Algorithm based smartphone apps to assess risk of skin cancer in adults: critical appraisal of a systematic review.

Related Articles
Algorithm based smartphone apps to assess risk of skin cancer in adults: critical appraisal of a systematic review.

Br J Dermatol. 2020 Aug 31;:
Authors: Malhi IS, Yiu ZZN

Abstract
Up to three million skin cancers occur worldwide annually, with an increasing burden over time1. Melanomas, accounting for 4% of skin cancers, are responsible for 75% of deaths1,2. An estimated 86% of melanomas in the UK are preventable3. Self-monitoring, earlier detection and improvement in survival from melanoma are therefore of interest. Algorithm based smartphone applications (apps) are based on artificial intelligence algorithms trained on images of diagnosed skin cancer. They have the potential to facilitate early detection of otherwise aggressive life-threatening skin cancers, thus prompting users to seek timely medical attention and improve survival.

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Desensitization of metastatic melanoma cells to therapeutic treatment through repeated exposure to dacarbazine.

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Desensitization of metastatic melanoma cells to therapeutic treatment through repeated exposure to dacarbazine.

J Photochem Photobiol B. 2020 Jul 31;211:111982
Authors: Biteghe FAN, Padayachee E, Davids LM, Chalomie NET, Ndong JC, Barth S

Abstract
Aberrant anti-cancer drug efflux mediated by membrane protein ABC transporters (ABCB5 and ABCG2) is thought to characterize melanoma heterogeneous chemoresistant populations, presumed to have unlimited proliferative and self-renewal abilities. Therefore, this study primarily aimed to investigate whether continuous exposure of melanoma cells to dacarbazine (DTIC) chemotherapeutic drug enriches cultures with therapy resistant cells. Thereafter, we sought to determine whether combining the genotoxic activity of DTIC with the oxidative insults of hypericin activated photodynamic therapy (HYP-PDT) could synergized to kill heterogenous chemoresistant melanoma populations. This study revealed that DTIC resistant (UCT Mel-1DTICR2) melanoma cells were less sensitive to all therapies than parental melanoma cells (UCT Mel-1), yet combination therapy was the most efficient. At the exception of DTIC treatment, both HYP-PDT and the combination therapy were effective in significantly reducing the Hoechst non-effluxing dye melanoma main populations (MP) compared to their side population (SP) counterparts. Likewise, HYP-PDT and combination therapy significantly reduced self-renewal capacity, increased expression of ABCB5 and ABCG2 transporters and differentially induced cell cycle arrest and cell death (apoptosis or necrosis) depending on the melanoma MP cell type. Collectively, combination therapy could synergistically reduce melanoma proliferative and clonogenic potential. However, further research is needed to decipher the cellular mechanisms underlying this resistance which would enable combination therapy to reach therapeutic fruition.

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Heterotypic signaling between dermal fibroblasts and melanoma cells induces phenotypic plasticity and proteome rearrangement in malignant cells.

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Heterotypic signaling between dermal fibroblasts and melanoma cells induces phenotypic plasticity and proteome rearrangement in malignant cells.

Biochim Biophys Acta Proteins Proteom. 2020 Aug 28;:140525
Authors: Pessotti DS, Andrade-Silva D, Serrano SMT, Zelanis A

Abstract
The signaling events triggered by soluble mediators released from both transformed and stromal cells shape the phenotype of
tumoral cells and have significant implications in cancer development and progression. In this study we performed an in vitro heterotypic signaling assays by evaluating the proteome diversity of human dermal fibroblasts after stimulation with the conditioned media obtained from malignant melanoma cells. In addition, we also evaluated the changes in the proteome of melanoma cells after stimulation with their own conditioned media as well as with the conditioned medium from melanoma-stimulated fibroblasts. Our results revealed a clear rearrangement in the proteome of stromal and malignant cells upon cross-talk of soluble mediators. The main proteome signature of fibroblasts stimulated with melanoma conditioned medium was related to protein synthesis, which indicates that this process might be an early response of stromal cells. In addition, the conditioned medium derived from 'primed' stromal cells (melanoma-stimulated fibroblasts) was more effective in altering the functional phenotype (cell migration) of malignant cells than the conditioned medium from non-stimulated fibroblasts. Collectively, self- and cross-stimulation may play a key role in shaping the tumor microenvironment and enable tumoral cells to succeed in the process of melanoma progression and metastasis. Although the proteome landscape of cells participating in such a heterotypic signaling represents a snapshot of a highly dynamic state, understanding the diversity of proteins and enriched biological pathways resulting from stimulated cell states may allow for targeting specific cell regulatory motifs involved in melanoma progression and metastasis.

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The effects of p53 gene inactivation on mutant proteome expression in a human melanoma cell model.

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The effects of p53 gene inactivation on mutant proteome expression in a human melanoma cell model.

Biochim Biophys Acta Gen Subj. 2020 Aug 28;129722


Abstract

BACKGROUND: The identification of mutated proteins in human cancer cells-termed proteogenomics, requires several technologically independent research methodologies including DNA variant identification, RNA sequencing, and mass spectrometry. Any one of these methodologies are not optimized for identifying potential mutated proteins and any one output fails to cover completely a specific landscape.

METHODS: An isogenic melanoma cell with a p53-null genotype was created by CRISPR/CAS9 system to determine how p53 gene inactivation affects mutant proteome expression. A mutant peptide reference database was developed by comparing two distinct DNA and RNA variant detection platforms using these isogenic cells. Chemically fractionated tryptic peptides from lysates were processed using a TripleTOF 5600+ mass spectrometer and their spectra were identified against this mutant reference database.

RESULTS: Approximately 190 mutated peptides were enriched in wt-p53 cells, 187 mutant peptides were enriched in p53-null cells, with an overlap of 147 mutated peptides. STRING analysis highlighted that the wt-p53 cell line was enriched for mutant protein pathways such as CDC5L and POLR1B, whilst the p53-null cell line was enriched for mutated proteins comprising EGF/YES, Ubiquitination, and RPL26/5 nodes.

CONCLUSION: Our study produces a well annotated p53-dependent and p53-independent mutant proteome of a common melanoma cell line model. Coupled to the application of an integrated DNA and RNA variant detection platform (CLCbio) and software for identification of proteins (ProteinPilot), this pipeline can be used to detect high confident mutant proteins in cells.

GENERAL SIGNIFICANCE: This pipeline forms a blueprint for identifying mutated proteins in diseased cell systems.

PMID: 32866596 [PubMed — as supplied by publisher]

Anticancer activity of functional polysuccinates with N-acetyl-cysteine in side chains.

Related Articles

Anticancer activity of functional polysuccinates with N-acetyl-cysteine in side chains.

Eur J Pharmacol. 2020 Aug 28;173501

Authors: Mrówka M, Jaszcz K, Skonieczna M

Abstract

The synthesis and characteristics of functional polyesters with a potential anticancer activity have been described, followed by a post-modification process of biologically active polymers. First, biodegradable functional polysuccinates possessing pendant allyl groups, that are susceptible to thiol-ene reaction, were obtained by polyaddition of succinic anhydride and allyl glycidyl ether. The functionality of such polyesters was regulated by replacing a part of unsaturated glycidyl ether with saturated ones. Polymers containing 20–100% mers with allyl groups were reacted with N-acetyl-cysteine (NAC). The use of simple click reaction allowed obtaining polyesters containing different amounts of N-acetyl-cysteine in side chains. The thus obtained polymers with a molecular weight of several thousand are characterized by solubility in methanol as opposed to their initial precursors. Modified polyesters show no toxicity to normal human keratinocytes (HaCaT) cells, similar to the NAC in normal human fibroblasts (NHDF), whereas the anticancer activities were observed against squamous carcinoma (SCC-25), and melanoma (Me45) cells. A standard colorimetric assay (MTS), to assessing cells viability and cytotoxicity of tested compounds, was performed against NHDF for NAC, HaCaT, SCC-25, and Me45 cells, within 24–144 h long-term expositions. Neither contact with NAC alone, and tested materials, nor long incubation decreased normal cell viability or induced inflammation. That reassumed the potential of anticancer activities of tested materials, with the tendency to visible selectivity against cancer cell lines in vitro, confirmed with
Angiosarcomatous transdifferentiation of metastatic melanoma.

Related Articles

Angiosarcomatous transdifferentiation of metastatic melanoma.
J Cutan Pathol. 2020 Aug 31:;
Authors: Kilsdonk MJ, Romeijn TR, Kelder W, van Kempen LC, Diercks GH

Abstract
Melanoma is known to show considerable variation in its histopathological presentation. In exceptional cases heterologous or divergent differentiation (metaplastic melanoma) can be observed. We report a case of a 69-year-old man who was diagnosed with nodular melanoma on the right upper leg. One year later, the patient presented with an inguinal lymph node metastasis and a lymph node dissection was carried out. In two out of five positive lymph nodes an angiosarcomatous component was found next to a ‘conventional melanoma’ component. Shortly after, the patient developed two in-transit metastases in which again an angiosarcomatous component was seen. The vascular component stained positive with ERG and CD31 and negative for melanocytic markers (Mart-1, S100, SOX-10), the ‘conventional melanoma’ had an opposite staining pattern. Molecular analysis on both components showed an identical mutation in the NRAS gene, which in our opinion proves the divergent differentiation. To our knowledge this is the first case report describing angiosarcomatous transdifferentiation of melanoma. This article is protected by copyright. All rights reserved.

PMID: 32865764 [PubMed — as supplied by publisher]

Development of new descriptor for melanoma detection on dermoscopic images.

Related Articles

Development of new descriptor for melanoma detection on dermoscopic images.
Authors: Akan H, Yildiz MZ

Abstract
Early detection of melanoma has critical importance for the success of the treatment. However, a successful early diagnosis is only possible with the existence of discriminative features. In this study, a new descriptor based on the number of colors was developed in order to successfully diagnose lesions of melanoma. The number of colors is the main feature in the identification of melanoma-type skin lesions. The user must select a threshold value when calculating the number of colors of the lesion. The incorrect threshold value selection of non-expert users disrupts the aforementioned feature and also leads to significant diagnostic errors. In this study, it was revealed that color counting threshold values have a significant effect on the distinctiveness of the number of colors. In the three dermoscopic databases, color counting threshold values that provide the maximum distinctiveness on melanoma and benign lesions were determined as 0 and 0.123 respectively. By using these color counting threshold values, the number of colors for each sample in the datasets was calculated separately. Following that, a novel attribute called the number of color difference was defined as a function of color counting threshold values. Experiments using only the proposed new descriptor yielded 52.7% higher f-measure and 84.5% higher true-positive performance than the number of colors used in the literature. The results obtained in this study revealed the importance of accurately determining the number of colors the lesions had and states that the applied color counting threshold significantly influences the classification results. Thereby, a new method is proposed for determining the critical color counting threshold. We claim that the classical ABCD rule should be improved by our new descriptor. Graphical abstract Fig. 1 Selection of threshold has vital effect on skin lesion classification. A new method to select the correct threshold value and a new attribute for correct classification were developed.

PMID: 32865830 [PubMed — as supplied by publisher]

A novel oncolytic virus engineered with PD-L1 scFv effectively inhibits tumor growth in a mouse model.

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A novel oncolytic virus engineered with PD-L1 scFv effectively inhibits tumor growth in a mouse model.
Cell Mol Immunol. 2019 09;16(9):780–782
Authors: Wu C, Wu M, Liang M, Xiong S, Dong C

PMID: 31363172 [PubMed — indexed for MEDLINE]

Cholesterol Induces CD8+ T Cell Exhaustion in the Tumor Microenvironment.

Related Articles

Cholesterol Induces CD8+ T Cell Exhaustion in the Tumor Microenvironment.
Cell Metab. 2019 07 02;30(1):143–156.e5
Abstract

Tumor-infiltrating T cells often lose their effector function; however, the mechanisms are incompletely understood. We report that cholesterol in the tumor microenvironment induces CD8+ T cell expression of immune checkpoints and exhaustion. Tumor tissues enriched with cholesterol and cholesterol content in tumor-infiltrating CD8+ T cells were positively and progressively associated with upregulated T cell expression of PD-1, 2B4, TIM-3, and LAG-3. Adoptively transferred CD8+ T cells acquired cholesterol, expressed high levels of immune checkpoints, and became exhausted upon entering a tumor. Tumor culture supernatant or cholesterol induced immune checkpoint expression by increasing endoplasmic reticulum (ER) stress in CD8+ T cells. Consequently, the ER stress sensor XBP1 was activated and regulated PD-1 and 2B4 transcription. Inhibiting XBP1 or reducing cholesterol in CD8+ T cells effectively restored antitumor activity. This study reveals a mechanism underlying T cell exhaustion and suggests a new strategy for restoring T cell function by reducing cholesterol to enhance T cell-based immunotherapy.

PMID: 31031094 [PubMed — indexed for MEDLINE]