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MOLECULAR DISCOVERIES SHED LIGHT ON LIVER CANCER -- HEPATOCELLULAR CARCINOMA (HCC)

- **Genomics improves our ability to target experimental cancer treatments**
 - **A promising new drug is in hand, and more are on the way**
 - **Improved ability to select patients to test particular drugs**

Milan, April 27th, 2008 – At today's sessions of this, the final day of the 43rd Annual Meeting of the European Association for the Study of the Liver (EASL), leading hepatologists described several important advances in understanding and provide novel treatments for hepatocellular carcinoma (HCC). Most notably, progress has been made by acquiring data that improve our understanding of the disease process at the molecular level... what is taking place in the body that leads to the development of HCC.

Applying the technologies of genomics and microarrays, scientists have discovered that there are a number of *different* biological pathways that result in HCC. Using this knowledge, they can now classify and explore various *subtypes* of HCC. This novel view contradicts the previous belief that the disease occurs in one way only, from a single disease mechanism.

The discovery of subtypes has significant implications. First, it raises the possibility of targeting treatments to particular patients, based on their respective cancer subtype ("targeted therapeutics"). Second, it enables more precise assessment of the response to specific experimental therapies. Moreover, it offers the possibility of refining each patient's prognosis, again based on his or her cancer subtype.

Malignancy is a complex process. It involves the accumulation of multiple independent gene mutations that lead to deregulation of cell pathways that influence cell growth and cell fate. The process itself is called the "oncogenic pathway." In the past, most scientists in the field believed that there was only one oncogenic "pathway" in HCC.

HCC is one of the most common tumors worldwide. Most cases of HCC result from a viral infection (Hepatitis B or C) or from cirrhosis. Obesity is an additional, recently recognized risk factor for HCC. Treatment options of HCC and prognosis are dependent on various factors, but chiefly on tumor size and staging.

Only a minority of hepatocellular carcinomas can be removed completely using surgery, and the tumor tends to recur. Other techniques are available to halt tumor progression, including percutaneous therapies such as radiofrequency ablation.



According to Professor Massimo Levrero, Associate Professor of Medicine at Italy's University of Cagliari, and Head of the Laboratory of Gene Expression, Fondazione Andrea Cesalpino, University of Rome La Sapienza, "Molecular approaches are starting to pay off. The years 2007 and 2008 are the 'years of the drug' for HCC. We now have Sorafenib, the first molecular targeted therapy for HCC that has been proven effective in a large clinical trial of patients with advanced cancers. Other drugs are coming soon. While Sorafenib is an efficient drug, our results need to be improved. We want to increase the cytotoxic potential of our treatments by combining drugs that can theoretically yield a synergistic effect. With recent advances regarding HCC subtypes, we know which patients can be selected for response to particular experimental therapies."

Scientists are continuing their search for the genes that are dysregulated in HCC. It is hoped that by improving our ability to identify aberrant genes, research will lead to the identification of new and more powerful pharmacological interventions for HCC.

About EASL

The European Association for the Study of the Liver (EASL) aims to promote investigation into liver disease and improve the treatments that currently exist for these conditions. The association, through its annual meetings, seeks to inform and educate both the scientific community as well as society in general about the increasing occurrence of liver diseases along with the importance of understanding these conditions in order to treat and prevent them. Since its creation in 1966, the EASL congress has been hosted in 20 different European countries. Currently the association has over 1400 members and the annual congress attracts over 6000 delegates from over 65 countries each year.

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