



Glioblastoma-associated stromal cells (GASCs) from histologically normal surgical margins have a myofibroblast phenotype and angiogenic properties.

Submitted by Anne Clavreul on Mon, 09/22/2014 - 15:33

Titre	Glioblastoma-associated stromal cells (GASCs) from histologically normal surgical margins have a myofibroblast phenotype and angiogenic properties.
Type de publication	Article de revue
Auteur	Clavreul, Anne [1], Guette, Catherine [2], Faguer, Rogatien [3], Tétaud, Clément [4], Boissard, Alice [5], Lemaire, Laurent [6], Rousseau, Audrey [7], Avril, Tony [8], Henry, Cécile [9], Coqueret, Olivier [10], Menei, Philippe [11]
Editeur	Wiley
Type	Article scientifique dans une revue à comité de lecture
Année	2014
Langue	Anglais
Date	2014 May
Pagination	74-88
Volume	233
Titre de la revue	The Journal of Pathology
ISSN	1096-9896
Mots-clés	Biopsy [12], Blotting, Western [13], Brain Neoplasms [14], Cell Communication [15], Cell Separation [16], Chemokine CXCL12 [17], Coculture Techniques [18], Flow Cytometry [19], Glioblastoma [20], Hepatocyte Growth Factor [21], Humans [22], Myofibroblasts [23], Neoplasm, Residual [24], Neovascularization, Pathologic [25], Phenotype [26], Primary Cell Culture [27], Proteomics [28], Reproducibility of Results [29], Spectrometry, Mass, Matrix-Assisted Laser Desorption-Ionization [30], Stromal Cells [31], Tandem Mass Spectrometry [32], Tumor Cells, Cultured [33], Tumor Markers, Biological [34], Wound Healing [35]

Résumé en anglais

Glioblastoma (GB) displays diffusely infiltrative growth patterns. Dispersive cells escape surgical resection and contribute to tumour recurrence within a few centimeters of the resection cavity in 90% of cases. We know that the non-neoplastic stromal compartment, in addition to infiltrative tumour cells, plays an active role in tumour recurrence. We isolated a new stromal cell population from the histologically normal surgical margins of GB by computer-guided stereotaxic biopsies and primary culture. These GB-associated stromal cells (GASCs) share phenotypic and functional properties with the cancer-associated fibroblasts (CAFs) described in the stroma of carcinomas. In particular, GASCs have tumour-promoting effects on glioma cells in vitro and in vivo. Here, we describe a quantitative proteomic analysis, using iTRAQ labelling and mass spectrometry, to compare GASCs with control stromal cells derived from non-GB peripheral brain tissues. A total of 1077 proteins were quantified and 67 proteins were found to differ between GASCs and control stromal cells. Several proteins changed in GASCs are related to a highly motile myofibroblast phenotype, and to wound healing and angiogenesis. The results for several selected proteins were validated by western blotting or flow cytometry. Furthermore, the effect of GASCs on angiogenesis was confirmed using the orthotopic U87MG glioma model. In conclusion, GASCs, isolated from GB histologically normal surgical margins and found mostly near blood vessels, could be a vascular niche constituent establishing a permissive environment, facilitating angiogenesis and possibly colonization of recurrence-initiating cells. We identify various proteins as being expressed in GASCs: some of these proteins may serve as prognostic factors for GB and/or targets for anti-glioma treatment.

URL de la notice	http://okina.univ-angers.fr/publications/ua4100 [36]
DOI	10.1002/path.4332 [37]
Autre titre	J. Pathol.
Identifiant (ID) PubMed	24481573 [38]

Liens

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