CURRICULUM VITAE

Richard A. Anderson

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Education:

B.S.	University of Minnesota, 1979, Biochemistry/Chemistry
Ph.D.	University of Minnesota, 1982, Biochemistry/Chemistry (R.E. Lovrien)
Postdoctoral	Yale University School of Medicine, 1982-1985, NIH Postdoctoral Fellow, Cell Biology and Protein Chemistry (V.T. Marchesi)

Academic positions:

1985-1986	Hull Cancer Research Fellow, Yale University School of Medicine
1987-1992	Assistant Professor, Department of Pharmacology, University of Wisconsin Medical School
1992-1996	Associate Professor, Department of Pharmacology, University of Wisconsin Medical School
1994-2011	Director and Founder, Molecular and Cellular Pharmacology Program
1999-2001	Chair and Vice chair, Biological Sciences Executive Committee and Tenure Committee
1996-2011	Professor, Department of Pharmacology, University of Wisconsin Medical School
2011-present	University Professor, University of Wisconsin-Madison School of Medicine and Public Health

Awards and Honors:

1979	American Chemical Society Award for Undergraduate Research
1979	Phi Beta Kappa
1981	Sigma Xi Graduate Research Award
1982	American Cancer Society Postdoctoral Fellowship
1982-1985	NIH Postdoctoral Fellowship
1983	Bacaner Basic Science Award
1986	Argall L. and Anna G. Hull Fund Cancer Research Fellowship Award
1988	March of Dimes Basil O'Connor Scholar Research Award
1992-2014	Wisconsin/Hilldale/Undergraduate/Faculty Research Awards (15 awards)
1996-2001	H.I. Romnes Faculty Fellow
1998-2002	Vilas Associate
2005	Visiting Professor, Stony Brook University
2004	William R. Kellett Midcareer Professor Award
2008	Keynote Speaker, Biomembrane Symposium, Purdue University, Biochemistry
2009	Vert Professor, K.U. Leuven and EMBO YIP, Department Human Genetics, Belgium
2010	Visiting Professor, Vollum Institute, Oregon
2010	Keynote Speaker, 27th Naito Conference on "Membrane Dynamics and Lipid Biology"
2012	Keynote Speaker, University of Marseille, France

Society membership:

American Association for the Advancement of Science; American Society for Cell Biology; RNA Society; American Heart Association; Biochemical Society; American Association for Molecular Biology and Biochemistry; American Society for Pharmacology and Experimental Therapeutics; American Association for Cancer Research

Service:

University Service:

1987-1990	Faculty Senate
1987-1988	Examinations Committee, Cell and Molecular Biology Program
1989-1998	Undergraduate Molecular Biology Advisory Committee
1989-1994	Admission Committee, Cell and Molecular Biology Program
1991-1994	Chair, Admissions Committee, Cell and Molecular Biology Program
1991-1994	Member, Coordinating Committee, Cell and Molecular Biology Program
1992-1993	Faculty Search and Screen Committee, Department of Pharmacology
1993-1995	Faculty Promotions Committee, Medical School
1994-1996	Faculty Search and Screen Committee, Department of Pharmacology
1996-1999	Faculty Advisory Committee, Medical School
1996-2000	Graduate Council, Medical School
1996-1999	Graduate School Research Committee
1996-1999	Faculty Awards Subcommittee, Graduate School Research Committee
1996-1997	Search and Screen Committee, Department of Pharmacology
1996-1997	Search and Screen Committee, School of Pharmacy
1997-2004	Steering Committee, Biotechnology Center
1997-1998	Search and Screen Committee, Department of Pharmacology
1995-1999	Chair, Mentoring Committee for Assistant Professor Emery Bresnick
1996-2003	Member, Mentoring Committees for Assistant Professor Shigeki Miyamoto, Assistant Professor Anna Huttenlocher
1997-2001	Executive Committee, Cell Adhesion and Signal Transduction Group
1998-2003	Member, Steering Committee, Cell and Molecular Biology Program
1998-2003	Member, Directors Committee, Biological Sciences
1998-2002	Member, Biological Sciences Executive Committee and Tenure Committee
1998-2002	Hilldale Award Selection Committee
1999-2000	Vice Chair, Biological Sciences Executive Committee and Tenure Committee
1999-2003	Co-Chair, Graduate Council, Medical School
2000-2001	Chair, Biological Sciences Executive Committee and Tenure Committee
2000-2001	Co-Chair, Cell Signaling Group, Cell and Molecular Biology Program
2000-2003	Member, Graduate School Fellowship Committee
2000-2006	Chair, Mentoring Committee for Assistant Professor Patricia Keely
2002-2007	Member, Mentoring Committee for Assistant Professor Randal Tibbetts
1994-2011	Chair, Steering Committee, Molecular and Cellular Pharmacology Program
1992-2011	Executive Committee, Department of Pharmacology
1994-2011	Director, Molecular and Cellular Pharmacology Program
1996-2011	Principal Investigator, Molecular and Cellular Pharmacology Training Grant
2012-present	Member, Hilldale Undergraduate/Faculty Research Fellowships Holstrom Environmental Scholarships selection committee

Professional Service:

Reviewer for:

Journals (since 2000):

Nature, *Journal of Cell Biology*, *Blood*, *Journal of Cellular Physiology*, *Journal of Biological Chemistry*, *Journal of Cell Science, Cell, Biochimica et Biophysica Acta*, *Biochemistry*, *Science, Molecular Endocrinology, Molecular Biology of the Cell, Molecular Cell, Nature Medicine, Nature Cell Biology, Nature Structure, Current Biology and others. On average about 50 manuscripts are reviewed each year.*

Outside Faculty Review and Promotion Evaluation Requests:

Each year since 1996 I have reviewed 1-4 faculty tenure, promotion, or continuation documents from institutions outside the University.

Editorial Boards (since 2008):

Journal of Biological Chemistry (1997-2008), Biochemical Journal (2006-2010), Cell Health and Cytoskeleton (2008-present), 'FACULTY OF 1000' (2010-present), *Molecular Biology of the Cell* Editorial Board (2012-prsent).

Current Society Committees:

ASCB* Public Policy Advocacy Team, *Project 50. Receive briefings on critical science policy issues, serve as contact in their state to work with the Public Policy Committee, and meet with Representatives and Senators to advocate support of biological research

Grant and Program Review Panels:

Biotechnology and Biological Sciences Research Council, UK (1990, 1992, 1996, 2001)
NIH BIOL-2, Biological Science 2 Study Section, Ad Hoc (1994)
National Science Foundation (1992-1996, 1998-2000)
Welcome Trust, UK (1993, 1996-2000)
NIDDK, Special Review Site Visit, Berkeley (1996)
External Reviewer, Babraham Institute, Cambridge, United Kingdom (1997-1998)
The Israel Science Foundation (1997-1999, 2003-2008)
Dutch Cancer Society (1997-1999, 2002)
NCI, Special Review Site Visit, Harvard (2000)
NCI, Scientific Review Group – Subcommittee C, Ad Hoc (2000)
NIGMS, Scientific Review Group Site Visit, University of Chicago (2001)
NIH/Physiological Chemistry Study section, Ad Hoc (2003)
NIH/Heart, Lung, and Blood Institute, Scientific Review Group Site Visit, UCSF (2003)
American Heart Association (Molecular and Cellular Biology Review Committee) (2003-2004)
National Institute of General Medical Sciences - BRT training grant review committee (2005-2009)
Chair - American Heart Association (Molecular and Cellular Biology Review Committee 3 (2005-2009)
NIDDK Institute, Scientific Review Group Site Visit (2005)
Chair, NIGM, Scientific Review Group Site Visits (2004, 2006, 2007, 2009)
Wisconsin Institutes for Discovery Review (2007)
Chair, NCI, Scientific Review Group Site Visit, UCSD (2009)
NCI, Tumor Progression and Metastasis Study Section (2010)
MRC Peer Review, Research Councils, UK (2010)
Chair, NIDDK, Special Emphasis Panel ZDK1-GRB-8 (2010)
NCI, EUREKA review panel (2010 and 2011)
NCI, Tumor Progression and Metastasis Study Section (2011)
MRC Peer Review, Research Councils, UK (2012)
NCI Omnibus R21/R03 Application Review Committee (2012)
NIH, ZRG1 IMST-R study section (NIH Program Project (P01) grant review) (2014-present)
Chair, American Heart Association (Molecular Signaling Review Committee 4) (2013-2015)
French National Research Agency (ANR) (2015)
MRC Peer Review, Research Councils, London, UK (2014-2016)
National Heart Lung and Blood Institute Board of Scientific Counselors Intramural Review (2016)
Israel Science Foundation, Peer Review (2016)
European Research Council (2016- present)
Austrian Science Fund review of Doctoral Programme (DK) BACCARINI Manuela, "Signaling Mechanisms in Cellular Homeostasis" site visit in Vienna, Austria (2016)
BBSRC Bioscience for the Future, Peer Review, Polaris House, London, UK (2016)
NIH review panel, "Maximizing Investigator's Research Award" ZGM1 TRN-7 (MIRA) (2016)

Meeting Organization:

Chair, Scientific Program Committee: International Symposium on "The Role of Phosphoinositides in

Cell Signaling", 1996, University of Wisconsin-Madison;
Chair, *ASCB 2014 Special Interest SUBGROUP meeting, "Nucleoskeletal Dynamics in Signaling and Gene Expression";*
Chair, FASEB Science Research Conference (2016), "*Phospholipid Signaling in Cancer, Neurodegeneration and Cardiovascular Disease.*"

Consulting:

Onyx Pharmaceuticals, 1995-1996, Amgen Inc., 2000, 2002, 2008, and 2011, Lilly Pharmaceuticals, 2004, 2006, 2009, and 2011, Echelon Biosciences (2015- present).

Training Program Leadership and Service:

Training Program Membership:

Cell and Molecular Biology Program (1987 – present)
Pharmacology Graduate Program (1987 – 1994)
Biomolecular Chemistry Graduate Program (1992 – 2009)
Molecular and Cellular Pharmacology program (1994 – present)
Medical Sciences Training Program (1988- present)
Molecular Biosciences Training Program (1988 – present)
Biotechnology Training Program (1998 – present)
Molecular & Environmental Toxicology (2006 – present)

Development and Direction for the Molecular and Cellular Pharmacology Program: Founding director of the Molecular and Cellular Pharmacology Program at Wisconsin. The University of Wisconsin has a rich tradition in the study of pharmacology with an emphasis on molecular and cellular approaches. A small, but excellent graduate programs leading to the Ph.D. in Pharmacology have been present at the University of Wisconsin since establishment of the School of Pharmacy and the School of Medicine in 1917. In addition, training in pharmacological research has occurred in departments beyond these two programs. In the early 1990's, it was clear that to develop the most outstanding training program, there must be change. Thus, to take advantage of the rich training environment at the University of Wisconsin, the Molecular and Cellular Pharmacology (MCP) Graduate Program was established in 1994 and I was appointed as the founding Director. The MCP Graduate Program is now the only degree-granting Pharmacology Program at Madison.

In 1996, an NIH Training Grant was awarded and renewed in 2002 and in 2007. Competitive extramural funding of trainees increased from $0/year in 1994 to ~$800,000/year in 2010 supporting ~24 student stipends/year from the NIH training grant and other competitive sources. During this time, the MCP Training Program has expanded from 21 to 49 faculty trainers associated with 15 different departments spanning five separate colleges. The student group grew from 4 students to a yearly average of ~50 doctoral students. The students published >400 manuscripts. The active participation of the Program faculty led to the offering of a cohesive curriculum in Molecular and Cellular Pharmacology. The curriculum includes didactic graduate courses, a research-oriented laboratory rotation program, and a weekly seminar schedule that focuses on visiting speakers, along with trainee and faculty presentations and a annual campus wide symposium. See http://molpharm.wisc.edu/. In late 2010, I stepped down as program director.

Graduate Student Doctoral Committees:

I currently serve on 3 Ph.D. Committees for students in four different Ph.D. programs on campus. I have served on over >100 Ph.D. Committees since coming to Madison.

Community Service:

President, Village of Cross Plains 2003-2005: Cross Plains, Wisconsin- a vibrant community of 3373 residents close to Madison. Annual budget of ~3.8 million dollars and employs over 20 people. The community is famous as the home of the Black Earth Creek, which is a world-class trout stream that flows through the village. The role of the Village President is to appoint all committees, commissions, develop the budget, and chair the village board.

Accomplishments in Office: Built the first "Environmentally Green" Library in the State of Wisconsin. Initiated and directed the private fund raising efforts for 60% of the $4.9 million cost. Sited and initiated the renovation of the village water purification facility ($6.9 million). Initiated and completed the economic development-plan for the village that emphasizes the Black Earth Creek of an economic development resource. Initiated the design of a "Water Quality Corridor" along the Black Earth Creek though and beyond the village that was adopted in a referendum of the voters. Initiated and chaired the Economic Development Committee in the village. Initiated and appointed the Budget Committee that defined and streamlined village spending resulting in annual savings of ~6% for village expenditures.

Continued Membership on Civic Committees:
Membership of advocacy groups: "Concerned Citizens of Cross Plains"; "Black Earth Creek Watershed Association" and the executive committee; Black Earth Creek Conservation Organization, and the executive committee.

Civic Awards:

"Water Champion of the Black Earth Creek", 2005; "Trout Unlimited Certificate of Appreciation", for establishment of the Water Quality Corridor along the Black Earth Creek, 2006.

Richard A. Anderson, Ph.D.

Kellett and University Professor

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Research Interests:

My early research led to the discovery that phosphatidylinositol-4,5-bisphosphate ($PI4,5P_2$) is a lipid messenger(*Nature, 318:295-8*). This discovery initiated a focus on the biochemistry, cell and molecular biology of phosphoinositide signal generating enzymes and $PI4,5P_2$ effectors. Today, it is clear that $PI4,5P_2$ and derived messengers control most aspects of cell biology including secretion/vesicular trafficking, cell migration, proliferation, cell morphogenesis, nuclear signaling, gene expression, cell differentiation and many disease processes.

My group discovered many of the enzymes and pathways that are key to these processes. Our current research goals are to understand the biological functions of phosphoinositide signaling and the underlying cellular and biochemical mechanisms by which these regulatory processes impact human diseases. A fundamental theme pioneered by my work is that phosphoinositide signaling and PIP kinases (PIPK) are spatially and temporally assembled into complexes that define signaling specificity and biological function. PIPKs directly associate with $PI4,5P_2$ effectors and these associations define signaling specificity(*J. Biol. Chem. 274:9907-9910*). These interactions are multifaceted, highly regulated and dependent on the cellular context or signaling pathway. We use a multiplicity of approaches including cell biological, chemical, biochemical, structural, molecular biological, mouse models, and a wide range of microscopic approaches. We currently focus on several major themes:

CURRENT PROJECTS:

Signaling pathways that regulate cell morphogenesis, cell polarity, proliferation, cell migration/invasion, receptor trafficking and cell survival. We focus on mechanisms by which cells regulate polarity with an emphasis on cytoskeletal dynamics and the trafficking of adhesion and growth factor receptors. These processes regulate the dynamics of cell-cell contacts assembly during epithelial morphorgenesis and cell to matrix adhesion during migration/invasion(*Nature, 420:89-93, Dev. Cell, 22, 116–130*). These combined events are the underpinnings of cancer metastasis. These projects have a translational emphasis on cancer progression and metastasis but are also fundamental in cardiovascular diseases and many biological processes. A current emphasis is the type Iγ PIP kinase (PIPKIγ) family of enzymes that are generated by pre-mRNA splicing(*Biochem. J.* **422**, 473-482). PIPKIγi1-7 family members are differentially targeted in cells and have distinct cellular functions.

Polarized membrane receptor trafficking – We discovered that PIPKI isoforms regulate membrane trafficking and secretion(*Nature* **374**, 173-177). Recently, we have defined a role for the PIPKIγi2 isoform and the exocyst in directional membrane trafficking that controls β-integrin (and other receptors) targeting to talin rich adhesion complexes at the leading edge of migrating cells(*Dev. Cell, 22, 116–130*). In this pathway (**Fig. 1**), PIPKIγi2 directly interact with both the exocyst and talin linking these two protein and delivers β-integrin containing vesicle to plasma membrane regions rich in talin (adhesion complexes). The

generation of PI4,5P_2 modulates both exocyst and also the talin interaction with β-integrins which controls focal adhesion assembly and cell-matrix interactions, key events in migration and invasion. This pathway also modulates trafficking of membrane receptors that control epithelial polarization(*Mol. Biol. Cell.* 23, 87-98). Currently, we are identifying specific receptors/membrane proteins trafficked by this pathway, the mechanisms for receptor specificity, and the role of this pathway in the metastasis of breast cancer cells using mouse models.

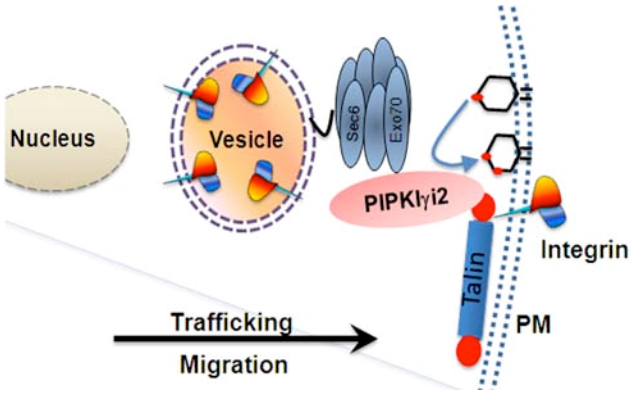


Figure 1. PIPKIγi2 regulated polarized trafficking of adhesion receptors controls directional cell migration(*Dev. Cell, 22*, 116–130).

Novel endosomal EGF receptor signaling in control of both proliferation and autophagy – We showed that PI4,5P_2 is generated at the late endosome(*J. Biol. Chem., 274:17794-17805*) and discovered an endosomal targeted PIPKIγi5 that selectively controls epidermal growth factor receptor (**EGFR**) sorting to the lysosome(*Dev. Cell, 25, 144–155*). Endosomal trafficking and degradation of the EGFR is essential for control of its signaling. PI4,5P_2 is an established regulator of endocytosis, whereas PI3P modulates endosomal trafficking. Yet, PIPKIγi5, an enzyme that synthesizes PI4,5P_2, controls endosome to lysosome sorting of EGFR (**Fig. 2left**). PIPKIγi5 is targeted to the endosomal where it interacts with sorting nexins, proteins that are PIP_2 effectors. The loss of PIPKIγi5, sorting nexin 5 (SNX5), or other PI4,5P_2 effector proteins in this pathway block EGFR sorting into intraluminal vesicles (ILVs) of the multivesicular body (MVB). Loss of ILV sorting enhances and prolongs EGFR signaling. These findings reveal that PIPKIγi5 and PI4,5P_2 form a unique signaling nexus that represents a paradigm shift in understanding the role of phosphoinositides in endosomal sorting (**Fig. 2left**). Remarkably, the PIPKIγi5 pathway is selective for EGFR(*Dev. Cell, 25, 144–155*).

We are defining components in this pathway, the receptor specificity and underlying mechanisms. Our studies show that PIPKIγi5 associates with lysosomal-associated transmembrane protein 4B (LAPTM4B) a known oncogene that is over expressed in many cancers and stimulates proliferation and anti-cancer drug resistance. We have shown that LAPTM4B blocks EGFR down regulation and enhances signaling by blocking sorting into ILVs(*EMBO J, 34, 475-90*). Our results indicate that the PIPKIγi5 and LAPTM4B pathway is a key regulator of EGFR signaling with broad implications for cancer progression.

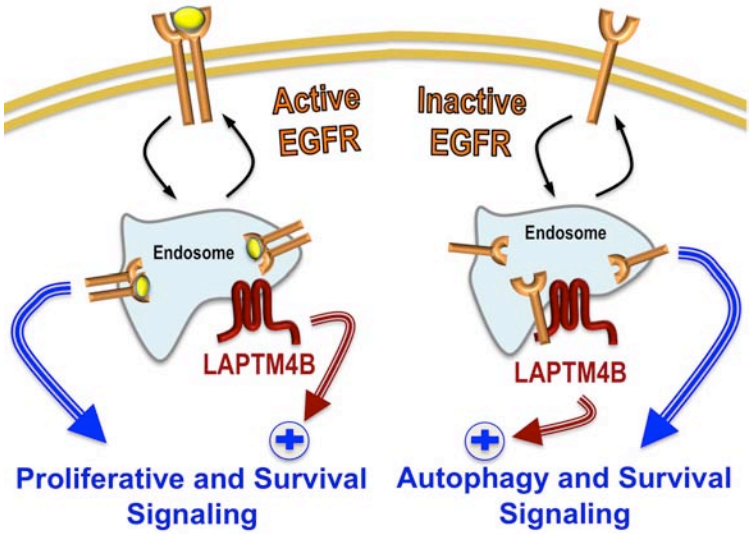


Figure 2. **Novel EGF receptor signaling pathways control proliferation and autophagy. Left**, the sorting of EGF activated EGFR to the endosome and then the lysosome terminates EGFR signaling (*Dev. Cell, 25, 144–155*). This pathway is regulated by LAPTM4B that enhances and prolongs EGFR signaling by blocking sorting to the lysosome(*EMBO J, 34, 475-90*). **Right**, remarkably the inactive EGFR also signals and is required for the initiation of autophagy. LAPTM4B also functions in this pathway as a co-activator of inactive EGFR's role in autophagy initiation (*Cell* 160, 145-160). PIPKIγi5 and PI4,5P_2 regulate both pathways.

A Kinase Independent Role for EGF Receptor in Autophagy Initiation - EGFR is over-expressed and/or over-activated in numerous human cancers. EGFR activation suppresses autophagy in tumor cells, and inhibition of EGFR signaling induces autophagy. We have discovered an unanticipated role for the inactive EGFR in autophagy initiation(*Cell* 160, 145-160). In this pathway inactive EGFR directly interacts with the oncoprotein LAPTM4B that is required for the endosomal accumulation of EGFR upon serum starvation. Inactive EGFR and LAPTM4B stabilize each other at endosomes and recruit and activate components required for basal and stress induced autophagy. Thus, the oncoprotein

LAPTM4B facilitates the role of inactive EGFR in autophagy initiation (see **Fig. 2Right**). This pathway is specific for the EGF receptor and positioned to control tumor metabolism and promote tumor cell survival upon stress induction of autophagy. Remarkably, EGFR kinase inhibitors also induces autophagy and may be a mechanism that impedes the effective use of these drugs as cancer therapies(*Cell* 160, 145-160)). These discoveries have opened unexpected mechanisms for EGFR in the proliferation and cell survival that appear specific for this receptor.

A switch in PIPKIγ isoform expression is an emerging mechanism for control of EGF receptor dependent cancer progression **-** There are four PIPKIγ isoforms that are expressed in mesenchymal and epitherial cells, these are the PIPKIγi1, 2, 4, and 5. Each of these isoforms has a distinct cellular function. PIPKIγi1 and 2 are required for EGF stimulated cell migration/invasion and for anchorage independent growth(*JBC* **288**, 34707–34718) and these activities are dose dependent. PIPKIγi4 and 5 isoforms control the expression of the PTEN tumor supressor and down regulation of the EGF receptor, respectively. Emerging data indicates that in triple negative breast cancers the PIPKIγi1 and 2 are overexpressed and the PIPKIγi4 and 5 are reduced or lost. The net effect would be enhanced survival, migration and invasion, and increased EGF receptor signaling. Where as a decrease of PTEN control of PI 3-kinase signaling enhances survival. Combined this could have a dramatic impact on the progression of cancers that are controlled by EGF receptor signaling (see discussion below).

Microenvironment regulation of cell growth **-** Emerging results indicate that PIP kinase family members integrate into multiple signaling pathways that are dependent upon environmental cues. For example, the PIPKIγi2 isoform integrates into a signaling nexus with Src and PI 3-kinase that is required for anchorage independent cell growth(*JBC* **288**, 34707–34718) and the development of breast cancer stem cell phenotypes. Yet growth of these cells in 2-D is independent of PIPKIγi2 but in this environment requires PIPKIα. Consistently, PIPKIγ isoforms are required for the metastasis of breast cancer cells and over expression (or loss of specific isoforms), as observed in triple negative breast cancers, enhances metastasis of breast cancer cells in a mouse model.

The Role Of Scaffolding Proteins In Phosphoinositide Signaling - $PI4,5P_2$ modulates actin assembly and dynamics at the leading edge of motile cells. We discovered that IQGAP1 scaffolds PIP kinases and is a $PI4,5P_2$ effector(*EMBO J. 32, 2617-30)*. IQGAP1 is a signaling scaffold that interact with multiple G-proteins, protein kinases, adhesion receptors and other signaling molecules. Type Iα and Iγ PIP kinase isoforms bind IQGAP1 and these PIP kinases and IQGAP1 have roles in multiple pathways. The assembly of PIPKIγ isoforms regulate IQGAP1's role in directional cell migration/invasion and cell polarization(*EMBO J. 32, 2617-30)*.

Agonist-stimulated $PI3,4,5P_3$ generation by scaffolded phosphoinositide kinases- The progression of most cancers is driven by receptor activation of the class I $PI4,5P_2$ 3-kinase composed of the regulatory p85 and the p110α catalytic subunits (**PI3K**) that generates phosphatidylinositol-3,4,5-trisphosphate (**$PI3,4,5P_3$**). We have discovered a mechanism for spatial and temporal activation of PI3K and $PI3,4,5P_3$ generation downstream of agonists that is selectively required for the survival of cancer cells. This pathway requires generation of PI4P and $PI4,5P_2$ by a PI 4-kinase and PI4P 5-kinase, respectively. We have discovered that agonists that stimulate proliferation and survival induce the assembly of an IQGAP1 complex containing Ras, PI 4-kinase (**PI4K**), PIP 5-kinase (**PIPKIα**), PI3K, and the 3-phosphoinositide dependent protein kinases PDK1 and Akt (**Fig. 3**). We have shown that activation of multiple growth factor receptors including EGFR,

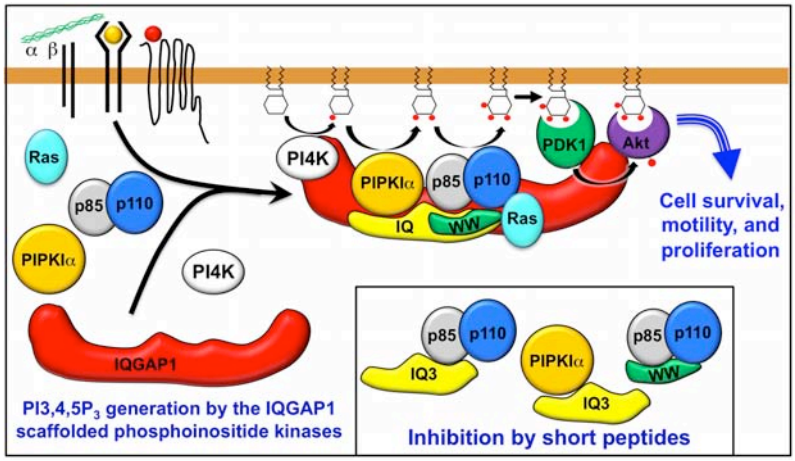


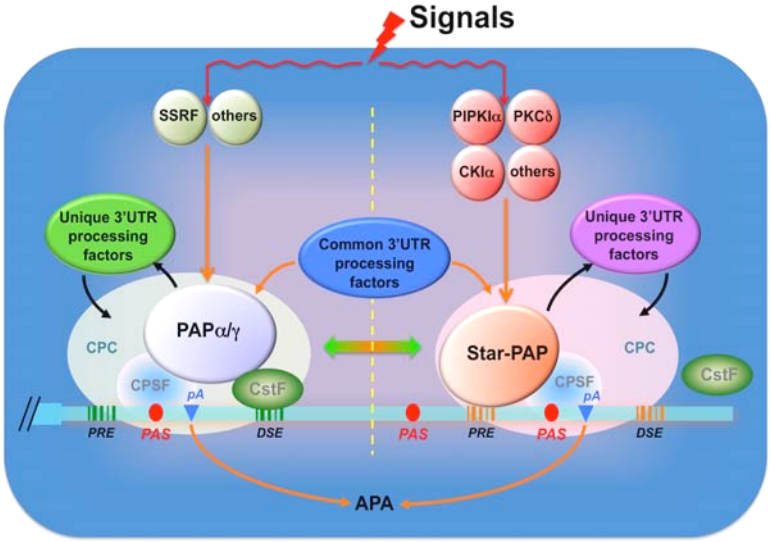
Figure 3. Receptors stimulate assembly of IQGAP1 with PI4K, PIPKIα, Ras, and PI3K resulting in concerted $PI3,4,5P_3$ generation with PDK1 and Akt signaling(*Nature Cell Biology* **18**, 1324–1335).

integrins and others stimulate assembly of this IQGAP1-phosphoinositide kinase complex, leading to concerted PI3,4,5P_3 synthesis and activation of PDK1 and Akt. This complex uses PI as the initial kinase substrate and as PI is ubiquitous, this IQGAP1 complex can generate PI3,4,5P_3 and activate PDK1 and AKT on any cellular membrane.

We have mapped the PIPKIα and PI3K binding site on IQGAP1 and have been able to make short IQGAP1 derived peptides that block PIPKIα and/or PI3K binding to IQGAP1. Blockade of this assembly with IQGAP1 derived peptides selectively block PI3,4,5P_3 synthesis and Akt signaling leading to cell survival. These peptides selectively kill many cancer cells. These indicate that the IQGAP1-phosphoinositide kinase complex is a novel drug target for cancer therapeutics. This combined work is published as an article at ***Nature Cell Biology*** **18**, 1324–1335**.**

Nuclear Phosphoinositide Signaling Controls Gene Expression. Almost 30 years ago Irvine and Cocco discovered that phosphoinositides could be generated in purified nuclei (see ***Trends Cell Biol.*, 20, 25-35**). Recently, we have discovered nuclear phosphoinositide signaling pathways that control mRNA processing and ultimately gene expression(***Nature, 451:1013-7***). Within the nucleus there are phosphoinositide pathways on the inner nuclear envelope. In addition, we discovered a novel phosphoinisitide compartment(s) associated with interchromatin granule clusters or nuclear speckles, which are compartments separate from known membrane structures(***Mol Biol Cell, 12:3547-60***). We have pioneered the investigation of the role of the nuclear phosphoinositide pathways and have shown that nuclear phosphoinositide pathways control 3'-end processing and polyadenylation of oxidative stress response, DNA damage and apopotosis mRNAs(***Nature, 451:1013-7, Mol. Cell, 45, 25–37***). These pathways are dependent on a novel non-canonical poly(A) polymerase that we named **Star-PAP** (for nuclear **S**peckle **Tar**geted **P**IPKIα **R**egulated-**P**oly(**A**) **P**olymerase)(**Nature, 451:1013-7**). Star-PAP is a nuclear PAP that is a PI4,5P_2 effector and requires PI4,5P_2 for it's poly(A) polymerase activity both *in vitro* and *in vivo*. *In vivo* Star-PAP controls the expression of key master genes that regulate cell stress pathways. Recently we have shown that Star-PAP controls expression genome wide.

Star-PAP controls genome wide alternative polyadenylation (APA) - Most genes in higher eukaryotes (~70% in humans) have multiple alternative 3'UTRs that are generated by APA. APA is significant as changes in the 3'-UTR control the stability and translation of mRNAs and thus protein expression. Changes in APA are implicated in cancer progression, stem cell differentiation, are cell type specific and are emerging as global regulatory mechanisms. Most recently, we have shown that the nuclear PAPs, PAPα, β, and γ and Star-PAP control genome wide APA and 3'-end processing of human genes (**Fig. 4**). Most significant each of the nuclear PAPs have specificity in control of individual and sets of genes by APA(*in revison,* ***Nature.comm***). Star-PAP is regulated by the lipid messenger PI4,5P_2 that is generated by PIP kinases that directly interact with Star-PAP. In addition, specific signaling pathways regulate the composition of Star-PAP complex which contains different phosphoinositide kinases, protein kinases and other signaling molecules that act as signaling transactivators. These signaling transactivators define Star-PAP's specificity toward genes and APA sites within a single gene. The canonical PAPα/γ also show specificity toward specific genes and APA sites but are regulated differently. The emerging data indicate that APA is regulated genome wide downstream of



CPC: *cleavage and polyadenylation complex;* ***PRE:*** *PAP regulatory element,* ***PAS:*** *poly(A) signal,* ***pA:*** *polyadenylation site,* ***SSRF:*** *specific signaling regulatory factors*

Figure 4. Regulation of 3'-end APA by the nuclear Star-PAP and PAPα/γ demonstrates that the PAPs have specificity toward genes. Star-PAP activity requires PI4,5P_2 stimulation suggesting spatial regulation of 3'UTR processing and control of expression(***Nature****, in revision*).

cellular signals and is a key mechanism for control of gene expression. In humans where the majority of genes have APA sites, the regulation of 3'-end processing may be equally important as 5' regulation of gene expression.

A current focus is to define the role and mechanisms of APA in expression of a key set of genes that control development, proliferation, cancer and cardiovascular disease. These genes include *PTEN*, *NQO1*, *MDM2*, *AKT1-3*, and *RhoA*, that contain between three and nine 3'-end APA sites. Star-PAP modulates a subset of APA sites for each of these genes. Star-PAP controls both distal and proximal APA sites. Significantly, Star-PAP regulated changes in APA have a dramatic impact on protein expression. For example, in the case of the PTEN tumor suppressor, Star-PAP controls all of the signal requlated APA sites (the most distal sites) and the expression of >80% of the cellular PTEN protein.

Star-PAP control of APA regulates expression of key regulatory genes and their expression is tightly controlled by signaling (**Fig. 4**). In higher eukaryotes most genes are regulated by APA. Thus, we hypothesize that 3'-end APA is a mechanism utilized in more complex organisms to fine tune gene expression. Our current objective is to define genome wide APA sites and transactivating factors for Star-PAP that are regulated by specific signaling pathways. A key aspect will be to define Star-PAP spatial modulation by lipid messengers within the nucleus.

Intranuclear spatial control of gene expression - The spatial organization of the nucleus and gene expression is dynamic and changes in disease states. The major cellular function of PIP_n isomers is to organize and assemble cellular compartments both temporally and spatially(***BioEssays***, **35**, 513–522). Thus, nuclear PIP_n isomers are positioned to play key roles in the organization of nuclear events including gene expression (**Fig. 5**). Synthesis of the lipid messenger $PI4,5P_2$ is required for Star-PAP control of 3'UTR processing. As $PI4,5P_2$ is found in membranes, this implies that the intranuclear organization of Star-PAP target gene expression and processing could spatially occur at the inner nuclear envelope (**Fig. 5**). Potentially, some Star-PAP target genes upon activation may become docked on the inner nuclear envelope (or nuclear pore complex) or the pre-mRNA maybe localized and processed at the envelope. There is evidence for these models and this could enhance gene expression and export of the resulting mRNA. In this paradigm, if spatial organization of a gene during expression is required for Star-PAP processing, the loss of normal intranuclear organization or changes in $PI4,5P_2$ spatial generation could dramatically change expression, consistent with changes in nuclear organization and expression in cancer cells.

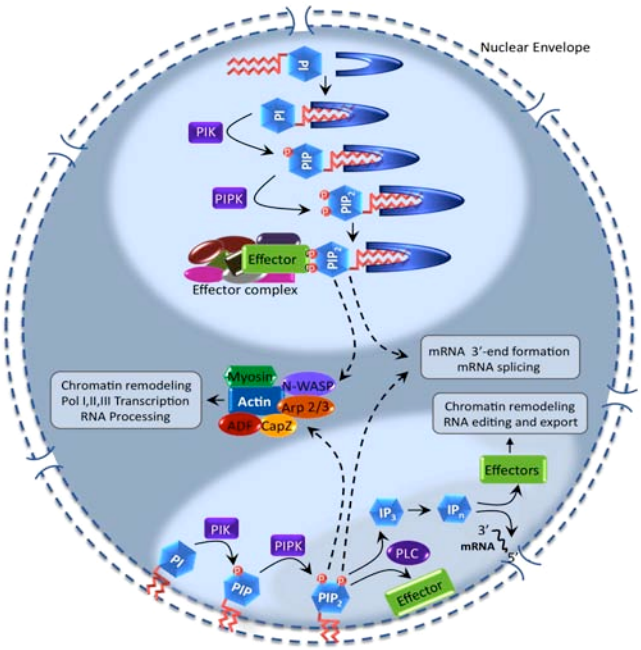


Figure 5. PIP_2 is localized to multiple intranuclear compartments and is positioned to regulate intranuclear organization. Generation of PIP_2 is required for Star-PAP control of gene expression through 3' APA(***Trends Cell Biology***, **20**, 25-35). Disruption of spatial PIP_2 synthesis may alter nuclear organization and may block Star-PAP dependent 3'-end processing of genes.

Alternatively, or in addition, there may be islands of phosphoinositides generated within the nucleus at non-membrane structures (**Fig. 5**). Our data also supports this model. Combined, these data indicate that lipid messengers are positioned to modulate spatial regulation of gene expression within the nucleus. This putative role for phosphoinositide lipid messengers appears to have evolved in higher eukaryotes and may represent an unexpected mechanism for spatial organization of gene expression and control of 3'-end processing is one example. We are determining if Star-PAP regulated genes are clustered when expressing, if Star-PAP regulated genes move to the nuclear envelop upon expression, the nature of the non-membrane PIP_2

compartment and if nuclear PIP kinases modulate nuclear organization by regulation of nuclear actin or other nuclear cytoskeletal components.

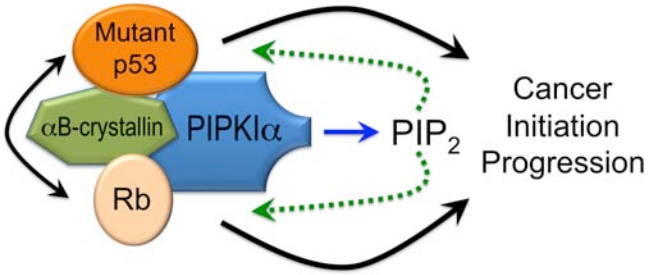


Figure 6. Mutant p53 stability requires PIPKIα, and αB-crystalin. Rb also interacts with PIPKIα and αB-crystalin and may function in the mutant p53 stability pathway.

Control of mutant p53 stability – Mutation of the p53 tumor suppressor is the most frequent event in cancers. Mutation of p53 gives rise to a stable mutant protein whose accumulation is a hallmark of cancer cells. Mutant p53 loses its ability to suppress tumors and often gains additional oncogenic functions that bestow growth and survival advantages. Mutations in p53 occur at different phases of malignant transformation and contribute to tumor initiation, promotion, aggressiveness, and metastasis. Turnover of mutant p53 is regulated differently from the wild type protein. The degradation mechanisms for mutant p53 are poorly defined.

Our emerging results have shown that the stability and turnover of mutant p53 is controlled by the nuclear PIPKIα and PIP_2. From these studies p53 directly interacts with PIPKIα and p53 appears to be a PIP_2 effector as it binds this phosphoinositide. Strickingly, PIPKIα controls the turnover of mutant but not wild type p53 (**Fig. 6**). The regulation of mutant p53 occurs by a ternary interaction between mutant p53, PIPKIα, and αB-crystalin. The αB-crystalin protein is a member of the small heat shock protein family and functions as molecular chaperone that binds misfolded proteins. Rb also interacts with PIPKIα and αB-crystalin and may function in the mutant p53 stability pathway, although this is less defined.

The kinase activatiy of PIPKIα is required for these functions indicating that generation of PIP_2 modulates these processes. Consistent with this, a recent inhibitor of PIPKIα activity (ISA-2011B) results in an *in vivo* loss of mutant p53 but not wild type p53. Remarkably, ISA-2011B also kills cancer cells but not normal cells. Because PIPKIα is required by the IQGAP1-PI3K pathway (**Fig. 3**) and for stability of p53 (**Fig. 6**), the ISA-2011B killing of cancer cells may occur by multiple mechanisms.

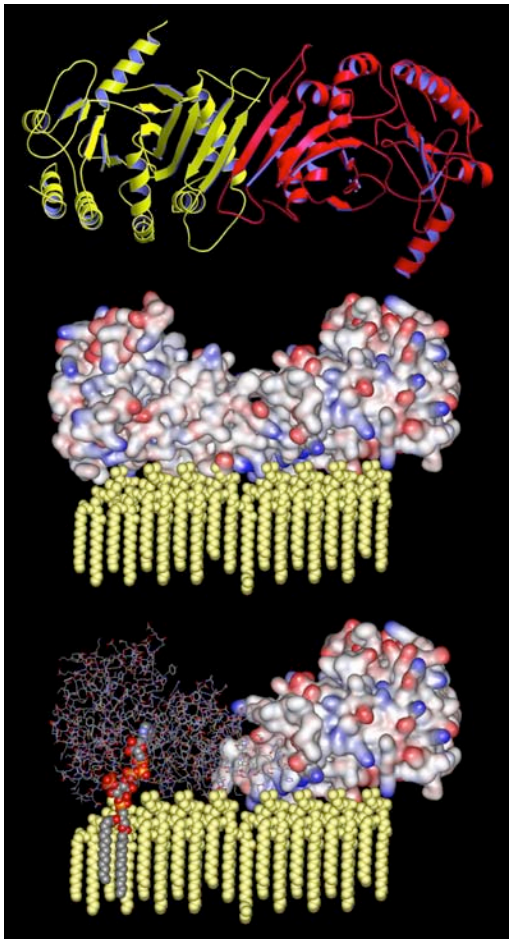


Figure 7. Structure of the PIPIIβ enzyme. Top, ribbon structure of PIPIIβ looking up from the membrane. Middle, a space filling model of the PIPIIβ docked on a membrane. A model showing the oreintaton of Mg-ATP and the substrate PI5P.

<u>Structure and Function of Signaling Molecules</u>: My group and I have had long term interest in the structure and function of signaling molecules. Although we do not solve 3-D structures of signaling molecules our selves, my group and I use structural data to define cellular functions and signaling mechanisms. As an example, in **Fig. 7** is the structure of the type II PI5P 4-kinase beta (PIPIIβ), we biochemically isolated and cloned this enzyme and worked with Jim Hurley at the NIH (now at Berkely) to solve the structure(***Cell 94***, 829-839). From this structure, we defined the mechanism for substrate usage and lipid messenger generation by making structure designed changes in the enzyme(***Mol. Cell 5***, 1–11). This structure fnction approach is a continuing emphasis in my laboratory, currently with many proteins and enzymes that we want to collaboratively define structures and use these structures to elucidate enzymatic and biological mechanims to address functional aspects. In each of the three current NIH funded projects we have a continuing structure/function emphasis.

The structures of Star-PAP, LAPTM4B, PIPKIγ isoforms, and complexes between PIPKI isoforms and interacting effectors would be of great interest to us and with strong translational significance.

Translational Applications to Human Diseases:

Cytosolic pathways - PIPKIγ is highly expressed in triple negative breast cancers and expression correlates with poor disease prognosis(*Breast Cancer Res.*, 12(1):R6). Emerging evidence indicates that in triple negative breast cancers there appears to be a switch in the expression of PIPKIγi1-5 isoforms, where PIPKIγi1 and PIPKIγi2 increase (pro-migration/invasion) with a loss of PIPKIγi5 (increased EGFR signaling) and PIPKIγi4 (loss nuclear signaling and PTEN expression). We plan to determine if such a switch may also occur in head and neck, small cell lung, colon, pancreatic, gliomas and other cancers. This PIPKIγ switch has significant therapeutic implications, as the role of PIPKIγi5 and pathway components in endosomal sorting of EGF receptor has strong implications in EGFR regulated cancers with potential roles in resistance to multiple therapies. LAPTM4B appears to be key oncogene that regulates EGFR signaling. LAPTM4B is regulated by both $PI4,5P_2$ and PIPKIγi5 binding that block LAPTM4B regulation of EGFR. A drug that would block LAPTM4B inhibition of EGFR downregulation may have theraputic potential.

IQGAP1 has known roles in cancer progression and metastasis (see discussion, ***EMBO J.*** **32**, 2617-30). The roles of IQGAP1 in cell migration, invasion and cell proliferation are controlled by the recruitement of specific signaling enzymes to the IQGAP1 complex. For IQGAP1's role in migration, invasion and cell proliferation this requires interactions with PI 3-kinase and PIP kinases. These interactions occur within defined IQGAP1 domains and are inhibited by short peptides that specifically block the PI 3-kinase and PIP kinase binding to IQGAP1. This indicates that peptides or small molecules that block PI 3-kinase and PIP kinase binding to IQGAP1 could be a theraputic approach to block metastasis and progression of some cancers. This approach has been validated for IQGAP1 control of the MAP kinase pathway which also requires interaction of MAP kinase components with IQGAP1. We have initiated a program lead by Alan Rapraeger with Paul Lambert and Randal Kimple to investigate the role of the IQGAP1-phosphoinoside signaling complex in head and neck cancers.

Gene expression, signaling and nuclear organization - Star-PAP controls PTEN, Mdm2, AKT1-3, NQO1, and human papillomavirus E6/E7 expression. These genes control p53 function, apoptosis, cell proliferation and cancer progression. The expression of these genes is controlled by DNA damage, oxidative stress, and growth factor signaling pathways that regulate Star-PAP 3'-end processing. We have shown that inhibition of Star-PAP modulates p53 and sensitizes cells to VP-16(*Oncogene doi:10.1038/onc.2013.14)*, indicating that Star-PAP is a putative anti-cancer therapeutic target. Defining Star-PAP's role in controlling expression of oncogenes and tumor suppressors is likely to identify drug targets that could control the expression of these genes.

The nuclear architecture is dramatically altered in cancer cells and these changes likely impact gene expression and mRNA processing. Phosphoinositide lipid messengers largely function as spatial signaling molecules that organize cellular architecture. As such, there is a potential role for nuclear PIP kinases and $PI4,5P_2$ generation in the spatial organization of gene expression and mRNA processing. A key example is control of *PTEN* expression by Star-PAP that is regulated by $PI4,5P_2$. Changes in nuclear organization have the potential to spatially disconnect $PI4,5P_2$ synthesis from regions of *PTEN* expression, this could block Star-PAP processing of the PTEN mRNA resulting in loss of PTEN and enhanced proliferation of cancer cells.

Mutation of p53 occurs in over 80% of cancers and mutant p53 is a major therapeutic target. The control of mutant and stress stimulated p53 expression by PIPKIα and PIP_2 indicates that PIPKIα and Pi 4-kinases in this pathway are key therapeutic targets. This concept is validated by the fact that the PIPKIα inhibitor ISA-2011B that blocks PIPKIa activity, resulting in a selective lose of mututant p53 with no impact on wild type p53. Further, ISA-2011B selectively kills a wild variety of cancer cells but only inhibits proliferation of normal cells. The role of this pathway in head and neck and breast cancers is being explored in collaboration with Alan Rapraeger, Paul Lambert and Vincent Cryns at the UW and Jenny L Persson at Lund and Umeå University in Sweden.

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Ling, K. Carbonara, C. Bairstow, S.F., Turbin, D.A., Huntsman, D.G. and Anderson, R.A. (2007) Type Iγ PIP Kinase Modulates Adherens Junction and E-cadherin Trafficking via a Direct Interaction with μ1B Adaptin. ***J. Cell Biology*****. 176**, 343-351. PMID: 17261850 **A novel mechanism for E-cadherin receptor mediated trafficking and epithelial morphogenesis by phosphoinositide kinases. Rated must read by Faculty of 1000 during February - May 2007. News and views - Caught in the middle, Mitch Leslie, J Cell Biol 2007 176:244a.*

Heck, J.N., Mellman, D.L., Ling, K. Sun, Y. Wagoner, M.P. Schill, N.J. and Anderson, R.A. (2007) A Conspicuous Connection: Structure Defines Function for the Phosphatidylinositol-Phosphate Kinase Family. ***Critical Rev. Biochem Mol. Biol.***, 42:15–39. PMID: 17364683

Sun, Y., Ling, K., Wagoner, M.P., and Anderson, R.A. (2007) Type Iγ PIP Kinase is Required for EGF-Stimulated Directional Cell Migration. ***J. Cell Biology*****, 178**, 297-308. PMID: 17635937

El Sayegh, T.Y. Arora, P.D., Ling, K., Laschinger, C., Janmey, P.A., Anderson, R.A., McCulloch, C.A. (2007) Phosphatidylinositol-4,5-bisphosphate Produced by PIP5KIγ Regulates Gelsolin, Actin Assembly and Adhesion Strength of N-Cadherin Junctions. ***Mol. Biol. Cell****.* 18, 3026–3038. PMID: 17538019

Mellman, D.L., Gonzales, M.L., Song, C., Barlow, C., Wang, P., Kendziorski, C. and Anderson, R.A. (2008) A Ptdins4,5P_2-Regulated Nuclear Poly(A) Polymerase Controls Expression of Select mRNAs. ***Nature,*** **451**, 1013-1017. PMID: 18288197 **Discovery of a novel gene expression pathway regulated by the lipid messenger PIP_2 and a novel poly(A) polymerase. Rated exceptional by Faculty of 1000 during Mar - Oct, 2008; Preview - A tail tale for U. Science. 2008 Mar 7;319(5868):1344-5. Emphasized J Cell Biol. 2008 March 24; 180(6): 1055.*

Publications (cont)**:**

Bunce, M.W., Boronenkov, I.V., and Anderson, R.A. (2008) Coordinated Activation the Nuclear Ubiquitin Ligase Cul3/Spop by the Generation of Phosphatidylinositol 5-Phosphate. ***J. Biol. Chem.*** **283**, 8678-8686. PMID: 18218622 **Discovery of a novel signaling pathway for phosphatidylinositol 5-phosphate.*

Gonzales, M.L., Mellman, D.L., and Anderson, R.A. (2008) Star-PAP is Associated with and Phosphorylated by the Protein Kinase CKIα that is also Required for Expression of Select Star-PAP Target Messenger RNA. ***J. Biol. Chem.*** **283**, 12665-12673 PMID: 18305108

Wagoner, M.P., Ling, K., and Anderson, R.A. (2008) Tracking the Transport of E-Cadherin to and from the Plasma Membrane. ***Methods in Molecular Biology***, **457**, 267-278. PMID: 19066034

Schill, N.J. and Anderson, R.A. (2009) Out, in, and back again: PtdIns(4,5)P_2 regulates cadherin trafficking in epithelial morphogenesis. ***Biochem. J.*****, 418**, 247-260. PMID: 19196245

Mellman, D.L. and Anderson, R.A. (2009) A Role for a Nuclear Localized Type Iα Phosphatidylinositol 4' Phosphate 5-kinase in 3' End Formation of Select mRNAs. ***Adv Enzyme Regul. 49****,* 11-28*. PMID: 19640411*

Thieman, J.R., Mishra, S.K., Ling, K., Doray, B., Anderson, R.A. and Traub, L.M. (2009) Clathrin Regulates the Association of PIPKIγ661 With The AP-2 Adaptor β2 Appendage. ***J. Biol. Chem. 284****,* 13924-13933. PMID: 19287005

Hedman, A.C. and Anderson, R.A. (2010) Regulation and Traffic of E-cadherin. in **Molecular and Functional Diversities of Cadherin and Protocadherin**, ISBN: 978-81-308-0395-1 Editor: Kenichi Yoshida.

Schill, N.J. and Anderson, R.A. (2009) Novel Splice Variants Of The Type Iγ Phosphatidylinositol 4' Phosphate 5'-Kinase Define A Diverse Family Of Signaling Enzymes. ***Biochem. J.*** **422**, 473-482. PMID: 19548880

Fairn, G.D., Ogata, K., Botelho, R., Stahl, P.D., De Camilli, P, Meyer, T, Anderson, R.A., Wodak, S., Grinstein, S. (2009) An Electrostatic Switch Displaces Phosphatidylinositol Phosphate Kinases from the Membrane During Phagocytosis. ***J. Cell Biology,*** **187**, 701-714**.** PMID: 19951917 ***Rated must read by Faculty of 1000 during May, 2009****.*

Barlow, C., Laishram, R.S., and Anderson, R.A. (2010) Nuclear Phosphoinositides: A Signaling Enigma Wrapped in a Compartmental Conundrum. ***Trends Cell Biology***, **20**, 25-35. PMID: 19846310

Sun, Y., Ling, K., Turbin, D., Huntsman, D. and Anderson, R.A. (2010) Type Iγ phosphatidylinositol phosphate kinase modulates invasion and proliferation and its expression correlates with poor prognosis in breast cancer. ***Breast Cancer Research****,* Jan 14;12(1):R6. [Epub ahead of print] PMID: 20074374, PMCID: PMC2880426. *Highly accessed article.*

Laishram, R.S. and Anderson, R.A. (2010) The poly A polymerase Star-PAP Controls 3'-end Cleavage by Recruiting CPSF Subunits to the Pre-mRNA. ***The EMBO Journal 29****, 4132–4145.* PMID: 21102410, PMCID: PMC3018792. *Highlight, "More than one way to make a tail." The EMBO Journal (2010) 29, 4066–4067*

Cho, I.J., Kim, Y.W., Kim, E.H., Hwang, S.J., Anderson, R.A. Lee, C.H. and Kim, S.G. (2010) E-Cadherin Antagonizes TGFβ1 Gene Induction in Hepatic Stellate Cells by Inhibiting RhoA-Dependent Smad3 Phosphorylation. ***Gastroenterology****, 52, 2053-64.* PMID: 20890948, PMCID: PMC3086490

Publications (cont)**:**

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Laishram, R.S., Barlow, C., and Anderson, R.A. (2011) CKI isoforms α and ε regulate Star–PAP target messages by controlling Star–PAP poly(A) polymerase activity and phosphoinositide stimulation. ***Nucleic Acid Research****.* 39(18), 7961-7973. PMID: 21729869, PMCID: PMC3185439

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Thapa, N., Sun, Y, Schramp, M., Choi, S., Ling, K., and Anderson, R. A. (2012) Phosphoinositide Signaling Regulates the Exocyst Complex and Polarized Integrin Trafficking in Directionally Migrating Cells. ***Dev. Cell, 22****,* 116–130*.* PMID: 22264730, PMCID: PMC3266520 *Rated must read by Faculty of 1000 during February - May 2012.*

Xiong, X, Xu, Q, Huang Y, Singh, R.D., Anderson, R., Leof, E., Hu, J., and Ling, K. (2012) An association between type Iγ PI4P 5-kinase and Exo70 directs E-cadherin clustering and epithelial polarization. ***Mol. Biol. Cell*****. 23**, 87-98. PMID: 22049025, PMCID: PMC3248907

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Shulga, Y.V., Anderson, R.A., Topham, M.K., and Epand, R.M. (2012). Phosphatidylinositol-4-phosphate 5-Kinase Isoforms Exhibit Acyl Chain Selectivity for Both Substrate and Lipid Activator. ***J Biol Chem*** *287*, 35953-35963. PMID: 22942276, PMCID: PMC3476263

Thapa, N., and Anderson, R.A. (2013). PIP_2 Signaling, an Integrator of Cell Polarity and Vesicle Trafficking in Directionally Migrating Cells. ***Cell Adh Migr*** *6*, 409-412. PMID: 23076053, PMCID: PMC3496677

Li, W., Laishram, R.S. and Anderson, R.A. (2013) The Novel Poly(A) Polymerase Star-PAP is a Signal-Regulated Switch at the 3'-end of mRNAs. ***Adv. Biol. Reg. 53, 64-76.*** *PMID: 23306079, PMCID: PMC3626085*

Li, W. & Anderson, R.A. (2014) Star-PAP controls HPV E6 regulation of p53 and sensitizes cells to VP-16. ***Oncogene*** **33**, 928-932. PMID: 23416977. NIHMSID: NIHMS554124.

Sun Y, Thapa N, Hedman AC, Anderson RA. (2013) Phosphatidylinositol 4,5-bisphosphate: targeted production and signaling. **Bioessays 35(6):513-22.** doi: 10.1002/bies.201200171. Epub 2013 Apr 10. Review. PMID: 23575577. NIHMSID: NIHMS506350

Sun, Y., Hedman, A.C., Tan, X., Schill, N.J. and Anderson, R.A. (2013) Endosomal Type Iγ PIP 5-Kinase Controls EGF Receptor Lysosomal Sorting. ***Dev. Cell****, 25, 144–155.* PMID: 23602387, PMCID: PMC3740164. *Rated must read by Faculty of 1000 during May - July 2013.*

Publications (cont)**:**

Ray D, Kazan H, Cook KB, Weirauch MT, Najafabadi HS, Li X, Gueroussov S, Albu M, Zheng H, Yang A, Na H, Irimia M, Matzat LH, Dale RK, Smith SA, Yarosh CA, Kelly SM, Nabet B, Mecenas D, Li W, Laishram RS, Qiao M, Lipshitz HD, Piano F, Corbett AH, Carstens RP, Frey BJ, Anderson RA, Lynch KW, Penalva LO, Lei EP, Fraser AG, Blencowe BJ, Morris QD, Hughes TR. (2013) A compendium of RNA-binding motifs for decoding gene regulation. **Nature. 499, 172-177**. doi: 10.1038/nature12311. PMID: 23846655. NIHMSID: NIHMS554111. *Rated must read by Faculty of 1000 during July 2013: New alert, Medical News Today*

Sun, Y., Hedman, A.C., Tan, X., and Anderson, R.A. (2013) An Unexpected Role for PI4,5P_2 in EGF Receptor Endosomal Trafficking. ***Cell Cycle 12:13,*** *1991–1992*. PMID: 23759577, PMCID: PMC3737296

Thapa, N., Choi, S., Sun, Y, and Anderson, R. A. (2013) Phosphatidylinositol Phosphate 5-Kinase Iγi2 in Association with Src Controls Anchorage-independent Growth of Tumor Cells. ***J. Biol. Chem.*** **288,** 34707–34718, *PMID: 24151076*, PMCID: PMC3843082

Choi, S., Thapa, N., Sacks, D., and Anderson, R.A. (2013) IQGAP1 is a novel phosphatidylinositol 4,5 bisphosphate effector in regulation of directional cell migration. ***The EMBO Journal.*** **32,** 2617-30, PMID: 23982733, PMCID: PMC3791370

Schill, N.J., Hedman, A.C., Choi, S. and Anderson, R.A. (2014) Isoform 5 of PIPKIγ regulates the endosomal trafficking and degradation of E-cadherin. ***J. Cell Science*** **127**, 2189-2203, PMID: 24610942, PMCID: PMC4021470 *Emphasized in the JCS Snapshot*

Tan, X., Thapa, N., Sun, Y. & Anderson, R.A. (2015) A kinase-independent role for EGF receptor in autophagy initiation. ***Cell 160,*** 145-160. PMID: 25594178, PMCID: PMC4297316. *News release UW, Emphasized in Science Comments, Oncology-central, Science Daily,* Cancer Discovery - *News in Brief, "Study Illuminates How Cancers Evade EGFR Inhibitors"*

Tan X, Sun Y, Thapa N, Liao Y, Hedman AC, Anderson RA. (2015) LAPTM4B is a PtdIns(4,5)P_2 effector that regulates EGFR signaling, lysosomal sorting, and degradation. ***The EMBO Journal***. ***34****, 475-90. PMID: 25588945, "PMCID: PMC4331002*

Choi, S., Thapa, N., Tan, X., Hedman, A.C. & Anderson, R.A. (2015) PIP kinases define PI4,5P_2 signaling specificity by association with effectors. ***Biochimica et biophysica acta 1851***, 711-723. PMID: 25617736, PMCID: PMC4380618

Thapa, N., Choi, S., Tan, X., Wise, T. & Anderson, R.A. (2015) Phosphatidylinositol Phosphate 5-Kinase Igamma and PI3K/Akt Signaling Couple to Promote Oncogenic Growth. ***J. Biol. Chem. 290****, 18843-54. PMID: 26070568, PMCID: PMC4513138*

Mohan N, Sudheesh AP, Francis N, Anderson. R.A. and Laishram, R.S., (2015) Phosphorylation regulates the Star-PAP-PIPKIα interaction and directs specificity toward mRNA targets. ***Nucleic Acids Res. 43***, 7005-20. *PMID: 26138484, PMCID: PMC4538844*

Tan, X., Thapa, N., Choi, S., and Anderson, R.A. (2015) Emerging roles of PtdIns(4,5)P_2 - beyond the plasma membrane. ***J. Cell Science, 128(22),*** *4047-56. PMID: 26574506, PMCID: PMC4712784*

Choi, S. and Anderson, R.A. (2015) IQGAP1 is a Phosphoinositide Effector and Kinase Scaffold. ***Adv Enzyme Regul:*** *S2212-4926(15)30027-0. PMID: 26554303, PMCID: PMC4729663*

Tan, X., Lambert, P.F., Rapraeger, A.C. & Anderson, R.A. (2106) Stress-Induced EGFR Trafficking: Mechanisms, Functions, and Therapeutic Implications. ***Trends in Cell Biology***, **26**, 352-66. PMID: 26827089, doi:10.1016/j.tcb.2015.12.006. PMC Journal – In Process.

Publications (cont)**:**

Thapa, N., Tan, X., Choi, S. & Anderson, R.A. (2016) PIPKIγ and Talin Couple Phosphoinositide and Adhesion Signaling to Control the Epithelial to Mesenchymal Transition. ***Oncogene.*** *PMID: 27452517 DOI: 10.1038/onc.2016.267. [Epub ahead of print] PMID: 27452517*

Thapa, N., Tan, X., Choi, S., Rapreager, A. Lambert, P. and Anderson, R. A. (2016) The Hidden Conundrum of Phosphoinositide Signaling in Cancer. **Trends in Cancer**, **2**, 378–390. *PMID: 27819060, PMCID: PMC5094282*

Tan X, Thapa, N., Liao, Y. and Anderson R.A. (2016) PtdIns(4,5)P_2 Signaling Regulates ATG14 and Autophagy. ***Proc. Natl. Acad. Sci. U.S.A.*** **113**, 10896-901. *PMID: 27621469, PMCID: PMC5047215*

Sun, M., Cai, J., Anderson, R.A., and Sun, Y. (2016) Type I Gamma Phosphatidylinositol Phosphate 5-kinase i5 Controls the Ubiquitination and Degradation of a Tumor Suppressor Mitogen-inducible Gene 6. ***J. Biol. Chem.*** 291(41):21461-21473. *PMID: 27557663, PMCID: PMC5076818*

Choi, S., Hedman, A.C. Sayedyahossein, S. Thapa, N. Sacks, D.B. and Anderson, R.A. (2016) Agonist-stimulated phosphatidylinositol-3,4,5-trisphosphate generation by scaffolded phosphoinositide kinases. ***Nature Cell Biology*** **18**, 1324–1335. *PMID: 27870828. See also News and Views, Nature Cell Biology 18, 1263–1265; News release University of Wisconsin-Madison. "Cancer signaling pathway could illuminate new avenue to therapy."; ScienceDaily, 23 November 2016, 9 others.*

Li*, W., Laishram*, R.S., Ji*, Z., Hoque, M., Tian, B., and Anderson, R.A. (2016) Genome-wide Alternative Polyadenylation is Specifically Regulated by the Different Nuclear Poly(A) Polymerases. **Co-first authors*. *In revision,* ***Genome.Research.***

Hedman, A.C., Sun, Y., Tan, X., and Anderson, R. A. (2016) Phosphoinositide Regulation of SNX5 and SNX6 Is Required for EGFR Lysosomal Degradation. *In revision,* ***J. Biol. Chem.***

Choi, S., Thapa, N., Cryns, V. and Anderson, R.A. (2017) The Stability of Mutant and Stress Induced p53 is Controlled by PIPKIα Stimulated Recruitment of αB-crystalin and Other Chaperones. *In preparation for* ***Nature.***

Laishram, R.S., Ji, Z., Hoque, M., Tian, B., and Anderson. R.A. (2017) Star-PAP Controls Expression of NQO1 by Regulation of Alternative Polyadenylation by Distinct Pathways and Mechanisms. *In preparation.*

Li, W., Li, W., Laishram, R.S., Ji, Z., Tian, B., and Anderson. R.A. (2017) Star-PAP and Nuclear PI 3-kinase Regulates PTEN, AKT, and MDM2 Expression by Alternative Polyadenylation. *In preparation.*

Contributed Abstracts: Approximately 153 (all but three have been published)

Patents:

Patent P03075US, Ling, K., Doughman, R.L., Firestone, and Anderson R.A. (2005) A Method for Identifying an Agent that Modulated Type I Phosphatidylinositol Phosphate Kinase Isoform Gamma-661.

Patent P03323US, Ling, K., Carbonara, C., Bairstow, S.F., and Anderson, R.A. (2006) Screening Method for identifying an agent that modulates PIPKIgamma trafficking of E-cadherin.

Patent P07036US, Mellman, D.L., Song, C., Gonzales, M.L. and Anderson, R.A. (2008) Discovery of a Novel Poly (A) Polymerase that Function in Nuclear Phosphoinositide Signaling Events that Regulate Specific mRNAs in Stress Response Pathways

Patent P07035US Schill, N.J. and Anderson, R.A. (2008), Unique Splice Variants of the Type I Phosphatidylinositol Phosphate Kinase Isoform Gamma as biomarkers for prognosis of Breast Cancer Progression.

Patent P150309 pending: Highly Selective Inhibition Of Cancer Cell Proliferation With IQGAP1-Derived Short-Length Peptides Via Blockade Of PI3,4,5P3 Synthesis And Signaling.

Invited Research Presentations (since 2006) (I tend not to keep track of these very well):

2006 Visiting University Professor, Stony Brook University, Department of Physiology
2006 Invited Speaker, Sloan-Kettering Memorial Cancer Center
2006 Invited Speaker, Gordon Research Conference on Cell Contact and Adhesion
2007 Invited Speaker, RNA Society Annual Meeting- presented by D. Mellman
2007 Invited Speaker, HHMI, Janelia Farms, Inositide Signaling Symposium
2007 Invited Speaker, University of Illinois, Department Pharmacology
2008 Invited Speaker, ASBMB Annual Meeting, RNA-Mediated Gene Expression Symposium
2008 Invited Speaker, Advances in Enzyme Regulation Symposium, *Bologna, Italy*
2008 Invited Speaker, Duke University, Pharmacology and Cancer Biology
2008 Keynote Speaker, Biomembrane Symposium, Purdue University, Biochemistry
2009 Invited Speaker, Mayo Clinic, Biochemistry and Molecular Biology
2009 Invited Speaker, Gordon Conference, Nuclear Signaling
2009 Invited Speaker, EMBO workshop, Messenger RNA 3' ends & gene expression, Oxford
2009 Invited Speaker, Laboratory of Signal Transduction, NIEHS
2009 Vert Professor, K.U. Leuven and EMBO YIP, Department Human Genetics, Belgium
2009 Invited Speaker, Vollum Institute, Oregon
2010 Keynote Speaker, 27th Naito Conference on "Membrane Dynamics and Lipid Biology"
2011 Did not accept speaking invitations this year
2012 Keynote speaker, CRCM, Cancer Research Center of Marseille, France
2012 Invited speaker, "Inositide signaling in health and disease", NCBS, Bangalore, India
2012 Invited speaker, "Symposium on "Biological Regulation and Enzyme Activity", Bologna, Italy
2012 Section Chair, Signaling Networks, Congress of Molecular & Cell Biology, Beijing, China
2012 Invited speaker, FASEB Summer Research Conference, Saxtons River, Vermont
2012 Invited speaker and session chair, *International Symposium on Signalling and Cancer*, Université de Montréal, Montreal, QC, Canada
2012 Invited speaker, McMaster University, Hamilton, ON, Canada
2013 Invited speaker, NCI workshop on "Endocytosis and Cancer", Washington, DC.
2013 Invited speaker, Columbia University, New York, NY.
2013 Invited speaker, Memorial Sloan-Kettering Cancer Center, New York, NY.
2013 Invited speaker, Albert Einstein College of Medicine, New York, NY.
2013 Invited speaker and Doctoral Juror, K.U. Leuven, Department Human Genetics, Belgium
2014 Invited speaker, 9th EMBO-Annaberg Workshop, Protein and Lipid Function in Secretion and Endocytosis, Goldegg, Austria)
2014 Invited speaker and Section Chair, FASEB SRC: Phospholipid Cell Signaling and Metabolism in Inflammation and Cancer
2014 Invited speaker, FASEB SRC: Lipids and Lipid Regulated Kinases in Cancer
2014 Invited speaker, Department of Biochemistry, Rutgers New Jersey Medical School
2014 Invited speaker, Van Andel Research Institute, Grand Rapids, Michigan
2014 Invited speaker, Department of Cell Biology, Johns Hopkins University, School of Medicine
2014 Invited speaker, Keystone Symposia on Autophagy: Fundamentals to Disease.
2014 Invited speaker, University of California San Francisco, San Francisco, CA
2014 Invited speaker, University of Texas Southwestern Medical Center, Dallas, TX
2014 Invited speaker, Yale University, New Haven, CT
2014 Invited speaker, The University of Texas Health Science Center at Houston
2014 Organizer and speaker, American Society for Cell Biology, Subgroup, "Nucleoskeletal Dynamics in Signaling and Gene Expression"
2015 Invited speaker, Fifty-Sixth International Symposium on "Biological Regulation and Enzyme Activity in Normal and Neoplastic Tissues" University of Bologna, Italy
2016 Chair and speaker, FASEB Science Research Conference (2016), "*Phospholipid Signaling in Cancer, Neurodegeneration and Cardiovascular Disease.*"
2016 Invited speaker, FASEB Science Research Conference (2016), "*Cell Signaling in Cancer: from Mechanisms to Therapy.*"
2016 Invited speaker, The University of Texas UT South Western
2016 Invited speaker, The University of Illinois
2016 Invited speaker, Worcester Polytechnic Institute
2016 Invited speaker, University of Massachusetts Medical School
2016 Invited speaker & reviewer, Austrian Science Fund and Doctoral Programme, Vienna, Austria
2016 Invited speaker, SFBD/SBCF "When Development meets Cell Biology", Lyon, France
2016 Keynote speaker, Cancer Research Center of Marseille, France

Past Funding (partial list of fellowships): Date/direct costs

Individual National Research Service Award (NIH Postdoctoral Fellowship) "Regulation of Protein 4.1-Glycophorin Associations by a Phosphoinositide" Grant #: 5 F32 GM09184-03 (score 1.1%)	11/01/82-10/31/85 $89,650
American Cancer Society Postdoctoral Fellowship "Regulation of Protein 4.1-Glycophorin Associations by a Phosphoinositide" Grant #: PF-746 (The grant was declined in favor of the NIH Postdoctoral Fellowship listed above)	11/01/82-10/31/85 $53,034
Argall L. and Anna G. Hull Fund Cancer Research Award "Structure of Nonerythroid Protein 4.1 Isoforms" Grant #: AAH-387	11/01/85-06/31/86 $31,000
National Institutes of Health (Anderson, PI) "Phosphoinositide Regulation of Erythrocyte Cytoskeleton" Grant #: R01 GM38906 (Score1.3%)	07/01/87-06/31/92 $460,333
March of Dimes Birth Defects Foundation Basil O'Connor Research Grant (Anderson, PI) "Regulation of Erythroid and Nonerythroid Protein 4.1 Associations with the Membrane by the Phosphoinositide Cycle" Grant #: 5-659	09/01/88-06/30/91 $70,000
American Heart Association (Anderson, PI) "Membrane Regulation of Phosphatidylinositol-4-P 5-Kinase" Grant #: 880934 (Score Outstanding)	07/01/88-06/31/91 $99,000
American Cancer Society (Anderson, PI) "Regulation of Membrane Proteins by Phosphoinositide Metabolism" Grant #: BC-639 (Score First decile)	07/01/88-06/30/90 $143,000
National Science Foundation Predoctoral Fellowship (to Jennifer Brockman)	10/01/90-09/30/93 $57,215
WARF Foundation Predoctoral Fellowship (to Jennifer Brockman)	10/1/93-08/31/94 $21,000
Council for Tobacco Research- U.S.A., Inc. (Anderson, PI) "Regulation of PIP Kinases and Protein 4.1 by Growth Factor Receptor Tyrosine Phosphorylation" Grant #: 3130	07/01/91-06/30/94 $207,825
American Heart Association Predoctoral Fellowship (to J. Brockman) "Identification and Characterization of a Casein Kinase 1 Isoform from Erythrocytes" (Score 1.3%)	09/01/94-08/31/95 $8,800
National Institutes of Health Predoctoral Traineeship (to Stefan Gross) Cell and Molecular Biology Training Grant	12/01/92-11/30/95 $69,000
American Heart Association Postdoctoral Fellowship (to M. D. Schroeder) "Determination of the Role of Casein Kinase I in the Regulation of the Cell Cycle" (Score 19%)	07/01/94-06/30/96 $38,300
University of Wisconsin Graduate School (Anderson, PI) "Regulation of Ca^{2+}- Stimulated Secretion by Phosphatidylinositol-4-Phosphate 5-Kinases" Grant #: 950736	07/01/94-06/30/95 $17,908

Past Funding (cont)**:**

University of Wisconsin Graduate School (Anderson, PI) "Casein Kinase I: A Role in Regulation of Nuclear Events" Grant #: 970323	07/01/96-06/30/97 $16,146
National Institutes of Health GMS R01 GM38906 (Anderson, PI) "Casein Kinase I Regulation by PI-4,5-P_2" (Score 11.2%)	07/01/92-06/30/97 $836,592
National Institutes of Health GMS R01 GM51968 (Anderson, PI) "Nuclear PIP 5-Kinases: Role in the Cell Proliferation" Grant #: (Score 3.6 %)	12/01/94-11/30/97 $726,837
UW Cancer Center Fund (Anderson, PI) "Control of Cancer Cell Motility and Metastasis"	06/17/96-08/31/97 $20,000
American Heart Association Postdoctoral Fellowship (to Feng Lu) "Type I Phosphatidylinositol 4-Phosphate 5-Kinase α and β in the Heart" Grant #: 96-F-Post-41	07/01/96-06/30/98 $61,000
National Institutes of Health Predoctoral Traineeship (to Gregory J. Parker) Molecular Biosciences Training Grant	07/01/96-06/30/98 $69,000
National Institutes of Health Predoctoral Traineeship (to Allison Freidlein) "Graduate Training in Molecular and Cellular Pharmacology" Grant #: T32 GM08688	07/01/98-06/30/00 $25,563
Swiss NSF Postdoctoral Fellowship (to Jeannette Kunz)	08/01/96-07/31/98 $108,000
American Heart Association Predoctoral Fellowship (to J. Loijens) "Type I Phosphatidylinositol-4-Phosphate 5-Kinases and their Regulation" Grant #: 97-F-Pre-27 (score 5.2%)	07/01/97-06/30/98 $36,000
National Institutes of Health Predoctoral Traineeship (to S. Nelson) "Environmental Toxicology (Predoctoral and Postdoctoral) Training Grant Grant #: T32 ES07015	07/01/98-06/30/00 $51,126
American Heart Association Predoctoral Fellowship (to S. Doughman) "Molecular Characterization of Nuclear Polyphosphoinositide Binding Proteins and their Role in Intranuclear Signalling"	07/01/99-06/30/00 $36,200
University of Wisconsin Graduate School (Anderson, PI) H.I. Romnes Faculty Fellowship	07/01/96-06/30/01 $60,000
WARF Fellowship (to Shawn Bairstow) Grant #: 98-F-PreDoc-23	09/01/99-08/31/00 $26,346
National Institutes of Health NIGMS R01 GM57549 (Anderson, PI) "Structure and Function of PIP Kinase in TNFR1 Signaling" (Score 19.1%)	05/01/98-04/30/02 $909,713
University of Wisconsin Graduate School Vilas Associate Award	07/01/99-06/30/01 $30,000

Past Funding (cont):

American Heart Association, Predoctoral Fellowship (to R. Dierckman) 07/01/00-06/30/02
"Functional Roles of the Type I Phosphatidylinositol Phosphate Kinases in Actin Reorganization and Cellular Migration. Grant #: 98-F-PreDoc-23 $37,000

National Institutes of Health NIGMS R01 GM51968 (Anderson, PI) 07/01/98-06/30/02
"Phosphoinositide Signaling to and within the Nucleus" $1,156,265
(Score 5.1%)

American Heart Association, Predoctoral Fellowship(to M. Bunce) 07/01/01-06/30/03
"Regulation of the Type I Phosphatidylinositol Phosphate Kinases by GTPase Arf6 in Actin Reorganization" $37,000
Grant #: 01-F-PreDoc-29 (Score 13.4%)

National Institutes of Health Predoctoral Traineeship (to S. Bairstow) 09/01/00-08/31/03
"Graduate Training in Biotechnology" $114,684
Grant #: T32 GM08349

National Institutes of Health NIGMS R01 GM57549 (Anderson, PI) 05/01/02-04/30/06
"Specificity and Targeting of Phosphoinositide Signaling" $1,307,844
(Score 156 and 17%)

National Institutes of Health Predoctoral Traineeship (to M. Gonzales) 07/01/01-06/30/03
"Graduate Training in Molecular and Cellular Pharmacology" $71,103
Grant #: T32 GM08688

National Institutes of Health Predoctoral Traineeship (to R. Doughman) 07/01/02-06/30/03
"Graduate Training in Molecular and Cellular Pharmacology" $35,563
Grant #: T32 GM08688

National Institutes of Health NIGMS R01 GM57549 (Anderson, PI) 05/01/03-04/30/07
"Specificity and Targeting of Phosphoinositide Signaling" $1,307,844
Grant #: (Score 17%)

American Heart Association Postdoctoral Fellowship (to K. Ling) 07/01/02-06/30/06
"The Role of the Phosphatidylinositol-4-Phosphate 5-Kinase Type I Gamma in Focal Adhesion Function" (Score 2.7%) $137,000
Grant # 0225401Z, Renewal for third year (Score 1.7%)

National Institutes of Health GMS T32 GM08688 (Anderson, PI) 07/01/03-06/30/08
"Graduate Training in Molecular and Cellular Pharmacology" $1,724,940
(Score 181)

National Institutes of Health 5 R01 GM051968-11 (Anderson) 07/01/03-06/30/08
"Phosphoinositide Signaling To and Within the Nucleus" $1,606,068
(Score 5.7%)

American Heart Association Postdoctoral Fellowship (to C. Song) 11/01/04-12/30/06
"Role of Type Ialpha Phosphatidylinositol-4- Phosphate 5-Kinase Targeting to and Generating PI4,5P2 in Nuclear Speckles" $87,000
Grant #: 01-F-PostDoc-29 (Score 7.4%)

Past Funding (cont):

American Heart Association Predoctoral Fellowship (to M. Gonzales) Phosphatidylinosotol-phosphate 5-kinases in nuclear signal transduction Grant #: 0315380Z (Score 13.6%)	11/01/04-12/31/06 $47,000
National Institutes of Health NIGMS R01 GM057549-08S1 (Anderson, PI) Specificity and Targeting of Phosphoinositide Signaling Transition funding. (Score 18.3%)	05/01/06-04/30/07 $123,000
National Institutes of Health Predoctoral Traineeships (J. Heck, M. Wagner, D, Mellman, A. Hedman, and N. Schill)	08/01/03-07/30/07 $192,285
National Institutes of Health R01 GM051968-11 (Anderson, PI) Phosphoinositide Signaling to and within the Nucleus" (Score 3.1%)	07/01/03-06/30/09 $1,184,912
National Institutes of Health NIGMS T32 GMGM08688-010 (Anderson, PI) Training in Molecular and Cellular Pharmacology (Score 168)	07/01/03-06/31/08 $1,808,200
American Heart Association Predoctoral Fellowship (to N. Schill) "Determining functional specificity of PIPKI splice variants in cell migration and cell-cell contact assembly" Grant #: 0610121Z (Score 19.4%)	06/01/05-05/31/07 $52,000
American Heart Association Predoctoral Fellowship (to D. Mellman) "Characterization of a Novel Poly(A) Polymerase that Functions in a Nuclear Phosphoinositide Signaling Pathway" Grant #: 0715661Z (Score 5.2%)	06/01/07-05/31/09 $52,000
American Heart Association Scientist Development Award (K. Ling/Anderson) "Role of type Igamma phosphatidylinositol phosphate kinase in endothelial cell adherens junction formation"(Score 2.84%)	06/01/04-05/31/09 $340,000
National Institutes of Health CA014520-AV-130 (Anderson, PI) Avon-NCI Progress for Patients' Awards Program Type Igamma PIP Kinases as Biomarkers for Breast Cancer Progression (Score 171)	07/01/07-06/31/09 $523,000
University of Wisconsin Kellet Award (Endowed) (Anderson, PI) "Award for Scholarly Activity"	07/01/04-06/31/09 $60,000
National Institutes of Health R01 CA104708-06 (Anderson, PI) PI Signaling Role in Epithelial/Mesenchymal Transition (Score 13.3%)	07/01/04-06/30/10 $1,414,890
American Heart Association Postdoctoral Fellowship (to R. Laishram) "PIPKIalpha and CKIalpha mediated Star-PAP function in cleavage and polyadenylation of target mRNAs" Grant #: 0920072G (Score 13%)	03/01/09-02/29/11 $94,000
National Institutes of Health NIGMS F32 GM082005-01 (to C. Barlow) Star-PAP and PIPKIalpha in the Regulation of Polyadenylation of Specific mRNAs. F32 GM082005 Postdoctoral Fellowship (Score 189)	06/01/09-05/31/11 $220,704

Past Funding (cont):

National Institutes of Health T32 GMGM08688-011 (Anderson, PI) 07/01/08-06/31/13
Training Grant for Molecular and Cellular Pharmacology $2,002,810
Score 162 (Funded with increased stipends/year)

American Heart Association Predoctoral Fellowship (to A. Hedman) 07/01/09-07/30/11
"Defining the Role of a PIPKIγ Interaction with SNX5 in E-cadherin Traffic" $61,000
Grant #: PRE2280534 (Score 8.1%)

National Institutes of Health R01 GM051968-13S1 (Anderson, PI) 04/01/09-05/31/13
"Phosphoinositide Signaling to and within the Nucleus" $100,000

National Institutes of Health NIGMS R01 GM057549-09 (Anderson, PI) 04/01/06-03/31/11
"Targeting of Phosphoinositide Signaling in Cell Migration $1,414,540
and Tumor Progression" (Score 23 / 16.5%).

American Heart Association Postdoctoral Fellowship (to N. Thapa) 07/01/11-06/30/13
"PIPKIγi2 modulates exocyst complex to regulate $94,000
directional cell migration" Grant #: 0980158G (Score 1.5 / 9%)

National Institutes of Health R01 GM051968-12 (Anderson, PI) 04/01/09-05/31/13
"Phosphoinositide Signaling to and within the Nucleus" $1,384,912
(Score 1.3 / 6.6%)

Wellcome Trust/DBT India Alliance fellowship has been awarded to Rakesh S, Laishram, Ph.D. This award is a transitional award for a faculty position at an Indian University. Professor Laishram continued in my laboratory through 2013 as a visiting scientist.

AHA Scientist Development Awards for Weimin Li, M.D., Ph.D. and Yue Sun, Ph.D. For 07/01/12 to 06/30/16. Each award is for $77,000 per year.

National Institutes of Health R01 CA104708-06 (Anderson, PI) 05/01/10-06/30/15
"PI Signaling Role in Epithelial/Mesenchymal Transition" $1,817,450.00
(Score 2.9 / 9%)

American Heart Association Predoctoral Fellowship (to S. Choi) 12/01/12-11/30/14
"Phosphatidylinositol phosphate kinase regulates IQGAP1 targeting $56,000
and activity required for directional cell migration"
Grant #: 13PRE14690057 (Score 1.15 / 5%)

Howard Hughes Medical Institute International Predoctoral Fellowship 08/01/12-08/30/14
(to Xiaojun Tan, Molecular and Cellular Pharmacology Program) $86,000
"An Endosomal Phosphatidylinositol4,5-bisphosphate Pathway Regulates
LAPTM4B Function in Epidermal Growth Factor Receptor Signaling,
Lysosomal Sorting and Degradation" (*One of 50 nation wide*)

National Institutes of Health R01 CA104708-06 (Anderson, PI) 05/01/10-06/30/15
"PI Signaling Role in Epithelial/Mesenchymal Transition" $1,817,450.00
(Score 2.9 / 9%)

National Institutes of Health, R01 GM057549 (Anderson, PI) 05/01/12-04/30/16
"Targeting of Phosphoinositide Signaling in Cell Migration, $2,315,224
Invasion and Metastasis" (Score 2.5 / 18%)

ACTIVE:

National Institutes of Health R01 GM114386 (Anderson, PI) "Nuclear Phosphoinositide Control of 3'-end mRNA Processing and Gene Expression". (Score 14 / 3%) The goal of this project is define the role of nuclear phosphoinositide signaling in control of 3'-end processing of mRNAs.	03/01/16-07/31/20	3.6 calendar $2,245,480
Robert Draper Technology Innovation Fund (Anderson, PI) P150309US01, TIF application The goal of this project is to further characterize the use of IQGAP1 derived peptides as potential anticancer agents.	03/01/16-02/31/16	0 calendar $50,000
UWCCC pilot project, "EGFR-coupled IQGAP1 (Anderson, PI) and PI 3-kinase signaling for HNC survival and invasion."	03/01/16-02/31/16	0 calendar $12,000
National Institutes of Health R01 GM057549-17 (Anderson, PI) "Agonist Activated Phosphoinositide Kinase Scaffolds Control Motility and Survival Signals' (Score 17 / 4%)	04/01/17-02/31/21	3.6 calendar $2,987,770

PENDING PROPOSALS:

National Institutes of Health New (Anderson, PI) "A Novel Endosomal Phosphoinositide Pathway Controls EGFR Signaling by Protein Turnover"	04/30/16-02/31/21	3.0 calendar $2,861,300
National Institutes of Health P01 NCI (Rapraeger, PI) "Novel Mechanisms of EGFR signaling in Head and Neck Cancer " A program project between Alan Rapraeger, Paul Lambert, and Richard Anderson ($328,942/year to Anderson)	01/01/17-12/31/23	3.0 calendar $9,380,000
National Institutes of Health New (Anderson, PI) "EGFR and HPV Regulation of PI 3-kinase Signaling and Tumorigenesis in Head and Neck Cancer (with co-Investigator Paul Lambert)	04/30/17-02/31/22	3.0 calendar $3,480,514
DOD BCRP Level 2 New (Anderson, PI) "PIPKIα control of mutant p53 and cell survival in triple negative breast cancer. (with co-PI Vincent Cryns)	04/30/17-02/31/20	1.8 calendar $500,000

Anderson career funding to date is >$25,000,000 to the University of Wisconsin
Annual Funding for which Anderson is PI or Sponsor has varied between $1.0 - 2.5 million.

Training Record:

1) Student: Chantal Bazenet, Ph.D.
Status: Postdoctoral
Dates: 1988-1991
Degrees: B.S., 1983; M.S., 1984; Ph.D., 1988, University of Lyon, France
Current: Senior Scientist and Adjunct Professor, Eisai London Research Laboratories, and King's College London

2) Student: Antonio Ruiz Ruano, Ph.D.
Status: Postdoctoral
Dates: 1989-1990
Degrees: B.S., 1975; Ph.D., 1984, University of Madrid, Spain
Last known: Research Scientist, Meharry Medical College in Nashville, Tennessee

3) Student: Gosukonda Subrahmanyam, Ph.D.
Status: Postdoctoral
Dates: 1989-1992
Degrees: B.S., 1977; M.S., 1979, Osmania University, Hyderabad, India;
Ph.D., 1983, Center for Cellular and Molecular Biology at Hyderabad, India
Current: Professor, Indian Agricultural Research Institute, New Delhi

4) Student: Glenn H. Jenkins
Status: Graduate student, Pharmacology Program
Dates: 1988-1994
Degrees: B.S., 1986, University of Georgia; Ph.D., 1994
Last known: Scientist, Merck & Co.

5) Student: Wensheng Wang
Status: Graduate student, Cell and Molecular Biology Program
Dates: 1990-1992
Degrees: B.S., 1987; M.S., 1989, Peking University; Ph.D., 1997
Last known: Postdoctoral, University of California, San Diego

6) Student: Jennifer L. Brockman
Status: Graduate student, Cell and Molecular Biology Program
NSF, WARF Foundation, and American Heart Fellow
Dates: 1989-1996
Degrees: B.S., 1987, University of Wisconsin, Stevens Point; Ph.D., 1996
Current: Scientist, University of Wisconsin-Madison

7) Student: Stefan D. Gross
Status: Graduate student, Cell and Molecular Biology Program
NIH Predoctoral Fellow
Dates: 1991-1997
Degrees: B.S., 1990, University of Colorado; Ph.D., 1997
Postdoctoral: James Maller, University of Colorado.
Current: Array BioPharma, Boulder, CO

8) Student: Jiren Zhang, Ph.D.
Status: Postdoctoral
Dates: 1992-1995
Degrees: B.S., 1978; M.S., 1982, Institute of Biophysics, Chinese Academy of Sciences, Beijing; Ph.D., 1992, University of Connecticut Health Center
Current: Researcher, Peking University, College Of Life Sciences, China,

Training Record: (cont)

9) Student: Joost C. Loijens
Status: Graduate student, Cell and Molecular Biology Program
Dates: 1992-1998
Degrees: B.S., 1992, University of Guelph, Canada; Ph.D., 1998
Postdoctoral, University of Virginia.
Current: Director, Product Management and Design at IGN Entertainment, Inc. (Fox Interactive Media)

10) Student: Igor V. Boronenkov
Status: Graduate student, Biomolecular Chemistry Training Program
Dates: 1993-2000
Degrees: B.S., 1992, Moscow State University, Russia; Ph.D., 2000
Current: Unknown

11) Student: Matthew D. Schroeder, Ph.D.
Status: American Heart Association Postdoctoral Fellow
Dates: 1993-1996
Degrees: B.S., 1988, University of Illinois, Champaigne-Urbana; Ph.D., 1993, Texas A&M University
Current: Scientist, Covance Pharmaceuticals

12) Student: Gregory J. Parker
Status: Graduate student, Cell and Molecular Biology, Program, NIH Predoctoral Trainee
Dates: 1994-1996
Degrees: B.S., 1994, Albion College, Albion, Michigan; M.S., 1996
Current: Scientist, Panvera Corp.

13) Student: Eric C. Gosink, Ph.D.
Status: Postdoctoral
Dates: 1995-1996
Degrees: B.S., 1988, University of California, San Diego; Ph.D., 1995, University of Wisconsin, Madison
Current: Business Development Manager at Life Technologies

14) Student: Kirsty J. Parker, Ph.D.
Status: American Heart Association Postdoctoral Fellow
Dates: 1996-1997
Degrees: B.S., 1992, Royal Holloway College, London, England; Ph.D., 1995, Kings College London, England
Current: Scientist, Kings College, Longdon.

15) Student: Jenneatte Kunz, Ph.D.
Status: Swiss NSF Postdoctoral Fellow
Dates: 1996-2001
Degrees: B.S., 1990, University of Basel, Basel, Switzerland; Ph.D., 1994, Biozentrum, University of Basel, Switzerland
Current: Associate Professor, Baylor College of Medicine

16) Student: Feng Lu, M.D., Ph.D.
Status: American Heart Association Postdoctoral Fellow
Dates: 1996-1998
Degrees: M.D., 1985, Shangdong Medical University; M.S., 1988, Shandong Medical University; Ph.D., 1994, University of Western Ontario
Current: Associate Professor, Marshfield Clinic

Training Record: (cont):

17) Student: Scott D. Doughman
Status: Graduate student, Cell and Molecular Biology Program
Dates: 1997-1999
Degrees: B.S., 1996, University of Wisconsin, Ph. D. 2004.
Current: President and Chief Scientific Officer Source-Omega Company

18) Student: Steve Watt, Ph.D.
Status: Postdoctoral
Dates: 1998-1999
Degrees: B.S., 1992, University of Toronto, Ph. D, 1997, University of Guelph, Canada
Current: Scientist, Promega Corp

19) Student: Mary Anne Watt, Ph.D.
Status: Postdoctoral
Dates: 1998-1999
Degrees: B.S., 1992, University of Toronto, Ph. D, 1998, University of Guelph, Canada
Current: Scientist, Ophidian Pharmaceuticals

20) Student: Thomas K. Zielinski
Status: Graduate student, Biomolecular Chemistry Training Program
Dates: 1999-2000
Degrees: B.S., 1998, Richard Stockton College
Current: Scientist, Promega Corp

21) Student: Renee L. Doughman (previously Dierckman)
Status: Graduate student, Molecular and Cellular Pharmacology Program
Dates: 1998-2003
Degrees: B.S., 1998, Purdue University; Ph.D. 2003
Current: Clinical Trials Regulatory Associate at UNC, University of North Carolina.

22) Student: Allison J. Friedlein
Status: Graduate student, Molecular and Cellular Pharmacology Program
Dates: 1998-1999
Degrees: B.S., 1998, Cornell College, M.S, 1999
Current: High School Teacher, Madison, Wisconsin

23) Student: Matthew W. Bunce
Status: Graduate student, Biomolecular Chemistry Training Program
Dates: 2000-2008
Degrees: B.S., 1999, Virginia Technical College; Ph.D. 2008
Current: Postdoctoral Fellow, University of Pennsylvania

24) Student: Shawn F. Bairstow
Status: Graduate student, Biomolecular Chemistry Training Program
Dates: 2000-2006
Degrees: B.S., 1999, University of Illinois; Ph.D. 2007
Current: Scientist, Baxter Pharmaceuticals

25) Student: Karen Abel
Status: Graduate student, Philipps-University in Marburg, Germany
Dates: 2000-2004
Degrees: B.S., 1999, Philipps-Universität in Marburg, Ph. D. University of Marburg/Wiscosin.
Current: Scientist, University of Tübingen, Germany

Training Record (cont):

26) Student: Michael L. Gonzales
Status: Graduate student, Molecular and Cellular Pharmacology
Dates: 2001-2007
Degrees: B.S., 1999, University of California, Davis; Ph.D. 2007
Current: Postdoctoral University of California-Davis

27) Student: Kun Ling, Ph.D.
Status: American Heart Association Postdoctoral Fellow
Dates: 2001-2006
Degrees: B.S., 1996, Qingdao University, China; Ph.D., 2001, Shanghai Institute of Cell Biology, Chinese Academy of Sciences, Shanghai, China
Current: Assistant Professor, Department of Biochemistry, Mayo College of Medicine

28) Student: Chunhua Song, M.D., Ph.D.
Status: American Heart Association Postdoctoral Fellow
Dates: 2002-2005
Degrees: M.D., 1985, Wannan Medical College, Wuhu, China; Ph.D., 2002, Molecular Biology, Kobe University, Japan
Current: Scientist, Pennsylvania State University Medical College
Pediatric Hematology/Oncology

29) Student: Xudong Shi, M.D., Ph.D.
Status: Research Associate
Dates: 2002 - 2003
Degrees: M.D., 1989, Beijing Medical University, Beijing, China; Ph.D., 2002, Cell and Molecular Biology, University of Illinois at Urbana-Champaign
Current: Assistant Scientist, Department of Urologic Surgery, University of Wisconsin

30) Student: Chateen Carbonara (now Chateen Krueger)
Status: Graduate student, Molecular and Cellular Pharmacology
Dates: 2002-2004
Degrees: B.S., 2002, State University of New York at Stony Brook; MS, 2005
Current: Research Specialist, Department of Oncology, University of Wisconsin

31) Student: David Mellman
Status: Graduate student, Molecular and Cellular Pharmacology, current Postdoctoral
Dates: 2003-2008,
Degrees: B.S., 2002, University of Colorado at Boulder, Ph.D. 2008.
Current Law School, University of Minnesota.

32) Student: Nicolas Schill
Status: Graduate student, Cellular and Molecular Biology
Dates: 2003-2009
Degrees: B.S., 2002, St. Norbert College, Ph.D. 2009
Current: Scientist Baxter Pharmaceuticals

33) Student: Yue Sun, Ph.D.
Status: Postdoctoral Fellow
Dates: 2003-2008, Scientist 2008-2014
Degrees: B.S., 1998, Lanzhou University, China; Ph.D. (Molecular Cell Biology), 2003, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences (CAS).
Current: Assistant Professor, University of Virginia, June 2014

Training Record (cont):

34) Student: Christy A. Barlow, Ph.D.
Status: Postdoctoral Fellow
Dates: 2006 - 2010
Degrees: Ph.D., 2006, University of Vermont, Cell and Molecular Biology
Current: Scientist ChemRisk, Boulder, CO

35) Student: Andrew F. Hedman
Status: Graduate student, Molecular and Cellular Pharmacology
Dates: 2007-2011, Postdoc 2012-2013
Degrees: B.S., 1999, University of Illinois, Ph.D. 2011.
Current Postdoctoral, NIH, Bethesda, MD

36) Student: Weimin Li, M.D., Ph.D.
Status: Postdoctoral Fellow
Dates: 2007- 2011, Scientist 2012-2014
Degrees: B.S., 1992, Shandong University; MD, 1999, Qingdao University; 2006, Ph.D. University of Basel, Switzerland
Current: Assistant Professor, University of Washington, June 2014

37) Student: Narendra Thapa, Ph.D.
Status: Postdoctoral Fellow
Dates: 2008-present
Degrees: B.S., 1996, Trichandra College, Nepal; Ph.D., 2006, Kyungpook National University, Republic of Korea

38) Student: Rakesh S. Laishram, Ph.D.
Status: Postdoctoral Fellow
Dates: 2008-2012, Visiting Professor, 2013 - 2014,
Degrees: B.Sc., 2004, in Chemistry, Manipur University; Ph.D., 2008, Centre for DNA Fingerprinting and Diagnostics, Hyderabad, India
Current: Assistant Professor, Rajiv Gandhi Centre for Biotechnology, Poojapura, Trivandrum - 695014, India

39) Student: Mark Schramp, Ph.D.
Status: Postdoctoral Fellow
Dates: 2008-2010
Degrees: B.S., 1994, in Biology, Marquette University; Ph.D., 2008, in Cell and Molecular Biology, University of California, Berkeley
Current: Assistant Professor, Dept. of Biology, Benedictine College

40) Student: Suyong Choi
Status: Graduate student, Cell and Molecular Biology
Dates: 2009-2015
Degrees: B.S., 2006, Seoul National University, M.S., 2008, Seoul National University.

41) Student: Xiaojun Tan
Status: Graduate student, Molecular and Cellular Pharmacology
Dates: 2009-2015
Degrees: B.S., 2009, Nanjing University.

Undergraduate training:

My laboratory has trained >60 undergraduate students in research scholarship. Most of these students (~90%) have gone on to Medical School or to Graduate School at excellent Universities, including Harvard (2), Yale (4), MIT (2), Michigan (8), Chicago (3), Wisconsin (20), Stanford (3), Johns Hopkins (2). There have been fifteen Wisconsin/Hilldale/Undergraduate/Faculty Research Awardees and nine Mary Shine fellows in my laboratory. These are highly competitive Wisconsin fellowships for undergraduate research.

Summary of Classroom Teaching Activities:

Pharmacology 901 Seminar Course
1 credit, Spring and Fall Semesters
1987-1989, Organizer

Pharmacology 710, Biochemical Pharmacology
3 credits, Spring Semester
1987–1997
12-15 lectures

Pharmacology 710, Cytosolic and Nuclear Signaling
2 credits, Spring Semester, Course Director
1998-2009
9 lectures and attended the remaining lectures

Pharmacology 717, Medical students
5 credits, Fall Semester
1987-1999
4 lectures

Pharmacology 875a, Kinase Regulation of Cell Growth and Development
2 credits, Spring Semester, Course Director
1989-1997
10-12 lectures

Pharmacology 875b, Signaling to the Nucleus
2 credits, Fall Semester
1995–1997, Co-Director
6 lectures

Zoology 570, Cell Biology
3 credits, Fall Semester, 1992
2 lectures

Pathology 709, Contemporary Topics in Cell Structure and Function
2 credits, Spring Semester, 1992
2 lectures

Biomolecular Chemistry 710, "Exploring Biochemical Functions of Macromolecules"
2 credits, Spring Semester, 2002-2004
2 lectures

Pharmacology 875c, Ethics in Molecular and Cellular Pharmacology.
1 Credit, Director and taught between 3 - 7 lectures. 1998-2006, 2008-2009, 2010.

Pharmacology 875d, Introduction to grant writing.
1 Credit, Course director and instructor. 2010 - 2012

Biochemistry 630/Pharmacology 630, Molecular and Cellular Mechanisms of Signal Transduction
3 credits, Fall Semester, with Tom Martin, Arnold Ruoho, Shigeki Myomoto, Beth Weaver, and Emery Bresnick.
1997-present
8-10 lectures

Student course evaluations over the past 30+ years have consistently ranked between 5.1 and 6.7 in a scale of 1 to 7, where 1 is poor and 7 is outstanding.