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Short CV in text – CURRENT RESEARCH INTERESTS

My research interests have been in the scientific areas of Biology of Cancer and Cell Death, towards exploitation of the interplay of proliferative with apoptotic/autophagic pathways for novel cancer therapeutics and their rational combinations. They are closely related to the scientific disciplines of the Institute of Biology, Medicinal Chemistry and Biotechnology.

Current studies in NHRF

The Research Group activities are focusing on the interplay between oncogenic and apoptotic signals and its exploitation towards uncovering sensitisation pathways to targeted cancer therapeutics and their rational combinations. The analysis of genetic and epigenetic events as well as global gene expression in physiological as compared to neoplastic cells. is the other focus of the lab.

a) Sensitisation to cancer therapeutic molecules and their rational combinations
Resistance mechanisms to BRAF inhibitors in BRAFV600E bearing colorectal cancer cells have been overcome by exploitation of BRAF associated autophagy. Rational combinatorial treatments of BRAF with autophagy inhibitors can overcome resistance of BRAFV600E colorectal cancer cells to BRAF inhibitors, and could be further tested in animal models and clinical studies (Goulielmaki et al., Oncotarget, 2016). Rational

combinatorial treatments of novel SMAC mimetics can cause synergistic cell death in cancer cells (Perimenis et al., BMC Cancer, 2016).

The interplay between oncogenic RAS with apoptotic signals induced by the cytokine TRAIL, a novel potent cancer therapeutic agent has been analysed. TRAIL induced apoptosis in mouse xenografts of primary colon tumour cells partially due to upregulation of DR5 (Oikonomou et al. Br. J. Cancer, 2007). Oncogenic forms of RAS sensitise human colon cells to TRAIL induced apoptosis by upregulating TRAIL receptors DR4 and DR5 through a MEK-dependent pathway (Drosopoulos et al. J. Biol. Chem. 2005, reviewed in: Oikonomou and Pintzas, Biofactors, 2013). Existence of KRAS and BRAF mutations in colorectal tumours is associated with DR overexpression, which indicates that these patients may potentially respond to TRAIL treatment (Oikonomou et al., Int J Cancer, 2009). Rational combination studies of TRAIL with small molecule inhibitors of activated kinase pathways have been performed. Interestingly, BRAF and PI3K inhibitors can synergise with TRAIL to sensitise tumour cells to apoptosis (Oikonomou et al., PLoS ONE, 2011). In addition, polyphenol quercetin has been shown to synergise with TRAIL on causing apoptotic death by inducing accumulation of TRAIL receptors in lipid rafts (Psahoulia et al., Mol. Cancer. Ther, 2007). The findings of an EU-funded consortium on the effect of kinase inhibitors on tumours and their combinatorial effect with TRAIL have been described (Pintzas et al., Cancer Biology and Therapy, 2012)

One other goal was the development of exploitable in vitro chemoprevention cell systems, based on the home made inducible oncogene expression systems In the same study, we have shown that the polyphenol quercetin induced autophagy in Ha-Ras transformed cells (Psahoulia et al. Carcinogenesis, 2007).

Currently, novel specific potential PI3K inhibitors are being screened in a drug discovery project in the frame of the POM programme. Also, new efficient anti-cancer rational combinations of TRAIL with apoptosis inhibitors are being developed in the frame of THERA-CAN programme. In parallel, other novel anti-tumour kinase inhibitors will be developed shortly in the frame of STHENOS project.

b) Oncogenic pathway analysis in human colorectal carcinogenesis

Analysis of gene expression profile during tumour progression in colon cancer cell lines has been performed (Roberts et al. Int. J. Cancer, 2006). Candidate genes to be involved in colon tumour progression have been identified by microarray analysis and their role is currently being validated. BRAFV600E target gene analysis (Joyce et al. Current Cancer Drug Targets, 2012) has being performed using the Illumina microarray platform. On the other hand, the comparative effect of KRASV12 vs BRAFV600E has being analysed (Oikonomou, Makrodouli, et al., Neoplasia, 2009; Makrodouli et al., Mol.

Cancer, 2012). Currently, the differential effects of PIK3CA mutant oncoproteins are being analysed, in the frame of POM project.

c) Genetic-epigenetic mechanisms of Epithelial-Mesenchymal Transition (EMT) in cancer
We have established a cell model of highly metastatic Epithelial to Mesenchymal Transition (EMT) phenotype in colon adenoma cells by Ha-RASV12 oncogene. Whole genome analysis has been performed and a signature of EMT has been revealed (Joyce et al., Clin. Exp. Metastasis, 2009). The role of EMT in resistance of cancer cells to therapies has been also reviewed (Voulgari et al., BBA Reviews on Cancer, 2009). Regulation of EMT associated genes by AP-1 and TFIID transcription factors has been shown (Andreolas et al., Int. J. Cancer, 2008, Kalogeropoulou et al., Mol. Cancer Res., 2010). On the other hand, selected histone modifications and modifiers associated with EMT have been identified (Mazon-Pelaez et al., Int J Biochem Cell Biol., 2010) and an important role of EZH2 histone methyltransferase in regulating EMT and anoikis has been revealed (Ferraro et al., Int J Biochem Cell Biol., 2013). A genome-wide ChIP-sequencing approach is currently in process for identification of global and novel EZH2 targets associated with tumour cell properties and EMT.

Previous studies in NHRF
d) Pathways and transcription factors associated with Ras signalling in mouse skin carcinogenesis /early Ras signalling studied by cell systems of inducible Ras)
Cells were derived from mice initiated by the chemical carcinogen DMBA and promoted by TPA. We found an important role of AP-1 in tumor progression of mouse epidermis, and have stressed the role of c-Jun, Fra-1 and ATF-2 factors in the process (Zoumpourlis et al. Oncogene, 2000; Papassava et al. Cancer Res. 2004). In parallel studies, an important role of serum response factor (SRF) during the epithelial to mesenchymal transition during tumor progression of mouse epidermis has been shown. (Psichari et al. J. Biol. Chem. 2002). On the other hand, an important role of TAFII55 in this process has been revealed on mechanisms of transcriptional regulation by the c-Jun transcription factor, (Munz et al. J. Biol. Chem. 2003).
In studies using inducible Ras systems, we had observed a novel rapid and transient mechanism of ERK1/2 activation and nuclear translocation dependent on ras that is phosphatase dependent (Plows et al. Biochem J., 2002). Macroarray analysis of early vs late Ras target genes has been performed (Moumtzi et al., Cancer Invest. 2010).

Studies prior to NHRF appointment (1985-1995)

-Activation of Ets oncogene family members by expression of other oncogenes and regulation of their DNA-binding and trans-activation activity on ets responsive genes (e.g. metalloproteases) (LGME-IGBMC, Strasbourg, France)
-DNA-binding and trans-activation properties of Jun proteins and role of activating mutations in v-Jun (Cancer Research UK Beatson Institute, Glasgow, UK)
-Regulation of human Ha-ras 1 oncogene by viral and cellular oncogenes. Oncogene expression in human neoplasias. (Hellenic Pasteur Institute, Athens, Greece).

EDUCATION AND QUALIFICATIONS

1992–1995: Senior Fellow, Institute of Biological Chemistry, LGME-CNRS, (currently IGBMC), School of Medicine, University of Strasbourg, France.
1989-1992: Post-doctoral Research Fellow, CRC (currently CRUK) Beatson Institute for Cancer Research, Glasgow, U.K.
1985-1989: PhD in Biochemistry- Molecular Biology, Dept. of Biology, University of Athens
1976-1981: BSc in Chemistry, Dept. of Chemistry, University of Athens

APPOINTMENTS

2020- : Director, Institute of Chemical Biology, National Hellenic Research Foundation, Athens
2020- : Vice President of NHRF's Board of Directors

2012-2019: Director, Institute of Biology, Medicinal Chemistry and Biotechnology (IBMCB), National Hellenic Research Foundation, Athens

2011- 2012: Director, Institute of Biological Research and Biotechnology (IBRB), National Hellenic Research Foundation, Athens

2002- : Research Director, Head of Signal Mediated Gene Expression Laboratory, Institute of Biological Research and Biotechnology, National Hellenic Research Foundation, Athens

1996- 2002: Research Associate Professor, Lab Head, Institute of Biological Research and Biotechnology, National Hellenic Research Foundation, Athens
1993-1996: Res. Assistant Prof., Inst. Biol. Res. Biotech., Nat. Hell. Res. Found.

1992–1995: Senior Fellow, Institute of Biological Chemistry, LGME-CNRS, (currently IGBMC), School of Medicine, University of Strasbourg, France.

1989-1992: Post-doctoral Research Fellow, CRC (currently CRUK) Beatson Institute for Cancer Research, Glasgow, U.K.

1985-1989: Functional Scientist, Dept. of Virology, Hellenic Pasteur Institute, Athens, Greece.

HONORS/AWARDS/DISTINCTIONS

1990-1991: Long-term EMBO (European Molecular Biology Organisation) Post-doctoral fellowship
1992-1993: Post-doctoral fellowship by the French Organisation against Cancer (ARC)
1993-1994: EU Marie Curie Post-doctoral fellowship (HCM)
1996: Fellowship from the Royal Society of U.K.

TEACHING AND TRAINING EXPERIENCE

2016-2022: Teaching In the frame of Master Courses co-organised by ICB/NHRF with the University of Thessaly ("Bioenterpreneurship") and with the University of Crete ("Oncology: from Oncogenesis to Therapy")
2003-2007: Visiting Professor on "Molecular Oncogenesis" at the Department of Molecular Biology and Genetics, Dimokriteio University, Greece
2004-2019: Teaching by Special Seminars on Biochemistry, Molecular Biology and Oncology in the frame of several post-graduate (Master) courses of Schools of Medicine, Biology, Athens University and of Oncology-Pathology Societies
1996-2015: Supervision of 16 (12 EU supported) post-doctoral fellows. Supervision of 10PhD students and 11 diploma students
1992-1995: Supervision of diploma students of Biotechnology School, Strasbourg University (ESBS-ULP), in the field of Molecular Biology of Cancer Cell

MEMBER OF SOCIETIES

-EMBO (European Molecular Biology Organisation) Fellows Network
- EACR (European Association for Cancer Research)
- EORTC (European Organisation for Research and Treatment of Cancer - PAMM group)
- Marie Curie Fellowship Association
- Greek Society of Biochemistry and Molecular Biology (EEBMB)
- Association of Greek Chemists (EEX)

RESEARCH FUNDING

Funding for the Institute:
1. 2018-2021: HNPM "Hellenic Network for Precision Medicine", a national network for precision oncology. Funding for the Institute: 250 kEuros

2. 2017-2020: «STHENOS-b", Targeted therapeutic approaches against degenerative diseases with special focus on cancer and ageing-optimisation of the targeted bioactive molecules. National Strategic Reference Framework. ""Competitiveness, entrepreneurship and innovation. Funding for the Institute: 790 kEuros (co-ordinator)

3. 2013-2015:"STHENOS", Targeted therapeutic approaches against degenerative diseases, with special focus on cancer and ageing. National Strategic Reference Framework, Action "Developmental Projects of Research Organisations- Kripis". Funding for the Institute: 1500 kEuros (co-ordinator)

TOTAL budget for the lab from competitive grants: > 4,000 kEuros
Selected grants:
1. 2016-2020: "TRANSAUTOPHAGY (COST Action CA15138)", a European Network for Multidisciplinary Research on Autophagy with emphasis on Translation of knowledge to applications.
2. 2012-2015: "THERACAN", Exploiting molecular pathways of apoptotic cell death for the rational design of therapeutic strategies for colon cancer. National Strategic Reference Framework, Action "Co-operation II". Funding for the lab: 200 kEuros
3. 2010-2015: "POM", PIK3CA Oncogenic Mutations in Breast and Colon Cancers: Development of Targeted Anticancer Drugs and Diagnostics. National Strategic Reference Framework, Action "Co-operation". Funding for the lab: 130 kEuros
4. 2009-2012: "EpiDiaCan", Development of sensitive methodologies for exploitation of early epigenetic marker diagnosis in major types of cancer. 7FP EU- Cooperation" – Theme "Health". Total funding 2.843 kEuros, for the lab 504 kEuros (co-ordinator)
5. 2012-2014: "CancerStem-Less", Establishment and characterization of cancer stem cells from colorectal tumours, towards their sensitisation to modern therapeutic pharmacological strategies. National Strategic Reference Framework, Action "Supporting Postdoctoral Researchers" Funding: 150 kEuros
6. 2006-2010: "Oncodeath" Resistant determinants and sensitisation of solid tumor cells to death receptor related therapies: combination of TRAIL with other therapeutic molecules. EU-Combating Cancer Programme. Total funding 2.345 kEuros , for the lab: 589 kEuros (co-ordinator)
7. 2006-2009: Functional oncogenomics: a powerful tool towards diagnosis and treatment of human colorectal cancer. Greek Research Network PENED. Funding 235 kEuros (co-ordinator)
8. 2004-2008: "Macromolecular assemblies involved in regulated gene expression: structural/functional characteristics, interplay and novel functions", EU Transfer of Knowledge (TOK) Research Programme, funding for the lab: 250 kEuros
9. 2004-2008: "TAF-Chromatin" EU Research Training Network (RTN) Programme. Participation of 7 labs from 6 countries. Funding for the lab: 370 kEuros.
10. 2004-2007: "Transcription complex dynamics controlling specific gene expression programs" EU- Fundamental Genomics Programme. Funding for the lab: 450 kEuros

11. 2004-2006: "Molecular mechanisms of tumour invasion and metastasis", Research cooperation programme between Greece and USA. Funding for the lab: 60 kEuros
12. 2003-2006: "In vivo and in silico analysis of gene expression induced by Ras oncogene in cancer", Greek Research Network PENED. Funding 140 kEuros (co-ordinator)
13. 2002-2005: "Regulation of transcription and mRNA processing by oncogenic signals", EU-IHP Research Programme. Funding: 228 kEuros (co-ordinator)
14. 1996-2001: "The AP-1 transcription factor", EU-TMR Research Network. Participation of 7 labs from 6 EU countries. Funding for the lab: 220 kEuros.
15.1996-2000: "Cell signalling in development and disease", EU-TMR Research Network. Participation of 9 labs from 7 EU countries. Funding for the lab: 55 kEuros

EXPERIENCE ON MANAGEMENT

2020-: Director, Institute of Chemical Biology (ICB), National Hellenic Research Foundation, Athens
2014-2019: Director, Institute of Biology, Medicinal Chemistry and Biotechnology (IBMCB), National Hellenic Research Foundation, Athens
2012-2014: Acting Director, Institute of Biology, Medicinal Chemistry and Biotechnology (IBMCB), National Hellenic Research Foundation, Athens
2011- 2012: Director, Institute of Biological Research and Biotechnology, National Hellenic Research Foundation, Athens
1996- : Head of Signal Mediated Gene Expression Group, National Hellenic Research Foundation, Athens

AS INSTITUTE DIRECTOR: SELECTED INITIATIVES- EVENTS

- Active participation as IBRB Director towards merging with IOPC to form the current Institute IBMCB (Institute of Biology, Medicinal Chemistry and Biotechnology) (2011-2012)
- Co-ordinated the IBMCB initiative on targeted therapeutics, which was accepted for funding with 1,5 million Euros: "STHENOS", Targeted therapeutic approaches against degenerative diseases, with special focus on cancer and ageing. National Strategic Reference Framework, Action, "Developmental Projects of Research Organisations- Kripis". Funding for the Institute: 1500 kEuros (co-ordinator) (2012)
- Active role, as the first IBMCB Director, for a functional start of the new Institute in NHRF (2012), by:
    a. Organisation of two-day workshop for Researchers of IBMCB (May 2012)

b. Co-ordination of the initial procedures towards a new structure of IBMCB, for exploitation of the existing multidisciplinary expertise of IBMCB Researchers on biology and chemistry in the areas of drug discovery, health and biotechnology-green chemistry

- Active support for IBMCB participation and membership in National and EU Infrastructures on Translational Research (EATRIS-GR), Biobanking (BBMRI-GR) and Structural biology (INSTRUCT). Supported IBMCB membership in the HELLENIC STEM CELL NETWORK Initiative
- Represented the Institute in meetings concerning research policy and thematic working groups on Health and Therapeutics

SCIENTIFIC AND FINANCIAL MANAGEMENT OF RESEARCH PROJECTS:

Scientific and financial management for 3 large European and 3 Greek research funded programmes of total 30 collaborating organizations and of total budget 5,8 million Eur

INTERNATIONAL COLLABORATIONS

- Cooperation with Czech Academy of Sciences, Prague, Czech Republic on mechanisms of anticancer properties of TRAIL and rational combinations with targeted drugs
- Cooperative studies with IGBMC, Strasbourg, France on the role of components of basal transcriptional machinery in tumour progression
- Cooperation with Medical School, Turin University and Illumina Inc. on microarray analysis of oncogenic pathways
- Collaboration with UCSF Cancer Center, San Francisco, USA on mechanisms of multistage carcinogenesis

CONFERENCES CHAIRED/ORGANISED

2008: 33rd FEBS-IUBMB Congress "Biochemistry of Cell Regulation", Athens, Greece
2008: FEBS Workshop "Lipids as regulators of cell function" Island of Spetses, Greece
2005: FEBS Advanced Study Institute on "Chemical Probes in Biology", Island of Spetses, Greece
2003: EMBO/FEBS advanced lecture course "Molecular Mechanisms in Signal Transduction", Island of Spetses, Greece
2003: 54th Conference of the Greek Society of Biochemistry and Molecular Biology, Athens, Greece
2002: NATO/FEBS Advanced Study Institute on "Chemical Probes in Biology", Island of Spetses, Greece
2001: FEBS/EMBO Advanced lecture Course on "Molecular Mechanisms in Signal Transduction", Island of Spetses, Greece

2001: 52nd Conference of the Greek Society of Biochemistry and Molecular Biology, Athens, Greece
2000: EU-FORTH-MCFA Conference on "Investing in Europe's Human Research Potential", Iraklio, Crete, Greece
1999: NATO/FEBS Advanced Study Institute on "Molecular Mechanisms of Signal Transduction", Island of Spetses, Greece
1999: 50th Conference of the Greek Society of Biochemistry and Molecular Biology, Athens, Greece
1988: NATO Advanced Research Workshop "Ras oncogenes",Vouliagmeni, Greece
1987: 35th Conference of European Tissue Culture Society, Athens, Greece

INVITED SPEAKER (SELECTED INVITATIONS)
EMBO Cancer Genomics Conference, Heidelberg, Germany
EORTC Meeting, Brussels, Belgium
EU EPITRON Meeting, Athens, Greece
European Cell Death Organisation Meeting, Ghent, Belgium
Institute for Cancer Research, London, U.K.
Cancer Research UK Beatson Institute for Cancer Research, Glasgow, U.K.
Institute of Molecular Biology and Biochemistry, FORTH, Heraklion, Greece
Karolinska Institute, Department of Biosciences and Nutrition, Stockholm, Sweden
UCSF - Cancer Research Institute, San Francisco, USA
IGBMC, Strasbourg, France
Biomedical Research Foundation, Athens Academy of Sciences, Greece
Demokritus Research Center, Athens, Greece
"Cell communication & Signalling", Workshop of the Hellenic Society of Biochemistry and Molecular Biology, Thessaloniki, Greece
FEBS Workshop, "Lipids as regulators of cell function", Island of Spetses, Greece
45th Congress of the European Society of Toxicology, Rhodes, Greece
IRCC, Medical School, University of Torino, Italy
7th INTERNATIONAL CONFERENCE OF ANTICANCER RESEARCH, Corfu, Greece
3rd Conference on Experimental and Translational Oncology, Kranjska gora, Slovenia
European Association for Cancer Research Conference, Granada, Spain
The Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus

Service/Consulting
Member of Advisory Board of EU Network on Cancer Genomics
Former Member of the National Assembly of Research and Technology (2003-2004)
National Expert of 7 FP ERC IDEAS Programme (2006-2009)

DUTIES AS REVIEWER/REFEREE

- For funding research organizations (selected): European Union (7th and 6th FP); Cancer Research UK (CRUK); Association for International Cancer Research (AICR); International Association for Cancer Research (UICC); National Research Funding Agencies of (selected) :The Netherlands, Switzerland, Singapore, Austria, Republic of Ireland, Czech Republic, Cyprus and funding research organizations of Greece (GSRT and other)
- For Scientific Journals (selected): Cell Death and Differentiation; Cancer Research; Gastroenterology; American Journal Pathology; Molecular and Cellular Biology, British Journal of Cancer; Carcinogenesis; Clinical Cancer Research; Apoptosis; Genome Research; International Journal Cancer; Molecular Cancer Therapeutics

SIGNAL MEDIATED GENE EXPRESSION (recent) GROUP MEMBERS

Vivian Kosmidou, MSc (Scientific Technical Personnel)
Eleni Poulou-Sidiropoulou, MSc (Scientific Personnel) (2022-)
Camelia Sidahmet, BSc (MSc student) (2020-2022)
Ioanna Giopanou, PhD (Postdoctoral Researcher) (2019-2020)
Marianna Kalioraki, MSc (Scientific Personnel) (2020-2021)
Salomi Skarmalioraki, MSc (Scientific Personnel) (2020-2021)
Kassandra Koumaki, MSc (PhD student) (2018-2020)
Eirini Kalogerakou (undergraduate student) (2017-2018)
Salomi Skarmalioraki (undergraduate-MSc student) (2018-2019)
Fani Pahitsa, BSc (MSc student) (2019-2020)

Distinctions-Prizes

Many invitations for seminars in Scientific Meetings and in University Departments-Research Institutes. Distinctions for Lab members in submitted presentations in scientific conferences.

Review of Prof. J. Taipale, Karolinska Institute, member of the external advisory group NHRF/IBRB, October 2009:

"Signal-mediated Gene Expression Programme, A. Pintzas: The signal-mediated gene-expression programme is one of the leading laboratories of the institute, and is currently highly active, and the laboratory's recent publication record is best of all the groups. I recommend additional funding for this group".

ARTICLES IN INTERNATIONAL PEER-REVIEWED SCIENTIFIC JOURNALS

63. Koumaki K., Skarmalioraki, S., Goulielmaki, M., Zoumpourlis, V., **Pintzas A.,** Souliotis, V.L. (2022). Antitumorigenic effect of combination treatment with BRAFi and cisplatin in colorectal cancer *in vitro* and *in vivo.* Submitted.

62. Koumaki K., Kontogianni, G., Kosmidou, V., Pachitsa, F., Kritsi, E., Zervou, M., Chatziioannou, A., Souliotis, V. L., Papadodima, O. and **Pintzas, A.*** (2021). BRAF paradox breakers PLX8394, PLX7904 are more effective against BRAFV600E CRC cells compared with the BRAF inhibitor PLX4720 and shown by detailed pathway analysis. *BBA Molecular Basis of Disease* 1867, 166061.

61. Kosmidou, V., Vlassi, M., Anagiotos, K., Raftopoulou, S., Kalogerakou, E., Aggeli, C., Choreftaki, T., Zografos, G., **Pintzas, A.*** (2021). Noxa upregulation and a 5-gene (Noxa, Mcl1, cIAP1, cIAP2, DR5) mRNA expression profile may provide an apoptotic biomarker panel with very significant differential diagnostic potential in colorectal cancer. *European Journal of Clinical Investigation* 51: e13353.

60. Giopanou, I*., **Pintzas, A.*** (2020). RAS and BRAF in the foreground for Non-Small Cell Lung Cancer and Colorectal Cancer: similarities and main differences for prognosis and therapies. *Critical Reviews in Oncology / Hematology*, 146, 102859.

59. Goulielmaki, M. Assimomytis, N., Rozanc, J., Taki, E., Christodoulou, I., Alexopoulos, L., Zoumpourlis, V., **Pintzas, A.,** Papahatjis, D. (2019). DPS-2: A novel dual MEK/ERK and PI3K/AKT pathway inhibitor with powerful ex vivo and in vivo anti-cancer properties. *Translational Oncology* 12: 932-950.

58. Vlachavas, E., Pilalis, E., Papadodima, O., Koczan, D., Willis, S., Klippel, S., Cheng, C., Pan, L., Sachpekidis, C., **Pintzas, A.,** Gregoriou, V., Dimitrakopoulou-Strauss, A., and Chatziioannou, A. (2019). Radiogenomic analysis of F-18-Fluorodeoxyglucose Positron Emission Tomography and gene expression data elucidates the epidemiological complexity of colorectal cancer landscape. *Computational and Structural Biotechnology Journal*.17:177-185.

57. Skaltsas, T., Goulielmaki, M., **Pintzas, A.,** Pispas, S., and Tagmatarchis, N. (2017). Carbon quantum dots/block copolymer ensembles for metal-ion sensing and bioimaging. *Journal of Materials Chemistry B.* 5, 5397 – 5402.

56. Theochari, I., Goulielmaki, M., Danino, D., Papadimitriou, V., **Pintzas, A.** and Xenakis, A. (2017). Drug nanocarriers for cancer chemotherapy based on microemulsions: the case of Vemurafenib analog PLX4720. *Colloids and Surfaces B*. 154, 350–356.

55. Devetzi, M., Kosmidou, V., Vlassi, M., Perysinakis, I., Aggeli, C., Zografos G.N., and **Pintzas A.*** (2016). Death receptor 5 (DR5) and a 5-gene apoptotic biomarker panel with significant differential diagnostic potential in colorectal cancer. *Sci. Rep*. 6:36532.

54. Goulielmaki, M., Koustas, E. Moisidou, E., Vlassi, M., Sasazuki, T., Shirasawa, S., Zografos, G., Oikonomou, E., and **Pintzas A.*** (2016). BRAF associated autophagy exploitation: BRAF and autophagy inhibitors synergise to efficiently overcome resistance of BRAF mutant colorectal cancer cells. *Oncotarget*. 7, 9188-9221.

53. Perimenis, P., Galaris, A., Voulgari, A., Prassa, M. and **Pintzas, A.*** (2016). IAP antagonists Birinapant and AT-406 efficiently synergise with either TRAIL, BRAF, or BCL-2 inhibitors to sensitise BRAFV600E colorectal tumour cells to apoptosis. *BMC Cancer* 16, 624.

52. Oikonomou, E., Koustas, E., Goulielmaki, M. and **Pintzas, A.*** (2014). BRAF vs RAS Oncogenes: Are Mutations of the Same Pathway Equal? Differential Signalling and Therapeutic Implications. *Oncotarget* 5, 11752-11777.

51. Ferraro, A., Boni T. and **Pintzas, A.*** (2014). EZH2 regulates cofilin activity and colon cancer cell migration by targeting ITGA2 gene. *PLoS ONE.* 9, e115276.

50. Kosmidou, V., Oikonomou, E., Vlassi, M., Avlonitis, S., Katseli, A., Tsipras, I., Mourtzoukou, D., Kontogeorgos, G., Zografos, G. and **Pintzas, A.*** (2014). Tumor heterogeneity revealed by *KRAS, BRAF* and *PIK3CA* pyrosequencing: *KRAS* and PIK3CA intratumor mutation profile differences and their therapeutic implications. *Human Mutation* 35, 329-340.

49. Ferraro, A., Kontos, C., Boni, T., Bantounas, I., Siakouli, D., Kosmidou, V., Vlassi, M., Spyridakis, Y., Tsipras, I., Zografos, G., and **Pintzas, A.*** (2014). Epigenetic regulation of miR-21 in colorectal cancer: ITGB4 as a novel miR-21 target and a three-gene network (miR-21-ITGB4-PCDC4) as predictor of metastatic tumor potential. *Epigenetics* 9, 129-141.

48. Ferraro, A., Mourtzoukou, D., Kosmidou, V., Avlonitis, S., Kontogeorgos, G., Zografos, G., and **Pintzas, A.*** (2013). EZH2 is regulated by ERK/AKT and targets Integrin α2 gene to control Epithelial-Mesenchymal Transition and anoikis in colon cancer cells. *Int J Biochem Cell Biol*, 45, 243-254.

47. Oikonomou E. and **Pintzas, A.*** (2013). The TRAIL of Oncogenes to Apoptosis. *BioFactors* 39, 343-354.

46. Joyce, T., Oikonomou, E., Kosmidou, V., Makrodouli, E., Bantounas, I., Avlonitis, S., Zografos, G., and **Pintzas A.*** (2012). A molecular signature for oncogenic BRAF in human colon cancer cells is revealed by microarray analysis. *Current Cancer Drug Targets* 12, 873-898.

45. **Pintzas, A.*,** Zhivotovsky, B., Workman, P., Clarke, P.A., Linardopoulos, S., Martinou, J-C., Lacal, JC, Robine, S., Nasioulas, G. and Andera, L. (2012). Sensitisation of (colon) cancer cells to death receptor related therapies: a report from the FP6-ONCODEATH research consortium. *Cancer Biology and Therapy* 13, 507 – 515.

44. Oikonomou E., Koc M., Sourkova, V., Andera, L., and **Pintzas A.*** (2011). Selective BRAFV600 inhibitor PLX4720, requires TRAIL assistance to overcome oncogenic PIK3CA resistance. *PLoS ONE*. 6, e21632,

43. Makrodouli, E., Oikonomou, E., Koc, M., Andera, L., Sasazuki, T., Shirasawa, S., and **Pintzas,** A.* (2011). BRAF and RAS oncogenes regulate Rho GTPase pathways to induce migration and invasion properties in human colon cancer cells: a comparative study. *Mol. Cancer* 10, 118.

42. Kalogeropoulou M., Voulgari A., Kostourou, V., Sandaltzopoulos, R., Dikstein, R., Davidson, I., Tora, L. and **Pintzas, A.*** (2010). TAF4b and Jun/AP-1 collaborate to regulate expression of Integrin α6 and cancer cell migration properties. *Mol. Cancer Res.* 8, 554-568.

41. Kerr, N., **Pintzas, A.,** Holmes, F., Hobson, S.-A., Pope, R., Wallace, M., Wasylyk, C., Wasylyk, B. and D. Wynick. (2010). Complexity in the expression of ELK transcription factors: Novel isoforms, antisense transcripts and upregulation by nerve damage. *Mol. Cell Neurosci.* 44. 165–177.

40. Mazón Peláez, I., Kalogeropoulou, M., Ferraro, A., Voulgari, A., Pankotai, T., Boros, I., and **Pintzas, A.*** (2010). Oncogenic RAS alters the global and gene specific Histone modification pattern during Epithelial-Mesenchymal Transition in colorectal carcinoma cells. *Int. J. Biochem. Cell Biol.* 42, 911–920.

39. Moumtzi, S., Roberts, M.L., Joyce, T., Euagelidou, M., Probert, L., Frillingos, S., Fotsis, T., and **Pintzas, A.*** (2010). Gene expression profile associated with oncogenic RAS-induced senescence, cell death and transforming properties in human cells. *Cancer Investigation* 28, 563-587.

38. Oikonomou E., Makrodouli E., Evagelidou, M., Joyce T., Probert, L. and **Pintzas A.*** (2009). BRAFV600E efficient transformation and induction of MSI versus KRASG12V induction of senescence markers in human colon cancer cells. *Neoplasia* 11, 1116-1131.

37. Joyce, T., Cantarella, D., Isella, C., Medico, E. and **Pintzas A.*** (2009). A molecular signature for Epithelial to Mesenchymal transition in a human colon cancer cell system is revealed by large-scale microarray analysis. *Clin Exp Metastasis* 26,569–587.

36. Oikonomou, E., Kosmidou, V., Katseli, A., Kothonidis, K., Mourtzoukou, D., Kontogeorgos, G., Andera, L., Zografos, G., and **Pintzas, A.*** (2009). TRAIL Receptor Upregulation Correlates to KRAS/ BRAF Mutations in Human Colon Cancer Tumours and Respective Normal Tissue. *Int. J. Cancer* 125, 2127-2135.

35. Voulgari A. and **Pintzas, A.*** (2009). Epithelial-Mesenchymal Transition in cancer metastasis: mechanisms, markers and strategies to overcome drug resistance in the clinic. *BBA Reviews on Cancer* 1796, 75-90. I.F.: 10.7. cited: 581 *(Web of Science Highly cited paper: As of September/October 2015, this highly cited paper received enough citations to place it in the top 1% of its academic field based on a highly cited threshold for the field and publication year). (2nd most cited Journal's article published 2008-)*

34. Voulgari, A., Voskou, S., Tora, L., Davidson, I. Sasazuki T., Shirasawa, S., and **Pintzas, A.*** (2008). TAF12 is important for Ras-induced transformation properties of colorectal cancer cells. *Mol. Cancer Res.* 6, 1071-1083.

33. Andreolas C., Kalogeropoulou, M., Voulgari, A. and **Pintzas, A.*** (2008). Fra-1 regulates vimentin during Ha-RAS-induced epithelial mesenchymal transition in human colon carcinoma cells. *Int. J. Cancer* 122, 1745–1756.

32. Fostira F, Apessos A, Oikonomou E, Kouklis P, Baratsis S, Manifikos G, Andera L, Yannoukakos D, **Pintzas A,** Nasioulas G. (2008). Culture of primary epithelial adenoma cells from familial adenomatous polyposis patients. *Anticancer Res.* 28, 843-846.

31. Psahoulia, F. H., Drosopoulos K. G., Doubravska, L., Andera, L. and **Pintzas, A.*** (2007). Quercetin enhances TRAIL-mediated apoptosis in colon cancer cells by inducing the accumulation of death receptors in lipid rafts. *Mol. Cancer. Ther* 6, 2591-2599.

30. Oikonomou, E., Kothonidis, K., Taoufik, E., Probert, L., Zografos, G., Nasioulas, G., Andera, L., and **Pintzas, A*.** (2007). Newly Established Tumourigenic Primary Human Colon Cancer Cell Lines are Sensitive to TRAIL Induced Apoptosis in vitro and in vivo. *Br. J. Cancer* 97, 73 – 84.

29. Joyce T. and **Pintzas, A.*** (2007) Microarray analysis to reveal genes involved in colon carcinogenesis. *Exp Opin Pharmacotherapy* 8, 895-900. (Review).

28. Psahoulia, F.H., Moumtzi, S., Roberts, M.L., Sasazuki T., Shirasawa S., and **Pintzas, A.*** (2007). Quercetin mediates preferential degradation of oncogenic Ras and causes autophagy in Ha-RAS-transformed human colon cells. *Carcinogenesis* 28, 1021-1031.

27. Drosopoulos, K. and **Pintzas, A.*** (2007). Multifaceted targeting in cancer: the recent death players meet the usual oncogene suspects. *Exp Opin Ther. Targets* 11, 641-659 (Review).

26. Oikonomou, E. and **Pintzas, A.*** (2006). Cancer Genetics of Sporadic Colorectal Cancer: BRAF and PI3KCA Mutations, their Impact on Signalling and Novel Targeted Therapies. *Anticancer Res.* 26, 1077-1084 (Review).

25. Roberts, M., Drosopoulos, K., Vasileiou, G., Stricker, M., Taoufik E., Maercker, C., Guialis, A., Alexis, MN. and **Pintzas, A.*** (2006). Microarray analysis of the differential transformation mediated by kirsten and harvey ras oncogenes in a human colon adenocarcinoma cell line. *Int. J. Cancer* 118, 616–627.

24. Drosopoulos, K. Roberts, M., Cermak, L., Sasazuki , T., Shirasawa, S., Andera L. and **Pintzas, A.*** (2005). Oncogenic Ras transformation sensitizes human colon cancer cells to TRAIL induced apoptosis by upregulating DR4 and DR5 receptors through a MEK dependent pathway. *J. Biol. Chem.* 280, 22856-22867.

23. Munz, C., Psichari, E., Mandilis, D., Lavigne, A.-C., Spiliotaki, M., Oehler, T., Davidson, I., Tora, L., Angel, P. and **Pintzas, A.*** (2003). TAF7 (TAFII55) plays a role in the transcription activation by c-Jun. *J. Biol. Chem.* 278, 21510-21516.

22. Psichari, E., Balmain, A., Plows, D. Zoumpourlis, V., and **Pintzas, A.*** (2002). High activity of serum response factor in the mesenchymal transition of epithelial tumor cells is regulated by RhoA signaling. *J. Biol. Chem.* 277, 29490-29495.

21. Plows, D., Briassouli, P., Owen, C., Zoumpourlis, V., Garrett, M. and **Pintzas, A.*** (2002). Ecdysone-inducible expression of oncogenic Ha-Ras in NIH3T3 cells leads to transient nuclear localisation of activated ERK regulated by MKP-1 phosphatase. *Biochem J.* 362, 305-315.

20. Cermak, L., Simova, S., **Pintzas, A.,** Horejsi, V. and Andera, L. (2002). Molecular mechanisms involved in CD43-mediated apoptosis of TF-1 cells: roles of transcription, Daxx expression and adhesion molecules. *J. Biol. Chem*. 277, 7955-7961.

19. Zoumpourlis, V.K., **Pintzas, A**., Papassava, P., Solakidi, S., Papaevangeliou, D. (2002). Biological and chemical approach of the inhibition of signaling cascades in mouse skin carcinogenesis. *Review of Clinical Pharmacology and Pharmacokinetics,* 16, 1,111.

18. Papathoma, A., Zoumpourlis, V., Balmain, A. and **Pintzas A.*** (2001). Role of matrix metalloproteinase-9 in progression of mouse skin carcinogenesis. *Mol. Carcinogenesis* 31, 74-82.

17. Zoumpourlis, V., Papassava, P., **Pintzas, A.,** Moutsatsou, P. and Katsanakis, K. (2001). AP-1 transcription factor and steroid hormone receptors in multistage mouse skin carcinogenesis. *Rev. Clin. Pharmacol. Pharmacokin.,* 15, 123-128.

16. Zoumpourlis, V., Papassava, P., Linardopoulos, S., Gillespie, D., Balmain, A. and **Pintzas, A.*** (2000). High levels of phosphorylated c-Jun, Fra-1, Fra-2 and ATF-2 proteins correlate with malignant phenotypes in the multistage mouse skin carcinogenesis model. *Oncogene* 19, 4011-4021.

15. Papathoma, A., Petraki, C., Grigorakis, A., Papakonstantinou, H., Karavana, V. Stefanakis, S., Sotsiou, F. and **Pintzas, A.*** (2000). Prognostic significance of matrix metalloproteinases 2 and 9 in bladder cancer. *Anticancer Res.* 20, 2009-2014.

14. Giovane, A., **Pintzas, A.,** Maira, M., Sobieszczuk, P. and Wasylyk, B. (1994). Net, a negative ets transcription factor that is activated by Ras. *Genes and Development* 8, 1502-1513.

13. Oehler, T., **Pintzas, A.**, Stumm, S., Darling, A., Gillespie, D. and Angel, P. (1993). Mutation of a phosphorylation site in the DNA binding domain is required for redox-independent transactivation of AP-1 dependent genes by vJun. *Oncogene*, 8, 1141-1147.

12. Hawker, K., **Pintzas, A.**, Hennigan, R., Gillespie, D.A.F. and Ozanne, B. Transformation by the fos and jun oncogenes does not increase AP-1 DNA binding activity (1993). *J. Virol.* 67, 5487-5495.

11. Frame, M., Wilkie, N.M., Darling, A. J., Chudleigh, A., **Pintzas, A.,** Lang, J.C. and Gillespie, D.A.F. (1991). Regulation of AP-1/DNA complex formation in vitro. *Oncogene*, 6, 205-209.

10. **Pintzas, A.**, and Spandidos, D. A. (1991). Sp1 specific binding sites within the human Ha-ras 1 promoter: potential role of the 6bp sequence in the T24 H-ras 1 gene. *Anticancer Res.* 11, 2067-2070.

9. Linardopoulos, S., Malliri, A., **Pintzas, A.**, Vassilaros, S., Tsikkinis, A. and Spandidos, D.A. (1990). Elevated expression of AP-1 activity in human breast tumors as compared to normal adjacent tissue. *Anticancer Res*. 10, 1711-1714.

8. Agnantis, N.J., Constantinidou, A., Poulios, C., **Pintzas, A.**, Kakkanas, A. and Spandidos, D.A. (1990). Immunohistochemical study of the ras oncogene expression in human bladder endoscopy specimens. *European Journal of Surgical Oncology* 16,153-160.

7. Tiniakos, D., Spandidos, D.A., Kakkanas, A., **Pintzas, A.**, Police, L. and Tiniakos, G. (1989). Expression of ras and myc oncogenes in hepatocellular carcinomas and other liver lesions. *Anticancer Res*. 9, 715-722.

6. Spandidos, D.A., Yiagnissis, M., and **Pintzas, A.** (1989). Human Immunodeficiency Virus Long Terminal Repeat responds to transformation by the mutant T24 H-ras 1 oncogene and it contains multiple AP-1 binding TPA inducible consensus sequence elements. *Anticancer Res.* 9, 383-386.

5. **Pintzas A.** and Spandidos, D.A. (1989). Ras p21 oncoproteinis autoregulated and acts as a potential mediator of insulin action on H-ras 1 promoter. *Gene Analysis Techniques* 6, 125-130.

4. Spandidos, D.A., Nichols, R. A. B., Wilkie, N. M. and **Pintzas, A. (**1988). Phorbol ester responsive H-ras 1 gene promoter contains multiple TPA-responsive/AP-1 binding consensus sequence elements. *FEBS Letters* 240, 191-195.

3. Agnantis, N.J., Spandidos, D.A., Mahera, H., Parisi, P., Kakkanas, A., **Pintzas, A.** and Papacharalambous, N.X. (1988). Immunohistochemical study of ras oncogene expression in endometrial and cervical human lesions. *European Journal of Gynaecological Oncology* 9, 360-365.

2. Spandidos, D.A. and **Pintzas, A.** (1988). Differential potency and trans-activation of normal and mutant T24 human H-ras gene promoters. *FEBS Letters* 232, 269-274.

1. Spandidos, D.A., **Pintzas, A.,** Kakkanas, A., Yiagnissis, M., Mahera, H., Patra, E., and Agnantis, N.J. (1987). Elevated expression of the myc gene in human benign and malignant breast lesions compared to normal tissue. *Anticancer Res.* 7, 1299-1304.

Articles in book chapters (international):

3. Pintzas, A. (2004). Signal regulated gene expression mediated by transcription factors-members of AP-1 and ets/SRF family members: pathways for potential therapeutic intervention. In:“Chemical probes in biology”, Kluwer Acad. Pub., M. Schneider (Ed.), NATO SCIENCE SERIES, SERIES II: MATHEMATICS, PHYSICS AND CHEMISTRY Volume: 129 Pages: 35-38

2. Pintzas, A., Zoumpourlis, V. and Plows, D. (2000). Regulation of components of AP-1 transcription factor by early and late Ras signals. In: MOLECULAR MECHANISMS OF SIGNAL TRANSDUCTION Book Series: NATO SCIENCE SERIES, SERIES A: LIFE SCIENCE Volume: 316 Pages: 57-62 “Molecular mechanisms of signal transduction”, pp 57-62, J. Bos (Ed.), IOS Press.

1. Pintzas, A., Kotsinas, A. and Spandidos, D.A. (1991). Transcriptional regulation of the c-Ha-ras gene. The superfamily of ras related genes. Plenum Publ. Corp. SUPERFAMILY OF RAS-RELATED GENES Book Series: NATO ADVANCED SCIENCE INSTITUTES SERIES, SERIES A, LIFE SCIENCES Volume: 220 Pages: 311-316