UNIVERSITY OF PENNSYLVANIA – SCHOOL OF MEDICINE
Curriculum Vitae

Date: February 2007

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Academic Title: Associate Professor, Department Radiation Oncology

Personal Information: Naturalized US Citizen

Education:

1989–1994	Ph.D. Biochemistry, Department of Biochemistry and Biophysics Sciences, University of Houston, Houston, Texas
1984–1989	B.S. Pharmacy (with honors), Aristotle University, Thessaloniki, Greece

Postdoctoral Training:

1994–1999	Postdoctoral Fellow, Department of Radiation Oncology, Stanford University School of Medicine

Area of Research: Tumor Biology

Advisor: Amato Giaccia, Ph.D.

Faculty Appointments:

2006-Present	Associate Professor (Tenured), Department of Radiation Oncology University of Pennsylvania School of Medicine
2005-2006	Associate Professor, Department of Radiation Oncology Wake Forest University School of Medicine
2005-2006	Associate Professor, Department of Neurosurgery Wake Forest University School of Medicine

1999-2005	Assistant Professor, Department of Radiation Oncology Wake Forest University School of Medicine
1999-Present	Associate, Department of Cancer Biology Wake Forest University School of Medicine
1994-1999	Postdoctoral Fellow, Department of Radiation Oncology Stanford University School of Medicine

Membership in Professional and Scientific Societies

Member, Radiation Research Society
Active Member, American Association for Cancer Research
Member, American Society for Microbiology

Fellowships:

1997-1999	National Research Service Award, (F-32 Postdoctoral Fellowship), NCI, NIH
1994-1996	Dean's Postdoctoral Fellowship, Stanford University School of Medicine

Honors and Awards:

1999	AACR/AFLAC Young Investigator Travel Award, Philadelphia, PA
1998	NIH Travel Fellowship Award, 10th p53 International Meeting, Crete, Greece
1994	Graduate Student Research Excellence Award, Department of Biochemistry and Biophysics Sciences, University of Houston

Invited Talks:

1. Genomics Institute of the Novartis Research Foundation, San Diego, CA; December 2006.
2. Bristol-Myers-Squibb Pharmaceutical Research Institute, Princeton, NJ; October 2006.
3. Wyeth Pharmaceuticals, Pearl River, NY; September 2006.
4. East Carolina University School of Medicine, Greenville, NC; March 2005.
5. University of Ottawa, Ottawa Regional Cancer Center, Canada. Sept. 2005.
6. McGill University, Lady Davis Institute for Medical Research, Montreal, Canada; May 2005.
7. University of Louisville Cancer Center, Louisville, KY; March 2005.
8. University of Pennsylvania School of Medicine, Department of Radiation Oncology; October 2004.

Oral Presentations at Meetings/Conferences

1. Keystone Meeting on "Hypoxia and Development, Physiology and Disease"; Breckenridge, Colorado. (Invited Speaker); January 2006. Title: The Role of the Unfolded Protein Response in Tumor Cell Resistance to Hypoxia/Anoxia.
2. NCI-sponsored workshop on "ER Stress and Cancer"; Bethesda, MD. October 2005. Title: An ER stress-regulated translation control program increases tolerance to hypoxia and promotes tumor growth.

3. 9th International Tumor Microenvironment Workshop Oxford, England; August 2005. Title: The Integrated Stress Response is required for tumor cell survival under hypoxia and for tumor growth.
4. Cold Spring Harbor Laboratory meeting on "Translational Control"; September 2004. Title: Activation of the endoplasmic reticulum kinase PERK and phosphorylation of the translation initiation factor eIF2α increases tumor cell resistance to hypoxic stress and contributes to tumor growth.
5. Cold Spring Harbor Laboratory meeting on "Translational Control"; September 2002. Title: Regulation of translation by hypoxia via activation of the endoplasmic reticulum kinase PERK and phosphorylation of the translation initiation factor eIF2α.
6. 48th Radiation Research Society Annual Meeting, San Juan, Puerto Rico; March 2001. Title: Phosphorylation of translation factor eIF2α in response to hypoxic stress.
7. NIH Campus, Bethesda, MD, 2nd International workshop on p53 modifications; September 1999. Title of talk: Post-translational modifications of p53 induced by hypoxia.
8. Montreal, Canada. International Tumor Microenvironment Meeting; October 1999. Title of talk: Regulation of p53 activity by tumor hypoxia.

Reviewing/Editing/Consulting Responsibilities:

Editorial Board Member, *Oncology Reports*

Guest Editor, Focused Review Series on "ER Stress and Cancer", *Cancer Biology & Therapy*, In Press.

Reviewer for the following journals: Cancer Research, Carcinogenesis, Clinical Cancer Research, Genes & Development, International Journal of Radiation Biology, Journal of Biological Chemistry, JNCI, Molecular Cancer Research, Molecular Cell, Molecular Cellular Biology, Molecular Pharmacology, Nature Reviews Cancer

Ad-hoc Reviewer for the following Granting Agencies:

- NIH, Basic Mechanisms of Cancer Therapeutics (BMCT) study section, Feb. 2007, June 2006, February 2006, November 2005.
- NIH, Drug Discovery and Molecular Pharmacology Study Section (DMP) study section, September 2006
- NIH, Oncology Fellowship and AREA Reviews (ZRG1 F09 20L), March 12-14, 2006
- Congressionally Directed Medical Research Program (CDMRP)-Breast Cancer Research Program Pathobiology-3, August 2005.
- NIH SEP, Innovative Molecular Analysis Technologies (IMAT) ZCA1 SRRB-C J1S. June-July 2005.
- NIH SEP, Innovative Molecular Analysis Technologies (IMAT) ZCA1 SRRB-C J1S. November 2004.
- NIH Special Emphasis Panel ZRG1, GGGE 02. October 22, 2004.
- Department of Veterans Affairs, Merit Review Subcommittee, ONC-A

- MRC (UK) Clinical Training and Career Development, February 2007.
- New Jersey Commission on Cancer Research grants, February 2007.
- Austrian Academy of Sciences, Austrian Program for Advanced Research and Technology, February 2006.
- Alberta, Canada Cancer Board-2004.
- United States-Israel Binational Foundation (Health Sciences)-Spring 2004.

Teaching Portfolio (WFUSM)

A. Medical Students

Lectures

1. Facilitator Small Group, Small Discussion Group; Phase 1-B, Prescription for excellence, WFUBMC. 10/1999-02/2000
2. Facilitator Small Group, Small Discussion Group; Phase 1-A, Prescription for excellence, WFUBMC. 09/2003-11/2003
3. Evaluator (objective structured clinical examination), Spring 2002 (2 hours)

B. Graduate Education (Master's and Doctoral candidates, Residents/fellows)

Lectures

1. Cancer Biology 708, "Molecular Targets of Cancer"
   Course director: Jim Vaughn
   Lecture title: "Tumor Microenvironment, Tumor chemotherapy and Apoptosis"
   Number of lectures (total time): 2 (3 hours)
   Taught: Spring 2000, 2001, 2002, and 2003
2. Cancer Biology 703 "Molecular Pathogenesis of Cancer".
   Course director: Suzi Torti.
   Lecture title "Radiation, p53 and the apoptotic decision".
   Number of lectures (total time): 2 (2 hours)
   Taught: Fall 2000, 2001, and 2002
3. Molecular Genetics 741 "Molecular Genetics Tutorials"
   Course co-directors: Gaddanamugu Prasad and Costas Koumenis
   Number of lectures (total time): 20 (30 hours)
   Taught: Spring 2003
4. Cancer Biology 704 "Cell Biology of Cancer"
   Course co-directors: Andrew Thorburn and Costas Koumenis
   Number of lectures (total time): 30 (45 hours)
   Taught: Spring 2003
5. Radiation Biology Course for Residents
   Course director: Mike Robbins
   Number of lectures (total time): 7 (7 hours)
   Taught: Summer 2003
6. Cancer Biology 715 " Introduction to Radiation Biology"
   Course director: Mike Robbins
   Number of lectures (total time) 16 (22 hours)
   Taught: Spring 2004, Spring 2006

Thesis and Examination Committees:

Thesis Advisor for the following graduate students:

1. Lori Hart, Dept. Cancer Biology, WFUSM (PhD, October 2006. Current Position: Postdoctoral Fellow, Lab of Dr. Wafik El-Deiry, University of Pennsylvania School of Medicine)
2. Diane Fels (5th year) Department of Cancer Biology, WFUSM
3. Prashanthi Javvadi (3rd year), Cancer Biology, WFUSM-now at University of Pennsylvania
4. Jiangbin Ye (3rd year), Cancer Biology, WFUSM-now at University of Pennsylvania

Committee member for the following graduate students (WFUSM):

1. JoLynn Turner, Biochemistry (Suzi Torti, Thesis Advisor)
2. Arta Monjazeb, Molecular Genetics (Ski Chilton, Thesis Advisor)
3. Virginia Young, Molecular Genetics (Griffith Parks, Thesis Advisor)
4. Zachary Whitlow, Molecular Genetics (Doug Lyles, Thesis Advisor)
5. Pameeka Smith, Cancer Biology (Mike Robbins, Thesis Advisor)
6. Michael Thomas, Cancer Biology (David Ornelles, Thesis Advisor)
7. Adrienne Smith, Cancer Biology (George Kulik, Thesis Advisor)
8. Joy Little, Cancer Biology (Steven Kridel, Thesis Advisor)

Mentoring/Advising

1. Mentor, Training Program in Translational Radiation Oncology (TRADONC). Fellow: Brian Lally, MD. (2005-present). Project title: "Unbiased screen of a chemical compound library for the identification of novel radiation sensitizers".
2. Mentor, Excellence in Cardiovascular Sciences Summer Research Program, Summer 2004. Student: Chelsie Swepson, undergraduate student, Fayetteville State University.
3. Mentor, C.E.R.T.L. Program, WFUBMC Summer 2002. Student: Jack Smallwood, high school junior.
4. Mentor, C.E.R.T.L. Program, WFUBMC Summer 2000. Student: Julie Erb, high school freshman

Teaching Portfolio (University of Pennsylvania)

A. Radiation Oncology Residents
Course Director, "Radiation Biology"; February-June 2007

B. Graduate Education
Co-director CAMB512 "Cancer Genetics"; January-May 2007

Thesis and Examination Committees:

Thesis Advisor for the following graduate students:

1. Prashanthi Javvadi (3rd year), CAMB Program, Cell Growth and Cancer group.
2. Jiangbin Ye (3rd year), CAMB program. Cell Growth and Cancer group.

Bibliography

Research Publications:

1. Raju, U.**, Koumenis, C.**, Nunez-Regueiro, M. and Eskin, A (1991). Alteration of the phase and period of a circadian oscillator by a reversible transcription inhibitor *Science*, 253: 673-675.
2. Noel, F., **Koumenis**, **C**., Raju, U., Nunez-Regueiro, M., Byrne, J. H. and Eskin, A. (1994) Novel effects on protein synthesis produced by pairing depolarization with serotonin, an analogue of associative learning in Aplysia. *Proc. Natl. Acad. Sci. USA*., 91:4150-4154.
3. **Koumenis**, **C**., Raju, U., Nunez-Regueiro, M. and Eskin, A (1995) Identification of three proteins in the eye of Aplysia whose synthesis is altered by serotonin *J. Biol. Chem*., 270: 14619-14627.
4. Girinsky, T.*, **Koumenis, C.***, Graeber, T.G., Peehl, D.M. and Giaccia A.J.(1995) Attenuated response of p53 and p21 in primary cultures of human prostatic epithelial cells exposed to DNA-damaging agents *Cancer Res*., 55: 3726-3731. * = co-first authors.
5. **Koumenis**, **C**., Tran, Q and Eskin, A (1996) The use of a reversible transcription inhibitor, DRB, to investigate the involvement of specific proteins in the ocular circadian system of Aplysia *J. Biol. Rhythms*, 11: 45-56.
6. Fried, L.*, **Koumenis, C**.*, Peterson, S., Green, S., van Zijl, P., Allalunis-Turner, J., Chen, D., Fishel, R., Giaccia, A.G., Brown, J.M. and Kirchgessner C. (1996) The DNA damage response in DNA-dependent protein kinase-deficient severe combined immunodeficient cells: Replication Protein A hyperphosphorylation and p53 induction *Proc. Natl. Acad. Sci. USA*, 93:13825-13830. * = co-first authors
7. **Koumenis, C**. and Giaccia, A.J. (1997) Ongoing activity of RNA Polymerase II is required for resistance to oncogene-induced apoptosis in transformed cells *Mol. Cell. Biol.*, 17:7306-7316.
8. Alarcon, R., **Koumenis, C**., Geyer R.K., Maki, C.G., Giaccia, A.J.(1999) Hypoxia induces p53 accumulation through MDM2 down-regulation and inhibition of E6-mediated degradation. *Cancer Res.* 59: 6046-6051.
9. Maecker, H., **Koumenis, C.*** and Giaccia, A.* (2000) p53 promotes selection for Fas-mediated apoptotic resistance. *Cancer Res.* 60:4638-44. *= corresponding authors.
10. **Koumenis, C.,** Alarcon, R., Maecker, H., Hoffman, W., Murphy, M., Derr, J., Taya, Y., Lowe, E., Kastan, M. and Giaccia, A. (2001) Regulation of p53 by hypoxia: dissociation of protein accumulation transcriptional repression and apoptosis from p53-dependent transactivation. *Mol. Cell. Biol.,* 21:1297-1310.
11. Parks G., Young V., **Koumenis C.**, Wansley E., Layer J., Cooke M. (2002) Controlled cell killing by a recombinant nonsegmented negative-strand RNA virus. *Virology*. 293:192-203.
12. Wade W., Willingham M., **Koumenis C.**, Cramer S.(2002) p27Kip1 is essential for the antiproliferative action of 1,25-dihydroxyvitamin D3 in primary, but not immortalized, mouse embryonic fibroblasts. *J Biol Chem*., 277: 37301-6.
13. **Koumenis C**., Naczki, C., Koritzinsky, M., Rastani, S., Diehl, A., Sonenberg, N. ,

Koromilas, A., and G. Wouters, BG. (2002) Regulation of protein synthesis by hypoxia via activation of the endoplasmic reticulum kinase PERK and phosphorylation of the translation initiation factor eIF2α. *Mol. Cell Biol*., 22: 7405-16.

14. Dunlap, N., Schwartz, G. G., Eads, D., Cramer, S. D., Sherk, A., John, V., **Koumenis, C.** (2003) 1alpha,25-dihydroxyvitamin D3 (Calcitriol) and its analogue, 19-nor-1alpha,25(OH)2D2, potentiate the effects of ionizing radiation on human prostate cancer cells. *Br. J. Cancer*, 89:46-53.
15. Schwartz, G.G., Eads, D., Rao, A., Cramer, S.D., Willingham, M.C., Chen, T.C., Jamieson, D.P., Wang, L., Burnstein, K.L., Michael F. Holick, M.F., and **Koumenis, C.** (2004) Pancreatic cancer cells express 25-Hydroxyvitamin D-1α-hydroxylase and their proliferation is inhibited by the prohormone 25-hydroxyvitamin D_3. *Carcinogenesis*, 25:1015-26.
16. Qu, L., Huang S., Baltzis, D., Rivas-Estilla A.-M., Pluquet, O., Hatzoglou, M., **Koumenis, C**., Taya, Y., Yoshimura, A., and Koromilas, A.E. (2004) Endoplasmic reticulum stress induces p53 cytoplasmic localization and prevents p53-dependent apoptosis by a pathway involving glycogen synthase kinase-3β. *Genes & Dev*., 18:261-77.
17. Rao, A., Coan, A., Welsh, J-E., Barclay, W.W., **Koumenis, C.**, Cramer, S.D. (2004) Vitamin D Receptor and p21/WAF1 are Targets of Genistein and 1,25-dihydroxyvitamin D3 in Human Prostate Cancer Cells. *Cancer Res*., 64:2143-7.
18. Connor, J., Naczki, C., **Koumenis, C**. and Lyles, D. (2004) Replication and Cytopathic Effect of Oncolytic Vesicular Stomatitis Virus in Hypoxic Tumor Cells In Vitro and In Vivo. *J. Virol.*, 78:8960-70.
19. Blais, J.D., Filipenko, V., Bi, M., Ron, D., **Koumenis, C**., Wouters, B.G., and Bell, J. C. (2004) Transcription Factor 4 is Translationally Regulated by Hypoxic Stress. *Mol. Cell. Biol*. 24:7469-82.
20. Hart, L., Yannone, S., Ornelles, D. and **Koumenis, C.** (2005) The Adenovirus E4orf6 protein inhibits double strand break repair and radiosensitizes human tumor cells in an E1B-55K-independent manner. *J. Biol. Chem*., 280: 1474–81.
21. Turner, J**., Koumenis, C**., Kute, T., Planalp, R.P., Brechbiel, M.W., Beardsley, D., Cody, B., Brown, K.D., Torti, F.M., Torti, S.V. (2005). An iron chelator, tachpyridine, induces G2 cell cycle arrest, activates checkpoint kinases, and sensitizes cells to ionizing radiation. *Blood*, 106:3191-9.
22. Bi, M., Hu, N., Blais, J., Fels, D., Koritzinsky, M., Naczki, C., Harding, H., Novoa, I., Kaufman, R., Ron, D., Bell, J., Wouters B. G., and **Koumenis, C.** (2005). ER stress-regulated translation increases tolerance to extreme hypoxia and promotes tumor growth. *EMBO J.* 24:3470-81.
23. Monjazeb AM, High KP, **Koumenis, C.**, Chilton, F.H. Inhibitors of arachidonic acid metabolism act synergistically to signal apoptosis in neoplastic cells. *Prostaglandins Leukot Essent Fatty Acids.* 2005 Dec;73(6):463-74.
24. Yacoub, A., Park, M.A., Hanna, D., Hong, Y., Mitchell, C., Pandya, A.P., Harada, H., Powis, G., Chen, C.S., **Koumenis, C.**, Grant, S., Dent, P. (2006). OSU-03012 promotes caspase-independent but PERK-, cathepsin B-, BID-, and AIF-dependent killing of transformed cells. *Mol Pharmacol*. 70:589-603.
25. Koritzinsky. M., Dostie, J., Pyronnet, S. Jaime, J., Bell, J., Lambin, P., Pettersen,

E.O., **Koumenis, C**., Sonenberg N., and Wouters, B.G. (2006). Hypoxia inhibits cap-dependent mRNA translation through eIF4F. *EMBO J.* 25:1114-25.

26. Blais, J.D., Addison, C.L., Edge, R., Falls, T., Zhao, H., Wary, K., **Koumenis, C.**, Harding, H.P., Ron, D., Holcik, M., Bell, J.C. (2006). Perk-dependent translational regulation promotes tumor cell adaptation and angiogenesis in response to hypoxic stress. *Mol Cell Biol.* 26(24):9517-32.
27. Hart, L.S., Ornelles, D.O., **Koumenis, C**. (2006). The adenoviral E4ORF6 protein induces atypical apoptosis in response to DNA damage. *J Biol Chem*. Dec 15; [Epub ahead of print]
28. Little J.L., Wheeler F.B., Fels D.R., **Koumenis, C**., Kridel S.J. (2007) Inhibition of Fatty Acid synthase induces endoplasmic reticulum stress in tumor cells. Cancer Res. 67:1262-9.

Invited Reviews/Meeting Reports/Commentaries:

1. Takahashi, J.S., Kornhauser, J., **Koumenis, C.** and Eskin, A. (1993). Molecular approaches to understanding circadian oscillators *Ann. Rev. Physiol*. 5: 729-753.
2. Wouters, B.G., Van Den Beucken, T., Magagnin, M.G., Lambin, P., **Koumenis, C**. (2004). Targeting hypoxia tolerance in cancer. *Drug Resist Updat*. 7:25-40.
3. Fels, D. and **Koumenis, C.** (2005). Hif1α and p53: The ODD couple? *Trends Biochem Sci*. 8:426-9.
4. **Koumenis, C**. (2006) ER stress, hypoxia tolerance and tumor progression. In "Role of Endoplasmic reticulum stress in physiology and disease. Soto, C. and Hetz, C. Eds., *Curr. Mol. Medicine,* 6:55-69.
5. Maxwell, P. and **Koumenis, C.** (2006). Low Oxygen stimulates the Intellect: Meeting report of Keystone Symposium on "Hypoxia and Development, Physiology and Disease", in Breckenridge, CO. *EMBO Rep.*, 7:679-684.
6. Fels, D. and **Koumenis, C.** (2006) The PERK/eIF2α/ATF4 module of the UPR in hypoxia resistance and tumor growth. *Cancer Biol & Ther* 5(7) [Epub ahead of print]
7. **Koumenis, C.** and Wouters, B.G. (2006) "Translating" Tumor Hypoxia: UPR-dependent and Independent Pathways. *Mol. Cancer Res*., 4:423-36.
8. Maity, M. and **Koumenis, C.** (2006). HIF and MIF – a nifty way to delay senescence? *Genes Dev.*, 20:3337-41.

Book Chapters:

1. **Koumenis, C**., Denko N., and Giaccia, A.J. (1998) Chemotherapy, the Tumor Microenvironment and Apoptosis in "Apoptosis and Cancer Chemotherapy". Hickman, J.A., Dive, C. Eds. Humana Press, pp.224-232.
2. Huang, T.W., Russo, S.M., Stieber, V.W., **Koumenis, C**., deGuzman, A.F., and Shaw, E.G. Radiation Therapy and Radiation Injury in "Basic Science for Surgeons: A Review". Argenta, L.C., Ed. Elsevier Science Health Science div. pp. 643-671.

Letters:

1. Giaccia, A.J., Brown, J.M., Wouters, B., Denko, N. and **Koumenis, C.** (1998) Cancer therapy and tumor physiology *Science,* 279:12-13.

Patents:

United States Patent 6,689,811: Koumenis, Constantinos *et al*. "**Method of using caffeic acid phenethyl ester and analogs thereof as radiation sensitizers**"

Funding

Ongoing:

1. 2 R01 CA094214-05 07/01/02-07/30/06
   NCI/NIH; Annual Direct Costs: $ 206,000
   "Role of eIF2α in tumor cell adaptation to hypoxic stress"
   The goal of this project is to investigate the molecular events that govern translational regulation by hypoxic stress in normal and malignant cells as a mechanism of adaptation to this stress. Specifically, the role of translation initiation factor eIF2α and of the upstream kinase PERK will be assessed by combined biochemical and genetic experiments.
   Competing renewal scored at 4th percentile, November 2006

2. 1 R01 CA104922; Koumenis (PI); 04/01/2005-03/30/2009
   NCI/NIH; Annual direct costs: $200,000
   "Phenolic antioxidants as tumor radio/chemosensitizers"
   The goal of this project is to evaluate the radiosensitizing and chemosensitizing properties of the phenolic antioxidants caffeic acid phenethyl ester (CAPE) and curcumin, *in vitro* and *in vivo*.

Completed:

1. Elekta RPG; Koumenis (PI); 01/01/2005-07/31/2006
   Annual direct costs: $125,000
   "A combined gene therapy and Gamma Knife radiosurgery approach to radiosensitize human glioma cells in a rat orthotopic tumor model"

2. Cancer Center Supplement; Koumenis (PI); 40% effort; 07/1/01-06/30/2002
   NCI/CAM; Annual direct costs: $108,000
   "Propolis and Caffeic Acid Phenethyl Ester (CAPE) as radiation sensitizers and pro-apoptotic agents in the treatment of prostate cancer".

3. WFU cross-campus collaboration grant; Koumenis (co-PI); Fantz (co-PI); 09/01/2003-08/31/2004,
   WFUSM; Annual direct costs $15,000
   "Genetic Screen for Regulators of Hypoxia Tolerance"