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Review Article

Talins and Cancer

Abstract

Talin is a large cytoskeletal adaptor protein that is an important component of focal adhesion complexes of adherent cells. It was originally identified as a component of focal adhesions and ruffling membranes of fibroblasts. It was the first cytoplasmic protein partner of integrins to be identified. Many studies proved that talin connects the intracellular actin cytoskeleton with the extracellular environment through interactions with integral membrane proteins in the dynamic focal adhesions. The modular structure of talin is responsible for its ability to serve as a linker protein. It was thought that animal cells contained only one talin. However, studies have been identified a second talin (Talin-2) in vertebrates. Talin-1 levels are very low in brain and striated muscle, but high in kidney, liver, spleen, stomach, lung, and rat vascular smooth muscle cells. Talin-2 levels are high in brain and striated muscle. The variable expression of Talin-2 in these differentiated cells reflects that these proteins have different roles, which would be reflected in different properties of each protein. Moreover, Talins may be a good target for treatment of certain types of cancers. Talins levels are altered in various types of cancer indicating its possible use as cancer biomarker.

Introduction

Talins and endometrioid carcinoma

It has been found that alpha-actinin and talin were completely de-expressed in both endometriosis and endometrioid carcinoma tissue. Some patchy, depolarized labeling for ezrin was noted in the endometrioid carcinoma but not in endometriosis.

Furthermore, the loss of these proteins in both endometriosis and endometrioid carcinoma tissue indicates a significant change in the integrity of these tissues compared with normal and the possibility that individual cells may break away from the parent histology due to loss of cell adhesion. It also indicates a similarity between endometrioid cancer and endometriosis with respect to epithelial cell function and adhesion [1].

Talins and prostate cancer progression to metastasis

It has been shown that, Talin1 overexpression enhanced prostate cancer cell adhesion, migration, and invasion by activating survival signals and conferring resistance to anoikis. Furthermore, ShRNA-mediated talin1 loss led to a significant suppression of prostate cancer cell migration and transendothelial invasion in vitro and a significant inhibition of prostate cancer metastasis in vivo. Talin1-regulated cell survival signals via phosphorylation of focal adhesion complex proteins, such as focal adhesion kinase and Src, and

downstream activation of AKT. Targeting AKT activation led to a significant reduction of talin1-mediated prostate cancer cell invasion.

Additionally, talin1 immunoreactivity directly correlated with prostate tumor progression to metastasis in the transgenic adenocarcinoma mouse prostate mouse model. These findings suggest a potential value for talin1 as a marker of tumor progression to metastasis [2].

Talins and aggressive oral squamous cell carcinoma

Oral squamous cell carcinoma (OSCC) is highly invasive and is associated with frequent tumour recurrences and lymph node metastases. Identification of genes involved in the aggressiveness of OSCC may give new targets for clinical intervention. A genome-wide study based on the Sty1 250K SNP array indicated the involvement of the Talin-1 (TLN1) gene in the 9p13.3 amplicon, which was further validated using dual colour fluorescence in situ hybridization (FISH).

Moreover, comparative analyses revealed that TLN1 was the most highly expressed integrin-cytoskeleton cross-linker that can trigger integrin activation. Immunohistochemistry (IHC) analyses and mouse study also showed a relation between TLN1 overexpression and advanced OSCC with invasion to adjacent tissues. Survival analyses revealed a significant association between TLN1 genetic gain/overexpression and a decreased overall survival in patients.

In addition, functional knockdown by a dominant negative TLN1 fragment reduced cell growth and invasiveness in TLN1-overexpressing cells through inactivation of downstream oncogenic signalling. Thus, TLN1 overexpression could serve as a diagnostic marker for aggressive phenotypes and a potential target for treating OSCC [3].

Talins and glioma cell-matrix tensional homeostasis

The ability of cells to adapt their mechanical properties to those of the surrounding microenvironment (tensional homeostasis) has been involved in the progression of a variety of solid tumours, including the brain tumour glioblastoma multiforme (GBM). GBM tumour cells are highly sensitive to extracellular matrix (ECM) stiffness and overexpress a variety of focal adhesion proteins, such as talin.

It has been shown that, talin-1 plays a critical role in enabling human GBM cells in ECM stiffness. Knock down of talin-1 strongly reduces both cell spreading area and random migration speed but does not significantly affect overall focal adhesion size distributions.

Furthermore, atomic force microscopy indentation reveals that talin-1 suppression compromises adaptation of cell stiffness to changes in ECM adaptation to stiffness. Consequently, these data support a role for talin-1 in the maintenance of tensional homeostasis in GBM and suggest a functional role for enriched talin expression in this tumour [4].

Talins and hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is characterized by a multistage process of tumor progression. Proteomic analysis using liquid chromatography-tandem mass spectrometry of early HCC and non-HCC has identified 61 proteins, including a cytoskeletal protein, talin-1 upregulated in HCC. Talin-1 expression levels in HCC nodules were significantly associated with the dedifferentiation of HCC.

Moreover, a follow-up survey of the examined clinical cases revealed a correlation between talin-1 upregulation Immunohistochemistry was performed on HCC nodules to confirm the results of the proteomic analysis.

Hence, from these data, talin-1 was identified as a promising HCC marker. Talin-1 upregulation is associated with HCC progression and may serve as a prognostic marker [5]. Another study has showed that talin1 is a valuable marker for diagnosis and prognostic assessment of human hepatocelluar carcinomas [6].

Talin as a target for treatment of colon cancer

It has been reported that, resveratrol (RSV) suppresses colon cancer cell proliferation and elevates apoptosis through targeting pentose phosphate pathway (PPP) and talin-p focal adhesion kinase (FAK) pathway in the colon cancer cell line HT-29 [7].

Conclusion

Talin analysis could be particularly helpful as a diagnostic or prognostic tool in many tumor types. Talin is overexpressed in various critically ill clinical states and correlated with disease severity that augments its role as a prognostic biomarker in clinical practice and as a good target for treatment of diseases. However, biomarkers should complement, rather than supersede the validated clinical severity scores and judgment skills of clinicians. Further studies using this biomarker in various clinical settings will ultimately prove their cost-effectiveness and clinical usefulness.

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