclovir is converted to a triphosphate by cellular enzymes, adding three phosphates to the right -OH group.



i) Use the web to find out what kind of viral infections are typically treated with acyclovir.

ii) How do you think acyclovir works to inhibit replication of the virus?

i) It is used to treat viral infections by herpes virus. (https://en.wikipedia.org/wiki/Aciclovir)

ii) Aciclovir lacks a 3'-OH group. It can be added to a growing DNA chain by a DNA polymerase, but once added the chain cannot be elongated since a 3'-OH is required.

5. Cystic fibrosis is a genetic disease that is caused by a single mutation in a chloride ion transporter (CFTR). The transporter is necessary to move Cl ions across mucus membranes. The chloride then causes water to move across the membrane to reduce the viscosity of mucus. When the transporter is defective the mucus is very thick, causing difficulty in breathing.

The gene for the CFTR protein is very long (over 180,000 bases). A segment of the DNA that codes for the middle section of the protein is shown below, beginning at the codon for residue 505 in the protein

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atc atc ttt ggt gtt
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The disease is recessive, meaning that an affected individual must have two copies of the mutation to have the disease. Heterozygous individuals do not have the disease but are carriers. There is a one-in-four chance that a child produced from two carriers will have the disease. Therefore, genetic testing for heterozygotes is very important if there is a family history of the disease.

You sequence DNA samples from an affected individual and find the following sequence for the same region of the DNA and find:

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atc atc ggt gtt
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i) What is the amino acid sequence of the normal and mutant proteins.

Normal: … Ile Ile Phe Gly Val

Mutant: Ile Ile Gly Val

ii) How does this mutation affect the protein sequence?

Deletion of Phe

iii) How might this change affect the structure of the protein?

This deletion prevents folding of the protein such that it cannot be inserted into the membrane to act as a chloride channel. It would also be acceptable to say that Phe is non-polar so its loss may affect insertion into the membrane.