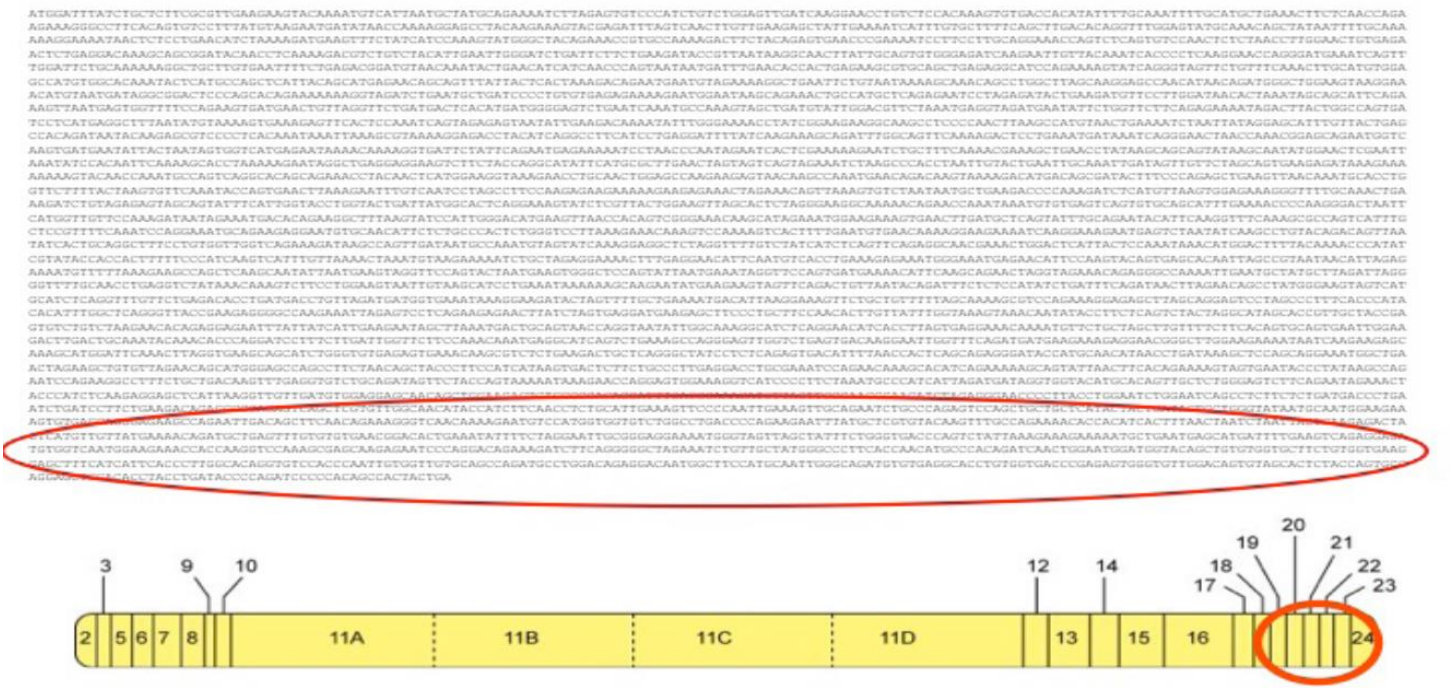
DNA Bioinformatics Study to Locate Human *BRCA* Cancer Genes

Bioinformatics is the study of genetics and molecular biology by retrieval and analysis of biochemical and biological data using mathematics and computer science. www.dictionary.reference.com At the National Center for Biotechnology Information (NCBI), genetic information from the genomes of many species has been stored. By comparing unknown sequences of DNA with known samples of DNA, information can be gained.

DNA sequences will be analyzed in this activity for mutations in the Human *BRCA1* Cancer Genes, which can cause breast and ovarian cancer. In addition to the DNA analysis, patient history will be considered to determine the likelihood of mutations in the *BRCA1* gene causing cancer.

Since the *BRCA1* gene is 81,188 base pairs long, only a small portion of the gene (below, circled in red) is used to make the comparisons with patient DNA. Within this small portion, there is at least one mutation that is implemented in causing breast cancer. With this bioinformatics tool, patient DNA will be compared with normal DNA to determine if there are mutations.

The *BRCA1* Gene



Because of a family history of breast and ovarian cancer, the following patients decided to undergo genetic testing for *BRCA1* cancer genes. A blood sample was collected to analyze their DNA. Using the information collected, you will analyze their DNA by going to the NCBI site at http://www.ncbi.nlm.nih.gov/ and using BLAST (Basic Local Alignment Search Tool) search engine to determine if these patients have a mutation within the *BRCA1* gene.

Patient A is a 33 year old mother of 4 children, 2 boys and 2 girls. Her mother and grandmother died of ovarian cancer at ages 54 and 48, respectively, and her aunt died of breast cancer at age 45.

Patient B is a 47 year old man that is of Ashkenazi Jewish descent.

Patient C is a 56 year old woman with no children. She eats a diet of lean meat, lots of fruits and vegetables, and whole grains and walks 4 miles each day.

Patient D is a 65 year old mother of 2 children, a boy and a girl, and 5 grandchildren, 3 boys and 2 girls. She has smoked for 45 years.

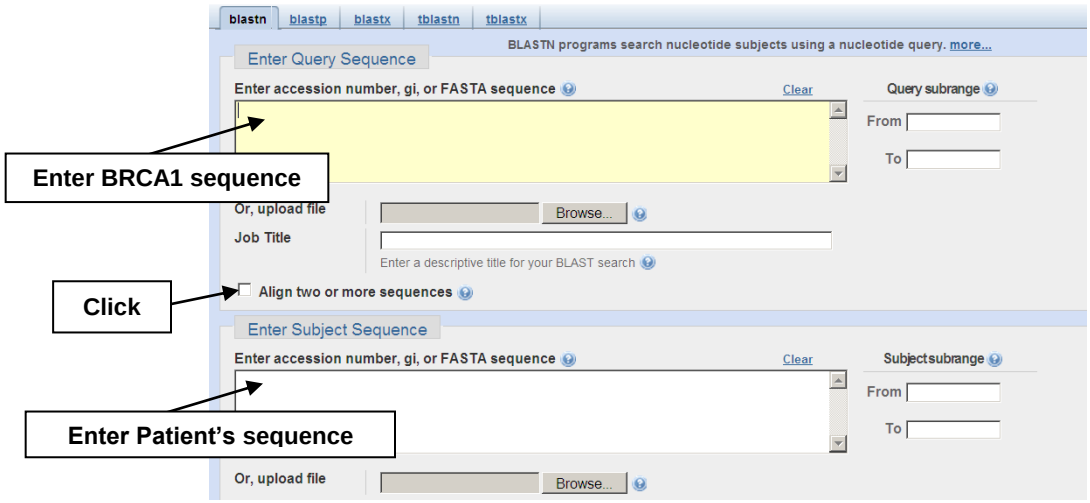
Patient E is a 45 year old woman whose father died from breast cancer at the age of 52. She has 3 children, 1 boy and 2 girls, and 1 grandchild, a girl.

Knowing that each patient came in for genetic testing because of a family history of breast and ovarian cancer and given their known life style, which patient(s) would you think has/have breast and/or ovarian cancer and why?

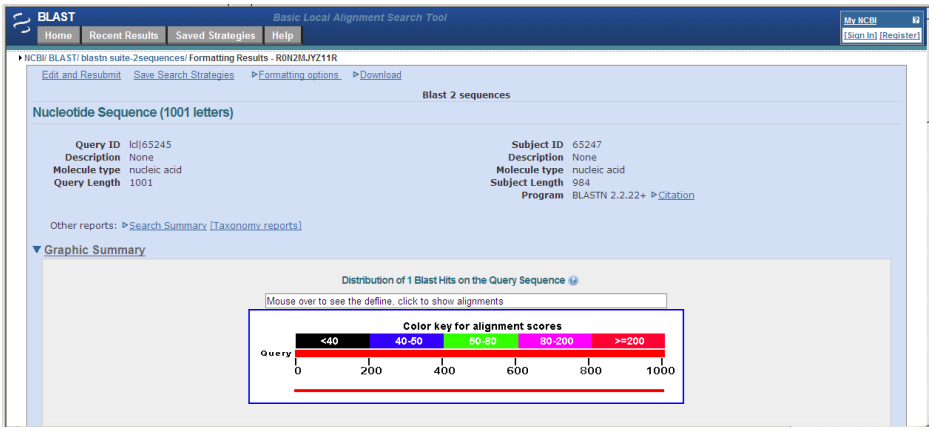
You will now align each patient's sequence to the functioning *BRCA1* gene using the following instructions.

1. Go to: http://www.ncbi.nlm.nih.gov/.
2. Click "BLAST" under "Popular Resources" on the right side of the page.
3. Under Basic BLAST: Chose a BLAST program to run.
4. Click on "nucleotide blast."
5. Open the *BRCA1* sequence file, copy the sequence and paste the sequence in the empty box titled: "Enter accession number, gi, or FASTA sequence." See diagram below.
6. Then click the box associated with the phrase "Align two or more sequences."

7. Then open Patient A's sequence file, copy the sequence and paste the sequence in the second empty box titled: "Enter accession number, gi or FASTA sequence." See diagram below.



8. Under "Program Selection: Optimize for," choose "Somewhat similar sequences (blastn)."
9. Then "BLAST" in a new window.
10. Wait until the following screen appears:



11. Then scroll down to observe the alignment of sequences between the BRCA1 sequence and the patient's sequence, record your observations on the following page.
    NOTE: Query represents BRCA1 Sequence and Sbjct represents Patient's sequence.
12. Repeat alignment sequence for all patients by clicking on "Edit and Resubmit" found on the top of the screen.

Observations:

Record the similarities/differences in alignment of the sequences.

Patient A alignment?

Patient B alignment?

Patient C alignment?

Patient D alignment?

Patient E alignment?

5 years later… the following information was collected about each patient.
Use the information from your BLAST alignments and the information below to answer the following questions.

Patient A was diagnosed with ovarian cancer at age 36 and continues to be treated.
Patient B was diagnosed with breast cancer at age 52 and just began treatment.
Patient C does not have breast or ovarian cancer.
Patient D was been diagnosed with breast cancer at age 68 and continues to be treated.
Patient E does not have breast or ovarian cancer but will have her children tested and depending on the results, perhaps her grandchild as well.

1. **When you aligned the patients' sequences compared to the normal *BRCA1* gene, what type(s) of mutation(s) did you observe in Patients A, B, C, D, E? Explain how you came to your conclusions.**

2. **When a mutation occurs within the *BRCA1* gene, or any gene, what happens when the protein is transcribed and translated from the mutated gene?**

3. **Do all individuals who have inherited the *BRCA1* mutation develop breast or ovarian cancer? Why or why not?**

4. **Should Patient A's children be tested for mutations in the *BRCA1* gene? Why or why not?**

5. **Other than mutations in the *BRCA1* gene, what other factor(s) can contribute to the development of breast or ovarian cancer?**

6. **Summarize important points from this activity.**

The student version of **DNA Bioinformatics Study to Locate Human *BRCA1* Cancer Genes** was adapted by Lynda Jones, MS, ONPRC, from Sample Lab #3 Using Bioinformatics to Sequence Cancer Genes (Looking for a BRCAI mutation in cancer patients) in the NUBIO Pilot Curriculum of the Oncofertility Consortium at Northwestern University, with permission. Sample Lab #3 was written by a teacher work team composed of Dr. David Bain, Kelly Breiner, Kevin McLean, Jeff Newton, Mark Prosise, Kate Silber, Jean Witty, and Christine Woods. The work was supported by Dr. Kemi Jona and Dr. Teresa Woodruff from Northwestern University and was directly supported through NIH grants RL5CA133836 (R25 Grant, Jona P.I.), 3RL5CA133836-02s1 (R25 Administrative Supplement Grant, Jona P.I.) and UL1RR024925 (Administrative Core, Woodruff P.I.).