Immunohistochemical Localization of Kallikrein 6 in the Brain

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OVERVIEW

2.2. Kallikrein 6 expression in patients with AD (Hippocampus)

Human kallikreins (hKs): A family of secreted serine proteinases localized in chr. 19q13.4 (Table 1).

hK6 is expressed in the brain (glial cells and oligodendrocytes) (Ref. 1)

hK6 is elevated in Alzheimer's disease patients (Ref. 2-5)

hK6: wide tissue distribution; highly expressed in the brain (Fig. 1).

The role of hK6 in the brain is not yet known: Although some targets have been identified (eg Myelin Basic Protein, Amyloid Precursor Protein, Proteinase-activated receptors) the relation of hK6 to brain physiology and/or pathology is unknown (Table 2).

hK6 expression in the brain: We found widespread and strong glial staining (ependyma, subependyma and choroid plexus, but also among fibrillary astroglial cells). In white matter, the oligodendrocytes demonstrated perinuclear cystoplastic staining, but the myelin appeared hK6-negative. The neurone of the grey matter displayed a distinct staining. As a rule, large neurones tended to display the most intense immunoreactivity, with some exceptions (e.g. Purkinje cells). The pial plasm (demonstrated reactivity within the adenosphenylosis, which appeared most strongly in corticotracts).

hK6 expression in patients with neurodegeneration: Expression pattern was similar to normal; However, Hirano bodies in the processes of pyramidal neurones were consistently and strikingly immunoreactive. hK6 expression in brain tumours: All samples of astrocytoma, glioblastoma multiforme, oligodendroglioma, ependymoma and meningioma were stained as hK6 positive.

Significance of study: hK6 should be further evaluated as a biomarker of brain malignancies, and its role in neuronal degeneration deserves further exploration.

Table 2: hK6 in the brain and potential substrates

- hK6 is expressed in the brain (glial cells and oligodendrocytes) (Ref. 1)
- hK6 is elevated in Alzheimer’s disease patients (Ref. 2-5)
- hK6 can potentially cleave APP (Ref. 6, 7)
- hK6 co-localizes with α-synuclein in Parkinson’s disease patients (Ref. 5, 8)
- hK6 can cleave MBP and localizes within multiple sclerosis lesions (Ref. 9, 10)
- hK6 has been related to brain tumourigenesis; high levels of the protein were detected in glioblastoma cells implanted intracranially in nude mice and were co-localized with an invasion-associated matricellular protein called SPARC (Ref. 11)
- hK6 is up-regulated during angiogenesis (Ref. 12)
- hK6 can cleave ECM proteins (Ref. 13, 14)
- hK6 expression in patients with neurodegeneration:
  - hK6 expression pattern was similar to normal; However, Hirano bodies in the processes of pyramidal neurones were consistently and strikingly immunoreactive.
  - hK6 expression in brain tumours:
    - All samples of astrocytoma, glioblastoma multiforme, oligodendroglioma, ependymoma and meningioma were stained as hK6 positive.

Results

1. Expression of kallikrein 6 in the cells of the brain tissue

Choroid Plexus

Neurupil (Inferior Olivary Nucleus)

Astrocytes; Medulla

Oligodendrocytes; Medulla

Trigeminal Neurons; Medulla

Figure 1: Human Kallikrein 6 (hK6)

Table 1: Human Tissue Kallikreins

Characteristics of the kallikrein family:
- The largest cluster of continuous serine proteinases
- Wide tissue distribution
- Trypsin or Chymotrypsin-like activity
- Secreted as zymogens
- Activated by different enzymes
- They can cleave several pro-uPA, GFs and ECM proteins

Future directions:
- Co-localization of hK6 with brain cells’ markers
- Significance of hK6 presence in Hirano Bodies

Selected references: