Chemoembolization relies on the knowledge that most HCC tumours receive nutrients from the liver's arterial system (França et al., 2004). Thus, blocking the hepatic artery is a definitive mode of treatment which has demonstrated great promise. As a non-surgical technique, chemoembolization utilizes interventional radiology to occlude the hepatic artery following identification with fluoroscopy (Befeler & Di Biscelgie, 2002). This technique effectively causes ischemic necrosis of approximately 80% of tumours, while leaving viable the unaffected hepatocytes and cells of the portal vein (França et al., 2004). Because of the specificity of this procedure, there is a realistic potential that high doses of chemotherapeutic agents may be delivered to the tumour with the result of high extraction rates following only one round of administration (Befeler & Di Biscelgie, 2002). The only clear limitation of this approach is that the blocking and chemotherapeutic agents must be re-administered every few months to maintain adequate functional levels in the liver.

When the affected liver has lost function and can no longer be treated by surgical resection, total liver transplantation is the recommended treatment for patients with HCC (Befeler & Di Biscelgie, 2002). Cases in which there is a small, single tumour, free of distant metastases and vascular invasion often have very encouraging prognoses following liver transplantation. Since the entire liver is replaced, any primary liver diseases are effectively removed along with the neoplasia. The limitation of this method lies in the extremely low number of liver donors (Bruix & Llovet, 2002). This creates a cascade effect which increases both the time on waiting lists and the monetary cost of the procedure to patients (França et al., 2004).

Conclusion

Preventing or modifying the risk factors associated with HCC is a critically important, yet often overlooked, means of decreasing the incidence of this cancer. The dissemination of information concerning lifestyle choices enables individuals to make healthier decisions in their daily lives (MD Consult, 2004). Tobacco and alcohol use have demonstrated a correlation with the presence of cirrhosis, and cirrhosis itself is the primary risk factor for the development of HCC (MD Consult, 2004). Drug abuse, an activity which substantially increases the risk of hepatitis B and C exposure, is a further lifestyle choice which can influence the presence of HCC. Furthermore, environmental carcinogenic agents should be avoided, participation in vaccination programs for hepatitis should be practiced, and screening programs should be attended by individuals who are aware of a family history of liver disease (MD Consult, 2004).

Congenital Insensitivity to Pain with Anhidrosis (CIPA)

Abdullah Alabousi

It is very easy to recognize. It is known all over the world and it breaks all language barriers. It is referred to as pain. This unpleasant experience notifies an individual that something is wrong in the body and needs to be corrected. It also serves a protective function by signalling the presence of harmful agents that may damage the body of an individual. However, pain is a complex perception that differs enormously amongst individuals (Tortora and Grabowski, 2003).

Pain, Nociception And CIPA

The perception of pain, referred to as nociception, depends on receptors and pathways that are specific to this sensation. Pain sensation begins in response to the stimulation of relatively unspecialized nerve cell endings called nociceptors (Tortora and Grabowski, 2003). Once nociceptors are stimulated, they convert a variety of stimuli into action potentials. They are then carried by nerve fibres to the spinal cord and the brain, where the nerve impulse is interpreted as pain (Tortora and Grabowski, 2003 & Purves et al., 2001).

Unfortunately, there are only a few individuals in the world who are born with a disease that renders them unable to feel pain. This disease is known as Congenital Insensitivity to Pain with Anhidrosis, or CIPA (Theodorou et al., 2000). CIPA is extremely rare and there is currently no data available as to the prevalence and incidence of this disease.

CIPA is an autosomal-recessive disorder characterized by recurrent episodic fevers, anhidrosis (inability to sweat), and absence of reaction to noxious or painful stimuli (Indo, 2002 & Guo et al., 2004). People with congenital insensitivity to pain go through life in danger of destroying their bodies because they do not realize the harm they are doing to themselves.

The main features of the disorder include lack of pain sensation, painless injuries of oral structures, fever during hot weather due to anhidrosis, mental retardation, as well as infection and scarring of the tongue, lips and gums (Theodorou et al., 2000). The lack of pain sensations in CIPA is due to the absence of unmyelinated fibres and reduced numbers of small myelinated afferent fibres that carry impulses to the spinal cord once they are activated by tissue-damaging stimuli (Rosemberg et al., 1994). Anhidrosis, on the other hand, is due to a loss of innervation of eccrine sweat glands, which are distributed throughout the skin and are responsible for the regulation of body temperature through sweat production (Indo, 2002; Tortora & Grabowski, 2003).

NGF And TRKA Mutations:

In normal individuals, Nerve Growth Factor (NGF) stimulates the growth and supports the survival of autonomic sympathetic neurons as well as nociceptive sensory neurons, which transmit pain sensations to the spinal cord and the brain (Alberts et al., 2002). NGF consists of three types of polypeptide chains; alpha, beta and gamma, which interact to form the protein. The NGF beta chain is the one responsible for the nerve growth stimulating activity of NGF (Petruska and Mendell, 2004). NGF functions as a survival signal and acts by suppressing programmed cell death, apoptosis (Yuan and Yankner, 2000).

The TRKA protein is a receptor tyrosine kinase (RTK), which has high affinity for NGF and phosphorylates itself in response to it (Figure 1). The autophosphorylation of TRKA activates various pathways of intracellular signal transduction that bring about support for the survival of nociceptive neurons (Indo, 2001). Not being able to transduce NGF into developing sympathetic and sensory neurons leads to the death of this class of neurons. Recent studies point to the TRKA gene as the site of the

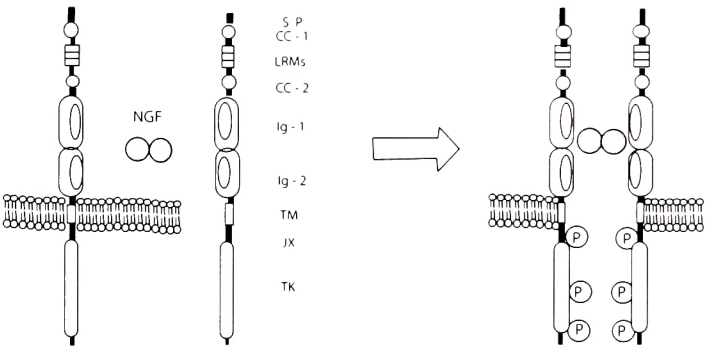

Figure 1: The binding of NGF to the TRKA protein, leads to its autophosphorylation, which is essential for intracellular signal transduction (Indo, 2002).

mutation that causes CIPA (Melamed et al., 2004, Indo, 2002, Rozentsveig et al., 2004, Sato et al., 2004, Mardy et al., 1999 & Guo et al., 2004). The mutation of the TRKA gene leads to the production of defective TRKA proteins. This, in turn, causes abnormalities in the NGF signal transduction pathway and various NGF dependent neurons are not maintained, mainly due to apoptosis during development (Indo, 2002 and Melamed et al., 2004). 37 different TRKA mutations have so far been identified in CIPA patients. These mutations include nine frameshift, seven nonsense, seven splice, and 14 missense mutations (Indo, 2001).

What's Next?

At this point in time there is no treatment available for CIPA patients but there is supportive therapy. Supportive therapy could include organizations that are dedicated to educating people about CIPA, as well as support groups for individuals who have to deal with the disease. From a clinical standpoint, CIPA is a serious illness that is very difficult to diagnose due to variable presentation in different patients and the lack of simple diagnostic tests to detect it (Rosemberg et al., 1994). However, a recent strategy has been developed that enables healthcare professionals to screen for TRKA mutations. This development should aid in the diagnosis and genetic counselling of this painless but severe genetic disorder with devastating complications (Indo, 2002). Also, understanding the molecular pathology of CIPA would provide unique opportunities to explore the critical role of the peripheral sensory nervous system, which transmits information about noxious stimuli for pain in humans (Indo, 2002). M