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Using OncoDB's Oncovirus Analysis for HBV-related HCC

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OncoDB and HCC

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Anna Claire Newman

Intro

- Hepatocellular carcinoma (HCC), or LIHC, is the sixth most common type of cancer and one of the most common causes of cancer death in the world (Su et al., 2007).
- The hepatitis B virus (HBV) can cause an increased risk of the development of HCC (Rizzo et al., 2022).
- There is already substantial research on HCC; however, analysis functions on viral infections such as HBV have not been given enough attention to be implemented into online tools.
- Evidence has found that oncoviruses are often behind cancer development, so to better evaluate these virus-related cancers, gene expression changes need to be identified.
- Data analysis needs to be made more accessible.
  - These are the goals of OncoDB.

Where do they get their data?

- The OncoDB database uses clinical data and information from more than 10,000 patients in the Cancer Genome Atlas study (TCGA), along with DNA methylation and RNA-seq.
- Tumor and matching normal tissue data was obtained from the GTEx study and the GDC data portal.
- OncoDB is open access, which makes it easily accessible for public use (Tang et al., 2022).

What is OncoDB?

- OncoDB's abilities are split into four sections
  - Expression analysis, methylation analysis, clinical analysis, and oncovirus analysis
- Clinical data is correlated with the DNA methylation and RNA expression data in order to identify relevant gene expression changes.
- Oncovirus analysis
  - Viral infections are used to give context to gene expression data in order to identify viral-related changes.

What is OncoDB?

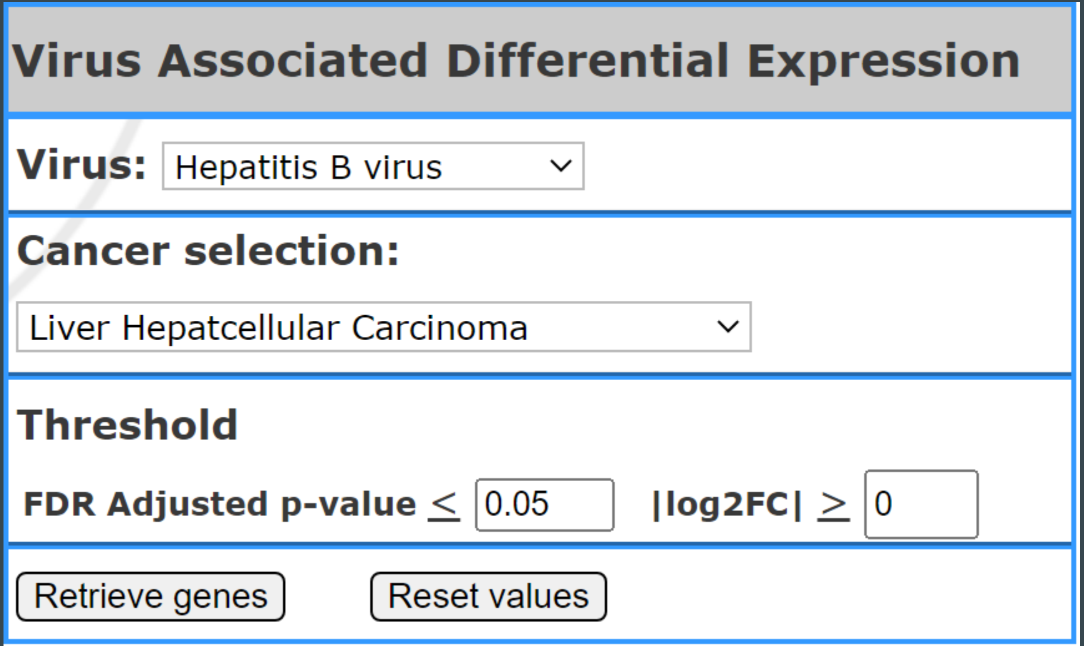
- The expression analysis section includes both cancer and gene-centered expression analysis and implements them into visualized results.
- The methylation analysis section compares matching tumor and normal tissue samples to evaluate patterns in differential methylation.
    - Summarized using a line graph of average methylation levels
- The clinical analysis section is a comparison of the DNA methylation and RNA expression data with the clinical data pulled from different sources.
    - Analysis of correlations
    - Expression box plot or a methylation line graph will be given, along with a summary table of statistical analysis results.

Oncovirus Analysis Capabilities

- Gene-centered analysis can be run to search for potential correlations between viral infection and a chosen gene from different types of cancer.
- Can also provide a list of the top genes that are correlated with a chosen virus and cancer.
- Users are able to obtain expression and methylation data concerning a virus-related cancer according to a certain parameter.
- Uses clinical data for gene analysis and gives a survival plot concerning the presence of a virus-related gene.
- Running a differential clinical analysis will provide a list of genes that present methylation and expression patterns correlated with a chosen virus and cancer.

Differential Expression

- User will input the virus and cancer they wish to analyze
- Gives list of genes in terms of expression
  - Also includes p-values, medians, and log2FC
- For Example
  - Chose top gene CLRN3



Virus Associated Differential Expression

Virus: Hepatitis B virus

Cancer selection:

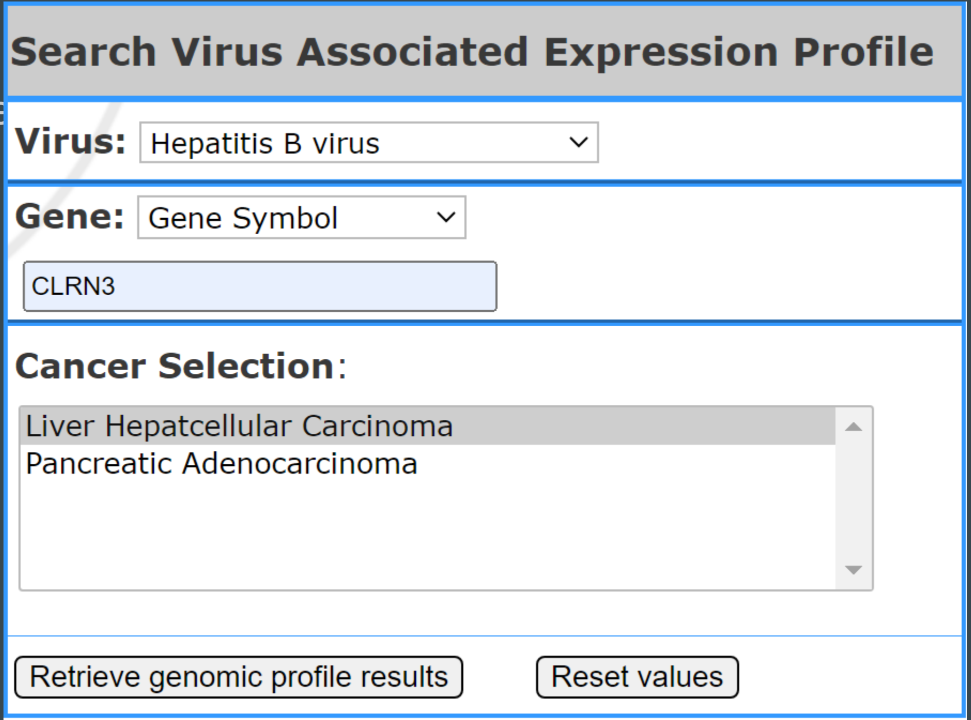
Liver Hepatcellular Carcinoma

Threshold

FDR Adjusted p-value ≤ 0.05 **|log2FC| ≥** 0

Expression profile

- Enter the cancer type, virus, and chosen gene on the expression profile page



Search Virus Associated Expression Profile

Virus: Hepatitis B virus

Gene: Gene Symbol

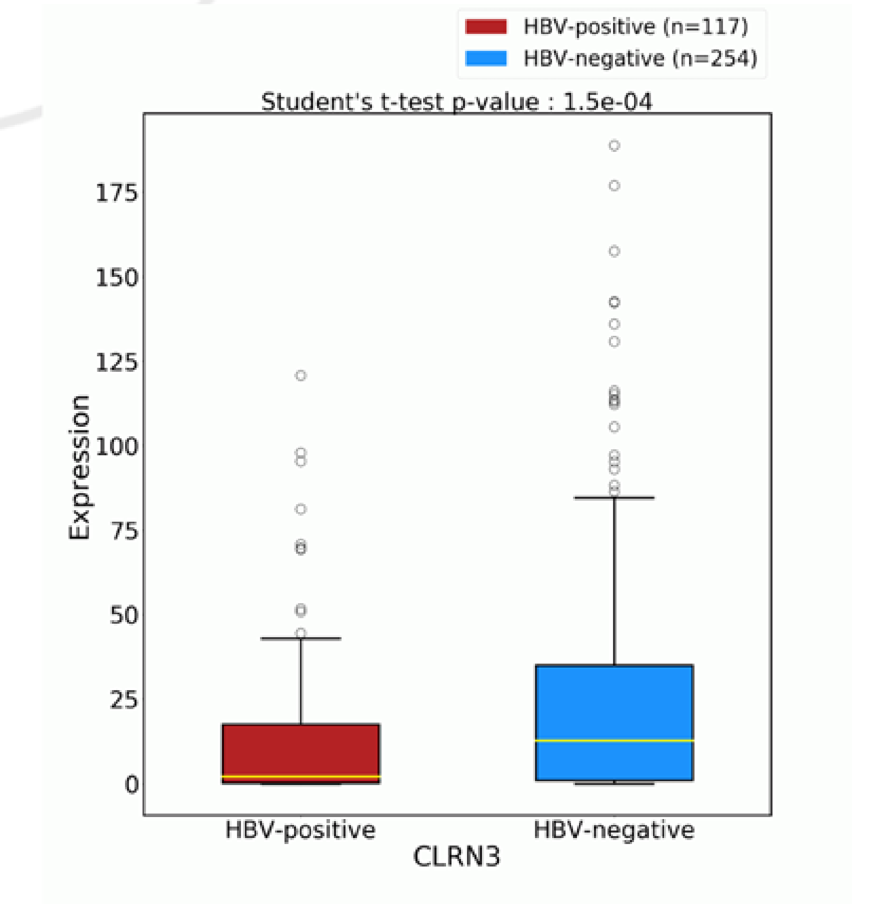
CLRN3

Cancer Selection:

Liver Hepatcellular Carcinoma
Pancreatic Adenocarcinoma

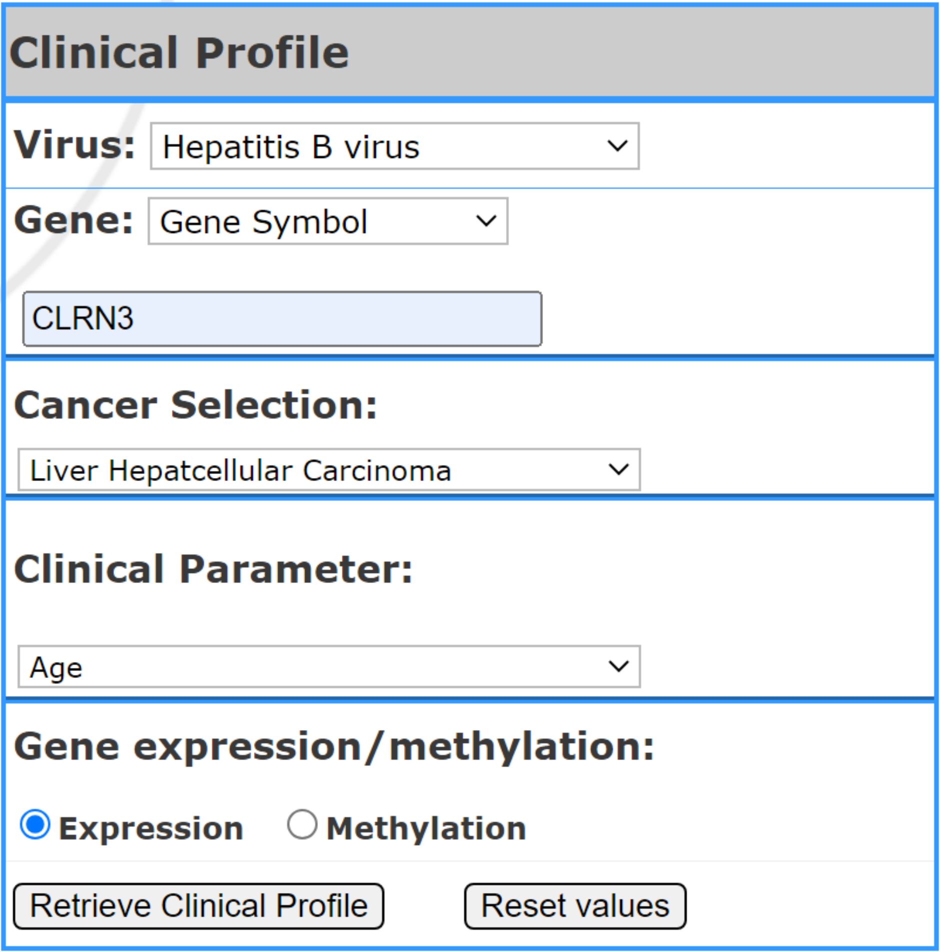
Results

- ➔ Higher expression of CLRN3 in HBV-negative LIHC compared to HBV-positive



Clinical profile

- ➔ Enter the selected virus, gene, cancer type, clinical parameter, and either expression or methylation
- ➔ Clinical parameter options
  - ◆ Pathological stage, age, gender, BMI, race, and histological grade
- ➔ For Example
  - ◆ Age chosen as parameter



Clinical Profile

Virus: Hepatitis B virus

Gene: Gene Symbol

CLRN3

Cancer Selection:

Liver Hepatcellular Carcinoma

Clinical Parameter:

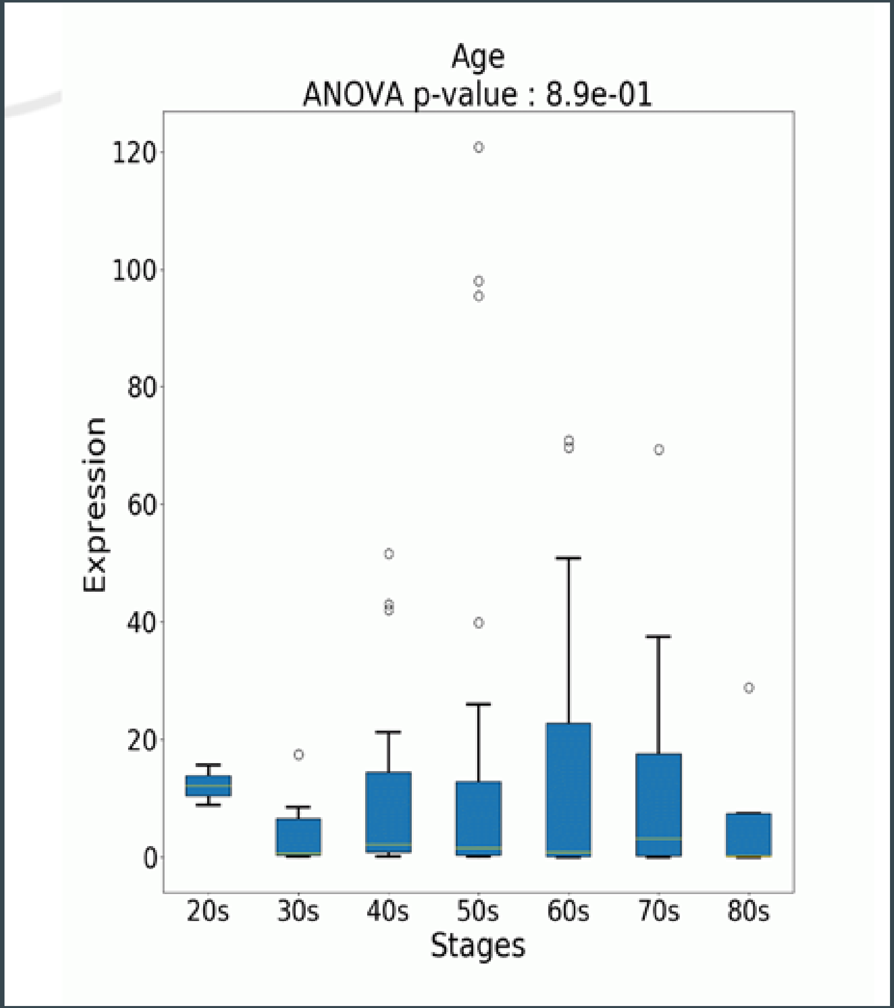
Age

Gene expression/methylation:

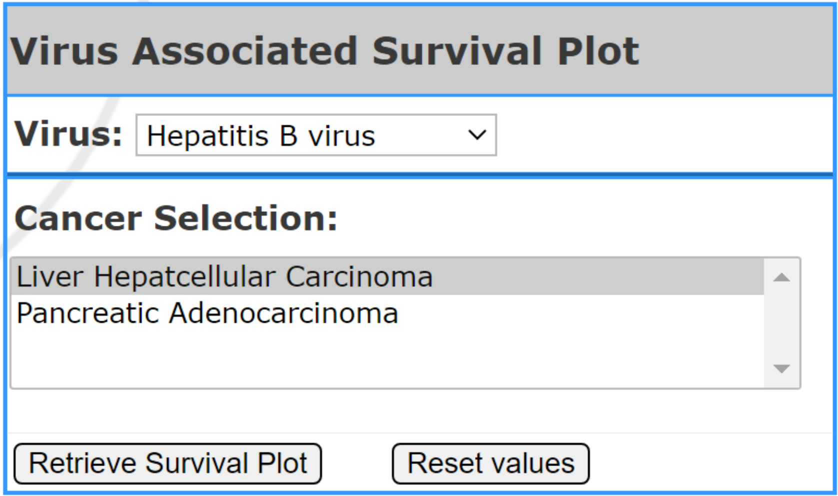
● **Expression** ○ **Methylation**

Results

- ➔ Compares the expression of CLRN3 in HBV-positive LIHC patients of different ages
- ➔ The highest average expression is in the 50s
- ➔ The lowest average expression is in the 30s



Survival Plots

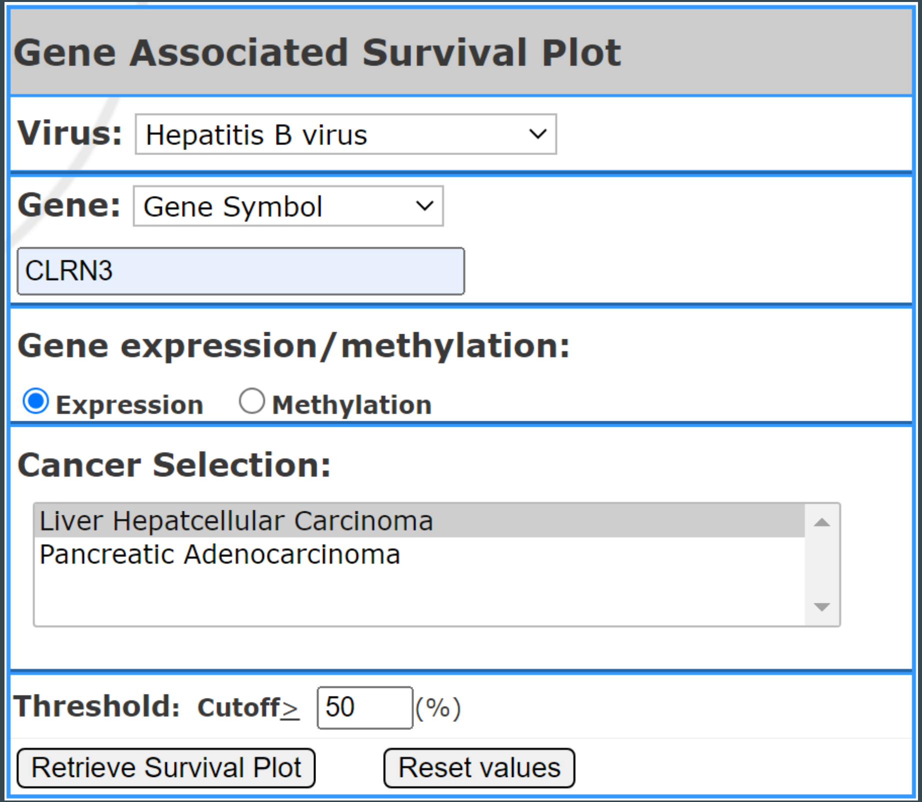


Virus Associated Survival Plot

Virus: Hepatitis B virus

Cancer Selection:

Liver Hepatocellular Carcinoma
Pancreatic Adenocarcinoma



Gene Associated Survival Plot

Virus: Hepatitis B virus

Gene: Gene Symbol

CLRN3

Gene expression/methylation:

● **Expression** ○ **Methylation**

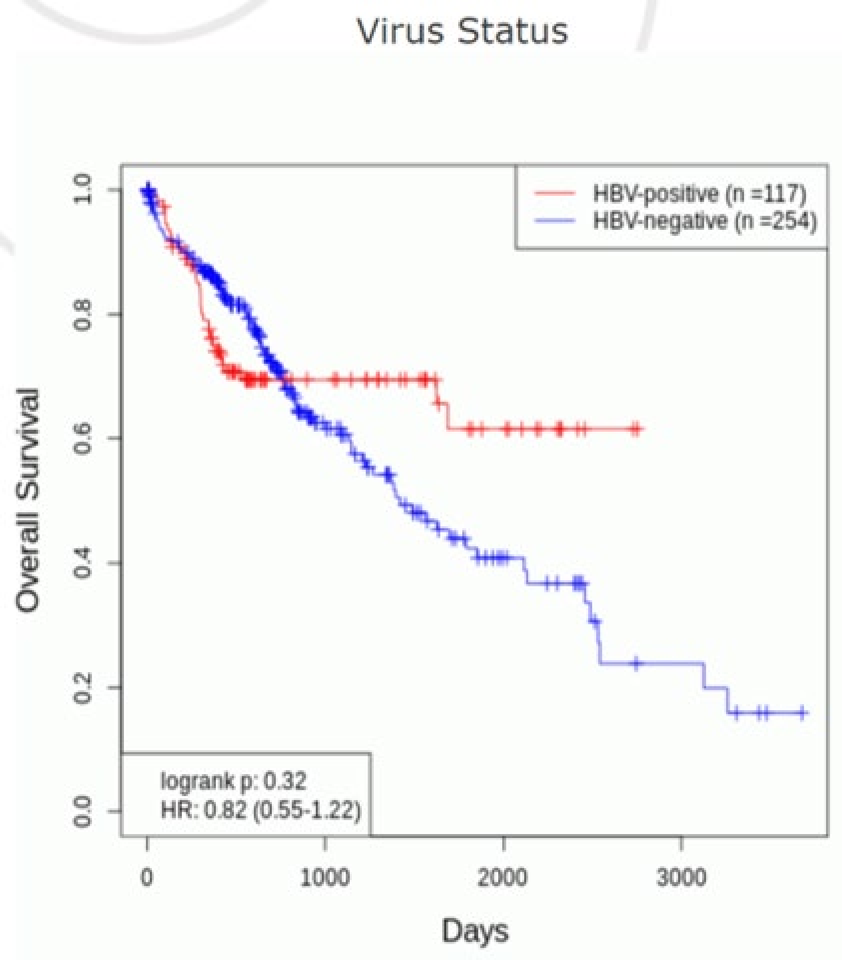
Cancer Selection:

Liver Hepatocellular Carcinoma
Pancreatic Adenocarcinoma

Threshold: **Cutoff≥** 50 (%)

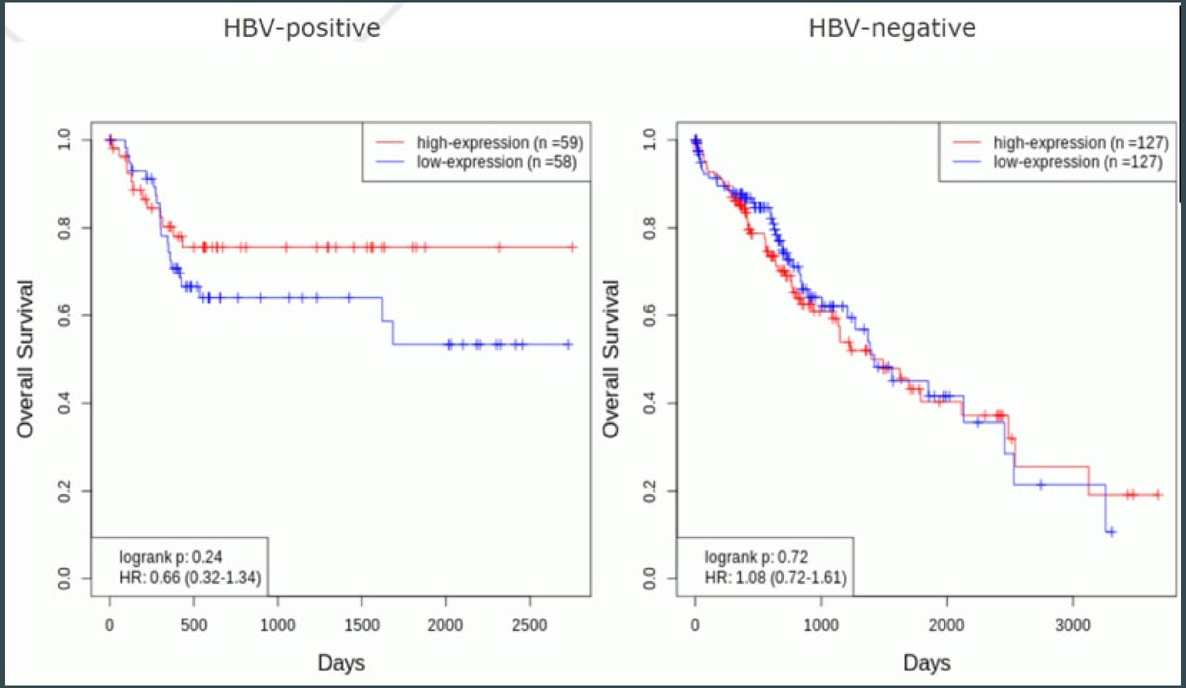
Results Virus Associated

- ➔ Gives a survival plot comparing HBV positive and HBV-negative patients
- ➔ Shows that HBV- positive patients have a higher survival rate than HBV negative patients
  - ◆ After a certain point



Results Gene Associated

- ➔ There is only a noticeable difference in survival rates for HBV-positive patients
- ➔ Those with higher expression of CLRN3 have a higher survival rate



Why is this important?

- One of the virus-related cancers that can benefit from OncoDB analysis is hepatitis B virus-related hepatocellular carcinoma.
- HCC is the leading cause of cancer death.
    - 10% survival rate for 5 years
- There is little known about targeted therapies for those who suffer with HCC (Todorova et al., 2023).
- HBV is also a large public health problem, with around two billion people affected.

Why is this important?

- ➔ HBV genomic mutations are what has been reported to correlate with the development of HCC, and HBV fragments are integrated into the genome in half of patients with HBV and HCC (Sukowati et al., 2016; Todorova et al., 2023).
- ➔ The immune response that is known to be from HBV infection could also lead to DNA damage and oxidative stress (Sukowati et al., 2016).
- ➔ The risk of developing HCC is not common knowledge, so many individuals with HBV could not only be uninformed of their increased risk, but are also not able to access testing, let alone treatment (Rizzo et al., 2022).

Summary

- OncoDB is a step in the right direction for research on viral related cancers and the development of more efficient treatment options.
- OncoDB provides an easy and efficient way to gather data and could have a huge impact on the future of cancer research.
- Being able to gain more insight into the mechanisms of HBV-related HCC is crucial as the prevalence of cases continues to rise in the US and treatment therapies fail to improve in efficacy.
  - OncoDB will have a crucial part to play.

Sources

OncoDB.HCC: an integrated oncogenomic database of hepatocellular carcinoma revealed aberrant cancer target genes and loci PMC

Role of hepatitis B virus DNA integration in human hepatocarcinogenesis - PMC.

Hepatitis B virus and hepatocellular carcinoma - PMC

The Functions of Hepatitis B Virus Encoding Proteins: Viral Persistence and Liver Pathogenesis - PMC

Hepatitis B Virus-Associated Hepatocellular Carcinoma - PMC

Significance of hepatitis virus infection in the oncogenic initiation of hepatocellular carcinoma - PMC

How did hepatitis B virus effect the host genome in the last decade? - PMC.

OncoDB