

Evgeny Nudler, Ph.D.

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Education

<u>Year</u>	<u>Degree</u>	<u>Field</u>	<u>Institution</u>
1989	B.A.	Biology	Division of Biology, Moscow State University, Moscow, USSR
1992	M.S.	Genetics	Department of Genetics, Moscow State University, Russia
1995	Ph.D.	Biochemistry	Institute of Molecular Genetics, Russian Academy of Sciences

Postdoctoral Training

<u>Dates</u>	<u>Specialty</u>	<u>Mentor</u>	<u>Place of Training</u>
1995-1997	Molecular Biology	Dr. A. Goldfarb	Public Health Research Institute, New York

Academic Appointments

1997-2003	Assistant Professor, New York University School of Medicine, New York, NY
2003-2005	Associate Professor (tenured), New York University School of Medicine
2005-2008	Professor, Dept. of Biochemistry, NYU School of Medicine
2008-	Julie Wilson Anderson Professor, NYU School of Medicine
2013-	Investigator, Howard Hughes Medical Institute

Awards/Honors

1997	The Helen Hay Whitney Foundation research fellowship (declined)
1998	The Searle Scholar Award
2001	The Irma T. Hirsch Career Scientist Award
2002	The Edward Mallinckrodt, Jr. Foundation Research Award
2002	Fogarty International Research Collaboration Award
2004	Keynote Lecture: The RNA Biochemistry Symposia. Blaubeuren, Germany
2004	United States-Israel Bi-national Science Foundation Award
2006	The Dynasty Foundation Award
2006	NIH Director's Pioneer Award
2008	Crain's "40 Under 40" Alumni
2008	Julie Wilson Anderson Professorship (endowment chair)
2009	The Vilcek Foundation Finalist Prize
2010	Keynote Lecture: The Harden Conference on Transcription. Cambridge, UK
2010	The Blavatnik Award, New York Academy of Science
2011	The Robertson Foundation Award
2012	Biogerontology Research Foundation Award
2013	Investigator, Howard Hughes Medical Institute
2013	Honorary Professor, Moscow Institute of Physics and Technology
2013	Master Scientist, NYU Langone Medical Center
2014	Dean's Honor Lecture, NYU School of Medicine
2016	The Neil Welker Memorial Award
2016	Engelhardt Memorial Lecture, IMB, Russian Academy of Science
2016	Elected Foreign Member, Russian Academy of Sciences
2017	Elected Fellow, American Academy of Arts and Sciences
2018	Glenn Award for Research in Biological Mechanisms of Aging
2019	Blavatnik Family Foundation Award

Research Statement (most significant contributions):

1. RNA polymerase *backtracking* and *ratcheting*: In 1997 we described back-and-forth sliding of RNAP along DNA and RNA (Nudler *Cell* 1997). Our group then showed that this universal phenomenon, which we called “backtracking”, plays a key role in controlling gene expression (e.g. Proshkin *Science* 2010), genome instability (e.g. Dutta *Cell* 2011), and DNA repair (e.g. Epshtein *Nature* 2014). We were also first to demonstrate that RNAP is a *Brownian ratchet* machine (Bar-Nahum *Cell* 2005). Our findings explained in mechanistical detail how RNAP translocates and responds to regulatory signals and elongation factors.

2. Transcription termination and antitermination: We have uncovered the mechanistical principles of the termination process in bacteria and formulated models explaining the molecular pathways leading to both intrinsic and Rho-dependent transcription termination (Gusarov *Mol Cell*, 1999; Epshtein *Mol Cell* 2007; Epshtein *Nature* 2010; Hao *Mol Cell* 2021). We also studied how these processes are regulated in the cell and formulated mechanistical models of factor-dependent (Gusarov *Cell* 2001) and factor-independent (Mironov *Cell* 2002; Sedlyarova *Mol Cell* 2017) modes of regulation. Our studies uncovered novel functions of Rho, such as silencing of horizontally transferred genes (Cardinal *Science* 2008) and preserving genomic integrity (Dutta *Cell* 2011). We also found that Rho functions as a global regulator of transcription, acting at 5'UTRs of numerous genes, and that sRNAs control Rho termination genome-wide, thus establishing sRNAs as transcription elongation factors (Sedlyarova *Cell* 2016).

3. Transcription-coupled DNA repair (TCR): In 2014 we uncovered a general mechanism of TCR that relies on RNAP backtracking (Epshtein *Nature* 2014). We found that the key DNA repair helicase UvrD binds RNAP during elongation and forces it to slide backward along DNA. By inducing backtracking, UvrD exposes DNA lesions shielded by RNAP, allowing the repair enzymes to access the damage sites. We also showed that bacterial alarmone ppGpp contributes to UvrD-mediated TCR by rendering RNAP backtracking-prone (Kamarthapu *Science* 2016; Weaver *NSMB* 2023). Because backtracking is a shared feature of all cellular RNAPs, this mechanism enables RNAP to function as a global DNA damage scanner in bacteria and eukaryotes. More recently we showed that RNAP serves as a platform for the assembly of functional nucleotide excision repair (NER) complexes (Bharati *Nature* 2022). Contrary to the conventional dogma, we show that TCR accounts for most chromosomal NER events and is largely independent of Mfd – a DNA translocase thought to be necessary and sufficient for TCR (Bharati *Nature* 2022; Martinez *Nat Commun* 2022). We also discovered that ribonucleotide excision repair (RER) is directly coupled to transcription in *E. coli* (Hao *Cell* 2023).

4. Riboswitches: In 2002, we discovered the first ligand-sensing mRNAs that regulate biosynthetic genes in *B. subtilis* (Mironov *Cell* 2002). Simultaneously, Breaker and colleagues reported similar findings in *E. coli*. Since then, dozens of riboswitches have been described in bacteria and eukaryotes where they control numerous genes. We have shown that riboswitches can activate and suppress gene expression acting at the level of transcription termination, translation initiation, and modulating alternative splicing and mRNA stability (reviewed in Serganov and Nudler *Cell* 2013).

5. Eukaryotic RNA *thermosensor*: In 2006 we isolated a complex composed of the translation elongation factor eEF1A1 and a novel non-coding RNA (HSR1) that is required for activation of heat shock genes in mammals (Shamovsky *Nature* 2006). We have shown that HSR1 serves as a molecular thermosensor. We also showed that eEF1A1 orchestrates the whole process of heat shock response, from transcription activation to mRNA stabilization, transport, and translation (Vera *eLife* 2014). These findings provide a new paradigm of cellular adaptation to stress, with implications in neurodegeneration and cancer.

6. Gas-defense system in bacteria: We showed that endogenously produced gases NO and H₂S protect bacteria from oxidative stress, immune attack, and many antibiotics (Gusarov *Science* 2009; Shatalin *Science* 2011). These results support the emerging concept of antibiotic killing, which relies in part on oxidative damage, and establish NO- and H₂S-producing enzymes as promising targets for antimicrobial therapy. We also discovered the critical role of endogenous H₂S in bacterial tolerance, including the formation of persister cells and biofilms (Shatalin *Science* 2021). In a separate line of investigation, we showed that NO produced by bacteria inside their host diffuses into animal tissues where it activates a defined set of genes that protect the host from environmental stress and extend its lifespan (Gusarov *Cell* 2013).

Complete list of published work (156 publications):

<https://pubmed.ncbi.nlm.nih.gov/?term=nudler+e&sort=date>