Liver cirrhosis is the late final stage of chronic liver disease and it has devastating consequences. Cirrhosis is accountable for 49,500 deaths annually, and in 2010 it was the eighth leading cause of death. What's more, cirrhosis is irreversible, and once it progresses to the point that liver function is severely compromised, the only remaining option is transplantation. Thus, it is vitally important to develop treatment options that would slow or possibly even stop the progression of cirrhosis.

Researchers in Barcelona are making some headway in doing just that, although it is early in the game. Scientists at the Institute for Research in Biomedicine (IRB Barcelona) and the August Pi i Sunyer Biomedical Research Institute (IDIBAPS) published a study in the journal, *Gastroenterology*, in which they reported the discovery of a new protein that involved in the pathological process of the progression of liver disease. The protein, which is called CPEB4, is involved in formation of new blood vessels called angiogenesis (angio = blood vessel; genesis = to create) one of the hallmarks in the development of cirrhosis.

Pathological angiogenesis is an abnormal process (and one of the most serious complications in patients with cirrhosis). It's characterized by a rapid proliferation of blood vessels a process that underlies many diseases such as cancer, psoriasis and age-related macular degeneration. There are many different endogenous factors that play a role in angiogenesis, one of the most important is called vascular endothelial growth factor (VEGF). This protein has been an important therapeutic target for key anti-cancer drugs. However, one of the biggest problems of anti-VEGF therapies is that they also affect healthy vessels.

The holy grail of successful therapy is the differentiation between normal cells, and the target of a drug. Sometimes this is easy. For example, antibiotic therapy targets components or mechanisms that are unique to bacteria, and are not present in human cells, which accounts for the generally low toxicity of antibiotics. But, this is much more difficult when treating cancer because cancerous
and normal cells share common processes. This is where CPEB4 enters the picture.

In mice and rat models of liver disease, as well as in tissue samples obtained from patients with liver cirrhosis and normal liver samples, the Barcelona researchers found an increased concentration in of the proteins CPEB1 and CPEB4 in patients with abnormal liver tissue samples as well as rats and mice with liver disease. When these two proteins were inactivated in rats and mice, there was no increase in VEGF and this translated into less severe forms of liver disease. CPEB1 and CPEB4 were associated with pathological angiogenesis as they were found only in abnormal tissue and in rats/mice with liver disease.

Thus, inactivating CPEBs may represent a safer therapeutic approach than VEGF in the development of liver disease treatments. Whereas targeting VEGF is indiscriminate (no selectivity) with regard to pathological and physiological states, again, CPEBs are promising in that they are only associated with disease states.

Understanding the mechanisms of cellular activity with respect to gene regulation is proving to be a fruitful area of research. The application of these findings could have significant impacts in the treatment of not just liver disease but many other diseases as well.

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