BIOGRAPHICAL SKETCH

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NAME: Kourtidis, Antonios (Antonis)

eRA COMMONS USER NAME (credential, e.g., agency login): akourtidis

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Aristotle University of Thessaloniki, Greece	BS	10/1998	Biology
Aristotle University of Thessaloniki, Greece	PhD	12/2004	Molecular Biology & Evolution
State University of New York at Albany, USA	Postdoctoral Fellow	07/2009	Molecular Biology of Cancer
Mayo Clinic Cancer Center, USA	Senior Research Fellow	08/2011	Epithelial Cell Biology

A. Personal Statement

I was trained as a Molecular Biologist at the School of Biology of the Aristotle University of Thessaloniki in Greece, where I obtained my PhD. I then came to the US and became involved in Cancer Biology as a Postdoctoral Fellow at the GenNYSis Center for Excellence in Cancer Genomics at the State University of New York at Albany, NY. I then moved on to specialize in Epithelial Biology as a Research Fellow and Research Associate at the Mayo Clinic Cancer Center in Jacksonville, FL. Current research in my lab focuses on the study of cell-cell adhesion complexes and their roles in cell signaling and behavior. My recent work led to a breakthrough finding: the adherens junctions associate with the RNA interference (RNAi) machinery, to regulate miRNA levels and function. Through this mechanism, the junctions suppress cell growth and expression of pro-tumorigenic and stem cell markers via miRNAs, in order to maintain the normal epithelial phenotype. I intend to fully explore this newly identified mechanism, of which we have only seen the tip of the iceberg: our follow-up data indicate that the interaction of the adherens junctions with RNA complexes and non-coding RNAs is extensive. I also intend to investigate the implications of this mechanism in disease. I am the lead author in several papers that have already been published from this work in top journals, such as ***Nature Cell Biology*** and ***Journal of Cell Biology***. This work has also already attracted competitive funding and earned me a faculty position at the Medical University of South Carolina. These are testaments both of the impact of this research as well as of my productivity and ability to lead cutting-edge projects as a mentor and an independent investigator. By combining my expertise in the areas of cellular, epithelial, cell-cell adhesion, and cancer biology, as well as molecular and RNA biology, I am fully and uniquely equipped to effectively conduct the proposed research. My recent findings bridged for the first time the fields of cell-cell adhesion and RNAi biology, initiating a new area of research, which I am eager to fully expand in my lab and to advance it into all directions.

B. Positions and Honors

Positions and Employment

2011-2016	Research Associate, Mayo Clinic Cancer Center, Mayo Clinic, Jacksonville, FL, USA
2014-2016	Instructor of Cancer Biology, Mayo Clinic College of Medicine, Mayo Clinic, Jacksonville, FL, USA
2016-present	Assistant Professor, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina, Charleston, SC, USA
2016-present	Associate Research Member, Cancer Genes & Molecular Regulation (CGMR) Program, Hollings Cancer Center, Medical University of South Carolina, Charleston, SC, USA

Honors

1997-1998	Tzivoglou Foundation award for undergraduate studies, Thessaloniki, Greece
2000-2002	Bodossaki Foundation fellowship award for PhD studies, Thessaloniki, Greece
2016	Abney Scholar, Hollings Cancer Center, Medical University of South Carolina (MUSC), USA
2016	Searle Award nomination, Medical University of South Carolina (MUSC), USA
2017	V Foundation Scholar Award nomination, Hollings Cancer Center, Medical University of South Carolina (MUSC), USA

Other Experience and Professional Memberships

2006-2009	Capital Region Cancer Research (CRCR) group, Albany, NY
2009-2016	Mayo Clinic Research Fellow Association (MRFA)
2010-present	Mayo Clinic Alumni Association
2009-present	Hellenic Bioscientific Association of the USA (HBA-USA) - Member
2015-present	American Society for Cell Biology (ASCB) - Member
2016-present	American Association for Cancer Research (AACR) - Member
2016-present	American Association for the Advancement of Science (AAAS) - Member
2016-present	Research Advisory Committee, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina (MUSC) - Member
2016-present	Faculty Search Committee, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina (MUSC) - Member
2016-present	Women Scholars Initiative Workshop Committee, Medical University of South Carolina (MUSC) - Member
2017-present	Seminar Series Supervisor, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina (MUSC)
2017-present	College of Graduate Studies Development Committee, Medical University of South Carolina (MUSC) - Member

C. Contribution to Science

1. Association of the adherens junctions with RNAi regulates epithelial cell behavior: In my most recent research effort, I dealt with the untangling of the conflicting pro- and anti-tumorigenic roles of the E-cadherin complexes, which were confusing the fields of adhesion and cancer biology for over a decade. My work resolved this apparent paradox by introducing three major conceptual advances: a) it revealed the presence of two spatially and functionally distinct E-cadherin-p120 catenin complexes at the junctions of non-transformed epithelial cells, one suppressing and one promoting cell growth; b) it uncovered the surprising association of the apical zonula adherens with a functional microprocessor complex and its core components DROSHA and DGCR8; c) it demonstrated association with of the zonula adherens with the RNA-induced silencing complex (RISC). By recruiting the RNAi machinery, the cadherin junctions maintain the normal epithelial phenotype via miRNA-mediated suppression of growth and stem cell markers. The discovery of a functional microprocessor outside the nucleus and the functional associations of RISC, miRNAs and mRNAs with the junctions, also consist major conceptual advances for the RNAi biology field. These findings bridged for the first time the fields of cell adhesion and RNAi biology, creating a new research field and introducing several novel research directions. A number of manuscripts were published or are in preparation from this work.

a. **Kourtidis A*,** Necela B, Lin WH, Lu R, Feathers RW, Asmann, YW, Thompson EA, Anastasiadis PZ. Cadherin complexes recruit mRNAs and RISC to regulate epithelial cell signaling. ***Journal of Cell Biology***, 2017, 216(10): 3073-85. PubMed PMID: 28877994. ***Co-corresponding author**
   (Faculty of 1000: Two Recommendations - 4 stars, to date)
b. **Kourtidis A,** Ngok SP, Pulimeno P, Feathers RW, Carpio L, Baker T, Carr JM, Yan IK, Borges S, Perez EA, Storz P, Copland JA, Patel T, Thompson EA, Citi S, Anastasiadis PZ. Distinct E-cadherin-based complexes regulate cell behaviour through miRNA processing or Src and p120-catenin activity. ***Nature Cell Biology****,* 2015, 17(9):1145-57. PubMed PMID: 26302406; PubMed Central PMCID: PMC4975377.
   (*Top read: in the top 1% of the 232,739 tracked articles of a similar age in all journals; Faculty of 1000: Two Recommendations - 4 stars, to date; Nature Medicine: News in Brief, October 2015, 21, 1112–13; Highlighted in BBC news and other news outlets*)
c. **Kourtidis A** and Anastasiadis PZ. PLEKHA7 defines an apical junctional complex with cytoskeletal associations and miRNA-mediated growth implications. ***Cell Cycle***, 2016, 15: 498-505. PubMed PMID: 26822694; PubMed Central PMCID: PMC5056615.
d. **Kourtidis A** and Anastasiadis PZ. Bringing together cell-to-cell adhesion and miRNA biology in cancer research. ***Future Oncology***, 2016, 12: 1211-1214. PubMed PMID: 26923006.

2. Identification of novel targets in cancer using RNAi-based functional genomics: Earlier in my career, I was involved in a research project to identify survival factors that the highly aggressive *ERBB2*-positive breast cancer cells depend upon to overcome *ERBB2*-targeting therapies and progress. During that work, I performed high-throughput RNAi screens that identified the metabolic regulators NR1D1, PBP and PPARγ as the strongest mediators of *ERBB2*-positive breast cancer cell survival, in addition to ERBB2. I have shown that these mediators boost a metabolic pathway that maximizes fatty acid production as a means of energy dependence for these cells, resulting in an altered physiology that is consistent with the Warburg effect. The two main research papers from this work have already been cited more than 80 times to date, in total. In parallel to this work, I also contributed articles and novel methods regarding the use of high-throughput RNAi applications in the discovery of targets in cancer.

a. **Kourtidis A**, Jain R, Carkner RD, Eifert C, Brosnan MJ, Conklin DS. An RNAi screen identifies metabolic regulators *NR1D1* and *PBP* as novel survival factors for breast cancer cells with the *ERBB2* signature. ***Cancer Research,*** 2010, 70:1783-92. PubMed PMID: 20160030; PubMed Central PMCID: PMC2837372.
b. **Kourtidis A**, Srinivasaiah R, Carkner RD, Brosnan MJ, Conklin DS. Peroxisome proliferator-activated receptor-γ protects ERBB2-positive breast cancer cells from palmitate toxicity. ***Breast Cancer Research***, 2009, 11:R16. PubMed PMID: 19298655; PubMed Central PMCID: PMC2688944.
c. **Kourtidis A**, Eifert C, Conklin DS. RNAi Applications in Target Validation. ***Ernst Schering Research Foundation Workshop***, 2007, 61:1-213. PubMed PMID: 17249494.
d. Evans SC, **Kourtidis A**, Markham TS, Miller J, Conklin DS, Torres A. microRNA target detection and analysis for genes related to breast cancer using MDLcompress. ***EURASIP Journal on Bioinformatics and Systems Biology*****,** 2007, 43670. PubMed PMID: 18317504; PubMed Central PMCID: PMC3171339.

3. Genomics and molecular evolution of heat-shock proteins: In my first research years during my PhD, I studied the molecular biology and evolution of the HSP70 and HSP90 family of heat-shock proteins. First, I constructed and screened whole genomic libraries from a mussel species, to fill the almost complete lack of knowledge for these proteins in mollusca, one of the largest animal phyla. This work identified many members of the HSP70 family and two members of the HSP90 family in mussels. A conceptual advance of this work included the discovery of satellite sequences and of a transposable element inside introns of the molluscan HSP70 genes, explaining the unusual large introns of these genes in these species and offering clues for the also unusual large molluscan genome, as opposed to its phylogenetic position.

a. **Kourtidis A**, Drosopoulou E, Nikolaidis N, Hatzi VI, Chintiroglou CC, Scouras ZG. Identification of several cytoplasmic HSP70 genes from the Mediterranean mussel (*Mytilus galloprovincialis*) and their long-term evolution in Mollusca and Metazoa. ***Journal of Molecular Evolution***, 2006, 62:446-459. PubMed PMID: 16547643.

b. **Kourtidis A**, Drosopoulou E, Pantzartzi CN, Chintiroglou CC, Scouras ZG. Three new satellite sequences and a mobile element found inside HSP70 introns of the Mediterranean mussel (*Mytilus galloprovincialis*). ***Genome***, 2006, 49:1451-1458. PubMed PMID: 17426760.
c. **Kourtidis A** and Scouras ZG. Analysis and characterization of the transcriptional unit of a new *Mytilus galloprovincialis* (Mollusca, Bivalvia) *hsp70* gene. ***DNA Sequence***, 2005, 16:36-43. PubMed PMID: 16040345.
d. Pantzartzi CN, **Kourtidis A**, Drosopoulou E, Yiangou M, Scouras ZG. Isolation and characterization of two cytoplasmic *hsp90* genes from *Mytilus galloprovincialis* (Mollusca: Bivalvia) that contain a complex promoter with a p53 binding site. ***Gene***, 2009, 431:47-54. PubMed PMID: 19061940.

Complete List of Published Work in MyBibliography.
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/46684716/?sort=date&direction=descending

D. Research Support

Ongoing

Start-up funding, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina
Kourtidis (PI) 08/01/16-07/31/19
Title: Association of the adherens junctions with the RNAi machinery regulates cell behavior
Goal: Explore a novel mechanism through which the adherens junctions recruit the RNAi mechanism to maintain cellular homeostasis
Role: PI

Abney Scholarship Award, Hollings Cancer Center, Medical University of South Carolina
Kourtidis (PI) 08/01/16-07/31/19
Title: The adherens junctions suppress pro-tumorigenic activity via RNAi
Goal: Investigate the implications of the adherens junctions-associated RNAi mechanism in cancer progression
Role: PI

American Cancer Society Institutional Research Grant, Hollings Cancer Center, Medical University of South Carolina
Kourtidis (PI) 01/01/17-12/31/17
Title: The Adherens Junctions suppress aberrant colon cell behavior via long non-coding RNAs
Goal: Explore the association and regulation of lncRNAs by the adherens junctions and the role of this cross-talk in colon cancer.
Role: PI

Digestive Diseases Research Core Center (DDRCC) Pilot & Feasibility Study Award, Medical University of South Carolina
Kourtidis (PI) 10/01/17-09/30/18
Title: The adherens junctions maintain colon cell homeostasis by recruiting the RNAi machinery
Goal: Investigate the implications and relevance of the adherens junctions-associated RNAi to colon cell behavior and intestinal disease.
Role: PI

Completed

Jay and Deanie Stein Career Development Award for Cancer Research - Mayo Clinic
Kourtidis (PI) 04/01/14-07/31/16
Title: Reversal of Ecad/p120-induced tumorigenicity of Inflammatory Breast Cancer cells via miRNA-mediated reprogramming
Goal: Investigate the role of adherens junctions-regulated miRNAs in inflammatory breast cancer
Role: PI