Lab sheet1: Information retrieval and sequence analysis

Q1

COX-2 (prostaglandin H2 synthase-2 (PTGS2)) gene

COX-2 has been thoroughly studied because of its role in prostaglandin synthesis. Prostaglandins have a wide range of roles in our body from aiding in digestion to propagating pain and inflammation.

Aspirin is a general inhibitor of prostaglandin synthesis and therefore, helps reduce pain.

However, aspirin also inhibits the synthesis of prostaglandins that aid in digestion. Therefore, aspirin is a poor choice for pain and inflammation management for those with ulcers or other digestion problems.

Recent advances in targeting specific prostaglandin-synthesizing enzymes have lead to the development of Celebrex, which is marketed as an arthritis therapy. Celebrex is a potent and specific inhibitor of COX-2. Celebrex is considered specific because it doesn't inhibit COX-1, which is involved in synthesizing prostaglandins that aid in digestion.

This is a remarkable accomplishment given the great similarity between COX-1 and COX-2.

This achievement has paved the way for developing new therapies that bind more specifically to their target and therefore have fewer side effects. Understanding the enzyme structures of COX-1 and COX-2 helped researchers develop a drug that would only bind and inhibit COX-2. Many of the types of information and tools used by researchers for these types of studies are freely available on the web.

GenBank, SwissProt, Sequence Manipulation suite are some of the websites.

- i. Access the entries for Human PTGS1 and PTGS2 in the "Gene" database at the NCBI (https://www.ncbi.nlm.nih.gov/) Website.
 - a. PTGS1 and PTGS2 are isozymes. Isozymes catalyze the same reaction but are separate genes. What types of reactions do PTGS enzymes catalyze? Also, what pathway are these enzymes a part of?
 - Catalyze the conversion of arachidonate to prostaglandin
 - PTGS1 is a part of the arachidonic acid metabolic pathway
 - b. How is the expression of PTGS1 and PTGS2 different?

PTGS1	PTSG2
Biased expression in skin (RPKM 36.8),	Biased expression in bone marrow (RPKM
esophagus (RPKM 21.4) and 12 other tissues	59.3), urinary bladder (RPKM 41.1) and 11
	other tissues

- c. Which isozyme (PTGS1 or PTGS2) is required to inhibit inflammation?
 - PTGS2
- d. The drug Celebrex selectively inhibits PTGS2 while aspirin and other NSAID's inhibit both PTGS1 and PTGS2 in the same way. Why do you think researchers wanted to discover a selective inhibitor to PTGS2?

- To discover a selective inhibitor for PTGS2 to avoid inhibiting PTGS1, which is involved in synthesizing prostaglandins for digestion
- Reduces side effects
- e. Describe how studying 3-D structures of PTGS1 and PTGS2 could help researchers design a drug that binds to PTGS1, but not to PTGS2.
 - Understanding structural nuances, such as flexibility and molecular interactions, enables the development of drugs with high specificity, reducing the risk of off target effects
- ii. Considering the Homo sapiens PTGS2 gene entry in NCBI gene https://www.ncbi.nlm.nih.gov/gene/ database,
 - a. What is the gene name?
 - Prostaglandin-endoperoxide synthase 2
 - b. What is the GeneID number?
 - 5743
 - c. Where in the human genome is this gene located?
 - The gene PTGS2 is located at complement (186,671,791..186,680,423) on chromosome NC 000001.11.
 - d. What is the RefSeq accession number for the mRNA sequence of Homo sapiens prostaglandin-endoperoxide synthase 2?
 - NM 000963.4
 - e. Download the prostaglandin-endoperoxide synthase 2 Reference mRNA sequence in "FASTA" format.
 - f. What is the RefSeq accession number for the Homo sapiens PTGS2 protein sequence? Download the sequence in "FASTA" format.
 - NP 000954.1
- iii. Search for the UniProt entry for PTGS2 in Expasy https://www.expasy.org/website.
 - a. What are the alternate names for this protein.
 - Prostaglandin G/H synthase 2
 - b. What types of drugs target this protein?
 - Nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin and ibuprofen
 - c. What amino acid is acetylated by aspirin (amino acid type)?
 - Serine
- iv. Translate the mRNA sequence of PTGS2 into Protein. Use "Translate " tool in ExPASy. Explain the output.
 - Every DNA sequence can be read in six possible frames three in the forward direction (5' to 3') and three in the reverse direction (3' to 5'). I have chosen the longest amino acid sequence which is in 5'3' Frame 2. Below are the equivalent fasta formats.

Fasta format

> VIRT-2302:5'3' Frame 2, start_pos=44
MLARALLLCAVLALSHTANPCCSHPCQNRGVCMSVGFDQYKCDCTRTGFY
GENCSTPEFLTRIKLFLKPTPNTVHYILTHFKGFWNVVNNIPFLRNAIMS
YVLTSRSHLIDSPPTYNADYGYKSWEAFSNLSYYTRALPPVPDDCPTPLG
VKGKKQLPDSNEIVEKLLLRRKFIPDPQGSNMMFAFFAQHFTHQFFKTDH
KRGPAFTNGLGHGVDLNHIYGETLARQRKLRLFKDGKMKYQIIDGEMYPP
TVKDTQAEMIYPPQVPEHLRFAVGQEVFGLVPGLMMYATIWLREHNRVCD
VLKQEHPEWGDEQLFQTSRLILIGETIKIVIEDYVQHLSGYHFKLKFDPE
LLFNKQFQYQNRIAAEFNTLYHWHPLLPDTFQIHDQKYNYQQFIYNNSIL
LEHGITQFVESFTRQIAGRVAGGRNVPPAVQKVSQASIDQSRQMKYQSFN
EYRKRFMLKPYESFEELTGEKEMSAELEALYGDIDAVELYPALLVEKPRP
DAIFGETMVEVGAPFSLKGLMGNVICSPAYWKPSTFGGEVGFQIINTASI
QSLICNNVKGCPFTSFSVPDPELIKTVTINASSSRSGLDDINPTVLLKER
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Readings:

http://www.aspree.org/AUS/aspree-content/aspirin/how-aspirin-works.aspx

Q2. Python Exercises

1. Below shows some files with embedded sample names:

```
lane1_NewCode_L001_R1.fastq.gz
lane1_NoIndex_L001_R1.fastq.gz
lane1_NoIndex_L001_R2.fastq.gz
pipeline_processing_output.log
lane7027_ACTGAT_JH25_L001_R1.fastq.gz
lane7027_ACTTGA_E30_1_2_Hap4_24h_L001_R1.fastq.gz
lane7027_AGTTCC_JH14_L001_R1.fastq.gz
lane7027_CGGAAT_JH37_L001_R1.fastq.gz
lane7027_GCCAAT_E30_1_21_Hap4_log_L001_R1.fastq.gz
lane7127_GGCTAC_E30_1_4_Hap4_48h_L001_R1.fastq.gz
```

Write a Python code to extract the sample name from these files ignoring any files which do not match the format given below.

The format is:

- 1. Written lane number
- 2. Barcode
- 3. Sample name
- 4. Numeric lane number (starting with L)
- 5. Read number (R1/2/3/4)
- 6. File extension

Eg. Lane8127_GCCAAT_S30_1_21_Hap4_log_L001_R1.fastq.gz the sample name would be, S30_1_21_Hap4_log

2. Create a FASTA file by obtaining 10 Dengue 1- Envelop gene DNA sequences from NCBI. Write a Python-program that reads the FASTA file, cleans up the header line to have only Accession number & gene-name and print headers and sequences to standard output as multi-FASTA-file again.

```
from Bio import Entrez, SeqIO
 def fetch_dengue_sequences():
    dengue_sequences = []
  for record_id in ids:
    return dengue_sequences
    with open(output_file, "w") as output_handle:
 def clean_up_header(header):
    if match:
       accession_number = match.group(1)
        gene_name = match.group(2)
def print_multi_fasta(file_path):
    sequences = list(SeqIO.parse(file_path, "fasta"))
        print(cleaned_header)
       print(seq_record.seq)
print_multi_fasta("dengue_sequences.fasta")
```

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 Write a Python program to search the DNA Sequence for the presence of one of the following Transcription Factor Binding Sites(TFBS) with ambiguity codes. Search for all the positions in the sequence where TFBS is located.

Transcription Factor	Consensus Sequence
RUNX1	BHTGTGGTYW
TGIF1	WGACAGB
IKZF1	BTGGGARD

Code	Represents
Α	Adenine
G	Guanine
С	Cytosine
Т	Thymine
Υ	Pyrimidine (C or T)
R	Purine (A or G)
W	weak (A or T)
S	strong (G or C)
К	keto (T or G)
М	amino (C or A)
D	A, G, T (not C)
V	A, C, G (not T)
Н	A, C, T (not G)
В	C, G, T (not A)

The sequence is shown below.

>search seq

```
def search_tfbs(sequence, tfbs_dict):
    for tf, consensus_seg in tfbs_dict.items():
```

```
def replace_ambiguous_bases(consensus_sequence):
            modified_sequence = consensus_sequence\
                .replace('K', '[TG]')\
.replace('M', '[AC]')\
.replace('D', '[AGT]')\
            return modified_sequence
        for tf, consensus_seq in tfbs_dict.items():
            modified_sequence = replace_ambiguous_bases(consensus_seq)
            tfbs_dict[tf] = modified_sequence
        results = search_tfbs(search_seq, tfbs_dict)
Sequence: GTGGGAAT
Process finished with exit code 0
```

Q3 – Biopython

Biopython Tutorial and Cookbook https://biopython.org/DIST/docs/tutorial/Tutorial.html#sec2

1. Write a Biopython program that asks the user to input a DNA-sequence and then translates the sequence to protein sequence.

```
from Bio.Seq import Seq

# Get user input for DNA sequence
dna_sequence = input("Enter the DNA sequence: ")

dna_seq = Seq(dna_sequence)

protein_seq = dna_seq.translate()

print("Translated Protein Sequence:", protein_seq)
```

```
C:\Users\maheshl\PycharmProjects\pythonProject1\venv\Scripts\python.exe C:\Users\maheshl\PycharmProjects\pythonProject1\Uni\CB\T1.py
Enter the DNA sequence: @10000ATMOTATIONGGGGGTGAAAGGGTGGGGGATAG
Translated Protein Sequence: VAIVMGR*KGAR*

Process finished with exit code 0
```

2. Write a Biopython program that will find all articles related to Alzheimer's in PubMed. Print the total number of articles available and the authors.

```
from Bio import Entrez

Entrez.email = "maheshlakshan760@gmail.com"

Anadle = Entrez.esearch(db="pubmed", teru="Alzheimen's")

record = Entrez.read(handle)

pubmed_ids = record["IdList"]

off pubmed_ids:

handle = Entrez.efetch(db="pubmed", id=pubmed_ids, rettype="xml")

records = Entrez.read(handle)

print("Total number of articles:", record["count"])

for record in records["PubmedArticle"]:

authors = ", ", "join(author("LastName") + " " + author["Initials"] for author in record("MedLimeCitation")["Articles"]["AuthorList"])

print("No articles found.")

print("No articles found.")

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Once It fetches only 20 records that's why there is only 20 authors entry in the Terminal.

3. Write a Biopython-program that finds CpG-islands from a given DNA-sequence.

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