Kininogen

Kininogens are proteins that are defined by their role as precursors for kinins, but that also can have additional roles. Kinins are biologically active peptides, the parent form is bradykinin.

The two main kininogen types are:

High-molecular-weight kininogen, which is produced mostly by the liver but is synthesized in endothelial cells and is present in platelets and neutrophils. It acts as a cofactor for prekallikrein, factor XI, and factor XII in the coagulation and inflammation systems. It has no intrinsic enzymatic activity. These high molecular weight kininogens are cleaved into bradykinin and kallidin by tissue and plasma kallikreins.

Low-molecular-weight kininogen, which is produced locally by numerous tissues, and secreted together with tissue kallikrein. They are both spliced from the same precursor.

A third type, T-kininogen, is found in rats but not humans.

Closely related proteins include cystatin.

Kininogen-1 (KNG1), also known as alpha-2-thiol proteinase inhibitor, Williams-Fitzgerald-Flaujeac factor or the HMWK-kallikrein factor is a protein that in humans is encoded by the KNG1 gene.

Kininogen-1 is the precursor protein to high-molecular-weight kininogen (HMWK), low-molecular-weight kininogen (LMWK), and bradykinin.

Kininogen-1 (KNG1) has demonstrated both tumor suppressor and angiogenesis inhibitor properties in glioblastoma cells.

Ren et al., analyzed the microarray and proteomics profiles of tumor tissues from glioblastoma patients (N = 180), and identified potential RNA regulators of the KNG1. Validation experiments in U87 glioblastoma cells showed that the regulation of KNG1 by CTU1, KIAA1274, and RAX was mediated by miR 138. The siRNA-mediated knockdown of CTU1, KIAA1274, or RAX in U87 cells and immortalized human endothelial cells (iHECs) significantly reduced KNG1 expression ($P < 0.05$ for all), which resulted in the upregulation of oncogenic EGFR signaling in both cell lines, and stimulated angiogenic processes in cultured iHECs and zebrafish and mouse xenograft models of glioblastoma-induced angiogenesis. Angiogenic transduction of iHECs occurred via the uptake of U87-derived exosomes enriched in miR-138, with the siRNA-mediated knockdown of KNG1, CTU1, KIAA1274, or RAX increasing the level of miR-138 enrichment to varying extents and enhancing the angiogenic effects of the U87-derived exosomes on iHECs. The competing endogenous RNA network of KNG1 represents potential targets for the development of novel therapeutic strategies for glioblastoma [1].

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Ren Y, Ji N, Kang X, Wang R, Ma W, Hu Z, Liu X, Wang Y. Aberrant ceRNA-mediated regulation of KNG1 contributes to glioblastoma-induced angiogenesis. Oncotarget. 2016 Oct 14. doi: 10.18632/oncotarget.12659. PubMed PMID: 27764797.