BIOGRAPHICAL SKETCH

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NAME: Copeland, Paul R.

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

POSITION TITLE: Professor of Biochemistry and Molecular Biology

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
Loyola University Chicago	B.S.	05/1990	Biology
University of Virginia	Ph.D.	05/1997	Biology
Cleveland Clinic Foundation	Postdoc	03/2002	Cell Biology

A. Personal Statement

My lab has been focused on deciphering the molecular mechanisms that are required for the utilization of the trace element selenium as the amino acid selenocysteine (Sec). A major focus in my lab has been on the role that RNA binding proteins play in promoting this unique incorporation event, which occurs at UGA codons that are found upstream of a kink turn RNA structure in selenoprotein mRNA 3' UTRs called a Sec insertion sequence (SECIS). A kink-turn binding protein known as SECIS binding protein 2 (SBP2) is required for efficient Sec incorporation, and it is important in the context of mutations in humans that cause SBP2 deficiency syndrome. Patients lacking two wild-type alleles are afflicted with a variety of downstream maladies that result from poor selenoprotein expression. We have a long term translational goal of identifying polymorphisms in the SBP2 gene that correlate with specific pathologies that may be the result of selenoprotein insufficiency. These would range in scope from hypothyroidism, cancer, heart disease and male fertility.

Ongoing projects that I would like to highlight include:

R01 GM077073
Copeland (PI)
2/1/19 – 1/31/23
Functional analysis of SBP2 and selenocysteine incorporation

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022 – Present	Associate Dean for Research, Robert Wood Johnson Medical School
2022 – Present	Director, Rutgers - Robert Wood Johnson Medical School/Princeton MD/PhD Program
2017 - Present	Professor, Department of Biochemistry and Molecular Biology, Rutgers - Robert Wood Johnson Medical School, Piscataway, NJ
2019 - 2022	Faculty Director, University Core Facilities, Rutgers Office of Research and Economic Development
2015 - 2019	Director of Research Development, Rutgers Office of Research and Economic Development
2011 - 2017	Associate Professor, Department of Biochemistry and Molecular Biology, Rutgers - Robert Wood Johnson Medical School, Piscataway, NJ
2002 - 2011	Assistant Professor, Department of Molecular Genetics, Microbiology and Immunology, UMDNJ - Robert Wood Johnson Medical School, Piscataway, NJ
1997 - 2002	Postdoctoral Fellow, Department of Cell Biology, Cleveland Clinic Foundation, Cleveland, OH
2014 - Present	NIH Pathways to Independence (K99) Study Section, NIGMS, ad hoc reviewer
2002 - Present	Member, American Society for Biochemistry and Molecular Biology
1997 - Present	Member, American Association for the Advancement of Science
1997 - Present	Member, The RNA Society

Honors

2015	Member of the RBHS Master Educator Guild
2011	UMDNJ Foundation Excellence in Teaching Award
2007	Graduate Student Association Professor of the Year
2002	Cancer Institute of New Jersey New Investigator Award
2000	Elsa Albrecht Fellow Award for Best Manuscript, Cleveland Clinic Foundation
1992	Kepner Teaching Award, Biology Department, University of Virginia

C. Contributions to Science

1. My graduate work resulted in the identification of a novel 3' exoribonuclease (PARN) that regulates protein synthesis by specifically degrading the poly(A) tails during early development. This cemented my interest in the mechanisms of post-transcriptional gene regulation.

   a. **Copeland, P.R**. and Wormington, M. (2001) The mechanism and regulation of deadenlyation: Identification and characterization of Xenopus PARN. *RNA* 7:875-886.

2. I began a postdoctoral stint at the Cleveland Clinic in January of 1997, joining the lab of Donna Driscoll, who had just begun investigating the mechanism of selenocysteine (Sec) incorporation as part of a larger project designed to investigate the function of the selenoprotein GPX4 in atherosclerosis. It was known at that time that a unique 3' UTR element called a selenocysteine insertion sequence was required for the incorporation of selenocysteine at specific UGA codons but none of the other required factors were known. Using my experience in protein purification, I purified and identified an essential factor, SECIS binding protein 2 (SBP2). I completed my postdoctoral stint by characterizing the function and regulation of this factor.

   a. **Copeland, P.R**. and D.M. Driscoll (1999). Purification, redox sensitivity and RNA binding properties of SECIS-binding protein 2, a protein involved in selenoprotein biosynthesis. *J. Biol Chem 274*: 25447-25454. PMID: 10464275

   b. **Copeland, P.R**., Fletcher, J.E. Carlson, B.A.. Hatfield, D.L. and Driscoll, D.M (2000). A novel RNA binding protein, SBP2, is required for the translation of mammalian selenoprotein mRNAs. *EMBO J*. 19:306-314. PMCID: PMC305564

c. Fletcher, J.E., **Copeland, P.R**. and Driscoll, D.M. (2000) Polysome distribution of phospholipid hydroperoxide glutathione peroxidase mRNA: Evidence for a block in elongation at the UGA/selenocysteine codon. *RNA* 6:1573-1584. PMCID: PMC1370027

d. **Copeland, P.R**., Stepanik, V.A., and Driscoll, D.M. (2001) Insights into mammalian selenocysteine incorporation: Domain structure and ribosome binding of SBP2. *Mol. Cell. Biol*. 21:1491-1498. PMCID: PMC86695

3. In 2002 I set up my own lab at what was then the University of Medicine and Dentistry of NJ, now part of Rutgers. During the first 8 years, my lab was engaged in two main projects surrounding the mechanism of Sec incorporation: identifying the role of the SBP2-ribosome interaction and examining the determinants for Sec incorporation efficiency. Together this work has formed the bulk of what we know about how Sec incorporation works in the mammalian system.

a. Caban, K., Kinzy, S.A. and **Copeland, P.R**. (2007) The L7Ae RNA binding motif is a multi-functional domain required for the ribosome-dependent Sec incorporation activity of SECIS binding protein-2. *Mol Cell Biol*, 27:6350-60. PMCID: PMC2099609

b. Gupta, M., and **Copeland P.R.** (2007) Functional analysis of the interplay between translation termination, selenocysteine codon context and SECIS binding protein 2. *J. Biol Chem*. 232:36797-36807. PMCID: PMC2820277

c. Donovan, J., Caban, K., Ranaweera, R., Gonzalez-Flores, J.N. and **Copeland P.R**. (2008) A Novel Protein Domain Induces High Affinity Selenocysteine Insertion Sequence Binding and Elongation Factor Recruitment. *J. Biol Chem.* 283(50):35129-35139. PMCID: PMC3073842

d. Donovan, J. and **Copeland, P.R**. (2010) The efficiency of selenocysteine incorporation is regulated by translation initiation factors. *J Mol Biol*. 400:659 PMCID: PMC3721751

4. Since 2010, my lab has branched into some new areas still within the confines of determining the mechanism of Sec incorporation but expanding into some of the regulatory mechanisms as well. Perhaps most importantly we have developed a system that allowed us to determine that the three known factors (*Sec-tRNA^{Sec}, eEFSec and SBP2) are all necessary and sufficient for Sec incorporation in vitro. This has proven useful in our collaborative work with the Howard lab as we can complement his ribosome profiling expertise with classical in vitro and cell based work.*

a. Gonzalez-Flores, J.N., Gupta, N., DeMong, L.W. and **Copeland, P.R**. (2012) The selenocysteine-specific elongation factor contains a novel and multi-functional domain. *J. Biol. Chem*. 287(46):38936-45 PMCID: PMC4269102

b. Gupta N, DeMong, L.W., Banda, S and **Copeland, P.R**. (2013) Reconstitution of selenocysteine incorporation reveals intrinsic regulation by SECIS elements. *J. Mol Biol*. 425:2415-22. *PMCID: PMC3699960*

c. Dobosz-Bartoszek, M., Pinkerton, M.H., Otwinowski, P., Söll, D., **Copeland, P.R**., Simonović, M. Crystal structures of human eEFSec suggest a non-canonical mechanism for selenocysteine incorporation. *Nat Commun*. 2016; 7: 12941, PMCID: PMC5059743

d. Dubey, A. and **Copeland, P.R**. The Selenocysteine-Specific Elongation Factor Contains Unique Sequences That Are Required for Both Nuclear Export and Selenocysteine Incorporation. *PLoS One*. 2016 Nov 1;11(11) PMCID: PMC5089774

5. More recent work has delved into the pre and post-translational aspects of selenocysteine utilization. This has partly focused on the unique selenium transport protein called Selenoprotein P (SELENOP). With up to 17 Sec codons, the synthesis of this protein challenges all of the mechanistic models we have thus far put forth. Additionally, we have started to use the zebrafish model system to answer key regulatory questions that require a systems biology context, specifically the role of selenoprotein synthesis in oxidative stress response pathways.

a. Shetty SP, **Copeland P.R**. The Selenium Transport Protein, Selenoprotein P, Requires Coding Sequence Determinants to Promote Efficient Selenocysteine Incorporation*. J Mol Biol.* 2018 Sep 20. pii: S0022-2836(18)30741-1. PMCID: PMC6289641

b. Shetty, SP., Kiledjian, NT and **Copeland, PR**. 2021. The Selenoprotein P 3' Untranslated Region Is an RNA Binding Protein Platform That Fine Tunes Selenocysteine Incorporation. *PLoS One* 2022.

c. Kiledjian NT, Shah R, Vetick MB, **Copeland PR**. The expression of essential selenoproteins during development requires SECIS-binding protein 2-like. *Life Sci Alliance.* 2022 May;5(5). PubMed PMID: 35210313; PubMed Central PMCID: PMC8881744

d. Hilal T, Killam BY, Grozdanović M, Dobosz-Bartoszek M, Loerke J, Bürger J, Mielke T, **Copeland PR**, Simonović M, Spahn CMT. Structure of the mammalian ribosome as it decodes the selenocysteine UGA codon. *Science*. 2022 Jun 17;376(6599):1338-1343. PMID: 35709277.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/paul.copeland.1/bibliography/public/