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研究團隊致力於新興檢驗技術之開發和基因檢測相關研究，研究成果包括:

可能性的生物因子參與在慢性肝炎誘發肝癌之機制:

1. 建立脂肪肝小鼠模式，從發炎誘導肝纖維化甚或是肝癌其可能參與之癌前病變機制之探討。
2. 開發和研究 C 型肝炎病毒相關肝癌之液態生物檢體-Exosomes 檢測因子開發液態檢測之精準醫療策略。
3. 血清中免疫相關蛋白表現對於慢性 C 肝感染病人其預後和產生肝癌的關係及機制之探討。
4. HCV 細胞內不同病毒量其和癌症相關基因表現之探討。

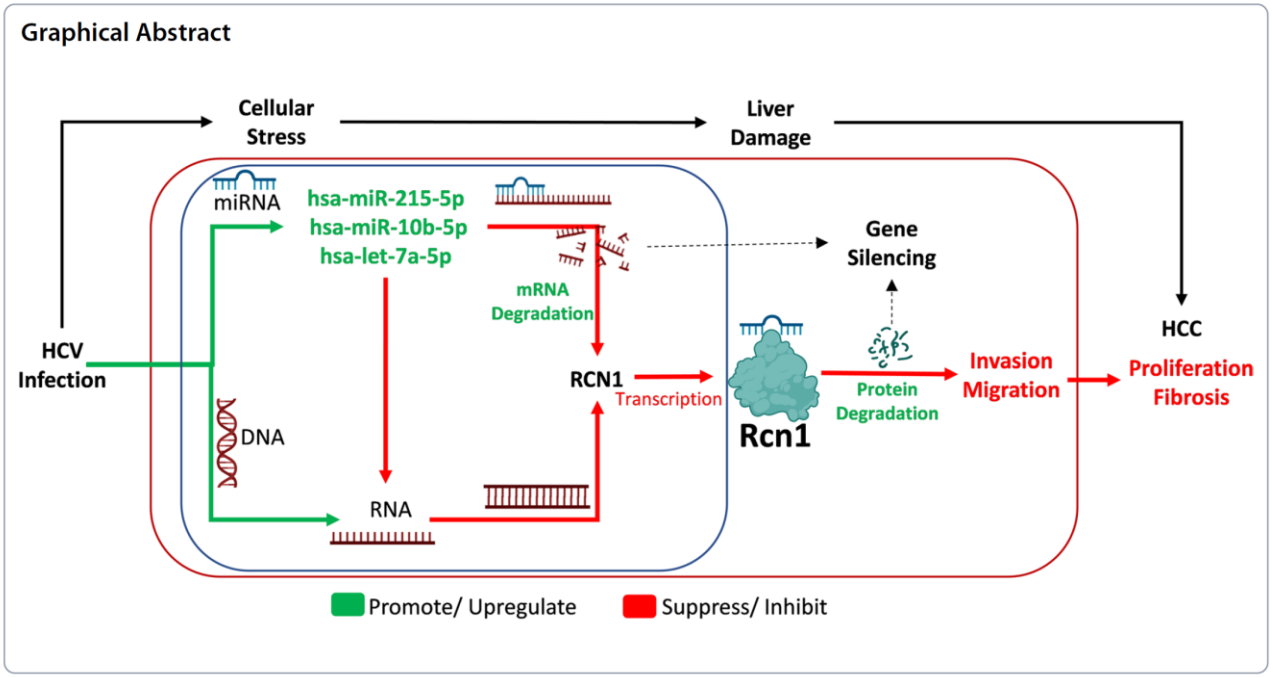
大數據分析到作用機制之探討:

1. 結合基因和微小 RNA 表現，我們發現長期低濃度潛伏 C 型肝炎病毒感染會造成癌細胞病變的相關基因檢測
2. 肥胖造成代謝性脂肪肝相關肝癌會有較差的預後以及和 ABCC8 的基因突變有關
3. 利用多體學探討細胞之間蛋白和細胞激素表現造成細胞趨化特性之調控監控癌細胞侵襲和轉移的指標

探究腫瘤發生和復發之相關機制:

1. 利用 SV40 Large T 抗原基因轉殖小鼠星狀膠質細胞(Astrocyte cells)建立腦腫瘤模式 ALTS1C1 建立小鼠腦腫瘤細胞和小鼠腦腫瘤動物模式研究腦腫瘤微環境變化。

2. 透過發炎調控腫瘤微環境的假說，找到不同的抗發炎藥物包括:Nordalbergin、Kurarinone、和 Punicalagin 皆會降低 ROS 的生成和抑制發炎小體的活化造成多種疾病的改善
3. 利用 cDNA 微陣列基因表現分析探討血管新生相關基因的關聯性。



具體成果：慢性 C 型肝炎病毒（HCV）感染會誘導某些 microRNA（miRNA）的表現，而這些 miRNA 具有抑制肝癌（HCC）的潛力，因為它們可以抑制癌基因的活性。在研究中發現，RCN1 基因的表現會被抑制，而 miRNA（例如 hsa-miR-215-5p、hsa-miR-10b-5p 和 hsa-let-7a-5p）的表現則會上升，呈現出一種相反的關係。因此，這些 miRNA 與它們的靶標基因 RCN1 有望成為監測由 HCV 引發的肝癌（HCV-HCC）進程的重要生物標記。這項研究的重要性在於提供病毒與癌症之間的相互作用機制，了解慢性 HCV 感染如何影響肝癌的發展。透過檢測這些 miRNA 和 RCN1 的表現，未來有可能更進一步發展出更有效的治療和預防策略，從而改善患者的預後。(*Journal of Translational Medicine.* 2024 Mar 12;22(1):268.)

【研究團隊】肝炎研究中心

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This Research Team focus to Development of Emerging Diagnostic Techniques and Genetic Testing Research. Key research findings include:

Potential Biomarkers in Chronic Hepatitis-Induced Hepatocarcinogenesis:

1. Establishment of Fatty Liver Mouse Models: Investigation of inflammation-

induced liver fibrosis and potential precancerous mechanisms leading to hepatocellular carcinoma (HCC).

2. Development of Liquid Biopsy Markers: Study of exosome-based biomarkers related to hepatitis C virus (HCV)-associated HCC to enable precise liquid biopsy strategies for personalized medicine.

3. Immune-Related Serum Proteins: Exploration of the relationship between immune protein expression in serum and the prognosis or HCC development in chronic hepatitis C patients.

4. HCV Viral Load and Cancer-Associated Gene Expression: Analysis of differential gene expression patterns under varying intracellular HCV viral loads.

From Big Data Analysis to Mechanistic Insights:

1. Gene and microRNA Expression: Discovery of cancer-related genetic alterations caused by long-term, low-level latent HCV infections through integration of gene and microRNA expression data.

2. Impact of Obesity on MASLD-Associated HCC: Identification of poorer prognosis in metabolic-associated steatotic liver disease (MASLD)-related HCC linked to ABCC8 gene mutations.

3. Omics-Based Analysis: Investigation of protein and cytokine expression between cells, highlighting regulatory mechanisms of chemotactic properties as indicators of cancer cell invasion and metastasis.

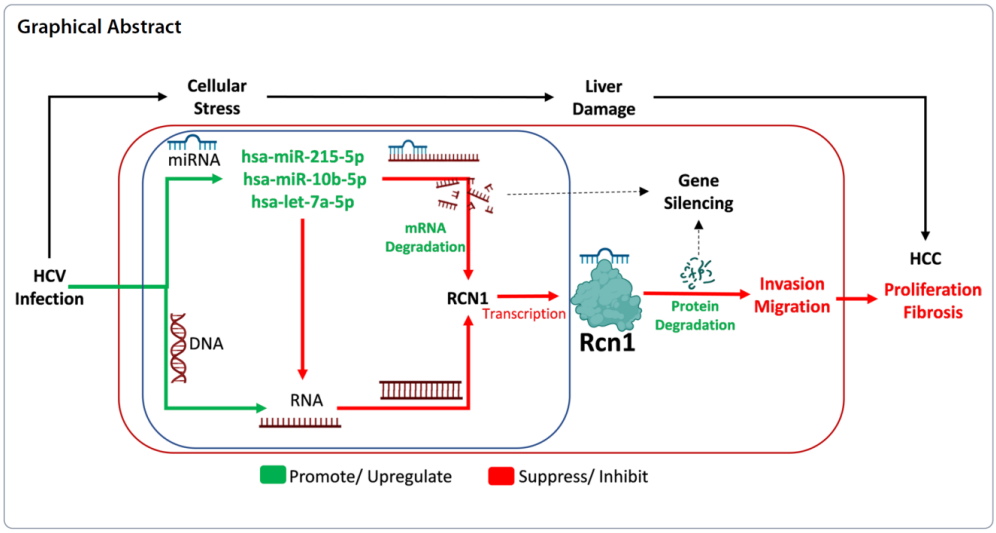
Mechanisms of Tumorigenesis and Recurrence:

1. Brain Tumor Models: Development of mouse astrocyte-based brain tumor models (ALTS1C1) using SV40 Large T antigen to study tumor microenvironmental changes.

2. Inflammation and Tumor Microenvironment: Identification of anti-inflammatory agents (e.g., Nordalbergin, Kurarinone, and Punicalagin) that reduce reactive oxygen species (ROS) generation and inflammasome activation, contributing to the mitigation of various diseases.

3. cDNA Microarray Analysis: Exploration of angiogenesis-related genes and their roles in tumor progression.

Our multidisciplinary approach integrates innovative technologies with mechanistic studies to advance precision diagnostics and therapeutic strategies for liver and other cancers.



Concrete Results:

Persistent HCV infection induced the expression of miRNAs that act as tumor suppressors by inhibiting oncogenes in HCC. RCN1 was suppressed while miRNAs were upregulated, demonstrating an inverse relationship. Therefore, hsa-miR-215-5p, hsa-miR-10b-5p, hsa-let-7a-5p and their target RCN1 may be ideal biomarkers for monitoring HCV-HCC progression. This research is significant as it elucidates the mechanisms of interaction between viruses and cancer, providing insights into how chronic HCV infection influences the development of liver cancer. By detecting the expression of these miRNAs and RCN1, there is potential to develop more effective therapeutic and preventive strategies in the future, ultimately improving patient outcomes. (*Journal of Translational Medicine.* 2024 Mar 12;22(1):268.)

【Research Team】

Research Team: Hepatitis Research Center.

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