A tumorigenic actin mutant alters fibroblast morphology and multicellular assembly properties

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 2098296
Author(s) Blache, Ulrich; Silván, Unai; Plodinec, Marija; Suetterlin, Rosmarie; Jakob, Roman; Klebba, Ina; Bentires-Alj, Mohamed; Aebi, Ueli; Schoenenberger, Cora-Ann
Author(s) at UniBasel Schönenberger, Cora-Ann ; Plodinec, Marija ; Jakob, Roman Peter ; Sütterlin, Rosmarie ;
Year 2013
Title A tumorigenic actin mutant alters fibroblast morphology and multicellular assembly properties
Journal Cytoskeleton
Volume 70
Number 10
Pages / **Article-Number** 635-50
Keywords actin mutation, membrane ruffling, multicellular spheroids, tumorigenic, transformation, actin polymerization
Tumor initiation and progression are accompanied by complex changes in the cytoarchitecture that at the cellular level involve remodeling of the cytoskeleton. We report on the impact of a mutant β-actin (G245D-actin) on cell structure and multicellular assembly properties. To appreciate the effects of the Gly245Asp substitution on the organization of the actin cytoskeleton, we examined the polymerization properties of G245D-actin in vitro by pyrene polymerization assays and total internal reflection fluorescence microscopy (TIRF). The mutant actin on its own has a significantly reduced polymerization efficiency compared to native actin but also modifies the polymerization of actin in copolymerization experiments. Comparison of the structure of Rat-2 fibroblasts and a stably transfected derivate called Rat-2-sm9 revealed the effects of G245D-actin in a cellular environment. The overall actin levels in Rat-2-sm9 show a 1.6-fold increase with similar amounts of mutant and wild-type actin. G245D-actin expression renders Rat-2-sm9 cells highly tumorigenic in nude mice. In Rat-2-sm9 monolayers, G245D-actin triggers the formation of extensive membrane ruffles, which is a characteristic feature of many transformed cells. To approximate complex cell-cell and cell-matrix interactions that occur in tumors and might modulate the effects of G245D-actin, we extended our studies to scaffold-free 3D spheroid cultures. Bright field and scanning electron microscopy (SEM) show that Rat-2-sm9 and Rat-2 cells share essential features of spheroid formation and compaction. However, the resulting spheroids exhibit distinct phenotypes that differ mainly in surface structure and size. The systematic comparison of transformed and normal spheroids by SEM provides new insights into scaffold-free fibroblast spheroid formation. ľ 2013 Wiley Periodicals, Inc.

Publisher Wiley
ISSN/ISBN 1949-3592
edoc-URL http://edoc.unibas.ch/dok/A6165218
Full Text on edoc No;
Digital Object Identifier DOI 10.1002/cm.21120
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/23804571
ISI-Number WOS:000326150300008
Document type (ISI) Journal Article