BIOGRAPHICAL SKETCH

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NAME: Rudolph. L. Juliano, Ph.D

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

POSITION TITLE: Professor Emeritus, Chief Scientific Officer

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
Cornell University	B.S.	June 1963	Physics
University of Rochester	Ph.D.	June 1971	Biophysics
Roswell Park Memorial Institute	Postdoc.	1970-72	Cell Biology

A. Personal Statement

I have extensive experience in the area of oligonucleotide chemistry and biology. My laboratory has made major contributions to the development of receptor targeted ligand oligonucleotide conjugates, to understanding intracellular trafficking of oligonucleotides, and most recently in the discovery of small molecules that dramatically enhance the pharmacological effects of oligonucleotides. Thus I am well positioned to contribute to this project.

Selected Recent Publications

Yang B, Ming X, Cao C, Laing B, Yuan A, Porter M, Hull-Ryde E, Maddry J, Suto M, Janzen W and Juliano RL (2015). High Throughput Screening Identifies Small Molecules that Enhance the Pharmacological Effects of Oligonucleotides. ***Nucleic Acids Research*** 43:1987-96 PMID 25662226 PMC4344505

Carver K, Ming X and Juliano RL (2014) Multicell Tumor Spheroids as a Model for Assessing Delivery of Oligonucleotides in Three Dimensions. ***Molecular Therapy - Nucleic Acids***. 11:e153. PMID:24618852 PMC4027982

Nakagawa O, Ming X, Carver K, Juliano R (2013) Conjugation With Receptor-Targeted Histidine-Rich Peptides Enhances the Pharmacological Effectiveness of Antisense Oligonucleotides. ***Bioconjug Chem***. 25:165-70. PMID 24354269; NIHMSID558329

Ming X , Carver K, Fisher M, Noel R, Cintrat JC, Gillet D, Barbier J, Cao C, Bauman J and Juliano RL. (2013) The Small Molecule Retro-1 Enhances the Pharmacological Actions of Antisense and Splice Switching Oligonucleotides ***Nucleic Acids Research***. 41: 3673-87 PMID:23396438; PMC3616695

B. Positions and Honors

1972-1978 Investigator, Research Institute, Hospital for Sick Children, Toronto
1973-1978 Assistant Professor of Biophysics, University of Toronto, Ontario
1978-1982 Associate Professor of Pharmacology, Univ. of Texas Medical School, Houston, TX
1982-1986 Professor of Pharmacology, Univ. Texas Medical School, Houston, TX

1987-2002	Professor and Chair, Department of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, NC
1993	Fogarty Fellow, J Gurdon lab, Wellcome-CRC Institute, Cambridge, UK
12/2002-07	Professor, Department of Pharmacology, University of North Carolina
2007-- 2015	Boshamer Distinguished Professor of Pharmacology
2008-2011	Assoc. Dean for Research & Graduate Education, UNC School of Pharmacy
July 2015-	Emeritus Professor of Pharmacology
Dec 2014-	Chief Scientific Officer and acting President, Initos Pharmaceuticals LLC

C. Contribution to Science

Throughout my career I have pursued three intertwined research themes (a) the basic biology of cell surface receptors and their signaling processes (b) the molecular pharmacology of anti-cancer and anti-infective drugs (c) novel approaches for enhanced drug delivery. From the 1980s to mid-2000's my laboratory made important contributions to study of integrins and their role in signaling processes. This included the co-discovery of a5b1 the first integrin to be described, as well as the first report of integrin signaling in nucleated mammalian cells (PMIDs: 11309409, 9082999, 1717976, 4012302). From the early 1990's until the present we have worked on the molecular pharmacology of antisense and siRNA oligonucleotides with emphasis on their targeting and intracellular trafficking (PMIDs : 25662226 , 20550198, 21755983 ,9655887). In the 1980's we worked very actively on liposomes, particularly for delivery of anti-infective agents (PMIDs 1272396: 6470530: 3807887), which ultimately resulted in a clinically utilized preparation of liposomal Amphotericin B. An important contribution in the 1970s was my role as co-discoverer of the P-glycoprotein (PMID: 990323) which is involved in multi-drug resistance in cancer.

http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/41161687/

D. Research Support

1 R41 TR 001330. 08/15/15—08/16/16
NIH (PI. R Juliiano)
Development of Small Molecules that Enhance the Delivery and the Pharmacological Effects of Oligonucleotides
A key impediment to oligonucleotide-based therapeutics is the difficulty in delivering these large, highly polar molecules to their sites of action in the cytosol or nucleus of tissue cells. While chemical modification of oligonucleotides and the utilization of various nanotechnology-based delivery approaches have been helpful, the delivery problem remains largely unresolved. We have taken an orthogonal approach to this problem and have developed small molecule compounds that enhance the functional delivery and pharmacological effectiveness of oligonucleotides by manipulating their intracellular trafficking. Here we propose to optimize compounds as *in vivo* probes; it seems likely that this effort will have a major impact on the entire field of oligonucleotide therapeutics.

R01CA151964 04/01/11 – 01/31/15 .
NIH (PI: Juliano) (unfunded extension)
Intracellular Trafficking of Antisense and siRNA Oligonucleotides in Cancer Cells
Aims: Antisense and siRNA oligonucleotides have great potential for cancer therapeutics. However our ability to use these molecules effectively is limited by lack of detailed molecular understanding of their cellular uptake and intracellular trafficking. This project will address these issues using a variety of pharmacological, molecular and imaging techniques. These studies will be pursued in single cells, multi-cellular assemblies, and tumors *in vivo*. This integrated approach will provide a rich stream of novel information that will enhance and expedite the development of oligonucleotides as therapeutic agents in cancer.

1 R21CA170332 7/01/2012-6/30/2015 .
NIH (PI: Juliano)(unfunded extension)

Title: ***Addressing Undruggable Targets Using Oligonucleotides and Small Organic Molecules (PQ 18)***
Aims: We pursue a novel approach for enhancing delivery of oligonucleotides and thus enhance their pharmacological actions in order to improve the therapeutic utility of oligonucleotides in cancer.

P30DK079312-06 7/01/12 – 6/30/17
Indiana University (Program PI: Molitoris); RJ Role: Core PI
Title: ***UNC Probe Delivery Core for the Center for Advanced Renal Microscopic Analysis***