



Ribonuclease III in Action: Catalytic Photographs of the Enzyme, Determined by X-ray Crystallography

**Jarosław
Błaszczyk**

This “mini-review”
e-poster
presentation
is dedicated
to
Professor Wojciech J. Stec
on the occasion
of
His 75th Birthday

*Financial support
by the
Polish National Science Center,
grant No.
DEC-2012/05/B/ST4/00075
is gratefully acknowledged.*

RCSB Protein Data Bank - Jmol Viewer for 1RC7 - Crystal structure of RNase III Mutant E110K from Aquifex Aeolicus complexed with ds-RNA at 2.15 Angstrom Resolution - Mozilla Firefox

http://www.pdb.org/pdb/explore/jmol.do?structureId=1RC7&opts=38&bionumber=1

RCSB Protein Data Bank - Jmol View...

RCSB PDB PROTEIN DATA BANK

A MEMBER OF THE PDB
An Information Portal to Biological Macromolecular Structures
As of Tuesday Oct 19, 2010 at 5 PM PDT there are 68701 Structures | PDB Statistics

Contact Us | Print

PDB ID or Text Search Advanced Search

MyPDB Hide
Login to your Account
Register a New Account

Home Hide
News & Publications
Usage/Reference Policies
Deposition Policies
Website FAQ
Deposition FAQ
Contact Us
About Us
Careers
External Links
Sitemap
New Website Features

Deposition Hide
All Deposit Services
Electron Microscopy
X-ray | NMR
Validation Server
BioSync Beamline
Related Tools

Search Hide
Advanced Search
Latest Release
New Structure Papers
Sequence Search
Chemical Components
Unreleased Entries
Browse Database
Histograms

Explorer:
Last Structure: 1RC7

Results:
Query (4):
• Query Results
• Query Details
• Query History (1)
• Save Query to MyPDB

Crystal structure of RNase III Mutant E110K from Aquifex Aeolicus complexed with ds-RNA at 2.15 Angstrom Resolution 1RC7

Display of Biological Assembly. [View Asymmetric Unit]

Jmol Version 12.0.2

Display Files
Download Files
Share this Page

Jmol_S

[G]8:8.P/2 #107 54.436 87.3 15.674

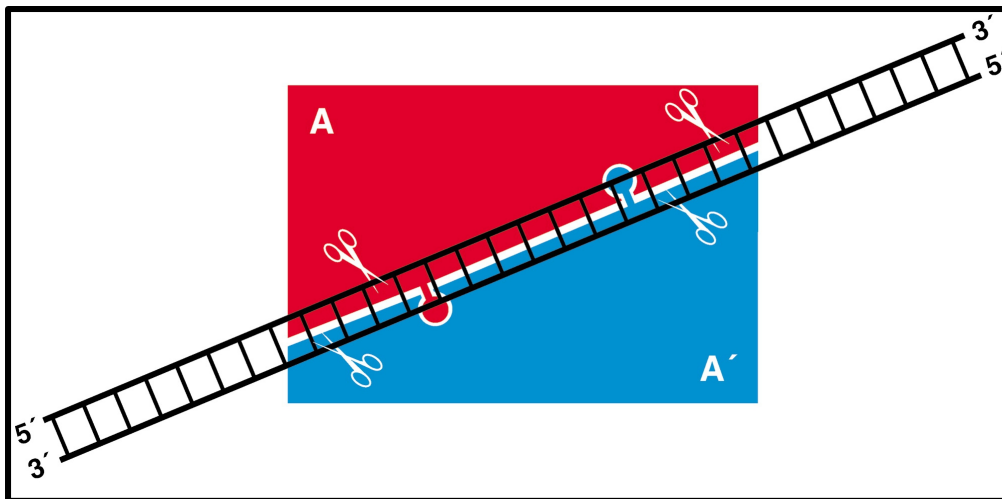
Ribonuclease III (RNase III)

an enzyme which catalyzes the cleavage of double-stranded RNA (dsRNA)

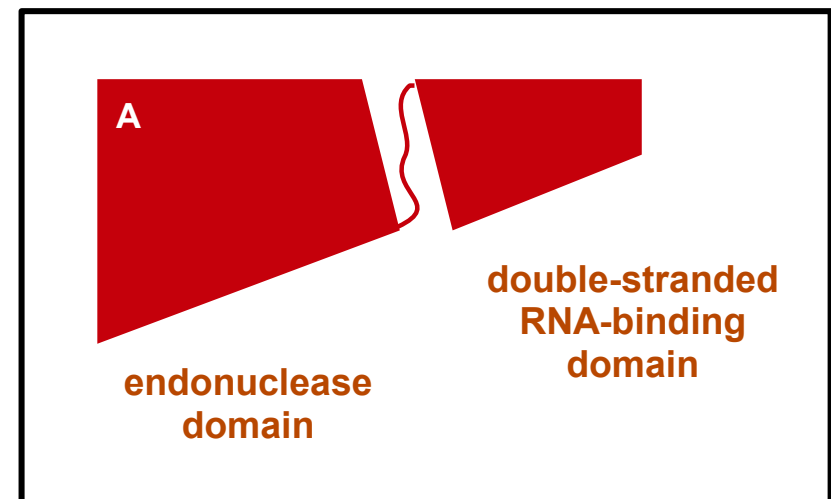
Ribonucleases (RNases) cleave RNA strands to shorter fragments or to single nucleotides by hydrolysis of the phosphodiester bonds.

Among ribonucleases, we can distinguish:

- **endoribonucleases**: they cleave RNA molecules inside the strands
- **exoribonucleases**: they detach nucleotides from RNA 3'- or 5'-ends.



Ribonuclease III is an endoribonuclease that catalyzes a cleavage of double-stranded RNA to short fragments



The RNase III monomer contains two very loosely connected domains

Very brief history of the struggle on determination of RNase III structure and function

1968: First time purified in *Escherichia coli*.

- [1]. H.D. Robertson, R.E. Webster and N.D. Zinder, *J. Biol. Chem.* (1968), **243**, 82-91.
 “Purification and properties of ribonuclease III from *Escherichia coli*.”

1968-1993: Investigation of enzyme functions.

- [2]. For example, see: H.L. Li, B.S. Chelladurai, K. Zhang, A.W. Nicholson, *Nucleic Acids Res.* (1993), **21**, 1919-1925. “Ribonuclease III cleavage of a bacteriophage T7 processing signal. Divalent cation specificity, and specific anion effects.”

1995: First X-ray structure: The double-stranded RNA-binding domain, PDB 1di2.

- [3.] A. Kharrat, J. Macias, T.J. Gibson, M. Nilges, A. Pastore, *EMBO J.* (1995), **14**, 3572-3584.
 “Structure of the dsRNA binding domain of *E. coli* RNase III.
 PDB 1di2, *Xenopus laevis* - frog.

double-stranded RNA-binding domain



1996-2004: The struggle to obtain pure protein and to get an X-ray structure of full-length RNase III

This includes my work in the National Cancer Institute at Frederick: in Macromolecular Crystallography Lab (Alex Wlodawer & Xinhua Ji; crystallization and structure determination), and in Gene Regulation and Chromosome Biology Lab (Don Court; where the expression and purification work I have done together with Daiguan Yu*)

Present: Daiguan Yu in his Lab in GIBH CAS in Guangzhou, China

Donald Court



Daiguan Yu



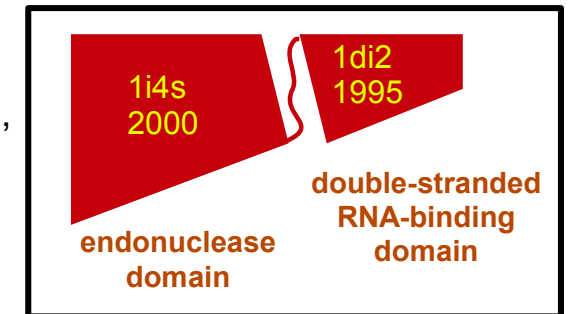
*Daiguan Yu is currently a Group Leader of the BioTherapeutics Core Technology Group at Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences



First X-ray structure which allowed to say something about the enzyme function

2000: X-ray structure of endonuclease domain, 1i4s. (not the full-length protein yet !)

[4]. J. Blaszczyk, J.E. Tropea, M. Bubunenko, K.M. Routzahn, D.S. Waugh, D.L. Court, X. Ji, *Structure* (2001), **9**, 1225-1236. "Crystallographic and modeling studies of RNase III suggest a mechanism for double-stranded RNA cleavage." PDB 1i4s, *Aquifex aeolicus*.



Endonuclease domain (PDB 1i4s) is a functional domain.

Based on this structure, I proposed a model of RNase III with the cleavage product, 22bp ds-RNA, with 2bp overhang on each side.

After years, my model was structurally proven: 2006, in entry 2ez6.

Molecular Cell

[5]. *Mol. Cell*, (2001), 8, 1158-1160.

Thirty-Three Years Later, a Glimpse at the Ribonuclease III Active Site

Phillip D. Zamore
Biochemistry and Molecular Pharmacology,
University of Massachusetts Medical School,
Worcester, MA 01655, USA

The paper which appreciates the impact of our work



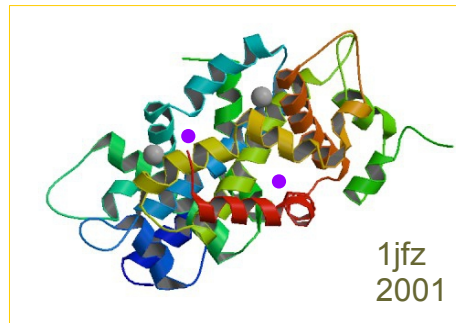
Our structure has been featured in December 2001 Issue cover



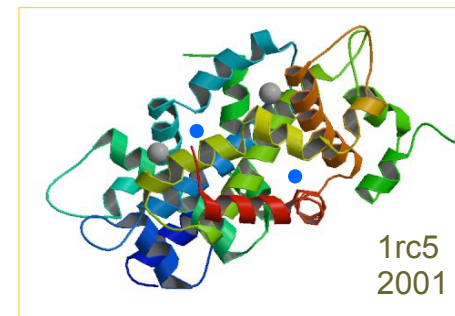
Our structure

First full-length RNase III structures

2001: Probing the RNase III active center: Two X-ray structures of endonuclease domain in complex with metal ions
 (1jfz: with Mn^{2+} , 1rc5: with Mg^{2+}) (still not the full-length protein!)



1rc5 : endonuclease domain, Mg^{2+} complex

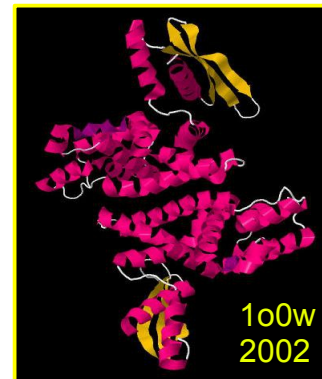


1jfz : endonuclease domain, Mn^{2+} complex

2002-2004: First structures of full-length RNase III (1o0w, 1rc7)

[6]. Joint Center for Structural Genomics (JCSG).
 “Crystal structure of ribonuclease III (TM1102) from *Thermotoga maritima* at 2.0 Å resolution.”
 PDB 1o0w. Apoenzyme, (2002), unpublished.

[7]. J. Blaszczyk, J. Gan, J.E. Tropea, D.L. Court, D.S. Waugh, X. Ji, *Structure* (2004), **12**, 457-466.
 “Noncatalytic assembly of ribonuclease III with double-stranded RNA.”
 PDB 1rc7. *Aquifex aeolicus*.



Full length, apo form (no RNA)

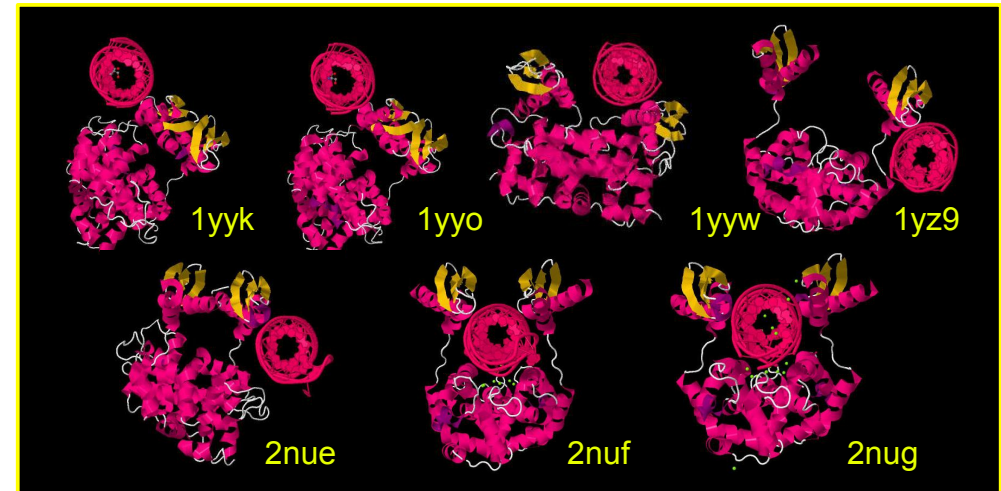


Full length, in complex with RNA

RNase III structural avalanche: the enzyme function disclosed in snapshots

2005-2007: “Catalytic photographs” of RNase III in action

- [8]. J. Gan, J.E. Tropea, B.P. Austin, D.L. Court, D.S. Waugh, X.Ji, *Structure* (2005), **13**, 1435-1442.
“Intermediate states of ribonuclease III in complex with double-stranded RNA.”
PDB 1yyk, 1yyo, 1yyw, 1yz9. *Aquifex aeolicus*.
- [9]. J. Gan, G. Shaw, J.E. Tropea, D.S. Waugh, D.L. Court, X.Ji *Mol. Microbiol.* (2007), **67**, 143-154.
“A stepwise model for double-stranded RNA processing by ribonuclease III.”
PDB 2nue, 2nuf, 2nug. *Aquifex aeolicus*.



2006: RNase III “Functional” complex with the product. Published in *Cell* !

- [10]. J. Gan, J.E. Tropea, B.P. Austin, D.L. Court, D.S. Waugh, X.Ji, *Cell* (2006), **124**, 355-366.
“Structural insight into the mechanism of double-stranded RNA processing by ribonuclease III.”
PDB 2ez6. *Aquifex aeolicus*.



Cell 124, 355–366, January 27, 2006 ©2006 Elsevier Inc.

Cell

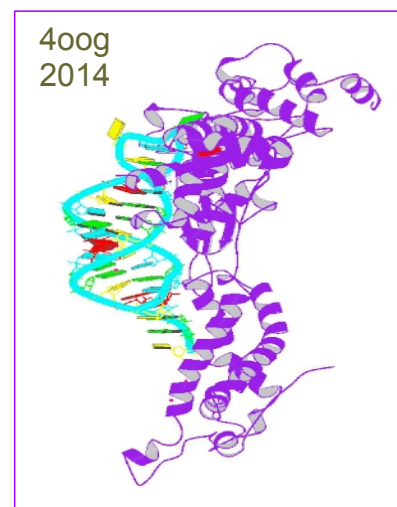
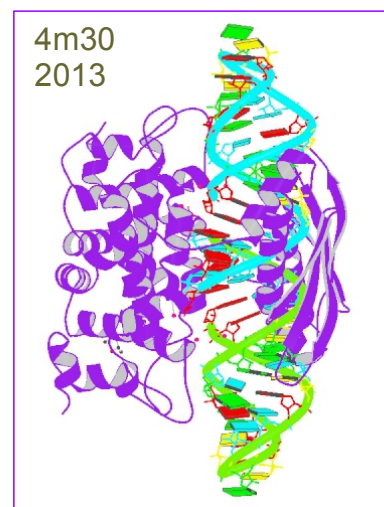
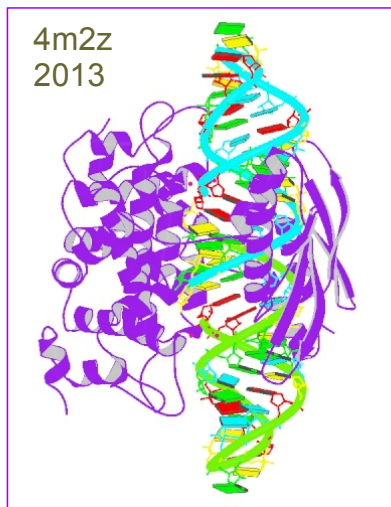
Structural Insight into the Mechanism of Double-Stranded RNA Processing by Ribonuclease III

Jianhua Gan,¹ Joseph E. Tropea,¹ Brian P. Austin,¹ Donald L. Court,¹ David S. Waugh,¹ and Xinhua Ji^{1*}
¹Center for Cancer Research, National Cancer Institute, National Institutes of Health, Frederick, MD 21702, USA
 *Contact: jix@ncifcrf.gov
 DOI 10.1016/j.cell.2005.11.034

RNase III structural avalanche: the enzyme function disclosed in snapshots (continued)

2008-2015: “Catalytic photographs” of RNase III in action (continued)

- [11]. D.L. Court, J. Gan, Y-H. Liang, G.X. Shaw, J.E. Tropea, N. Costantino, D.S. Waugh, X. Ji, *Annu. Rev. Genet.* (2013), **47**, 405-431. “RNase III: Genetics and Function; Structure and Mechanism.” PDB 4m2z, 4m30. *Aquifex aeolicus*.
- [12]. Y.H. Liang, M. Lavoie, M.A. Comeau, S. Abou Elela, X. Ji, *Mol. Cell* (2014), **54**, 431-444. “Structure of a eukaryotic RNase III postcleavage complex reveals a double-ruler mechanism for substrate selection.” PDB 4oog. *Aquifex aeolicus*.



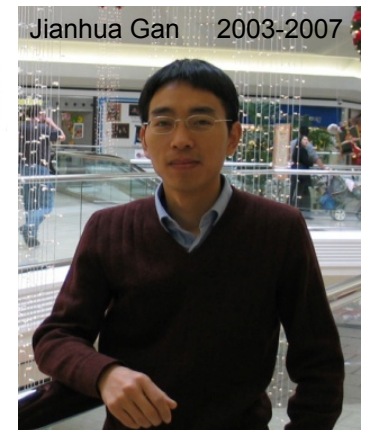
My (1996-2004) successors:

The two meanings of the word “successor”:

1. “The person who took charge of the project”
2. “The author of the success; the success holder”

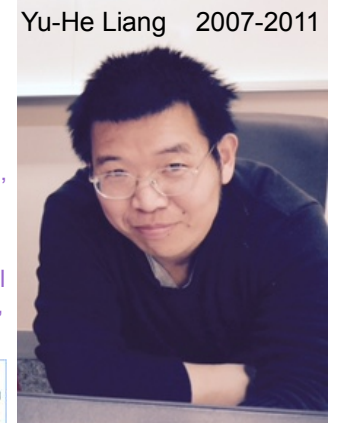


Jianhua Gan
is currently a
Full-Time
Professor at the
Department of
Physiology
and Biophysics,
School of Life
Sciences,
Fudan University,
Shanghai, China



Yu-He Liang 2007-2011

Yu-He Liang
is currently a
Research Associate,
a PDB annotator at
Rutgers University,
Department of Chem-
istry and Chemical
Biology, Piscataway,
New Jersey, USA

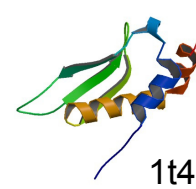


The aftermath of our RNase III structural work

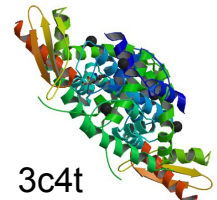
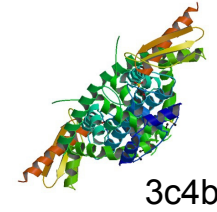
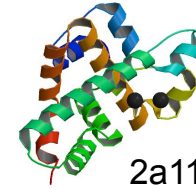
8



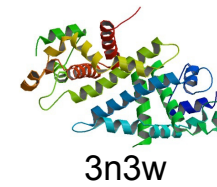
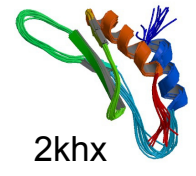
1t4o Rnt1p dsRNA-binding domain of RNase III
 [13]. N. Leulliot, S. Quevillon-Cheruel, M. Graille, H. Van Tilbeurgh, T.C. Leeper, K.S. Godin, T.E. Edwards, S.T. Sigurdsson, N. Rozenkrants, R.J. Nagel, M. Ares, G. Varani, *Embo J.* (2004), **23**, 2468-2477. "A new alpha-helical extension promotes RNA binding by the dsRBD of Rnt1p RNase III."



2a11 Endonuclease Domain of RNase III from *Mycobacterium tuberculosis*
 [14]. D.L. Akey, J.M. Berger, *Protein Sci.* (2005), **14**: 2744-2750. "Structure of the nuclease domain of ribonuclease III from *M. tuberculosis* at 2.1 Å."



2khx Drosha double-stranded RNA binding motif
 [15]. G.A. Mueller, M.T. Miller, E.F. Derose, M. Ghosh, R.E. London, T.M. Hall, *Silence* (2010), **1**:2. "Solution structure of the Drosha double-stranded RNA-binding domain."



3c4b RNase IIIb and dsRNA binding domains of mouse Dicer (form 1)
3c4t RNase IIIb and dsRNA binding domains of mouse Dicer (form 2)
 [16]. Z. Du, J.K. Lee, R. Tjhen, R.M. Stroud, T.L. James, *Proc. Natl. Acad. Sci. USA* (2008), **105**, 2391-2396. "Structural and biochemical insights into the dicing mechanism of mouse Dicer: a conserved lysine is critical for dsRNA cleavage."

2eb1 C-Terminal RNase III Domain of Human Dicer
 [17]. D. Takeshita, S. Zenno, W.C. Lee, K. Nagata, K. Saigo, M. Tanokura, *J. Mol. Biol.* (2007), **374**, 106-120. "Homodimeric structure and double-stranded RNA cleavage activity of the C-terminal RNase III domain of human dicer."

3n3w Nuclease Domain of RNase III from *Campylobacter jejuni* (form 1)
3o2r Nuclease Domain of RNase III from *Campylobacter jejuni* (form 2)
 [18]. G. Minasov, A. Halavaty, L. Shuvalova, I. Dubrovskaya, J. Winsor, L. Papazisi, W.F. Anderson, *Center for Structural Genomics of Infectious Diseases* (2010). Unpublished.

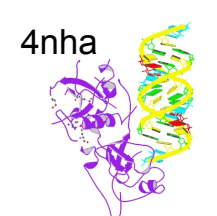
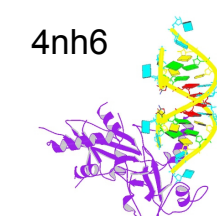
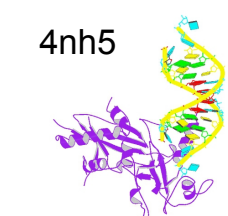
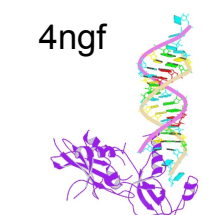
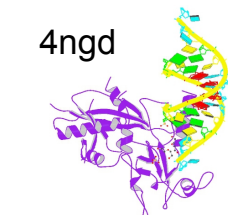
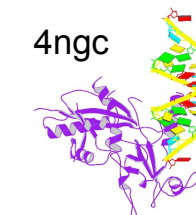
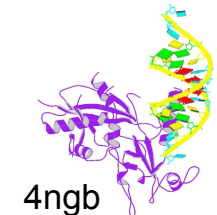
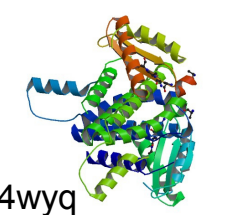
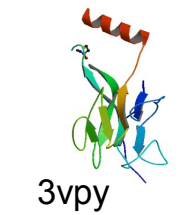
3vpy Conserved phospho-threonine recognition cleft for dicer binding
 [19]. S. Machida, Y.A. Yuan, *Mol Plant* (2013), **6**, 1290-1300. "Crystal structure of *Arabidopsis thaliana* Dawdle forkhead-associated domain reveals a conserved phospho-threonine recognition cleft for dicer-like 1 binding."

Human Dicer Platform-PAZ-Connector Helix cassette in complex with:

4ngb	12-mer siRNA, UU-3' ends	4nh3	13-mer siRNA, 5'-pU and UU-3' ends
4ngc	12-mer siRNA, UA-3' ends	4nh5	14-mer siRNA, 5'-pUU; UU-3' ends
4ngd	12-mer siRNA, 5'-p and UU-3' ends	4nh6	15-mer siRNA, 5'-pUUU; UU-3' ends
4ngf	17-mer siRNA, 5'-p and UU-3' ends	4nha	16-mer siRNA, 5'-p and UU-3' ends
4ngg	13-mer siRNA, 5'-A and UU-3' ends		

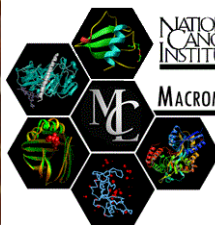
[20]. Y. Tian, D.K. Simanshu, J.B. Ma, J.E. Park, I. Heo, V.N. Kim, D.J. Patel, *Mol. Cell* (2014), **53**, 606-616. "A phosphate-binding pocket within the platform-PAZ-connector helix cassette of human Dicer."

4wyq Dicer / TRNA-Binding Protein interface
 [21]. R.C. Wilson, A. Tambe, M.A. Kidwell, C.L. Noland, C.P. Schneider, J.A. Doudna, *Mol. Cell*, (2015), **57**: 397-407. "Dicer-TRNABindingProtein Complex Formation Ensures Accurate Mammalian MicroRNA Biogenesis."





NCI 1996-2004



NATIONAL
CANCER
INSTITUTE
MACROMOLECULAR CRYSTALLOGRAPHY LABORATORY

NCI-Frederick

9



MICHIGAN STATE UNIVERSITY
MSU 2004-2006
Biochemistry & Molecular Biology



ACKNOWLEDGEMENTS

Jarosław Błaszczyk -
- performed structural study in:
National Cancer Institute
Frederick, Maryland, USA, 1996-2004
Michigan State University
East Lansing, Michigan, USA, 2004-2006

- collected synchrotron data at:
National Synchrotron Light Source, X9B beamline
Brookhaven National Laboratory, Upton, New York, USA
Argonne National Laboratory, Advanced Photon Source
Argonne near Chicago, Illinois, USA

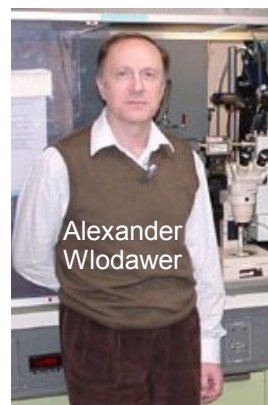
- and thanks to:
Alexander Wlodawer
*Director, Macromolecular Crystallography Laboratory,
NCI-Frederick, Maryland, USA*
Xinhua Ji
*My then supervisor, Section Chief, Macromolecular Crystallo-
graphy Laboratory, NCI-Frederick, Maryland, USA*
David Waugh
*Collaborator, Section Chief, Macromolecular Crystallography
Laboratory, NCI-Frederick, Maryland, USA*
Zbigniew (Zbyszek) Dauter
*Beamline X9B Director, National Synchrotron Light Source,
Brookhaven National Laboratory. Currently: Advanced Photon Source,
Argonne National Laboratory, Chicago-Argonne, Illinois, USA*
Krzysztof (Christopher) Michejda
*Collaborator, Section Chief († 2007), Structural Biophysics Laboratory,
NCI-Frederick, Maryland, USA*



NSLS



NSLS X9B



Alexander
Wlodawer



Xinhua
Ji



David Waugh



Krzysztof
Michejda



Zbigniew
Dauter

The aftermath of our RNase III structural work - - Selected reading (in chronological order)

- [22]. P.D. Zamore, *Mol. Cell* (2001), **8**, 1158-1160.
"Thirty-three years later, a glimpse at the ribonuclease III active site."
- [23]. P. Provost, D. Dishart, J. Doucet, D. Frendewey, B. Samuelsson, O. Radmark, *EMBO J.* (2002), **21**, 5864-5874.
"Ribonuclease activity and RNA binding of recombinant human Dicer."
- [24]. C. Arenz, U. Schepers, *Naturwissenschaften* (2003), **90**, 345-359. "RNA interference: from an ancient mechanism to a state of the art therapeutic application?"
- [25]. D. Drider, C. Condon, *J. Mol. Microbiol. Biotechnol.*, (2004), **8**, 195-200. "The continuing story of endoribonuclease III."
- [26]. B. Lamontagne, S. Abou Elela, *J. Biol. Chem.* (2004), **279**, 2231-2241. "Evaluation of the RNA determinants for bacterial and yeast RNase III binding and cleavage."
- [27]. M.A. Carmell, G.J. Hannon, *Nat. Struct. Mol. Biol.*, (2004), **11**, 214-218. "RNase III enzymes and the initiation of gene silencing."
- [28]. Y.S. Lee, K. Nakahara, J.W. Pham, K. Kim, Z.Y. He, E.J. Sontheimer, R.W. Carthew, *Cell* (2004), **117**, 69-81
"Distinct roles for *Drosophila* Dicer-1 and Dicer-2 in the siRNA/miRNA silencing pathways."
- [29]. B. Lamontagne, R.N. Hannoush, M.J. Damha, S. Abou Elela, *J. Mol. Biol.* (2004), **338**, 401-418. "Molecular requirements for duplex recognition and cleavage by eukaryotic RNase III: Discovery of an RNA-dependent DNA cleavage activity of yeast Rnt1p."
- [30]. H.D. Zhang, F.A. Kolb, L. Jaskiewicz, E. Westhof, W. Filipowicz, *Cell* (2004), **118**, 57-68. "Single processing center models for human dicer and bacterial RNase III."
- [31]. J.J. Han, Y. Lee, K.H. Yeom, Y.K. Kim, H. Jin, V.N. Kim, *Genes & Development* (2004), **18**, 3016-3027.
"The Drosha-DGCR8 complex in primary microRNA processing."
- [32]. W. Sun, A. Pertzev, A.W. Nicholson, *Nucl. Acids Res.* (2005), **33**, 807-815. "Catalytic mechanism of *Escherichia coli* ribonuclease III: kinetic and inhibitor evidence for the involvement of two magnesium ions in RNA phosphodiester hydrolysis."
- [33]. F.A. Kolb, H.D. Zhang, K. Jaronczyk, N. Tahbaz, T.C. Hobman, W. Filipowicz, *RNA Interference*. Book Series: Methods in Enzymology (2005), **392**, 316-399. "Human dicer: Purification, properties, and interaction with PAZ PIWI domain proteins."
- [34]. V.N. Kim, *Nat. Rev. Mol. Cell Biol.* (2005), **6**, 376-385.
"MicroRNA biogenesis: Coordinated cropping and dicing."
- [35]. J.F. Kreuzer, E.I. Savenkov, W. Cuellar, X.D. Li, J.P.T. Valkonen, *J. Virol.* (2005), **79**, 7227-7238. "Viral class 1 RNase III involved in suppression of RNA silencing."
- [36]. S.M. Hammond, *FEBS Lett.* (2005), **579**, 5822-5829. "Dicing and slicing - The core machinery of the RNA interference pathway."
- [37]. I.J. MacRae, K.H. Zhou, F. Li, A. Repic, A.N. Brooks, W.Z. Cande, P.D. Adams, J.A. Doudna, *Science* (2006), **311**, 195-198.
"Structural basis for double-stranded RNA processing by dicer."
- [38]. J.J. Han, Y. Lee, K.H. Yeom, J.W. Nam, I. Heo, J.K. Rhee, S.Y. Sohn, Y.J. Cho, B.T. Zhang, V.N. Kim, *Cell* (2006), **125**, 887-901. "Molecular basis for the recognition of primary microRNAs by the Drosha-DGCR8 complex."
- [39]. C. Gaudin, G. Ghazal, S. Yoshizawa, S. Abou Elela, D. Fourmy, *J. Mol. Biol.* (2006), **363**, 322-331. "Structure of an AAGU tetraloop and its contribution to substrate selection by yeast RNase III."
- [40]. K.P. Watkins, T.S. Kroeger, A.M. Cooke, R.E. Williams-Carrier, G. Friso, S.E. Belcher, K.J. Van Wijk, A. Bark, *Plant Cell* (2007), **19**, 2606-2623. "A ribonuclease III domain protein functions in group II intron splicing in maize chloroplasts."
- [41]. I.J. MacRae, J.A. Doudna, *Curr. Opin Struct. Biol.* (2007), **17**, 138-145. "Ribonuclease revisited: structural insights into ribonuclease III family enzymes."
- [42]. I.J. MacRae, K. Zhou, J.A. Doudna, *Nat. Struct. Mol. Biol.* (2007), **14**, 934-940. "Structural determinants of RNA recognition and cleavage by Dicer."
- [43]. A. Orlacchio, G. Bernardi, A. Orlacchi, S. Martin, *Mini-Reviews In Medicinal Chem.* (2007), **7**, 1166-1176. "RNA interference as a tool for Alzheimer's disease therapy."
- [44]. L. Jaskiewicz, W. Filipowicz, *RNA Interference*. Book Series: Current Topics In Microbiology and Immunology (2008), **320**, 77-97. "Role of Dicer in posttranscriptional RNA silencing."
- [45]. X. Ji, *RNA Interference*. Book Series: Current Topics In Microbiology and Immunology (2008), **320**, 99-116. "The mechanism of RNase III action: How Dicer dices."
- [46]. Z. Du, J.K. Lee, R. Tjhen, R.M. Strould, T.L. James, *Proc. Natl. Acad. Sci. USA* (2008), **105**, 2391-2396. "Structural and biochemical insights into the dicing mechanism of mouse Dicer: A conserved lysine is critical for dsRNA cleavage."
- [47]. P. Comella, F. Pontvianne, S. Lahmy, F. Vignols, N. Barbezier, A. DeBures, E. Jobet, E. Brugidou, M. Echeverria, J. Saez-Vasquez, *Nucleic Acids Res.* (2008), **36**, 1163-1175. "Characterization of a ribonuclease III-like protein required for cleavage of the pre-rRNA in the 3'ETS in *Arabidopsis*."
- [48]. M. Lavoie, S. Abou Elela, *Biochemistry* (2008), **47**, 8514-8526.
"Yeast ribonuclease III uses a network of multiple hydrogen bonds for RNA binding and cleavage."
- [49]. K. Zenke, K.H. Kim, *Archives of Virology* (2008), **153**, 1651-1656.
"Functional characterization of the RNase III gene of rock bream iridovirus."
- [50]. M. Jinek, A.J. Doudna, *Nature* (2009), **457**, 405-412. "A three-dimensional view of the molecular machinery of RNA interference."
- [51]. V.N. Kim, J. Han, M.C. Siomi, *Nat. Rev. Mol. Cell Biol.* (2009), **10**, 126-139. "Biogenesis of small RNAs in animals."
- [52]. J.P. Xiao, C.E. Feehery, G. Tzertzinis, C.V. Maina, *RNA - A Publication of the RNA Society* (2009), **15**, 984-991. "*E. coli* RNase III(E38A) generates discrete-sized products from long dsRNA."
- [53]. Q. Liu, Z. Paroo, Book Series: Annual Review of Biochemistry (2010), **79**, 295-319. (Kornberg RD, Raetz CRH, Rothman JE, eds). "Biochemical Principles of Small RNA Pathways."
- [54]. L. Nathania, A.W. Nicholson, *Biochemistry* (2010), **49**, 7164-7178.
"Thermotoga maritima Ribonuclease III. Characterization of Thermostable Biochemical Behavior and Analysis of Conserved Base Pairs That Function as Reactivity Epitopes for the Thermotoga 23S rRNA Precursor."
- [55]. C.M. Arraiano, J.M. Andrade, S. Domingues, I.B. Guinote, M. Malecki, R.G. Matos, R.N. Moreira, V. Pobre, F.P. Reis, M. Saramago, I.J. Silva, S.C. Viegas, *FEMS Microbiology Rev.* (2010), **34**, 883-923.
"The critical role of RNA processing and degradation in the control of gene expression."
- [56]. A.W. Nicholson, *Ribonucleases*. Book Series: Nucleic Acids and Molecular Biology (2011), **26**, 269-297. "Ribonuclease III and the Role of Double-Stranded RNA Processing in Bacterial Systems."
- [57]. Z.J. Shi, R.H. Nicholson, R. Jaggi, A.W. Nicholson, *Nucleic Acids Res.* (2011), **39**, 2756-2768. "Characterization of *Aquifex aeolicus* ribonuclease III and the reactivity epitopes of its pre-ribosomal RNA substrates."
- [58]. B.R. Madina, G. Kuppan, A.A. Vashisht, Y.H. Liang, K.M. Downey, J.A. Wohlschlegel, X. Ji, et al., *RNA - A Publication of the RNA Society* (2011), **17**, 1821-1830. "Guide RNA biogenesis involves a novel RNase III family endoribonuclease in *Trypanosoma brucei*."
- [59]. D.E. Weinberg, K. Nakanishi, D.J. Patel, D.P. Bartel, *Cell* (2011), **146**, 262-276. "The Inside-Out Mechanism of Dicers from Budding Yeasts."
- [60]. M. Doyle, L. Jaskiewicz, W. Filipowicz, in *Enzymes* (Guo F, Tamano F, eds), Eukaryotic RNases and Their Partners in RNA Degradation and Biogenesis, pt B. (2012), **32**, 1-35. "Dicer Proteins and Their Role in Gene Silencing Pathways."
- [61]. K. Okamoto, Y. Murawaki, *Curr Pharmaceut. Biotechnol.* (2012), **13**, 2235-2247. "The Therapeutic Potential of RNA Interference: Novel Approaches for Cancer Treatment."
- [62]. D.A. Bernstein, K.V. Vyas, G.R. Fink, *RNA Biology* (2012), **9**, 1123-1128. "Genes come and go The evolutionarily plastic path of budding yeast RNase III enzymes."
- [63]. N. Haddad, M. Saramago, R.G. Matos, H. Prevost, C.M. Arraiano, *Bioscience Reports* (2013), **33**, 889-901. "Characterization of the biochemical properties of *Campylobacter jejuni* RNase III"
- [64]. J.M. Lee, Y. Kojin, T. Tatsuke, H. Mon, Y. Miyagawa, T. Kusakabe, *Insect Sci* (2013), **20**, 69-77. "Coexpression of *Escherichia coli* RNase III in silkworm cells improves the efficiency of RNA interference induced by long hairpin dsRNAs."
- [65]. C.M. Arraiano, F. Mauxion, S.C. Viegas, R.G. Matos, B. Seraphin, *Biochim Biophys Acta* (2013), **1829**, 491-513.
"Intracellular ribonucleases involved in transcript processing and decay: Precision tools for RNA."
- [66]. L. Yuan, H.Y. Chu, M.L. Wang, X.J. Gu, D. Shi, L. Ma, D.Y. Zhong, M.L. Du, P. Li, N. Tong, G.B. Fu, C. Qin, C.J. Yin, Z.D. Zhang, *PLoS One* (2013), **8**, e81524. "Genetic Variation in DROSHA 3'UTR Regulated by hsa-miR-27b Is Associated with Bladder Cancer Risk."
- [67]. A.W. Nicholson, *Wiley Interdisciplinary Reviews-RNA* (2014), **5**, 31-48. "Ribonuclease III mechanisms of double-stranded RNA cleavage."
- [68]. I. Weinheimer, K. Boonrod, M. Moser, M. Wassenegger, G. Krczal, S.J. Butcher, J.P.T. Valkonen, *J. Gen. Virol.* (2014), **95**, 486-495.
"Binding and processing of small dsRNA molecules by the class 1 RNase III protein encoded by sweet potato chlorotic stunt virus."
- [69]. N. Sabbaghian, A. Srivastava, N. Hamel, F. Plourde, M. Gajtko-Metera, M. Niedziela, W.D. Foulkes, *Eur J. Human Genet.* (2014), **22**, 564-567. "Germ-line deletion in DICER1 revealed by a novel MLPA assay using synthetic oligonucleotides."
- [70]. Z.Q. Gao, M. Wang, D. Blair, Y.D. Zheng, Y.X. Dou, *PLoS One* (2014), **9**, e95350. "Phylogenetic Analysis of the Endoribonuclease Dicer Family."
- [71]. G. Torrezan, E. Ferreira, A. Nakahata, B. Barros, M. Castro, B. Correa, A. Krepisch, E. Olivieri, I. Cunha, U. Tabori, P. Grundy, C. Costa, B. de Camargo, P. Galante, D. Carraro, *Nat. Commun.* (2014), **5**:4039.
"Recurrent somatic mutation in DROSHA induces microRNA profile changes in Wilms tumour."
- [72]. M. Ha, V.N. Kim, *Nat. Rev. Mol. Cell Biol.* (2014), **15**, 509-524.
"Regulation of microRNA biogenesis."
- [73]. D. Rakheja, K.S. Chen, Y.J. Liu, A.A. Shukla, V. Schmid, T.C. Chang, S. Khokhar, J.E. Wickiser, N.J. Karandikar, J.S. Malter, J.T. Mendell, J.F. Amatruda, *Nat. Commun.* (2014), **5**:4802. "Somatic mutations in Drosha and Dicer1 impair microRNA biogenesis through distinct mechanisms in Wilms tumours."
- [74]. J.M. Pompey, B. Foda, U. Singh, *PLoS One* (2015), **10**, e0133740.
"A Single RNaseIII Domain Protein from *Entamoeba histolytica* Has dsRNA Cleavage Activity and Can Help Mediate RNAi Gene Silencing in a Heterologous System."
- [75]. B. Lim, M. Sim, H. Lee, S. Hyun, Y. Lee, Y. Hahn, E. Shin, K. Lee, *J. Microbiol.* (2015), **53**, 487-494. "Regulation of *Escherichia coli* RNase III activity."