SMART DIASPORA 2023

ABORDĂRI MULTI-OMICE ÎN MEDICINA PERSONALIZATĂ, PREZENT ȘI VIITOR

Prof Dr Cristiana Tanase

ABORDĂRI MULTI-OMICE ÎN MEDICINA PERSONALIZATĂ, PREZENT ȘI VIITOR

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- În ultimii ani, înțelegerea mecanismelor moleculare și a interacțiunilor celulare relevante pentru afecțiunile maligne s-a îmbunătățit substanțial.

- Termenii „**medicină de precizie**” și „**medicină**
- **personalizată**” sunt utilizați frecvent în comunitatea științifică, sistemele de sănătate , mass-media. Acești termeni precum si „P4 medicine”, „stratified medicine”, „medicina genomică” sau „medicina bazată pe dovezi”, sunt adesea folosiți în mod interschimbabil pentru a descrie abordări specifice bolii legate de pacient - cu privire la impactul clinic al profilurilor moleculare, genetice, epigenetice, proteomice, metabolice și funcționale asupra diagnosticului, prognosticului și evoluției individuale a pacientului.

Medicina de precizie –

concept nou pentru realizarea dezideratului

medicina personalizata.

- Principiile de bază ale medicinei personalizate- „aplicarea terpiei potrivite pentru pacientul potrivit la momentul potrivit”, nu sunt noi.
- O descriere a teoriei medicinei personalizate a fost deja elaborată de grecii antici - Hipocrate (460-370 î.Hr.).
- Hipocrate a subliniat importanța individualizării managementului pacientului

- **Medicina personalizata si de precizie** se concentrează pe **abordarea individuala**, fiind **proactive**, au fost rapid preluate în **cercetarea biomedicală fundamentală** și **clinică** de avangardă.
- Au fost incluse în programe de finanțare atât în Uniunea Europeană, cât și în Statele Unite ale Americii, fiind **componente-cheie** a programelor **Horizon2020** și **White House's Precision Medicine Initiative**.

Peste 50% din manifestarile stiintifice au in componenta sectiunile ***medicina de precizie – medicina personalizata***.

- Precision Center Medicine: The Future is Now, Only Better
- Personalised and Precision Medicine in Cancer Clinical Trials: Panacea for Progress or Pandora's Box?
- Precision Medicine: Personal Omics Profile for Understanding & Managing Health and Disease
- Enterprises and challenges in diagnostics for precision medicine
- Precision medicine: an evolving paradigm in 21st century healthcare
- Problems, challenges and promises: perspectives on precision medicine

Abordarea cercetarii medicale fundamentale si clinice – o noua era: **medicina de precizie** pentru diagnostic si **tratament personalizat**

= medicina de precizie – medicina personalizata.

PubMed

Ultimii 5 ani:

personalized medicine:

- > 85000 (2023)

precision medicine:

- > 60000 (2023)

personalized and precision medicine:

- > 8700 (2023)

omics personalized cancer:

- > 1200 (2023)

omics personalized regeneration

- > 30 (2023)

Medicina personalizata - OMS (2013) - model medical ce folosește profilul molecular realizat prin tehnologii „omice” pentru configurarea unei strategii terapeutice adecvate, pentru pacientul potrivit, la momentul potrivit și evaluează predispoziția pentru o boală la nivelul populației, oferind posibilități de prevenție adecvată la momentul potrivit.

- **Medicina personalizata** reprezinta o noua abordare inovatoare pentru tratamentul si preventia bolii, luand in considerare **variabilitatea individuala** la nivel **genetic**, **de mediu** si **stil de viata** al fiecarei persoane.

The New England Journal of Medicine, 2015

Medicina de precizie

• Concept sau abordare în medicina preclinică, translațională sau aplicată care ia în considerare una sau mai multe molecule , celule și/sau interacțiuni între (rețele de) molecule și celule, cu scopul de a îmbunătăți diagnosticul, prognosticul, preventia și/sau terapia în patologia tumorală.

Medicina personalizata

• Concept sau abordare în medicina translațională sau aplicată care ia în considerare una sau mai multe molecule, celule și/sau interacțiuni relevante din punct de vedere clinic între (rețele de) molecule si celule, precum și mai mulți (sau toți) factorii relevanți legați de pacient cu scopul aplicarii unui diagnostic optim, algoritmi pentru prognostic și să selecteze strategia optimă de preventie și/sau abordare terapeutica pentru pacientul **potrivit** sau **cohorta de pacienți** la momentul **potrivit** în patologia tumorală.

- Definiția „medicinei personalizate” este în conformitate cu principiile străvechi definite de Hipocrate și cu definițiile mai recente folosite de Comisia Europeană în programul Orizont 2020. Ca atare, reprezintă, de asemenea, o extensie a „conceptului de medicină de precizie”, cu un domeniu de aplicare mai larg, bazat pe variabile individuale legate de pacient.
- Utilizarea comună a acestor termeni ar trebui să faciliteze comunicarea între cercetare, medicina aplicată și ar trebui să sprijine dezvoltarea științifică în domeniu..

MEDICINA PERSONALIZATA –tehnologii OMICE

- Integrarea datelor *omice* la mai multe niveluri poate defini granița dintre sănătate și boală.

- Utilizarea abordării de **tip machine learning** pentru a integra profilurilor genomic, transcriptomic, epigenomic, proteomic, metabolomic la scară largă, va permite o evaluarea a borderline-ului: sănătate - boală.
- În special, integrarea diferitelor tehnici ***omice***, cum ar fi *single cell DNA and RNA sequencing* cu *single cell proteomics*, va avea un impact profund asupra interpretării diferitelor fenotipuri de boală, elucidând heterogenitatea probelor

- Descifrarea bolilor complexe prin integrarea datelor omice pe modele de linii celulare sau modele animale a condus la o provocare - ….necesitatea de a reproduce fenotipurile complexe ale bolii umane. Aceasta a condus la dezvoltarea de modele mai apropiate de realitatea biologica, cum ar fi culturi celulare și organoizi derivați din probe de la pacienti sau din celule stem pluripotente induse (iPSC).

- Valorificarea *deep-learning* pentru integrarea datelor multi-omice poate solutiona multe provocări în analiza profilului molecular,

Prin aplicarea unor algoritmi de inteligență artificială la seturi de date biologice multidimensionale (care surprind variabilitățile individuale asociate cu un fenotip particular), medicina de precizie si medicina personalizata permit realizarea predicției riscului de boală, răspunsul la tratament și evolutia

Profilul omic:

transcriptome, proteome, epigenom, cytokinome, kinome, metabolome releva varietatea componentelor moleculare pe parcursul progresiei bolii.

Analiza integrata multi-omica – identificarea riscului de boala si predictibilitatea evolutiei bolii.

Dezvoltarea agentilor terapeutici ce vizeaza **mecanismele moleculare** constituie aspecte inovatoare in strategia trialurilor clinice.

“Individual omes - integrated profiles of **multiple omes”:** genome, epigenome, transcriptome, proteome, metabolome, antibodyome

monitorizare, preventie

medicina de precizie,personalizata

Medicina de precizie –personalizata- o noua paradigma in sistemul de sanatate, datorita dezvoltarii tehnologiilor high-throughput -

statusul fiziologic in timp real –

“integrated Personal Omics Profile” (iPOP).

INTEGRATIVE OMICS IN "PREVENTATIVE" MEDICINE

International Cancer Genome Consortium (http://www.icgc.org/)

Cancer Genome Atlas (http://cancergenome.nih.gov/).

Abordarea iPOP permite o perspectiva a diferentierii moleculare detaliata dintre statusurile fiziologice.

Alt avantaj al **abordarii iPOP** il reprezinta modularitatea - informatii **omice** cuantificabile pot fi incluse in **profilul iPOP**, care poate fi **personalizat** pentru a monitoriza orice eveniment biologic sau patologic.

- Medicina de precizie - punct central in terapia tintita, bazata pe informatii despre **modificarile cailor de semnalizare** și a componentelor acestora, implicate in transformarea tumorală.
- **farmacogenetica**
- **farmacogenomica**
- **farmacoproteomica**.
- În timp ce farmacogenetica și farmacogenomica oferă informaţii la nivel de genom și transcriptom, farmacoproteomica urmărește schimbările produse la nivel funcţional/translaţional.

MEDICINA DE PRECIZIE/PERSONALIZATE IN CANCER

- Amplificarea eforturilor in domeniul genomicii/proteomicii in vederea preventiei si tratamentului in cancer
- Terapia tintita in cancer pe baza semnaturii moleculare aplicabila in studii clinice in parteneriat cu companiile farmaceutice
- Dezvoltarea de noi abordari in evaluarea raspunsului la terapie
- Identificarea unor solutii fezabile pentru limitarea rezistentei la medicatie pe baza terapiei tintite

- Pe masura ce noi biomarkeri capata semnificatie clinica se contureaza schimbarea paradigmei diagnostic unic/terapie unica spre diagnostic complex/ terapie complexa

TEHNOLOGII *OMICE* - REZULTATE

Hindawi
Disease Markers
Volume 2019, Article ID 1814304, 12 pages
https://doi.org/10.1155/2019/1814304

Research Article

Inflammation-Related Patterns in the Clinical Staging and Severity Assessment of Chronic Kidney Disease

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Guest Editor: Christos Chadjichristos

Chronic kidney disease (CKD) is an irreversible loss of kidney function, and it represents a major global public health burden due to both its prevalence and its continuously increasing incidence. Mineral bone disorders (MBDs) constitute a hallmark of CKD, and alongside cardiovascular complications, they underlie a poor prognosis for these patients. Thus, our study focused on novel CKD biomarker patterns and their impact on the clinical staging of the disease. As a first testing approach, the relative expression levels of 105 proteins were assessed by the Proteome Profiler Cytokine Array Kit for pooled CKD stage 2–4 serum samples to establish an overall view regarding the proteins involved in CKD pathogenesis. Among the molecules that displayed significant dysregulation in the CKD stages, we further explored the involvement of Dickkopf-related protein 1 (Dkk-1), a recognised inhibitor of the Wnt signalling pathway, and its crosstalk with $1,25OH_2D_3$ (calcitriol) as new players in renal bone and vascular disease. The serum levels of these two molecules were quantified by an ELISA (76 samples), and the results reveal decreasing

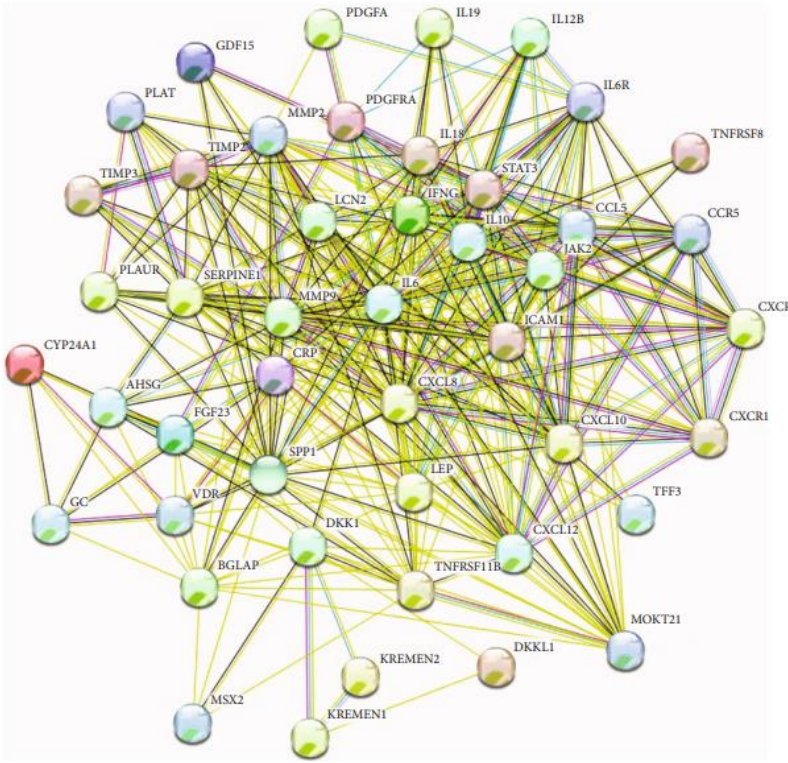

FIGURE 7: Functional interaction between different molecules involved in inflammation and MBDs in CKD. The coloured nodes are represented by query proteins and the first shell of interactors. Edges represent protein-protein functional associations, assigned with different colour codes, as follows: a blue edge indicates known interactions from curated databases, a pink edge indicates known interactions that have been experimentally determined, a green edge indicates predicted interactions in the gene neighbourhood, a red edge indicates predicted interactions for gene fusions, a blue-ink edge indicates predicted interactions for gene cooccurrences, a light-green edge indicates other interactions derived from text mining, and a black edge indicates gene coexpression derived from other databases. Abbreviations: CYP24A1: calcitriol, 1,25-dihydroxyvitamin D_3, and $1,25OH_2D_3$; SPP1: osteopontin, OPN; TNFRSF11B: osteoprotegerin, OPG; BGLAP: osteocalcin, OC; CXCL8: IL-8, interleukin-8; GC: vitamin D binding protein, DBP; VDR: vitamin D receptor.

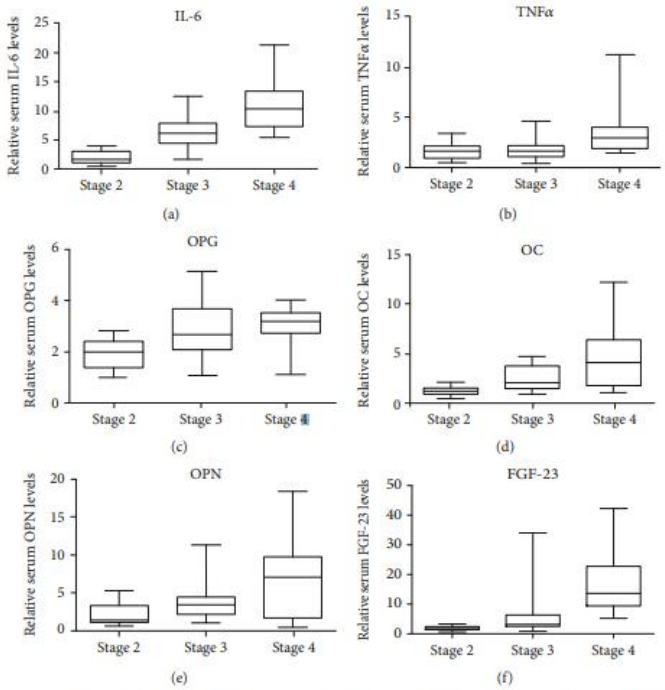

FIGURE 6: Fold change in serum IL-6 (a), TNFα (b), OPG (c), OC (d), OPN (e), and FGF-23 (f) expressions in CKD stages 4, 3, and 2 versus the control, assessed by xMAP array.

Journal List > Int J Mol Sci > v.21(16); 2020 Aug > PMC7460590

International Journal of Molecular Sciences

MDPI

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PMID: 32781778

CD36 and CD97 in Pancreatic Cancer versus Other Malignancies

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Abstract

Go to:

Starting from the recent identification of CD36 and CD97 as a novel marker combination of fibroblast quiescence in lung during fibrosis, we aimed to survey the literature in search for facts about the separate (or concomitant) expression of clusters of differentiation CD36 and CD97 in either tumor- or pancreatic-cancer-associated cells. Here, we provide an account of the current knowledge on the diversity of the cellular functions of CD36 and CD97 and explore their potential (common) contributions to key cellular events in oncogenesis or metastasis development. Emphasis is placed on quiescence as an underexplored mechanism and/or potential target in therapy. Furthermore, we discuss intricate signaling mechanisms and networks involving CD36 and CD97 that may regulate different subpopulations of tumor-associated cells,

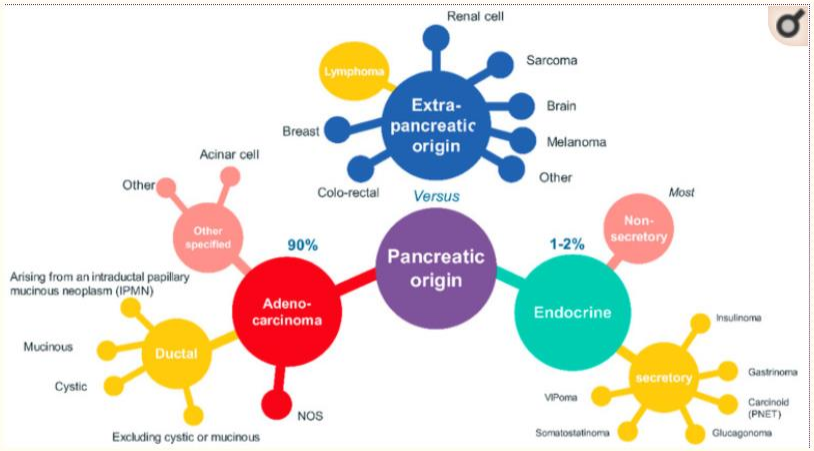


Figure 1

Histological types of pancreatic cancer, based on References [15,16].

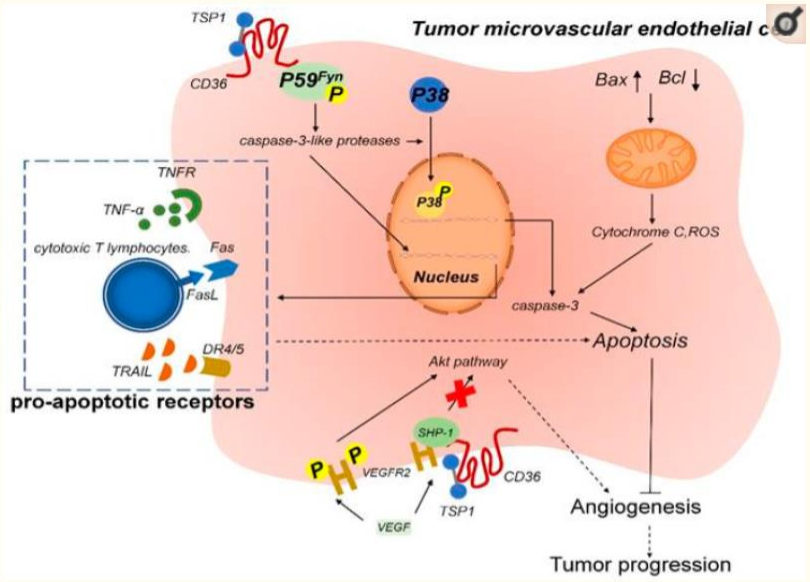


Figure 4

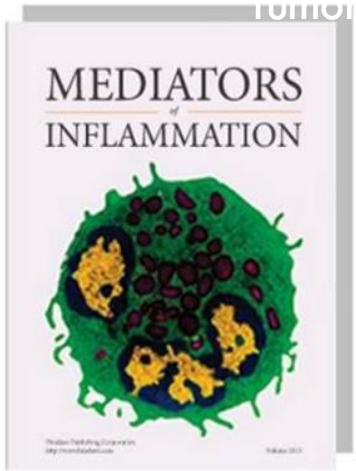
TSP-1-CD36 signaling is inducing apoptosis of tumor associated epithelial cells. As a result of TSP-1 binding to CD36 on microvascular endothelial cells, phosphorylation and, therefore, activation of P59fyn (cytoplasmic protein kinase) occur. This in turn stimulates caspase-like proteases, which induce the phosphorylation of MAPK. Nuclear translocation of MAPK generates increased expression of caspase-3 and of proapoptotic receptors, leading to apoptosis. Mitochondrial damage leads to the release of reactive oxygen species and of cytochrome C, which are also triggers of apoptosis. Moreover, the binding of THC-1 to CD36 induces the recruitment of SHP-1 to the VEGFR2 complex, followed by VEGFR2 dephosphorylation and inhibition of the VEGF pathway and leading to anti-angiogenesis. (Reproduced with permission from Reference [53].)

ABORDARI OMICE -TUMORI CEREBRALE

3. Albulescu R, Elena Codrici E, Popescu ID, Mihai S, Necula LG, Petrescu D, Teodoru M, Tanase C. *Cytokine Patterns in Brain Tumour Progression*, Mediators of Inflammation, 2013, doi:10.1155/2013/979748

Hindawi Publishing Corporation
Mediators of Inflammation
Volume 2013, Article ID 979748, 7 pages
http://dx.doi.org/10.1155/2013/979748

Hindawi



Research Article

Cytokine Patterns in Brain Tumour Progression

Radu Albulescu,[1,2] Elena Codrici,[1] Ionela Daniela Popescu,[1] Simona Mihai,[1] Laura Georgiana Necula,[1,3] Daniel Petrescu,[4] Mihaela Teodoru,[5] and Cristiana Pistol Tanase[1]

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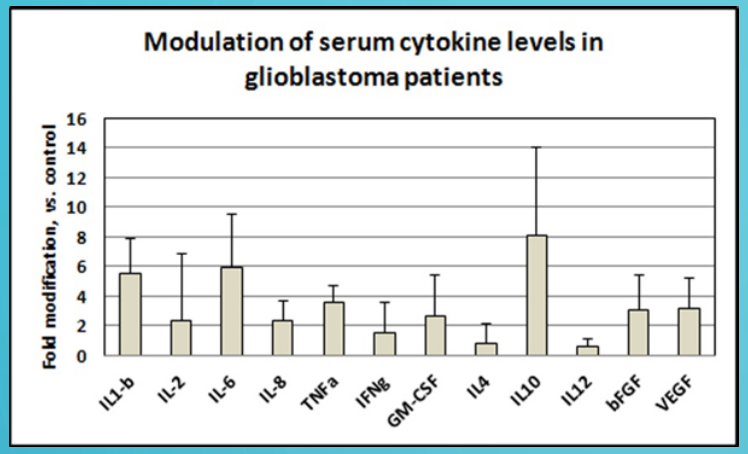
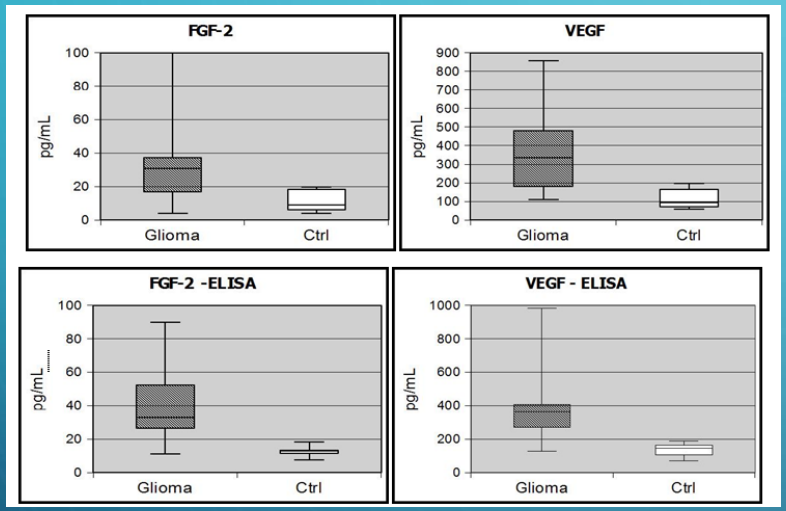
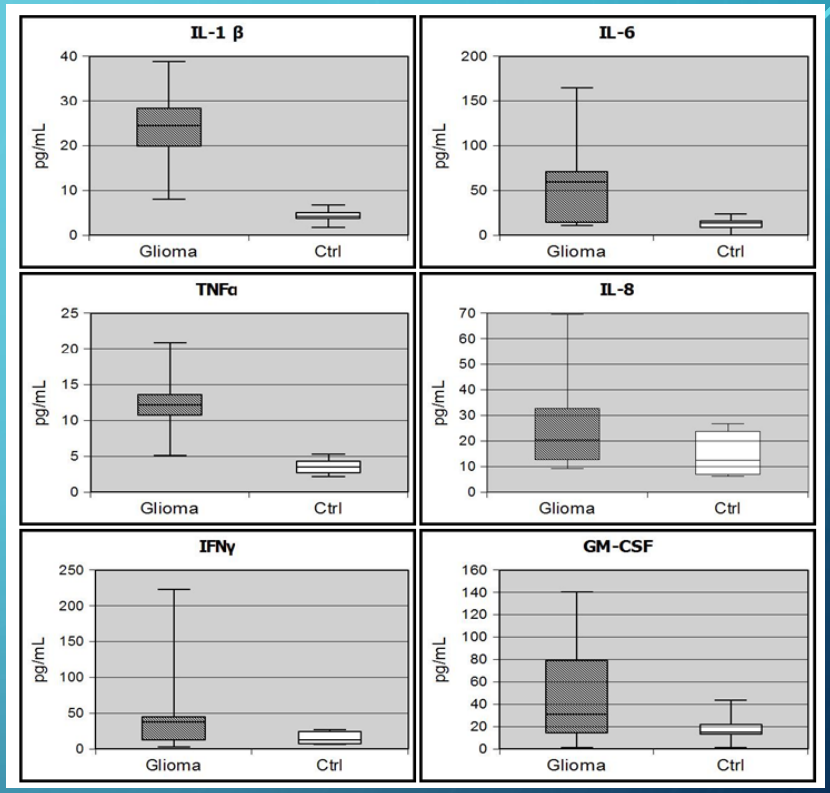
Academic Editor: Gila Moalem-Taylor

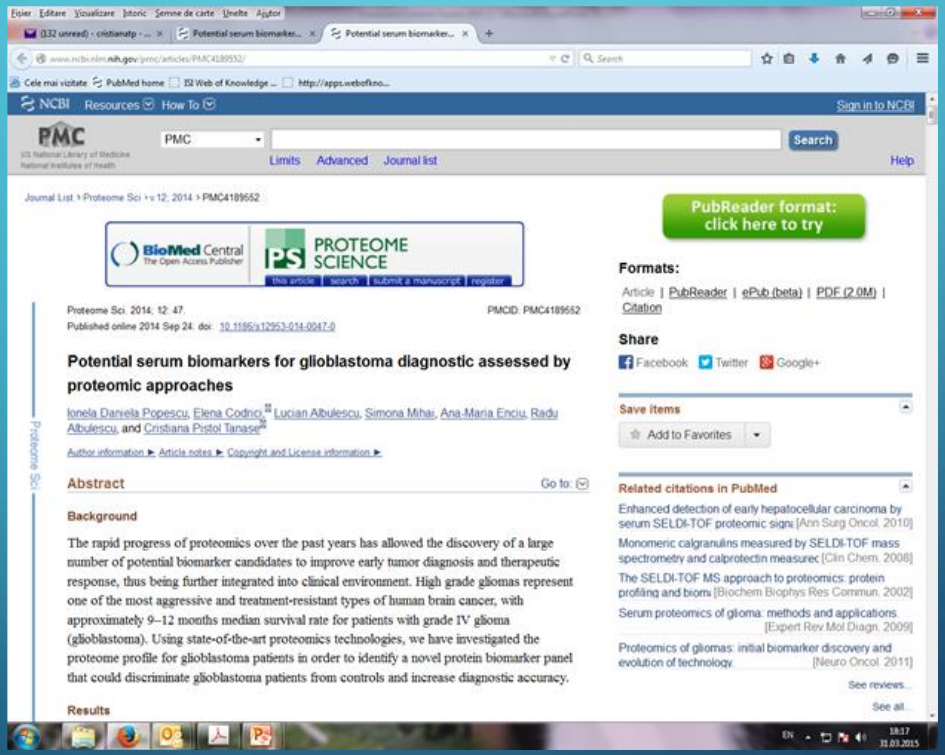




Expression levels of angiogenic factors, by xMAP analysis (A,B) and ELISA (C,D). Statistical significance (one way Anova): $p<0.05$ for bFGF and VEGF over-expression in sera from glioblastoma patients vs. control, by both methods



Serum levels of pro-inflammatory cytokines by xMAP analysis. The values represent averages +/- standard deviation of the group patients. Statistical significance (one way Anova): $p<0.05$ for IL-1β, TNFα, IL-6 and GM-CSF over-expression in sera from glioblastoma patients vs. controls.



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Proteome Sci. 2014; 12: 47. PMCID: PMC4189552
Published online 2014 Sep 24. doi: 10.1186/s12953-014-0047-0

Potential serum biomarkers for glioblastoma diagnostic assessed by proteomic approaches

Ionela Daniela Popescu, Elena Codrici, Lucian Albulescu, Simona Mihai, Ana-Maria Enciu, Radu Albulescu, and Cristiana Pistol Tanase

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Formats: Article | PubReader | ePub (beta) | PDF (2.0M) | Citation

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Abstract

Background

The rapid progress of proteomics over the past years has allowed the discovery of a large number of potential biomarker candidates to improve early tumor diagnosis and therapeutic response, thus being further integrated into clinical environment. High grade gliomas represent one of the most aggressive and treatment-resistant types of human brain cancer, with approximately 9–12 months median survival rate for patients with grade IV glioma (glioblastoma). Using state-of-the-art proteomics technologies, we have investigated the proteome profile for glioblastoma patients in order to identify a novel protein biomarker panel that could discriminate glioblastoma patients from controls and increase diagnostic accuracy.

Results

Related citations in PubMed

Enhanced detection of early hepatocellular carcinoma by serum SELDI-TOF proteomic signa [Ann Surg Oncol. 2010]

Monomeric calgranulins measured by SELDI-TOF mass spectrometry and calprotectin measurec [Clin Chem. 2008]

The SELDI-TOF MS approach to proteomics: protein profiling and biom [Biochem Biophys Res Commun. 2002]

Serum proteomics of glioma: methods and applications [Expert Rev Mol Diagn. 2009]

Proteomics of gliomas: initial biomarker discovery and evolution of technology [Neuro Oncol. 2011]

See reviews...

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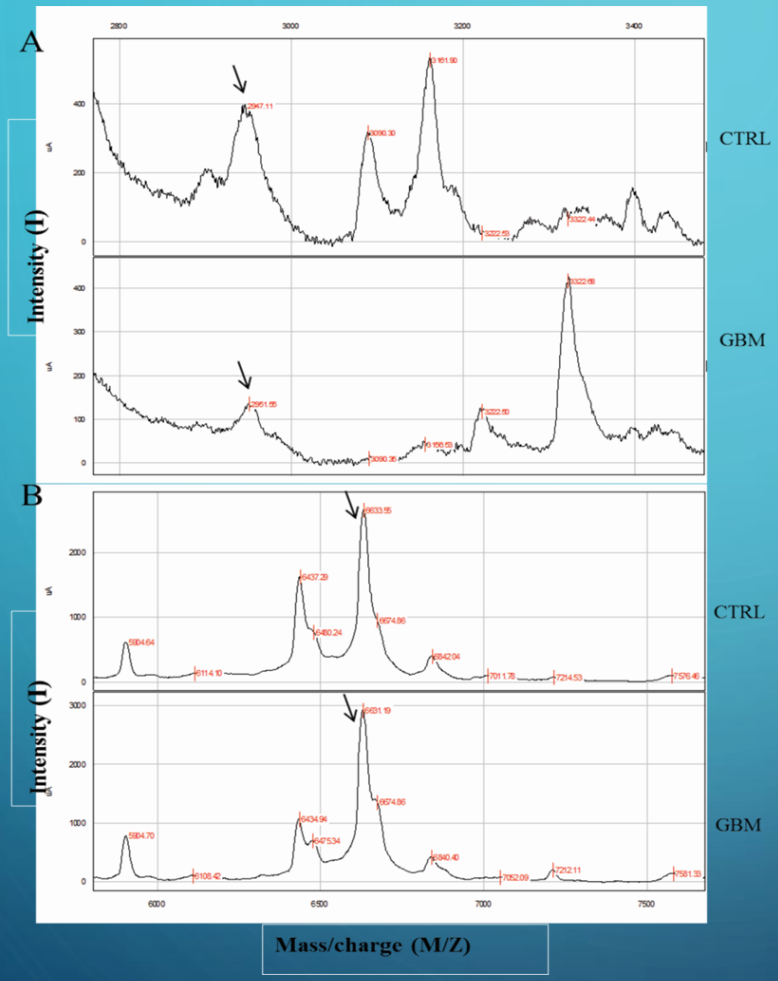

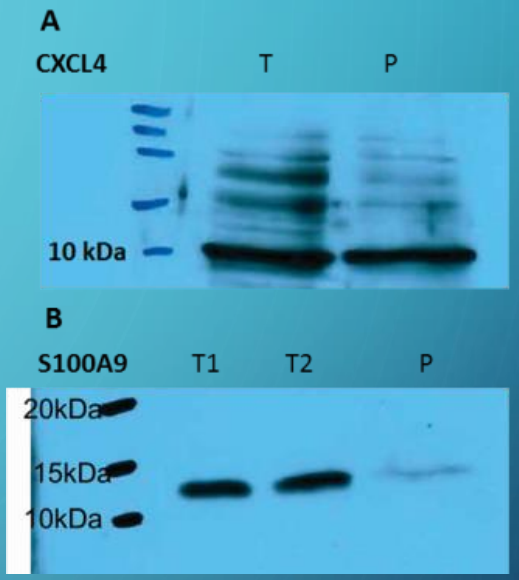

Validation of proteins by Western blot. CXCL4 (A) and S100-A9 (B) expression in tumoral (T) and peritumoral (P) tissues of glioblastoma.

6. Cruceru ML, Enciu AM, Popa AC, Albulescu R, Neagu M, Tanase CP, Constantinescu SN. *Signal transduction molecule patterns indicating potential glioblastoma therapy approaches*. OncoTargets and Therapy, 6:1737-1749, 2013

OncoTargets and Therapy

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ORIGINAL RESEARCH

Signal transduction molecule patterns indicating potential glioblastoma therapy approaches

This article was published in the following Dove Press journal:
OncoTargets and Therapy
28 November 2013
Number of times this article has been viewed

Maria Linda Cruceru[1]
Ana-Maria Enciu[1,2,7]
Adrian Claudiu Popa[1,3]
Radu Albulescu[2,4,7]
Monica Neagu[2,7]
Cristiana Pistol Tanase[2,7]
Stefan N Constantinescu[5–7]

Purpose: The expression of an array of signaling molecules, along with the assessment of real-time cell proliferation, has been performed in U87 glioma cell line and in patients' glioblastoma established cell cultures in order to provide a better understanding of cellular and molecular events involved in glioblastoma pathogenesis. Experimental therapy was performed using a phosphatidylinositol-3′-kinase (PI3K) inhibitor.

Patients and methods: xMAP technology was employed to assess expression levels of several signal transduction molecules and real-time xCELLigence platform for cell behavior.

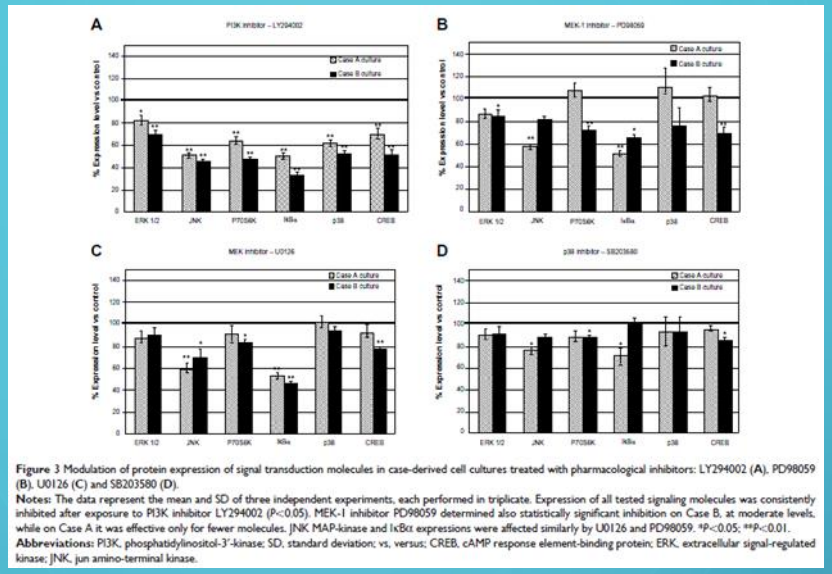
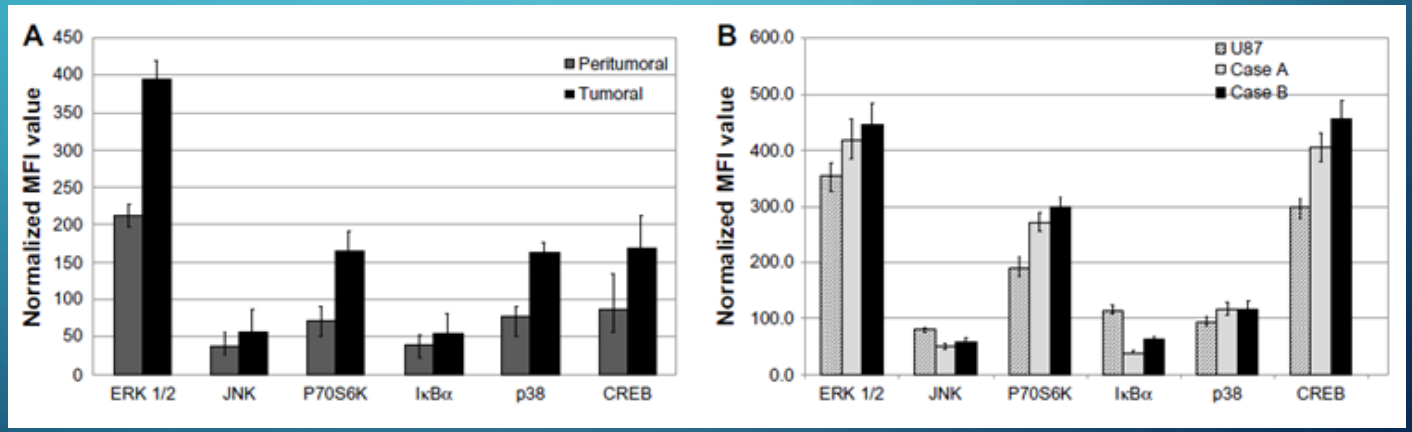


Figure 3 Modulation of protein expression of signal transduction molecules in case-derived cell cultures treated with pharmacological inhibitors: LY294002 (**A**), PD98059 (**B**), U0126 (**C**) and SB203580 (**D**).

Notes: The data represent the mean and SD of three independent experiments, each performed in triplicate. Expression of all tested signaling molecules was consistently inhibited after exposure to PI3K inhibitor LY294002 ($P<0.05$). MEK-1 inhibitor PD98059 determined also statistically significant inhibition on Case B, at moderate levels, while on Case A it was effective only for fewer molecules. JNK MAP-kinase and IκBα expressions were affected similarly by U0126 and PD98059. $^{*}P<0.05$; $^{**}P<0.01$.

Abbreviations: PI3K, phosphatidylinositol-3'-kinase; SD, standard deviation; vs, versus; CREB, cAMP response element-binding protein; ERK, extracellular signal-regulated kinase; JNK, jun amino-terminal kinase.



Expression profiles of signaling transduction proteins quantified by xMAP analysis

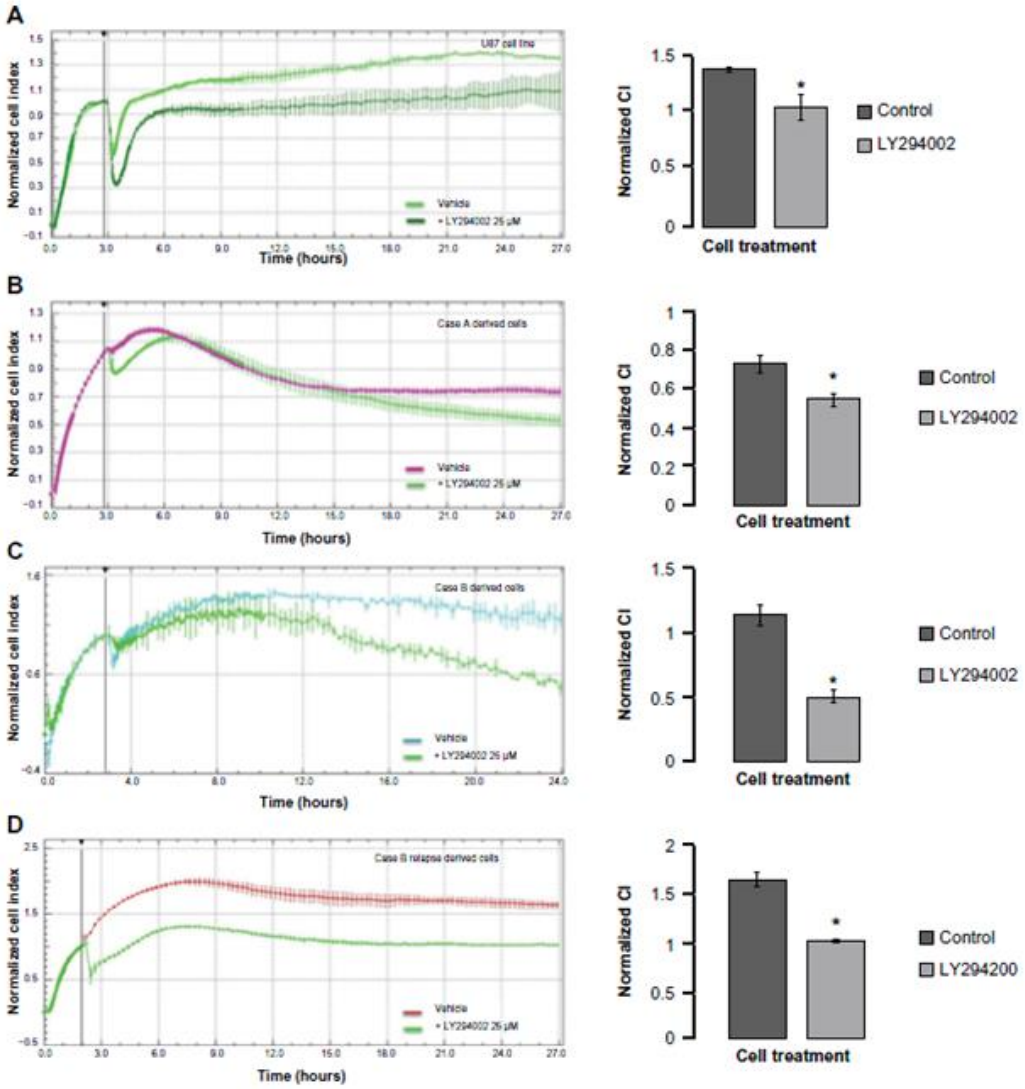


Figure 5 Real-time impedance analysis of cell proliferation under PI3K inhibition.

Notes: Five thousand U87 cells (**A**), Case A derived culture cells (**B**), Case B derived culture cells (**C**), and Case B relapse derived culture cells (**D**) were plated on collagen-coated cells and left to adhere for 2 hours. After the plating period, vehicle comprising 1/400 DMSO or 25µM LY294002, PI3K inhibitor, were added to the wells; cells were further incubated in standard cell culture conditions for 48 hours. LY294002 inhibited proliferation in all experimental setups, yet at different amplitudes and times. Proliferation CI were normalized after an initial 2-hour plating period. Readings were collected every minute for the first 2 hours, then every 15 minutes for the remainder of the experiment. Statistical analysis was carried out using Student's *t*-test (two-tailed) for normalized cell indexes at 24 hours *($P<0.01$). The data represent the mean and SD of three independent experiments.

Abbreviations: CI, cell indexes; DMSO, dimethyl sulfoxide; SD, standard deviation.

BREVETE

- ***Metodă de stabilire a unui set de biomarkeri solubili pentru diagnosticul, prognosticul sau monitorizarea glioblastomului, și metodă pentru diagnosticul, prognosticul sau monitorizarea glioblastomului bazată pe utilizarea acestui set*** - Brevet acordat OSIM RO 130590 B1

- ***Metodă de stabilire a unui set de biomarkeri proteici pentru diagnosticul glioblastomului*** - Brevet acordat OSIM RO 130589 B1

Review

Fatty Acids, CD36, Thrombospondin-1, and CD47 in Glioblastoma: Together and/or Separately?

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Abstract: Glioblastoma (GBM) is one of the most aggressive tumors of the central nervous system, characterized by a wide range of inter- and intratumor heterogeneity. Accumulation of fatty acids (FA) metabolites was associated with a low survival rate in high-grade glioma patients. The diversity of brain lipids, especially polyunsaturated fatty acids (PUFAs), is greater than in all other organs and several classes of proteins, such as FA transport proteins (FATPs), and FA translocases are considered principal candidates for PUFAs transport through BBB and delivery of PUFAs to brain cells. Among these, the CD36 FA translocase promotes long-chain FA uptake as well as oxidated lipoproteins. Moreover, CD36 binds and recognizes thrombospondin-1 (TSP-1), an extracellular matrix protein that was shown to play a multifaceted role in cancer as part of the tumor microenvironment. Effects on tumor cells are mediated by TSP-1 through the interaction with CD36 as well as CD47, a member of the immunoglobulin superfamily. TSP-1/CD47 interactions have an important role in the modulation of glioma cell invasion and angiogenesis in GBM. Separately, FA, the two membrane receptors CD36, CD47, and their joint ligand TSP-1 all play a part in GBM pathogenesis. The last research has put in light their interconnection/interrelationship in order to exert a cumulative effect in the modulation of the GBM molecular network.

check for updates

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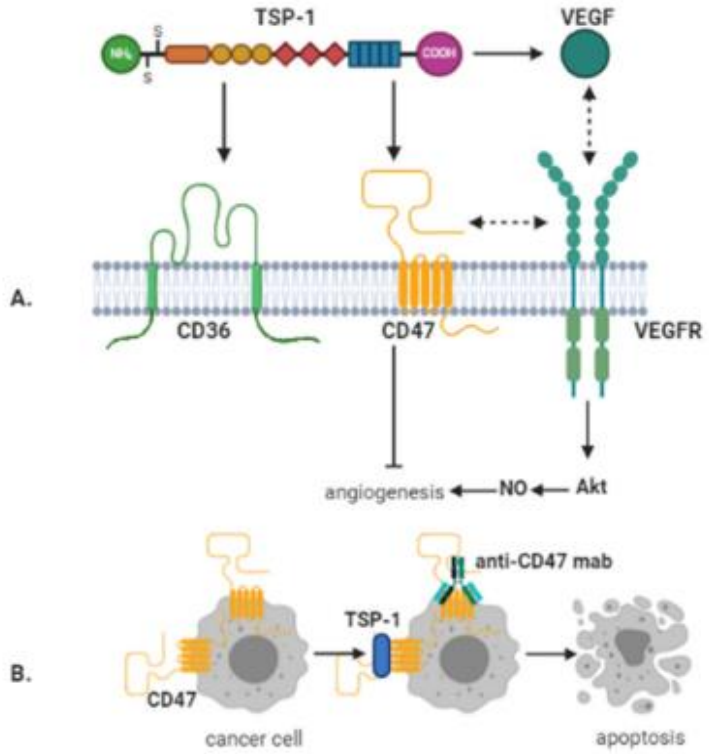


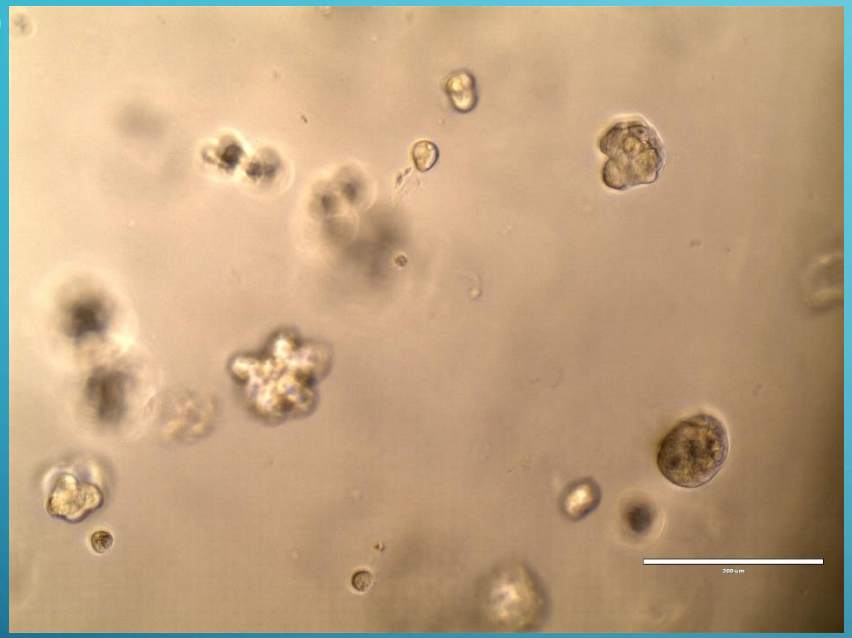
Figure 2. Anti-angiogenic and direct anti-cancer effects mediated by CD47. (**A**) TSP-1 inhibits angiogenesis via binding to CD36 and CD47. However, TSP-1 mediated inhibition of angiogenesis by binding to CD36 is also regulated via CD47. In addition, CD47 directly interacts with vascular endothelial growth factor receptor-2 (VEGFR-2) on endothelial cells. By binding to CD47, this interaction is abrogated by TSP-1, whereby angiogenesis is inhibited. Further, TSP-1 can directly bind to VEGF, thereby preventing its interaction with VEGFR-2. (**B**) Crosslinking of CD47 by antibodies or TSP-1 can lead to caspase-independent cancer cell death. Image created with BioRender.com (accessed on 14 January 2021).

PN 23.16.02.03- ABORDĂRI MOLECULARE ÎN MODELE 3D (SFEROIZI TUMORALI) EDITATE GENIC PRIN METODA CRISPR/CAS9 ÎN DEZVOLTAREA DE SOLUȚII PENTRU MEDICINA PERSONALIZATĂ ÎN CANCER (2023-2026)

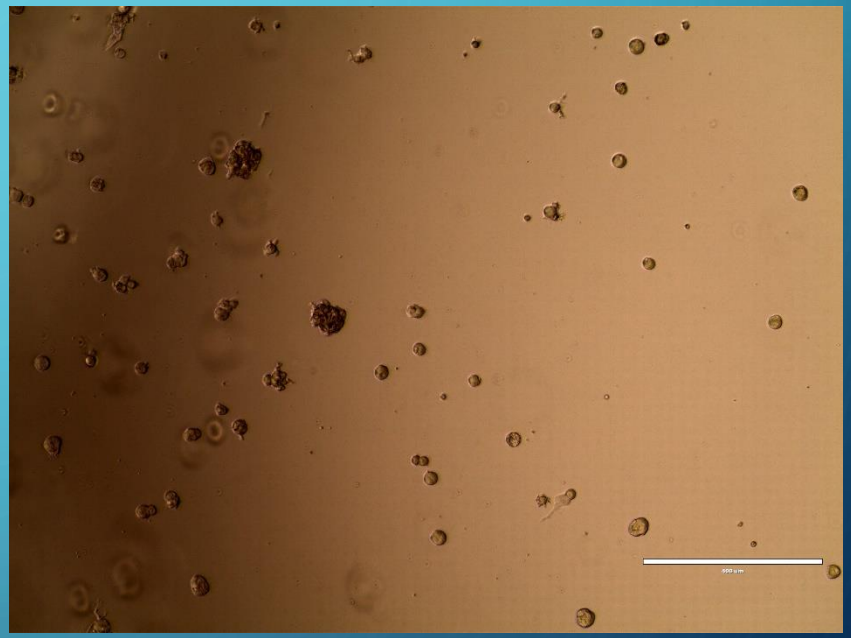
- SCOP - dezvoltarea de modele experimentale tumorale 3D *in vitro* (sferoizi tumorali multicelulari), pornind de la celule editate genic pentru gene cu impact în reprogramarea metabolică (IDH1, CD36), ca abordare inovatoare în screeningul rezistenței la chimioterapie.
- modele experimentale de sferoizi editați genic prin CRISRP/Cas9 vor fi utilizate pentru demonstrarea fezabilității sistemului propus.
- pe baza modelelor funcționale nou create se va realiza validarea în condiții de laborator a sferoizilor editați genic, respectiv investigarea răspunsului la tratament, fiind identificate posibile cauze de rezistență la chimioterapie sau de evoluție nefavorabilă a bolii, în vederea adaptării strategiei terapeutice la caracteristicile individuale.

NOI DIRECȚII DE ABORDARE

Sferoizi tumorali de
carcinom mamar (celule MCF-7)



Sferoizi tumorali de
glioblastom(celule U87)



Modelele 3D sunt utile pentru aprecierea penetrabilității medicamentelor
Și pentru aprecierea rezistenței la chimioterapie

Generarea de modele 3D pornind de la celule tumorale obținute
de la pacienți sunt utile pentru evaluarea răspunsului la tratament

Dextran-based polymers can be used as first choice to generate tumor spheroids *in vitro*

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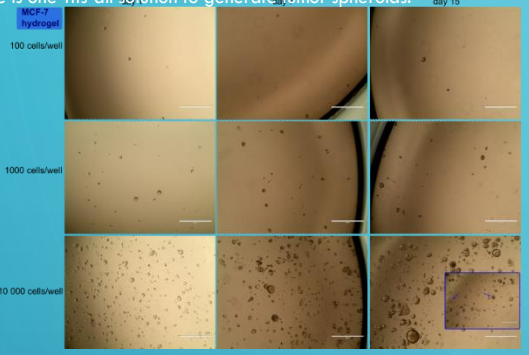
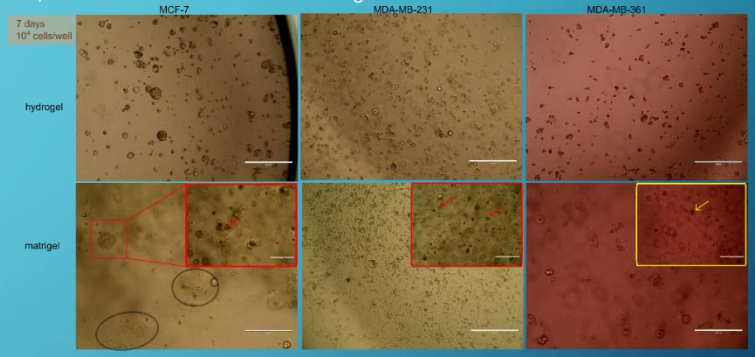
Background. 3D tumor cell cultures are currently emerging as the novel standard for cytotoxicity testing as well as *in vitro* molecular studies, but various solutions are available to generate them.
Aim. We tested whether there is one-fits-all solution to generate tumor spheroids.

Results.

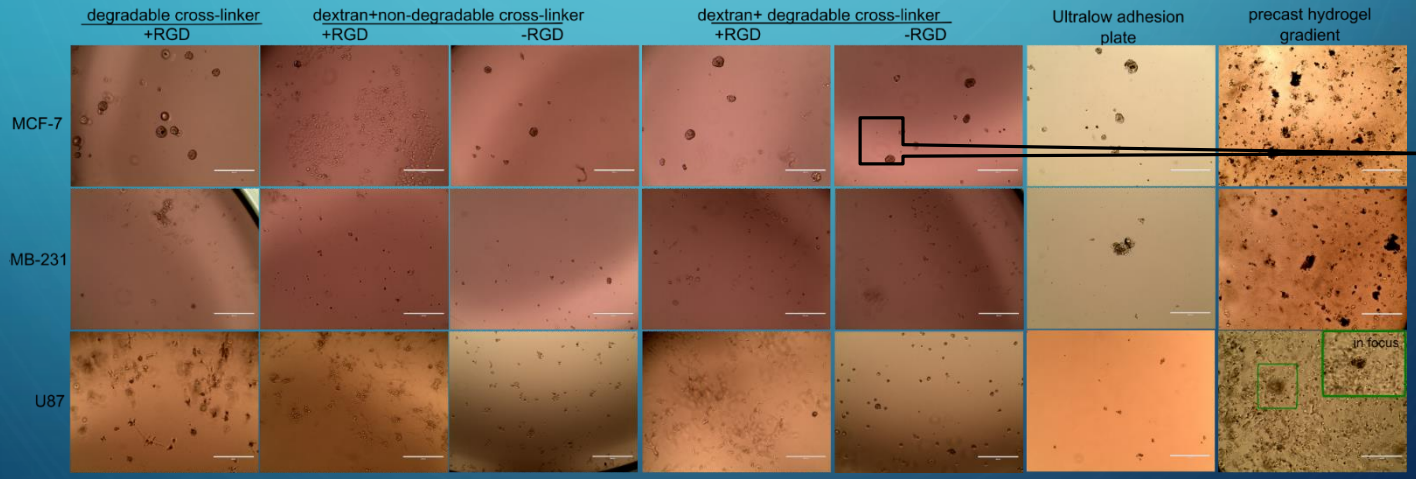
1. For higher cell numbers, presence of spheroids can be documented as early as 5 days, but at least 7 days are recommended. Once formed, spheroids can be maintained more than 28 days, with twice a week cell medium change.



2. Presence of organic molecules (basement membrane matrix) impaired formation of tumor spheroids for the aggressive cell line MDA-MB-231. The other two mammary carcinoma cell lines yielded mixed cultures (2D and 3D – the latter shown in inserts).



3. A non-degradable cell linker prevented proliferation of cells and formation of spheroids, regardless of cell type. A cross-linker gradient, yielded mixed cultures (2D and spheroids). Ultra-low adherence plates allowed formation of spheroids only for MCF-7 cells, whereas for the rest, irregular cell aggregates were observed at higher cell number. The only solution which generated spheroids for all tested lines is a dextran-base recipe, with no adherence peptide added.

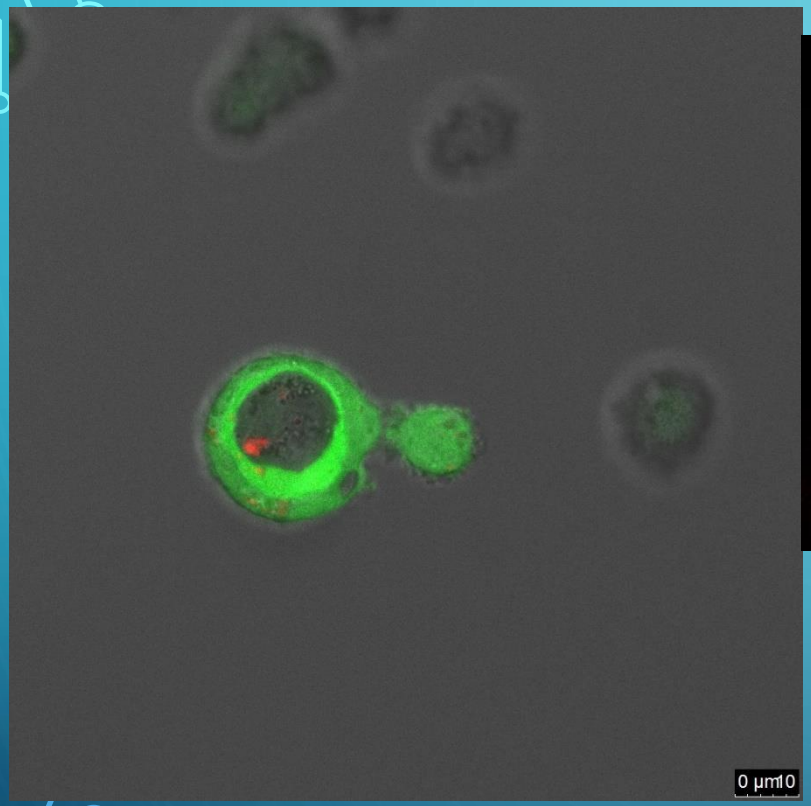


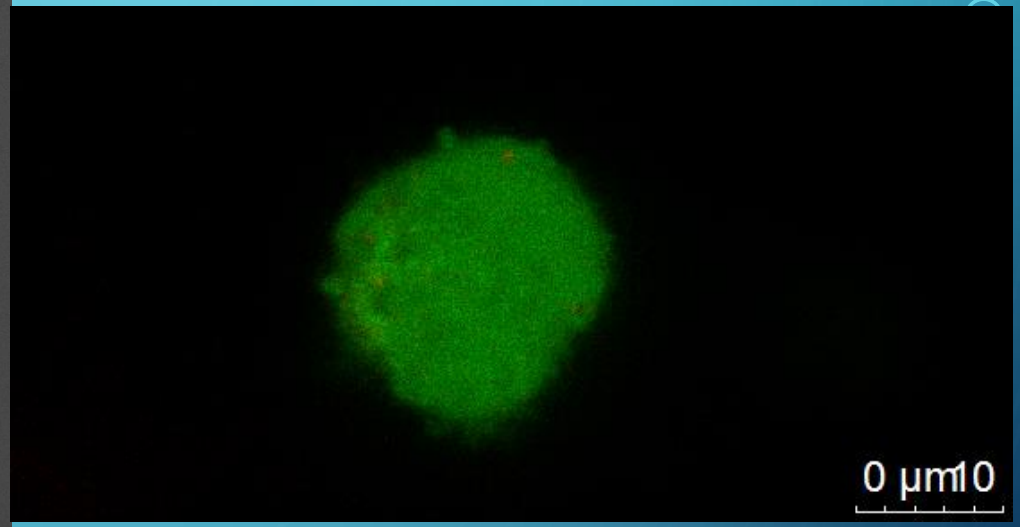
Live - dead assay of a 14d MCF-7 spheroid, in a dextran-based scaffold.

Conclusion. Dextran-based polymers can be used for tumor spheroid formation regardless of cell type, provided that no adhesion peptides are added.

Conflict of interest: The authors have no conflicts of

VIZUALIZARE 3D – LIVE/DEAD ASSAY





Verde – celule vii
Roșu – nuclei de celule moarte

Medicina de precizie-personalizata
O abordare translationala transdisciplinara

- Determinata de progresul tehnologic:
- platforme omice;
- abordare computationala;
- integrarea informatiei.

- Accelereaza calea de la cercetarea fundamentala la clinica.

Aceste preocupări constituie obiectul unor colaborări globale care reunesc oameni de știință, profesioniști din domeniul medical, politicieni, asociații de pacienți, reprezentanți ai industriei, ce își propun să exploreze posibilități de cooperare în vederea realizării conceptului de medicină personalizata.

“Un medic bun trateaza boala;
un medic exceptional
trateaza pacientul ce sufera de boala.”

William Osler
Parintele Medicinei Moderne
(1849 – 1919)

Towards Individualized Medicine