

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	Cellular and Molecular Biology of Cancer

A. Personal Statement

I was originally 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 to become an expert in Cancer Biology, first as a Postdoctoral Fellow at the GenNYSis Center for Excellence in Cancer Genomics at the State University of New York at Albany, NY, and then as a Research Fellow and Research Associate at the Mayo Clinic Cancer Center in Jacksonville, FL. My current research focuses on the study of cell-cell adhesion complexes and their roles in cell behavior and tumorigenic transformation. 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 markers via miRNAs, in order to maintain the normal epithelial phenotype. This was an unexpected finding, revealing for the first time the presence of the microprocessor complex outside the nucleus and its association with the adherens junctions. I intend to fully explore the newly identified AJs-RNAi mechanism, of which we have only seen the tip of the iceberg: follow-up data indicate that the interaction of the AJs with RNA complexes is extensive. I also intend to investigate the implications of this mechanism in tumor progression. I am strongly motivated to work on this novel fundamental mechanism and to advance it into new directions, also by collaborating with a broad group of experts from different fields. I am the lead author in several papers that have already been published or are in preparation to be submitted from this work in top journals, such as *Nature Cell Biology*. This work has also already attracted competitive funding. These are testaments both of the impact of this research as well as of my productivity and ability to lead cutting-edge projects as an independent investigator. As an expert in the areas of Molecular and Cellular Biology, cell-cell adhesion, RNAi, systems biology, functional genomics, epithelial and cancer biology, I am fully equipped to effectively conduct this research. My recent findings bridged for the first time the fields of adhesion biology and of RNAi biology, essentially creating a whole new area of research, which I am eager to fully expand in my lab.

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

Honors

1997-1998	Tzivoglou Foundation award for undergraduate studies, Thessaloniki, Greece
2000-2002	Bodossaki Foundation fellowship award for PhD studies, Thessaloniki, Greece

Professional Memberships

2006-2009	Capital Region Cancer Research (CRCR) group, Albany, NY
2009-2016	Mayo Clinic Research Fellow Association (MRFA)
2010-2016	Mayo Clinic Alumni Association
2009-present	Hellenic Bioscientific Association in the USA (HBA-USA)
2015-present	American Society for Cell Biology (ASCB)
2016-present	American Association for Cancer Research (AACR)
2016-present	American Association for the Advancement of Science (AAAS)

C. Contribution to Science

1. Association of the adherens junctions with RNAi regulates cell behavior in cancer: In my most recent research effort, I dealt with the untangling of the conflicting pro- and anti-tumorigenic roles of the E-cadherin and p120-catenin core adhesion proteins, which were confusing the fields of adhesion and cancer biology for over a decade. My work resolved this apparent paradox by introducing two 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; this interaction confers the anti-tumorigenic properties of the cadherin junctions, via miRNA-mediated regulation of growth markers. The discovery of a functional microprocessor outside the nucleus and its regulation by junctional proteins also consists a major conceptual advance for the RNAi biology field, since until now it was thought that the microprocessor resides and functions solely in the nucleus. 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**, 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.
(Top read: ~29,000 views to date; 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)
- b. **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
- c. **Kourtidis A** and Anastasiadis PZ. Bringing together cell-to-cell adhesion and miRNA biology in cancer research. **Future Oncology**, 2016, 12: 1211-1214

- d. **Kourtidis A**, Huvelde D, Yanagisawa M, Copland JA, Anastasiadis PZ. Pro-tumorigenic phosphorylation of p120 catenin in renal and breast cancer. *PLOS ONE*, 2015, 10(6):e0129964.

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 PPAR γ 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 54 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
- 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
- c. **Kourtidis A**, Eifert C, Conklin DS. RNAi Applications in Target Validation. *Ernst Schering Research Foundation Workshop*, 2007, 61:1-213.
- 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.

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
- 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
- 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.
- 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.

Complete List of Published Work in: [PubMed - Kourtidis, A](#)

D. Research Support

Ongoing Research Support

Abney Scholarship Award, Hollings Cancer Center, Medical University of South Carolina
Kourtidis (PI) 08/01/16-07/31/19

Association of the adherens junctions with the RNAi machinery regulates cell behavior

The goal of this study is to explore the novel mechanism through which the adherens junctions recruit the RNAi mechanism to suppress expression of pro-tumorigenic markers and maintain cellular homeostasis.

Role: PI

Completed Research Support

Jay and Deanie Stein Career Development Award for Cancer Research - Mayo Clinic
Kourtidis (PI) 04/01/14-07/31/16

Reversal of Ecad/p120-induced tumorigenicity of Inflammatory Breast Cancer cells via miRNA-mediated reprogramming

The goal of this project was to explore the relevance of adherens junctions-regulated miRNAs in inflammatory breast cancer and generate preliminary data for upcoming proposals

Role: PI