There are no translations available.
Η Δράση «Αναπτυξιακές προτάσεις Ερευνητικών Φορέων-ΚΡΗΠΙΣ» στοχεύει στην ενίσχυση των στρατηγικών επιλογών των εποπτευομένων από τη Γενική Γραμματεία Έρευνας & Τεχνολογίας Ερευνητικών Φορέων για την προαγωγή της αναπτυξιακής πορείας, της Αριστείας και της ποιότητας των προσφερομένων προϊόντων και υπηρεσιών. Στο πλαίσιο της Δράσης αυτής υλοποιείται στο Ινστιτούτο Βιοεπιστημών & Εφαρμογών (ΙΒ-Ε) του ΕΚΕΦΕ "Δημόκριτος" το έργο "ΔΙΑΣ" ("Ταυτοποίηση στόχων για τη διάγνωση και αντιμετώπιση ασθενειών").

Το ερευνητικό αντικείμενο του έργου ΔΙΑΣ συνίσταται στην ταυτοποίηση μοριακών και κυτταρικών στόχων και την ανάπτυξη καινοτόμων μεθόδων διάγνωσης και αντιμετώπισης ασθενειών και εντάσσεται σε μία από τις βασικές στοχεύσεις, προτεραιότητες και πεδία ανταγωνιστικής έρευνας τόσο σε Ευρωπαϊκό όσο και σε παγκόσμιο επίπεδο, ήτοι την τεκμηρίωση, εφαρμογή και προώθηση της προσωπικής/εξατομικευμένης Ιατρικής (personalized medicine).

Στο πλαίσιο του έργου ΔΙΑΣ έχει προγραμματισθεί η αναβάθμιση της απεικονιστικής μονάδας του ΙΒ-Ε και η πρόσληψη νέου υποστηρικτικού και επιστημονικού προσωπικού, για την προαγωγή των σχετικών με το έργο δραστηριοτήτων εντός του Ινστιτούτου. Τελικός στόχος θα είναι η δημιουργία μιας πλατφόρμας τεχνογνωσίας κυτταρικών και μοριακών στόχων που θα χρησιμοποιηθούν για την ανάπτυξη α) πρωτότυπων διαγνωστικών τεχνικών, β) στοχευμένων ιχνηθετών ή/και θεραπευτικών παρασκευασμάτων καθώς και γ) καινοτόμων νανοϋλικών με εξειδικευμένη και εκλεκτική αντικαρκινική δράση.

Επιπροσθέτως θα υποστηριχθεί η δυνατότητα εξωτερικών χρηστών των μονάδων παροχής υπηρεσιών του Ινστιτούτου να εφαρμόσουν καινοτόμους πειραματικούς σχεδιασμούς, αποκομίζοντας σημαντικά ερευνητικά οφέλη.

Συνεργάτες:

Με την υποστήριξη του έργου "ΔΙΑΣ" έχουν προσληφθεί οι ακόλουθοι εξωτερικοί συνεργάτες:

Αλεξίου Πολυξένη

Βαγενός Δημήτριος

Βλάχος Παναγιώτης

Ζαρκάδας Χριστόφορος

Ζωγραφίδης Αριστείδης

Κουτλόγλου Σοφία

Λιονής Ιωάννης

Μαυρογονάτου Ελένη

Μπιράτση Άλντα

Νασοπούλου Μαρία

Νινιός Ιωάννης

Ξυδάκη Δέσποινα

Ξυδούς Μάριος

Τροχάτου Ουρανία

Τσαλαβούτας-Ψαρράς Ελευθέριος

Δημοσιεύσεις:

Οι ακόλουθες δημοσιεύσεις έχουν προκύψει με την υποστήριξη του έργου "ΔΙΑΣ":

Effect of nanostructured TiO_2 crystal phase on photoinduced apoptosis of breast cancer epithelial cells (2014)

Nefeli Lagopati, Effie-Photini Tsilibary, Polycarpos Falaras, Panagiota Papazafiri, Evangelia A Pavlatou, Eleni Kotsopoulou, Paraskevi Kitsiou

International Journal of Nanomedicine 9: 3219–3230

(doi: 10.2147/IJN.S62972)

Purpose: The use of nanoparticles has seen exponential growth in the area of health care, due to the unique physicochemical properties of nanomaterials that make them desirable for medical

applications. The aim of this study was to examine the effects of crystal phase-nanostructured titanium dioxide particles on bioactivity/cytotoxicity in breast cancer epithelial cells.

Materials and methods: Cultured Michigan Cancer Foundation (MCF)-7 and human breastadenocarcinoma (MDA-MB-468) breast cancer epithelial cells were exposed to ultraviolet A light (wavelength 350 nm) for 20 minutes in the presence of aqueous dispersions of two different nanostructured titanium dioxide (TiO_2) crystal phases: anatase and an anatase–rutile mixture. Detailed characterization of each titanium dispersion was performed by dynamic light scattering. A 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide (MTT) colorimetric assay was employed to estimate the percentage of viable cells after each treatment. Western blot analysis of protein expression and characterization, as well as a deoxyribonucleic acid (DNA)-laddering assay, were used to detect cell apoptosis.

Results: Our results documented that 100% anatase TiO2 nanoparticles (110–130 nm) exhibited significantly higher cytotoxicity in the highly malignant MDA-MB-468 cancer cells than anatase–rutile mixtures (75%/25%) with the same size. On the contrary, MCF-7 cells (characterized by low invasive properties) were not considerably affected. Exposure of MDA-MB-468 cells to pure anatase nanoparticles or anatase–rutile mixtures for 48 hours resulted in increased proapoptotic Bax expression, caspase-mediated poly(adenosine diphosphate ribose) polymerase (PARP) cleavage, DNA fragmentation, and programmed cell death/apoptosis.

Conclusion: The obtained results indicated that pure anatase TiO2 nanoparticles exhibit superior cytotoxic effects compared to anatase–rutile mixtures of the same size. The molecular mechanism of TiO2 nanoparticle cytotoxicity involved increased Bax expression and caspase-mediated PARP inactivation, thus resulting in DNA fragmentation and cell apoptosis.

The Catabolic Effect of TNF α on Bovine Nucleus Pulposus Intervertebral Disc Cells and the Restraining Role of Glucosamine Sulfate in the TNF α

-Mediated up-Regulation of MMP-3
(2014)

Eleni Mavrogonatou, Maria T. Angelopoulou, Dimitris Kletsas

Journal of Orthopaedic Research 32 (12):1701-1707 (doi: 10.1002/jor.22725)

Glucosamine is an endogenous amino monosaccharide naturally occurring in the cartilage. We have recently shown that glucosamine sulfate promotes the biosynthesis of glycosaminoglycans in intervertebral disc cells. Here we assessed the role of glucosamine sulfate in the response of bovine nucleus pulposus cell monolayers to TNFα that constitutes an early signal of disc degeneration. TNFα was not found to affect nucleus pulposus cells' viability, while it resulted in a 2.5-fold increase of the intracellular ROS levels, a rapid transient phosphorylation of p38 MAPK and a ROS-dependent activation of JNKs. In addition, TNFα had a prominent inflammatory effect on nucleus pulposus cells by up-regulating MMP-3 expression that was reversed when inhibiting the kinase activity of p38 MAPK. Glucosamine sulfate also diminished the increased by TNFα MMP-3 mRNA levels, but this was unrelated to the p38 MAPK or ROS-mediated JNK activation. Even though the mode of action of glucosamine towards TNFα remains to be elucidated, to the best of our knowledge, this is the first report providing evidence for the protective role of glucosamine against this early mediator of disc degeneration that could support the potential usage of this molecule as a treatment for preventing disc degenerative disorders.

Conserved Noncoding Elements Follow Power-Law-Like Distributions in Several Genomes as a Result of Genome Dynamics (2014)

Dimitris Polychronopoulos, Diamantis Sellis, Yannis Almirantis

PLoS ONE 9(5): e95437 (doi:10.1371/journal.pone.0095437)

Conserved, ultraconserved and other classes of constrained elements (collectively referred as CNEs here), identified by comparative genomics in a wide variety of genomes, are non-randomly distributed across chromosomes. These elements are defined using various degrees of conservation between organisms and several thresholds of minimal length. We here investigate the chromosomal distribution of CNEs by studying the statistical properties of distances between consecutive CNEs. We find widespread power-law-like distributions, i.e. linearity in double logarithmic scale, in the inter-CNE distances, a feature which is connected with fractality and self-similarity. Given that CNEs are often found to be spatially associated with genes, especially with those that regulate developmental processes, we verify by appropriate gene masking that a powerlaw-like pattern emerges irrespectively of whether elements found close or inside genes are excluded or not. An evolutionary model is put forward for the understanding of these findings that includes *segmental or whole genome duplication* events and
eliminations
(
loss
) of most of the duplicated CNEs. Simulations reproduce the main features of the observed size distributions. Power-law-like patterns in the genomic distributions of CNEs are in accordance with current knowledge about their evolutionary history in several genomes.

A Study of Fractality and Long-Range Order in the Distribution of Transposable Elements in Eukaryotic Genomes Using the Scaling Properties of Block Entropy and Box-Counting (2014)

Labrini Athanasopoulou, Diamantis Sellis, Yannis Almirantis

Entropy 16: 1860-1882 (doi:10.3390/e16041860)

Repeats or Transposable Elements (TEs) are highly repeated sequence stretches, present in virtually all eukaryotic genomes. We explore the distribution of representative TEs from all major classes in entire chromosomes across various organisms. We employ two complementary approaches, the scaling of block entropy and box-counting. Both converge to the conclusion

that well-developed fractality is typical of small genomes while in large genomes it appears sporadically and in some cases is rudimentary. The human genome is particularly prone to develop this pattern, as TE chromosomal distributions therein are often highly clustered and inhomogeneous. Comparing with previous works, where occurrence of power-law-like size distributions in inter-repeat distances is studied, we conclude that fractality in entire chromosomes is a more stringent (thus less often encountered) condition. We have formulated a simple evolutionary scenario for the genomic dynamics of TEs, which may account for their fractal distribution in real genomes. The observed fractality and long-range properties of TE genomic distributions have probably contributed to the formation of the “fractal globule”, a model for the confined chromatin organization of the eukaryotic nucleus proposed on the basis of experimental evidence.

Nephrin, a transmembrane protein, is involved in pancreatic beta-cell survival signaling (2015)

Katerina Kapodistria, Effie-Photini Tsilibary, Panagiotis Politis, Petros Moustardas, Aristidis Charonis, Paraskevi Kitsiou

Molecular and Cellular Endocrinology 400: 112–128

(doi: 10.1016/j.mce.2014.11.003)

Nephrin, a cell surface signaling receptor, regulates podocyte function in health and disease. We study the role of nephrin in β-cell survival signaling. We report that in mouse islet β-cells and the mouse pancreatic beta-cell line (βTC-6 cells) nephrin is associated and partly co-localized with PI3-kinase. Incubation of cells with functional anti-nephrin antibodies induced nephrin clustering at the plasma membrane, nephrin phosphorylation and recruitment of PI3-kinase to nephrin thus resulting in increased PI3K-dependent Akt phosphorylation and augmented

phosphorylation/inhibition of pro-apoptotic Bad and FoxO. Nephrin silencing abolished Akt activation and increased susceptibility of cells to apoptosis. High glucose impaired nephrin signaling, increased nephrin internalization and up-regulated PKCα expression. Interestingly, a marked decrease in nephrin expression and phosphorylated Akt was observed in pancreatic islets of db/db lepr-/- diabetic mice. Our findings revealed that nephrin is involved in β-cell survival and suggest that glucose-induced changes in nephrin signaling may contribute to gradual pancreatic β-cell loss in type 2 diabetes.

Organotypic Cultures of Intervertebral Disc Cells: Responses to Growth Factors and Signaling Pathways Involved (2015)

Harris Pratsinis, Dimitris Kletsas

BioMed Research International Vol. 2015, *Article ID 427138*

(doi:10.1155/2015/427138)

Intervertebral disc (IVD) degeneration is strongly associated with low back pain, a major cause of disability worldwide. An in-depth understanding of IVD cell physiology is required for the design of novel regenerative therapies. Accordingly, aim of this work was the study of IVD cell responses to mitogenic growth factors in a three-dimensional (3D) organotypic milieu, comprising characteristic molecules of IVD's extracellular matrix. In particular, annulus fibrosus (AF) cells were cultured inside collagen type-I gels, while nucleus pulposus (NP) cells in chondroitin sulfate A (CSA) supplemented collagen gels, and the effects of Platelet-Derived Growth Factor (PDGF), basic Fibroblast Growth Factor (bFGF), and Insulin-Like Growth Factor-I (IGF-I) were assessed. All three growth factors stimulated DNA synthesis in both AF and NP 3D cell cultures, with potencies similar to those observed previously in monolayers. CSA supplementation inhibited basal DNA synthesis rates, without affecting the response to growth factors. ERK and Akt were found to be phosphorylated following growth factor stimulation. Blockade of these two signaling pathways using pharmacologic inhibitors significantly, though not completely, inhibited growth factor-induced DNA synthesis. The proposed culture systems may prove useful for further in vitro studies aiming at future interventions for IVD regeneration

Viral Small-RNA Analysis of *Bombyx mori* Larval Midgut during Persistent and Pathogenic Cytoplasmic Polyhedrosis Virus Infection
(2015)

Aris Zografidis, Filip Van Nieuwerburgh, Anna Kolliopoulou, Konstantinos Apostolou-Karampelis, Steven R. Head, Dieter Deforce, Guy Smagghe, Luc Swevers

Journal of Virology 89: 11473-11486 (doi:10.1128/JVI.01695-15)

The lepidopteran innate immune response against RNA viruses remains poorly understood, while in other insects several studies have highlighted an essential role for the exo-RNAi pathway in combating viral infection. Here, by using deep-sequencing technology for viral small-RNA (vsRNA) assessment, we provide evidence that exo-RNAi is operative in the silkworm *Bombyx mori* against both persistent and pathogenic infection of *B. mori* cytoplasmic polyhedrosis virus (BmCPV) which is characterized by a segmented double-stranded RNA (dsRNA) genome. Further, we show that Dicer-2 predominantly targets viral dsRNA and produces 20-nucleotide (nt) vsRNAs, whereas an additional pathway is responsive to viral mRNA derived from segment 10. Importantly, vsRNA distributions, which define specific hot and cold spot profiles for each viral segment, to a considerable degree overlap between Dicer-2-related (19 to 21 nt) and Dicer-2-unrelated vsRNAs, suggesting a common origin for these profiles. We found a degenerate motif significantly enriched at the cut sites of vsRNAs of various lengths which link an unknown RNase to the origins of vsRNAs biogenesis and distribution. Accordingly, the indicated RNase activity may be an important early factor for the host’s antiviral defense in Lepidoptera.

Ανακοινώσεις:

Οι ακόλουθες ανακοινώσεις έχουν προκύψει με την υποστήριξη του έργου "ΔΙΑΣ":

Zografidis A., A. Kolliopoulou, K. Iatrou, L. Swevers and V. Labropoulou: "The impact of PDV protein expression on the insect RNAi mechanism". The 9th International Workshop on MOLECULAR BIOLOGY AND GENETICS OF THE LEPIDOPTERA, 17-23 August, 2014,

Orthodox Academy of Crete, Kolympari, Crete, Greece.

Zarkadas C., D. Sellis and M. Vlassi “GROMITA-4.6: A Graphical User Interface to facilitate molecular simulations with GROMACS GPU-CPU versions 4.6.x.”. Current Trends in Structural Biology & 7th International Conference of the Hellenic Crystallographic Association, FORTH, 19-21 September 2014, Crete, Greece.

Zarkadas C. and M. Vlassi. “Molecular dynamics simulations of the human apolipoprotein E3”. 9th Conference of the Hellenic Society for Computational Biology and Bioinformatics (HSCBB14), 10-12 October 2014, Agricultural University of Athens, Greece.

Zografidis A., F. Van Nieuwerburgh, A. Kolliopoulou, K. Apostolou-Karampelis, S.R. Head, D. Deforce, G. Smagghe and L. Swevers: "Viral small analysis of Bombyxmori larval midgut during persistent and pathogenic cytoplasmic polyhedrosis virus infection". 2015, Viruses & Cells Gordon Research Conference, “From Molecular Mechanism to Pathogenesis and Prevention”, 21-26 June 2015, PGA Catalunya Business and Convention Centre, Girona, Spain.

Galeou A., and A. Prombona: "Chromatin remodeling and the *Phaseolus vulgaris* circadian clock: effect of TSA on the expression of core clock genes". 2015, 66
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Πανελλήνιο Συνέδριο Ελληνικής Εταιρείας Βιοχημείας και Μοριακής Βιολογίας, 11-13 Δεκεμβρίου 2015, Αθήνα.

Pratsinis H., and D. Kletsas: "Intervertebral disc cells in three-dimensional cultures: Proliferative response to growth factors and the underlying signaling pathways". 2015, 66ο Πανελλήνιο Συνέδριο Ελληνικής Εταιρείας Βιοχημείας και Μοριακής Βιολογίας, 11-13 Δεκεμβρίου 2015, Αθήνα.

Trohatou O., E.-P. Tsilibary, A.S. Charonis, E.A. Lianos, C. Iatrou and G. Drossopoulou: "Vitamin D3 ameliorates podocyte injury through the nephrin signaling pathway in isolated diabetic rat glomeruli". 2015, 66ο Πανελλήνιο Συνέδριο Ελληνικής Εταιρείας Βιοχημείας και Μοριακής Βιολογίας, 11-13 Δεκεμβρίου 2015, Αθήνα.

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Ευθυμίου Α., Λ. Ευθυμίου, Δ. Θεοφιλόπουλος, Ε. Τσιλιμάρη, Μ. Σαγνού, Μ. Νασοπούλου και Ε. Βαβουράκη: «Χρήση του αλλομοσχεύματος του ΕΚΕΦΕ «Δημόκριτος» στην αποκατάσταση οστικού κενού μετά την αφαίρεση κύστης», 8η Διημερίδας της Ελληνικής Εταιρείας Βιοϋλικών, 15-16 Νοεμβρίου 2013, Αθήνα.

Ξυδάκη Δ., Λ. Τσαλαβούτας-Ψαρράς, Ε. Βαβουράκη, Μ. Σαγνού και Ε. Φ. Τσιλιμπάρη: Παραγωγή και χαρακτηρισμός καινοτόμου υλικού οστικής αποκατάστασης βόειας προέλευσης: μελέτες τροποποιημένων σταδίων παραγωγής, 10η Επετειακή Εκδήλωση της Ελληνικής Εταιρείας Βιοϋλικών, 26 -28 Νοεμβρίου 2015, Αθήνα

Διπλώματα ευρεσιτεχνίας:

Στο πλαίσιο του έργου "ΔΙΑΣ" έχουν υποβληθεί αιτήσεις για τα εξής διπλώματα ευρεσιτεχνίας:

Pharmaceutical preparation of the N20 antibody recognizing the renin-dependent anti-apoptotic signaling in the pancreatic B-cells by promoting the survival of these last *by* Tsilimpari Foteini and Kitsiou Paraskevi (GR20130100425 20130719).

New Derivatives of 3,5-divinyl-pyrazole for medical applications *by* Kolotova Ekaterina Sergeevna, Shtil Alexander Albertovich, Novikov Fedor Nikolaevich, Chilov Germes Grigorievich, Stroganov Oleg Valentinovich, Stroilov Victor Sergeevich, Zeifman Alexey Alexandrovich, Titov Ilya Yurievich, Sagnou Marina and Alexiou Polyxeni (PCT/RU2015/000323).


Ευρωπαϊκή Ένωση
Ευρωπαϊκό Ταμείο
Περιφερειακής Ανάπτυξης
ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Υπουργείο Πολιτισμού, Παιδείας & Θρησκευμάτων
Γενική Γραμματεία Έρευνας & Τεχνολογίας
η περιφέρεια στο
Με τη συγχρηματοδότηση της Ελλάδας και της Ευρωπαϊκ
στο πλαίσιο του Ε.Π. Ανταγωνιστικότητα και Επιχειρηματικ