Curriculum Vitae

Vassiliki Kostourou, PhD

Institute of Immunology
Biomedical Sciences Research Centre "Al. Fleming" Vari, 16672, Attiki
email: kostourou@fleming.gr, tel: +30 210 9654465, Fax:: +30 210 9653934
http://www.fleming.gr/en/investigators/Kostourou/index.html

Education

31/12/2002 Ph.D. at St. George's Medical School, Department of Biochemistry-Immunology, University of London, UK.
30/9/1998 MSc in Biochemical Research, Imperial College London, Department of Biochemistry, University of London, UK.
30/9/1998 Diploma in Biochemistry, Imperial College London, Department of Biochemistry, University of London, UK.
30/6/1997 BSc. in Biology, University of Patras, Greece (honors-upper 2nd class)

Research apointments

sep2007-present Researcher C, Head of the Laboratory of endothelial biology and pathophysiology, BSRC Al. Fleming.
2005-2007 Research Fellow at Institute of Cancer, Dept. Tumour Biology, CRUK Clinical Center, UK, Cell Adhesion and Disease Laboratory (Advisor: Dr K. Hodivala-Dilke
2002-2005 Research Fellow in London Research Institute -CRUK, UK, Vascular Development Laboratory, (Advisor: Dr R. Adams)

Fellowships awarded

PhD studentship, St George's Medical School, University of London, (1998-2005)
CRUK Postdoctoral Research Fellowship (2002-2005).

Research Interests

The main research interest of our recently established group is to study the molecular mechanisms that control endothelial cell function during blood vessel development. Our approach utilizes genetically modified mouse models and various cellular and molecular assays in primary endothelial cells and ex vivo tissues to elucidate the function of adhesion dynamics in vascular morphogenesis during embryonic development and in pathological conditions such as cancer. Major emphasis is placed on identifying the functional relationships among intracellular adhesion proteins and their role in cell adhesion remodelling and cell migration during angiogenesis. In recent studies, we have established the role of integrins and focal adhesion kinase (FAK) in pathological angiogenesis. Our ongoing projects are focusing on intracellular adhesion molecules that associate with integrins and provide a molecular link to cytoskeleton such as Talin, ILK and PINCH. Recently we demonstrated the functional requirement of Talin1 in embryonic vascular development. We aim to dissect further the molecular mechanisms of intracellular adhesion protein function during physiological and pathological angiogenesis.

Teaching experience

2010. Invited lecturer on "Cell Adhesion dynamics" and "Molecular mechanisms of angiogenesis" at the PhD programme of Gulbenkian Institute, Lisbon, Portugal.
Since 2008. Invited lecturer at the course "Multicellular Organisation of life" postgraduate programme of "Molecular Medicine", Medical School, University of Athens, Greece.
2006-2007. Invited lecturer at the course "Inside the cell", PhD programme of Gulbenkian Institute, Lisbon, Portugal.
1999-2001. Co-organiser and teaching of the practical courses in biochemistry, St George's Medical School, University of London, UK.

Supervising of students

PhD student
Katerina Ntakou, current
Bernardo Tavora, (2006-2010), Queen Mary University London, UK, co-supervising
MSc students
Evagelia Papageorgopoulou current
Katerina Ntakou, (2010-2011) Medical School, University of Athens
Sofia Birmpili, (2008) Université de Paris VI, Pierre et Marie Curie, France
Diploma student
Kleanthi Xanthopoulos (2012) Department of Medical Laboratories, TEI Athens
Gundrun VonHaven (2003) London Research Institute-Cancer Research UK.

Reviewer of International Scientific Journals

Journal of Cell Science (Impact Factor 6,427)

Reviewer of funding bodies

- General Secretary of Research and Technology, Ministry of Education, Greece
- Cancer Research UK, UK

Organisation of conferences/chair at sessions

- Member of the organizing committee for the 62nd conference of Hellenic Society of Biochemistry and Molecular Biology (HSBMB), Dec Athens 2011.
- Co-organising the session: Dynamic Imaging: from single cell to whole animal, 62nd HSBMB conference, Athens, Dec 2011.
- Chair at the International ELMI meeting on Advanced Light Microscopy, Alexandroupolis, Greece, June 2011.
- Chair of session at the "Imaging Biomolecules in Time and Space", An advanced light microscopy symposium, University of Patras, Patra, Greece, Sep 2010.

Member of scientific societies

- European Association for Cancer Research
- Hellenic Society of Biochemistry and Molecular Biology.
- Hellenic Society of BioImaging
- British Biochemical Society
- British Society of Cell and Developmental Biology
- Imperial College London Alumni Society.

Publications

Ikonomou G, **Kostourou V**, Shirasawa S, Sasazuki T, Samiotaki M, Panayotou G. (2012) "Interplay between oncogenic K-Ras and wild-type H-Ras in Caco2 cell transformation". ***Journal of Proteomics.*** 75(17):5356-69.

Monkley S., **Kostourou V.**, Spence L., Petrich B., Coleman S., Ginsberg M., Pritchard C. & Critchley D. (2011) "Endothelial cell talin1 is essential for embryonic angiogenesis". ***Developmental Biology*** (IF 4.7) 349:494-502.

Kostourou V., Cartwright J., Johnstone A., Boult J., Cullis E., Whitley G. & Robinson S. (2011) "The Role of Tumour Derived iNOS in Tumour Progression and Angiogenesis". ***British Journal of Cancer*** (IF 4.51) 104:83-90.

Tavora B., Batista S., Reynolds L., Robinson S., Jajida S., **Kostourou V.,** Hart I., Fruttiger M., Parsons M. & Hodivala-Dilke K. (2010). "Endothelial Cell FAK is required for tumour angiogenesis" ***EMBO Molecular Medicine*** (IF 8.83) 2: 516-528

Silva R., Tavora B., Reynolds L., Szekeres C., Lamar J., Batista S., Robinson S., **Kostourou V.**, Germain M., Reynolds A., Jones D., Watson A., Jones J., Harris A., Hart I., Iruela-Arispe L., DiPersio M., Kreidberg J. & Hodivala-Dilke K. (2010) "Endothelial α3β1-integrin represses pathological angiogenesis and sustains endothelial-VEGF" ***American Journal of Pathology*** (IF 5.7) 177:1534-1548

Kalogeropoulou M., Voulgari A., **Kostourou V.**, Sandaltzopoulos R., Dikstein R., Davidson I., Tora L. & Pintzas A. (2010) "TAF4b and Jun/AP-1 Collaborate to Regulate Expression of Integrin α6 and Cancer Cell Migration Properties" ***Molecular Cancer Research*** (IF 4.5) 8:554-68

Germain M., De Arcangelis A., Robinson S., Baker M., Tavora B., D'Amico G., Silva R., **Kostourou V.**, Reynolds L., Ramjaun A., Jones J., Georges-Labousesse E. & Hodivala-Dilke K. (2010) "Genetic ablation of the alpha 6-integrin subunit in Tie1Cre mice enhances tumour angiogenesis" ***Journal of Pathology*** (IF 6.5) 220:370-381.

D'Amico G., Jones D., Nye E., Spienza K., Ramjuan A., Reynolds A., Robinson S., **Kostourou V.**, Martinez D., Aubyn D., Grose R., Thomas G., Spencer-Dene B., Zicha D., Davies D., Tybulewicz V., & Hodivala-Dilke K. (2009) "Regulation of lymphatic-blood vessel separation by Rac-1" ***Development*** (IF 7.2) 136(23): 4043-4053.

Robinson S., Reynolds L., **Kostourou V.,** Reynolds A., Silva R., Marshall J. & Hodivala-Dilke K. (2009) "αvβ3-integrin limits the contribution of Neuropilin-1 to VEGF-induced angiogenesis". ***Journal of Biological Chemistry*** (IF 5.5) 284: 33966-33981

Reynolds A., Hart I., Watson A., Welti J., Silva R., Robinson S., Da Violante G., Gourlaouen M., Salih M., Jones M., Jones D., Saunders G., **Kostourou V.**, Perron-Sierra F., Norman J., Tucker G. & Hodivala-Dilke K. (2009) "Stimulation of tumor growth and angiogenesis by low concentrations of RGD mimetic integrin inhibitors". ***Nature Medicine*** (IF 28) 15:372-400

Claxton S., **Kostourou V.**, Jadeja S., Chambon P., Hodivala-Dilke K. & Fruttiger M. (2008) "Efficient, inducible Cre-recombinase activation in vascular endothelium". ***Genesis*** (IF 2.6) 46:74-80

Takamiya K., **Kostourou V.**, Adams S., Jadeja S., Chalepakis G., Scambler P., Huganir R & Adams R. (2004) "A direct functional link between the multi-PDZ domain protein GRIP1 and the Frazer syndrome protein Fras1". ***Nature Genetics*** (IF 34.3) 36:172-177

Kostourou V., Troy H., Murray J., Whitley G, Griffiths JR. & Robinson SP. (2004) "Overexpression of Dimethylarginine Dimethylaminohydrolase enhances tumour hypoxia: An insight into the relationship of hypoxia and angiogenesis in vivo" ***Neoplasia*** (IF 5) 6:401-404

Kostourou V., Robinson SP., Whitley G. & Griffiths JR. (2003) "Effects of Overexpression of Dimethylarginine Dimethylaminohydrolase on Tumour Angiogenesis Assesed by Susceptibility Magnetic Resonance Imaging" ***Cancer Research*** (IF 7.7) 63: 4960-4966

Kostourou V., Robinson SP., Cartwright JE. & Whitley G. (2002) "Dimethylarginine Dimethylaminohydrolase I enhances tumour growth and angiogenesis". ***British Journal of Cancer*** (IF 4.5) 9:673-680

Thiru A., Hodach M., Eloranta J., **Kostourou V.**, Weinzierl ROJ. & Matthews S. (1999) "RNA polymerase subunit H features a beta-ribbon motif within a novel fold that is present in archaea and eukaryotes" ***Journal of Molecular Biology*** (IF 3.8) 287:753-760.

Revised

Kostourou V.*, Lechtier T., Reynolds L.E., Jones D., Ramjaun A., Baker M., Robinson S., Hart I. and Hodivala-Dilke K. "FAK heterozygocity enhance pathological angiogenesis" ***Nature Communication***
* corresponding author

Research achievements in the last 10 years

My scientific career has followed my interest in angiogenesis both during development and in cancer pathology. Having gained initial research experience during my master course at Imperial College, I was awarded a PhD studentship from the St George's Hospital Medical School to study the role of angiogenesis in tumour development (supervisor: Prof. G.St.Whitley). My PhD work focused on the role of nitric oxide in tumour growth and angiogenesis (Br.J.Cancer 2002, Canc. Res 2003, Neoplasia 2004). To explore more the molecular pathways regulating blood vessel formation in embryonic development I moved to the Vascular Development laboratory of Dr R. Adams at LRI-CRUK where I was awarded a CRUK-Research Fellowship. In my postdoctoral work, I studied the molecular mechanisms of vascular development and organ formation. In particular, I characterised the function of a PDZ-domain containing protein, GRIP1 (**G**lutamate **R**eceptor **I**nteracting **P**rotein 1), in embryonic development using knockout and transgenic mouse models as well as biochemical and imaging analysis of primary cells. These studies revealed that GRIP1 is required for the localisation of Fras1, a protein linked to Fraser syndrome, to the basal side of epithelial cells (Nature Genetics 2004). I further demonstrated a novel role for GRIP1 in the remodeling of adhesion sites and cell migration through its negative regulation of the activity of the GIT1-□Pix-Pak signalling complex (manuscript submitted). Having gained extensive experience in analysing cell adhesion dynamics, I, then, moved to Dr. Hodivala-Dilke lab (Dept. Tumour Biology, CRUK Clinical Center), a world expert on the role of integrins in angiogenesis. I was involved in investigated the function of integrins in pathological angiogenesis. Our studies showed that integrin regulate angiogenesis by fine-tuning the angiogenic responses of growth factors, such as Vascular Endothelial Growth Factor (Nat. Med. 2009, J Biol. Chem. 2009, J. Pathol 2010, Am.J. Pathol. 2010). My main work focused on elucidating the role of FAK (Focal Adhesion Kinase) in pathological angiogenesis *in vivo*. Since endothelial deletion of FAK is embryonic lethal, there was a requirement for a mouse model that enables the deletion of the gene of interest specifically in endothelial cells and in an inducible time- controlled manner. Hence, I participated in the characterization of the PdgfBicreER^{T2} transgenic mouse that was generated by Dr M. Fruttiger (UCL, UK) (Genesis, 2008). We used this model to delete FAK in adult endothelial cells and showed that FAK is essential for tumour angiogenesis (EMBO Mol Med. 2010). Additionally, I demonstrated that FAK heterozygous mice display increased tumour growth and angiogenesis and enhanced *in vitro* and *in vivo* angiogenic responses due to elevated Akt activity (manuscript under revision to Nat Commun-corresponding author). Having gained valuable experience in several in vivo and ex vivo models of angiogenesis and expertise in integrin signaling, I joined BSRC Al. Fleming in sep 2007 and started my own group effectively in 2008. Our current projects are focusing on elucidating the role of intracellular adhesion proteins in regulating blood vessel formation. Although, it becomes increasingly evident that adhesion signaling mechanisms are equally important to growth factor signaling for controlling cellular responses, very little is known about the in vivo requirement of intracellular adhesion proteins in angiogenesis. Only 5 intracellular adhesion proteins (PI3K, Rac, FAK, ILK, Talin) have been examined in vivo and we have been involved in analyzing 4 of these, in past (FAK, Rac) and current projects (Talin, ILK). Specifically, we have established collaborations with leading figures in the field of adhesion (Prof. D. Critchley and Prof. R. Fassler) and obtained genetically modified mice and reagents to study the role of Talin, ILK and PINCH in developmental and pathological angiogenesis. Recently, we showed that Talin is requited for blood vessel formation during developmental angiogenesis (Dev Biol, 2011). We are now exploring their role in tumour angiogenesis and cancer progression.

Monkley S., **Kostourou V.**, Spence L., Petrich B., Coleman S., Ginsberg M., Pritchard C. & Critchley D. (2011) "Endothelial cell talin1 is essential for embryonic angiogenesis". ***Developmental Biology*** (IF 4.7) 349:494-502.

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Reynolds A., Hart I., Watson A., Welti J., Silva R., Robinson S., Da Violante G., Gourlaouen M., Salih M., Jones M., Jones D., Saunders G., **Kostourou V.**, Perron-Sierra F., Norman J., Tucker G. & Hodivala-Dilke K. (2009) "Stimulation of tumor growth and angiogenesis by low concentrations of RGD mimetic integrin inhibitors". ***Nature Medicine*** (IF 28) 15:372-400

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Invited speaker/conferences

- 63rd National Conference, Hellenic Society of Biochemistry and Molecular Biology, Hrakleio, Crete, Greece, 9-11 Nov, "FAK-heterozygous mice display enhanced pathological angiogenesis".
- 22nd European Tissue Repair Society (ETRS) meeting, Athens, Greece, 4-5 Oct, "The role of adhesion protein Talin in wound angiogenesis and repair".
- Confererence of the Hellenic association of Bioscientists, Athens, Greece, 9-10 Oct 2010 "To move or not to move? Important decisions in blood vessel formation".
- Gulbenkian Institute, Lisbon, Portugal, 22 Nov 2010 "Vascular Development in health and disease".
- University of Leicester, Leicester, UK, 23 March 2007 "The role of focal adhesion proteins in angiogenesis".
- 58th National Conference, Hellenic Society of Biochemistry and Molecular Biology, Patras, Greece, Nov 2006 "Investigating the role of Focal adhesion kinase in pathological angiogenesis".
- BSRC Al. Fleming, Athens, Greece, June 2006 "Identifying the dynamic nature of cell adhesion".
- Queen Mary's College, CRUK Clinical Centre, London, UK, Sep 2005 " GRIP regulates cell migration and focal adhesion remodelling".
- IIBEAA, Athens, Greece, Feb 2005 "Getting to GRIPs with cell adhesion remodelling".

- London Research Institute –CRUK, London, UK, Nov 2000. “The role of DDAH in tumour growth and angiogenesis”.
- Cancer Research Theme Group Meeting, St. George's Hospital Medical School, Feb 2000 “The role of DDAH in tumour growth and angiogenesis”.

Projects grants

Cancer Research UK- project grant, CRUK 2005-2007 “The role of FAK in pathological angiogenesis” (Co-applicant, PI: Dr. Kairbaan Hodivala-Dilke).
Budget: 300000 £

SYNERGASIA action, GSRT, 2011-2014 “From targets to Leads: Innovative therapeutics for Arthritis (TheRAlead)” (Co-applicant, Co-ordinator: Dr G. Kollias)
Budget for the lab: 8000€

Postdoctoral grant, GSRT, 2011 “The role of Talin in physiological and pathological angiogenesis (AngioTalin)” (Postdoctoral applicant: Dr A. Anagnostopoulou)
Budget: 150000€- not initiated

ELPEN, 2011 “Studying blood vessels during wound healing in diabetic conditions” (Co-ordinator)
Budget: 10000€