Nestin

Nestin (acronym for neuroectodermal stem cell marker) is a type VI intermediate filament (IF) protein.

These intermediate filament proteins are expressed mostly in nerve cells where they are implicated in the radial growth of the axon. Seven genes encode for the heavy (NF-H), medium (NF-M) and light neurofilament (NF-L) proteins, nestin and α-internexin in nerve cells, synemin α and desmuslin/synemin β (two alternative transcripts of the DMN gene) in muscle cells, and syncoilin (also in muscle cells). Members of this group mostly preferentially coassemble as heteropolymers in tissues. Steinert et al. has shown that nestin forms homodimers and homotetramers but does not form IF by itself in vitro. In mixtures, nestin preferentially co-assembles with purified vimentin or the type IV IF protein -internexin to form heterodimer coiled-coil molecules.

Malignant gliomas have disproportionally high morbidity and mortality. Heterozygous mutations in the isocitrate dehydrogenase 1 (IDH1) gene are most common in glioma, resulting in predominantly arginine to histidine substitution at codon 132. Because IDH1 R132H requires a wild-type allele to produce (D)-2-hydroxyglutarate for epigenetic reprogramming, loss of IDH1R132H heterozygosity is associated with glioma progression in an IDH1-wildtype-like phenotype. Although previous studies have reported that transgenic IDH1R132H induces the expression of a nestin-a neural stem-cell marker, the underlying mechanism remains unclear. Furthermore, this finding seems at odds with a better outcome of IDH1R132H glioma because of a negative association of nestin with overall survival [1].

Nestin+cells from spheroid aggregates display typical histopathological features compatible with cell stemness. Nestin and CD133+cells found in glioblastomas, distributed frequently around aberrant vessels, are considered as potential cancer stem cells. They are possible targets for antitumoral therapy because they lead the tumorigenesis, invasiveness and angiogenesis. However, little is known about their role and presence in low-grade gliomas. The aim of this work is to localize and characterize the distribution of these cells inside tumors during the development of experimental endogenous glioma. For this study, a single dose of Ethyl-nitrosourea was injected into pregnant rats. Double immunofluorescences were performed in order to identify stem-like and differentiated cells. Low-grade gliomas display Nestin+cells distributed throughout the tumor. More malignant gliomas show, in addition to that, a perivascular location with some Nestin+cells co-expressing CD133 or VEGF, and the intratumoral spheroid aggregates of Nestin/CD133+cells. These structures are encapsulated by well-differentiated VEGF/GFAP+cells. Spheroid aggregates increase in size in the most malignant stages. Spheroid aggregates have morphological and phenotypic similarities to in vitro neurospheres and could be an in vivo analogue of them. These arrangements could be a reservoir of undifferentiated cells formed to escape adverse microenvironments [2].

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Tiburcio PDB, Locke MC, Bhaskara S, Chandrasekharan MB, Huang LE. The neural stem-cell marker CD24 is specifically upregulated in IDH-mutant glioma [published online ahead of print, 2020 Jul 1]. Transl Oncol. 2020;13(10):100819. doi:10.1016/j.tranon.2020.100819
2)
García-Blanco A, Bulnes S, Pomposo I, Carrasco A, Lafuente JV. Nestin+cells forming spheroids aggregates resembling tumorspheres in experimental ENU-induced gliomas. Histol Histopathol. 2016

Apr 1:11763. [Epub ahead of print] PubMed PMID: 27033357.