Welcome to your Patient!

Jeff, 46 year old American male of Scots descent has come to you for a second opinion...

**Diagnosis:** Cirrhosis of the liver and Type 1 Diabetes due to chronic alcoholism

**Key Symptoms:** Elevated liver enzymes, excess ascites fluid and an enlarged spleen (splenomegaly)

In the two months since his diagnosis, the insulin treatment and significant dietary changes have not seemed to improve things much, indeed his condition has deteriorated (severe fatigue). He claims he is not, nor has he been an alcoholic – used to have 1-2 glasses of beer a few times a week and had not had anything for a time before being diagnosed – so he really doesn’t think this diagnosis makes any sense.

Clinical Research

1. **Search MedGen with symptoms** *(click on “Limits” and in the “Field” pull-down menu select “Clinical Features”):*
   
   cirrhosis AND diabetes AND ascites AND splenomegaly

   Scan the descriptions provided in the retrieved list. **WHAT IS A POSSIBLE DIAGNOSIS FOR JEFF?**

2. To **confirm this diagnosis**, **WHAT LABORATORY TEST(S) COULD YOU ORDER?**
   (Hint: Check the GeneReviews>Diagnosis Link or take a look at PubMed articles listed in the Recent clinical studies>Diagnosis section.)

   ➢ Click here (access this URL) to see the Lab Test results: [http://1.usa.gov/1lQz8Rd](http://1.usa.gov/1lQz8Rd)

   **NOTES:**

   Based on your research and the results of the Lab Test, **WHAT DO YOU THINK IS WRONG WITH JEFF?**
3. There are many relevant publications on the MedGen record – about Recent clinical studies and Recent systematic reviews. Write down PMIDs for those of interest to you.

4. What is the name of the link that would you click to find relevant Clinical Trials?

5. Find some helpful Patient Education Materials - Write in the link name(s).

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You discuss the diagnosis and hand Jeff some Patient Education materials. He has heard that this is may be a genetic condition. He has a twin sister and a brother and is concerned that they may be effected.

He’d like to have a DNA test to see if the cause of his disease is genetic and also see if he can find out specifically what is wrong with him on a personal level, even though it may not change his prognosis or therapy.

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**Genetics Research**

6. From the MedGen record, find a genetic test that you could order for him. (For this case-study, this should be a CLIA-certified clinical lab in California.) Write down the GTR Test ID.

- Click here (access this URL) to see the Genetic Test results: [http://1.usa.gov/1scRJHC](http://1.usa.gov/1scRJHC)

NOTES:

What is the specific gene and variation identified in Jeff?
7. Back on the MedGen record, click the gene link for the one identified as having a variant in Jeff. What is this gene normally purported to do?

8. From the Gene record, click the UniGene link to find out in which tissues this gene is expressed and also, since it stays within the cell, where it functions. Which tissues found to express this gene correlate with some of Jeff’s symptoms?

9. From the Gene record, click the RefSeq Proteins link, then the one entitled “isoform 1 precursor”. Click Graphics to see defined regions on the protein sequence. Then, click “Identify Conserved Domains” to display a graphic displaying more specific information about the main functional regions on this protein.

   Based on the location of Jeff’s genetic variant and the description of the functional regions, what might the variant might do to the protein function or structure?

10. From both the Gene and Protein records, there are links to 3D Structures….examine a structure to see precisely where the amino acid affected by the genetic variation is located.

   ➢ Click here (access this URL) to open an annotated 3D Structure:  http://1.usa.gov/WNP3nL

   NOTES:

   What do you think the change in amino acid might do to the protein?
NOTES & THOUGHTS: