

## Double Retrograde Tracer Study of the Thalamostriatal Projections to the Cat Caudate Nucleus

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Abstract of:

SYNAPSE 32:80-92 (1999)

The distribution of thalamostriatal neurons projecting to the cat caudate nucleus was examined by retrograde fluorescent tracers. Thus, Fast Blue and Diamidino Yellow were concomitantly injected in different rostrocaudal, dorsoventral, or mediolateral sectors of the caudate nucleus. The main findings of this study are as follows: (1) few double-labeled cells were found after two injections in different sectors of the caudate nucleus; (2) dou-

ble-labeled neurons were more abundant after adjacent injections and they were mainly located in the caudal intralaminar nuclei, in the rhomboid nucleus and in the dorsal mediodorsal nucleus; and (3) there were variations in the spatial organization of the thalamostriatal neurons projecting to various sectors of the caudate nucleus in the different thalamic nuclei known to project to this part of the striatum.

**Key Words:** striatum, caudate nucleus, thalamus, fluorescent tracers, thalamostriatal projections, basal ganglia, cat.

## Gene therapy of viral hepatitis and hepatocellular carcinoma

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Abstract of:

Journal of Viral Hepatitis 1999;6:17-34

**Summary:** Gene therapy, represents an attractive approach to treat a great variety of diseases, both inherited and acquired. And it is moving slowly from a proof-of-principle phase to a wide application in most medical fields. Liver cancer and viral hepatitis are natural targets for this new therapeutic alternative due to the lack of success of conventional antitumoral and antiviral treatments and the ominous prognosis related with liver tumours. Gene therapy for viral hepatitis is aimed to boost the patient immune response against viral antigens or to make cells resistant to infection by blocking the viral life cycle. Gene trans-

fer techniques applied to the treatment of hepatocellular carcinoma include drug sensitization by suicide genes, genetic immunotherapy, normal tissue protection by transfer of the multidrug resistance gene, replacement of tumour suppressor genes, inhibition of oncogenes and modifications of the biology of the tumour (antiangiogenesis). However, major advances in our understanding of the regulation of gene expression cassettes and development of more efficient gene transfer vectors are mandatory before gene therapy can become a widely used therapeutic modality.

**Key Words:** Gene therapy, hepatitis B virus, hepatitis C virus, cancer, hepatocellular carcinoma.

## Assessment of Biliary Bicarbonate Secretion in Humans by Positron Emission Tomography

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Abstract of:

Gastroenterology 1999;117:167-172

**Background & Aims:** Positron emission tomography (PET) allows imaging and quantitative analysis of organ functions in basal and stimulated conditions. We have applied this method to the study of biliary bicarbonate secretion in humans.

**Methods:** PET was performed in 5 healthy subjects and 13 patients with hepatobiliary disorders after intravenous injection of  $\text{NaH}^{11}\text{CO}_3$ . In each case the study was performed in basal conditions and after secretin stimulation. Positron emission from the hepatic area was scanned, and normalized uptake values for parenchymal and hilar regions were estimated.

**Results:** In healthy individuals, the injection of  $\text{NaH}^{11}\text{CO}_3$  resulted in a peak uptake of the label in parenchymal and hilar regions 2-3 minutes after the injection. In both normal and cirrhotic subjects, secretin administration increased bicarbonate uptake in the parenchymal region, followed by accumulation of the label in the perihilar area. Normal basal uptake with absent response to secretin was registered in extrahepatic biliary obstruction and in untreated primary biliary cirrhosis (PCB). The secretin response was present in patients with PBC undergoing treatment with ursodeoxycholic acid.

**Conclusions:** PET allows investigation of biliary bicarbonate secretion in humans. An impaired response to secretin was observed in cholestatic conditions. Preliminary data suggest that ursodeoxycholic acid might improve the response to secretin in PCB.