

**Robustness and Fragility**  
**- Gene regulation based on N:N reaction system -**

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I will talk about my scientific research experiences for the last 30 years. The content of my talk is as follows. The main topics are “How I could carry out the world-leading science on different topics” and “How I could survive in the non-creative science world”.

I. Across the science universe

Research life at The University of Tokyo

Research life at The Rockefeller University, U.S.A.

The study of eukaryotic transcription focused on “RNA polymerase II and S-II” at The University of Tokyo and “the action of TFIID and general transcription factors” at The Rockefeller University

II. The long and winding science road

Research life as an independent researcher at The University of Tokyo - I

Histone, nucleosome and chromatin studies mainly focused on “Isolation of chromatin-related components”, “Histone modification to nucleosome structural change”, “Formation of heterochromatin and euchromatin” and “Nucleosome-mediated gene regulation”

III. Let it be or not

Research life as an independent researcher at The University of Tokyo - II

The study on the complex network system of “histone modification network structure” and “modification web theory and signal router theory”

IV. Get back science

Research life as an independent researcher at The University of Tokyo - III

The study to solve “the remaining problems in my research life”

The studies on “intrinsically disordered region, structural change and N:N reaction system” and mechanistic evolution

**Major publications:** (Horikoshi published 164 papers including major papers described below in eukaryotic gene regulation.)  
(Papers in **red** are Horikoshi's favorites and in **blue** the next favorites.)

### Structure-function relationship of eukaryotic transcription factor S-II (TFIIS)

[J.Biol.Chem., 259, 608-611 \(1984\)](#), [J.Biol.Chem., 260, 5739-5744 \(1985\)](#)

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### Mechanism of transcriptional activation

[Cell, 54, 665-669 \(1988\)](#), [Cell, 54, 1033-1042 \(1988\)](#), [Cell, 54, 1043-1051 \(1988\)](#), [Proc.Natl.Acad.Sci.U.S.A., 87, 2289-2293 \(1990\)](#), [Proc.Natl.Acad.Sci.U.S.A., 87, 9153-9157 \(1990\)](#), [Cell, 61, 475-484 \(1990\)](#), [Nature, 348, 86-88 \(1990\)](#), [Genes Dev., 4, 1899-1909 \(1990\)](#), [Science, 251, 1476-1479 \(1991\)](#), [Cell, 69, 401-412 \(1992\)](#), [J.Biol.Chem., 268, 17554-17558 \(1993\)](#), [Nature, 369, 252-255 \(1994\)](#)

### Isolation and characterization of TATA box-binding protein

[J.Biol.Chem., 263, 12596-12601 \(1988\)](#), [Mol.Cell.Biol., 8, 4028-4040 \(1988\)](#), [Proc.Natl.Acad.Sci.U.S.A., 86, 4843-4847 \(1989\)](#), [Nature, 341, 299-303 \(1989\)](#), [Cell, 61, 1171-1178 \(1990\)](#), [Genes Dev., 4, 1141-1148 \(1990\)](#), [Nature, 346, 387-390 \(1990\)](#), [Nature, 346, 390-394 \(1990\)](#), [Proc.Natl.Acad.Sci.U.S.A., 87, 9148-9152 \(1990\)](#), [Mol.Cell.Biol., 11, 4809-4821 \(1991\)](#), [Cell, 67, 1241-1250 \(1991\)](#), [Proc.Natl.Acad.Sci.U.S.A., 89, 1060-1064 \(1992\)](#), [Proc.Natl.Acad.Sci.U.S.A., 89, 2844-2848 \(1992\)](#), [Nature, 360, 40-46 \(1992\)](#), [J.Biol.Chem., 268, 5005-5013 \(1993\)](#)

### Isolation and characterization of general transcription initiation factors

[J.Biol.Chem., 262, 3322-3330 \(1987\)](#), [Proc.Natl.Acad.Sci.U.S.A., 87, 9158-9162 \(1990\)](#), [Proc.Natl.Acad.Sci.U.S.A., 87, 9163-9167 \(1990\)](#), [Proc.Natl.Acad.Sci.U.S.A., 88, 9553-9557 \(1991\)](#), [Nature, 354, 398-401 \(1991\)](#), [Nature, 354, 401-404 \(1991\)](#), [Mol.Cell.Biol., 12, 5189-5196 \(1992\)](#), [Proc.Natl.Acad.Sci.U.S.A., 89, 2839-2843 \(1992\)](#), [Nature, 363, 744-747 \(1993\)](#), [Science, 261, 463-466 \(1993\)](#), [Mol.Cell.Biol., 15, 4856-4866 \(1995\)](#)

### Isolation and characterization of TFIID complex

[Proc.Natl.Acad.Sci.U.S.A., 89, 11809-11813 \(1992\)](#), [Nature, 362, 179-181 \(1993\)](#), [Genes Dev., 7, 1033-1046 \(1993\)](#), [Proc.Natl.Acad.Sci.U.S.A., 90, 5896-5900 \(1993\)](#), [J.Biol.Chem., 268, 17554-17558 \(1993\)](#), [Mol.Cell.Biol., 13, 7859-7863 \(1993\)](#), [Nature, 367, 484-487 \(1994\)](#), [Proc.Natl.Acad.Sci.U.S.A., 91, 3520-3524 \(1994\)](#), [Proc.Natl.Acad.Sci.U.S.A., 92, 8195-8199 \(1995\)](#), [Proc.Natl.Acad.Sci.U.S.A., 94, 85-90 \(1997\)](#), [J.Biol.Chem., 272, 6714-6721 \(1997\)](#), [Genes Cells, 3, 347-355 \(1998\)](#)

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### Isolation and characterization of histone acetyltransferase Tip60

[J.Biol.Chem., 272, 30595-30598 \(1997\)](#), [FEBS Lett., 431, 131-133 \(1998\)](#), [Genes Cells, 3, 789-800 \(1998\)](#), [Cell, 102, 463-473 \(2000\)](#), [J.Biol.Chem., 277, 35688-35695 \(2002\)](#), [J.Mol.Biol., 365, 1047-1062 \(2007\)](#), [J.Biol.Chem., 282, 4193-4201 \(2007\)](#), [J.Mol.Biol., 378, 987-1001 \(2008\)](#)

### Isolation and characterization of histone chaperone CIA (Asf1)

[Genes Cells, 5, 221-233 \(2000\)](#), [Genes Cells, 6, 1043-1054 \(2001\)](#), [Genes Cells, 7, 59-73 \(2002\)](#), [Proc.Natl.Acad.Sci.U.S.A., 99, 9334-9339 \(2002\)](#), [J.Biol.Chem., 278, 35660-35667 \(2003\)](#), [Genes Cells, 16, 1050-1062 \(2011\)](#)

### Discovery of histone chaperone activities in a variety of proteins

[Genes Cells, 5, 251-263 \(2000\)](#), [J.Biol.Chem., 278, 28758-28764 \(2003\)](#), [Mol.Cell.Biol., 23, 8528-8541 \(2003\)](#), [Nature Struct.Mol.Biol., 11, 275-283 \(2004\)](#), [Nature Struct.Mol.Biol., 13, 331-338 \(2006\)](#), [Proc.Natl.Acad.Sci.U.S.A., 104, 4285-4290 \(2007\)](#), [Mol.Cell.Biol., 28, 1171-1181 \(2008\)](#), [Cell.Mol.Life Sci., 65, 414-444 \(2008\)](#), [Genes Cells, 15, 945-958 \(2010\)](#), [J.Biol.Chem., 286, 30504-30512 \(2011\)](#)

### Action of chromatin-related components

[Genes Cells, 5, 29-42 \(2000\)](#), [J.Biol.Chem., 280, 12123-12129 \(2005\)](#), [J.Biol.Chem., 282, 9895-9901 \(2007\)](#), [Genes Cells, 15, 945-958 \(2010\)](#)

### Structural analysis of various factors

[J.Biol.Chem., 279, 1546-1552 \(2004\)](#), [J.Biol.Chem., 279, 9615-9624 \(2004\)](#), [J.Biochem., 138, 821-829 \(2005\)](#), [J.Biol.Chem., 282, 4193-4201 \(2007\)](#), [Structure, 15, 179-189 \(2007\)](#), [Biochem. Biophys. Res. Commun., 359, 503-509 \(2007\)](#), [Genes Cells, 13, 1127-1140 \(2008\)](#)

### Construction of histone GLibrary and its application

[Genes Cells, 12, 13-33 \(2007\)](#), [Genes Cells, 14, 1271-1330 \(2009\)](#), [Genes Cells, 16, 590-607 \(2011\)](#), [EMBO J., 30, 3353-3367 \(2011\)](#), [Genes Cells, 17, 65-81 \(2012\)](#)

### Mechanism of nucleosome structural change through histone modifications

[Nature, 446, 338-341 \(2007\)](#), [Proc.Natl.Acad.Sci.U.S.A., 107, 8153-8158 \(2010\)](#)

### Mechanism of formation of the border between euchromatin and heterochromatin

[Nature Genet., 32, 370-377 \(2002\)](#), [Genes Cells, 9, 499-508 \(2004\)](#)

### Theoretical framework of the histone modification network

[Genes Cells, 14, 789-806 \(2009\)](#), [Genes Cells, 15, 553-594 \(2010\)](#), [Curr. Pharm. Design, 19, 5019-5042 \(2013\)](#)

### Roles of common subunits of distinct multisubunit complexes

[Proc.Natl.Acad.Sci.U.S.A., 111, 699-704 \(2014\)](#)