



[Outline](#) [Download](#) [Export](#) ▾

Developmental Biology

Volume 249, Issue 1, 1 September 2002, Pages 156-173

Regular Article

Multiple Cdk1 Inhibitory Kinases Regulate the Cell Cycle during Development

Walter F. Leise III^a ... Paul R. Mueller^{b1}

[Show more](#)

<https://doi.org/10.1006/dbio.2002.0743>

[Get rights and content](#)

Under an Elsevier user license

[open archive](#)

Abstract

The Wee kinases block entry into mitosis by phosphorylating and inhibiting the activity of the mitotic cyclin-dependent kinase, Cdk1. We have found that the various *Xenopus* Wee kinases have unique temporal and spatial patterns of expression during development. In addition, we have isolated and characterized a new Wee1-like kinase, *Xenopus* Wee2. By both *in vivo* and *in vitro* tests, *Xenopus* Wee2 functions as a Wee1-like kinase. The previously isolated Wee1-like kinase, *Xenopus* Wee1, is expressed only as maternal gene product. In contrast, *Xenopus* Wee2 is predominantly a zygotic gene product, while the third Wee kinase, *Xenopus* Myt1, is both a maternal and zygotic gene product. Concurrent with the changing levels of these Cdk inhibitory kinases, the pattern of embryonic cell division becomes asynchronous and spatially restricted in the *Xenopus* embryo. Interestingly, once zygotic transcription begins, *Xenopus* Wee2 is expressed in regions of the embryo that are devoid of mitotic cells, such as the involuting mesoderm. In contrast, *Xenopus* Myt1 is expressed in regions of the embryo that have high levels of proliferation, such as the developing neural tissues. The existence of multiple Wee kinases may help explain how distinct patterns of cell division arise and are regulated during development.

Keywords

Wee1; Myt1; Wee2; Cdc2; gastrulation; cell cycle; *Xenopus*; cell division; morphogenesis; embryogenesis

[Recommended articles](#) [Citing articles \(29\)](#)

References

REFERENCES

- 1 R. Aligue, L. Wu, P. Russell
Regulation of *Schizosaccharomyces pombe* Wee1 tyrosine kinase
J. Biol. Chem., 272 (1997), pp. 13320-13325
- 2 E. Apolinario, M. Nocero, M. Jin, C.S. Hoffman
Cloning and manipulation of the *Schizosaccharomyces pombe* his7+ gene as a new selectable marker for molecular genetic studies
Curr. Genet., 24 (1993), pp. 491-495
- 3 Y. Audic, B. Boyle, M. Slevin, R.S. Hartley

Feedback

Cyclin E morpholino delays embryogenesis in Xenopus

Genesis, 30 (2001), pp. 107-109

- 4 R.N. Booher, R.J. Deshaies, M.W. Kirschner
Properties of *Saccharomyces cerevisiae wee1* and its differential regulation of p34CDC28 in response to G1 and G2 cyclins
EMBO J., 12 (1993), pp. 3417-3426
- 5 R.N. Booher, P.S. Holman, A. Fattaey
Human Myt1 is a cell cycle-regulated kinase that inhibits Cdc2 but not Cdk2 activity
J. Biol. Chem., 272 (1997), pp. 22300-22306
- 6 S. Bryant, D.L. Manning
Formaldehyde gel electrophoresis of total RNA
Methods Mol. Biol., 86 (1998), pp. 69-72
- 7 S.D. Campbell, F. Sprenger, B.A. Edgar, P.H. O'Farrell
Drosophila Wee1 kinase rescues fission yeast from mitotic catastrophe and phosphorylates Drosophila Cdc2 in vitro
Mol. Biol. Cell, 6 (1995), pp. 1333-1347
- 8 P.B. Carpenter, P.R. Mueller, W.G. Dunphy
Role for a Xenopus Orc2-related protein in controlling DNA replication
Nature, 379 (1996), pp. 357-360
- 9 A. Charlesworth, J. Welk, A.M. MacNicol
The temporal control of Wee1 mRNA translation during Xenopus oocyte maturation is regulated by cytoplasmic polyadenylation elements within the 3'-untranslated region
Dev. Biol., 227 (2000), pp. 706-719
Article  PDF (319KB)
- 10 T.R. Coleman, Z. Tang, W.G. Dunphy
Negative regulation of the Wee1 protein kinase by direct action of the Nim1/Cdr1 mitotic inducer
Cell, 72 (1993), pp. 919-929
Article  PDF (1MB)
- 11 F. Corpet
Multiple sequence alignment with hierarchical clustering
Nucleic Acids Res., 16 (1988), pp. 10881-10890
- 12 B.A. Edgar, P.H. O'Farrell
Genetic control of cell division patterns in the Drosophila embryo
Cell, 57 (1989), pp. 177-187
Article  PDF (7MB)
- 13 F. Fagotto, K. Guger, B.M. Gumbiner
Induction of the primary dorsalizing center in Xenopus by the Wnt/GSK/beta-catenin signaling pathway, but not by Vg1, Activin or Noggin
Development, 124 (1997), pp. 453-460
- 14 F. Fagotto, B.M. Gumbiner
Beta-catenin localization during Xenopus embryogenesis: Accumulation at tissue and somite boundaries
Development, 120 (1994), pp. 3667-3679
- 15 V.E. Foe
Mitotic domains reveal early commitment of cells in Drosophila embryos
Development, 107 (1989), pp. 1-22
- 16 S.L. Forsburg
Comparison of *Schizosaccharomyces pombe* expression systems
Nucleic Acids Res., 21 (1993), pp. 2955-2956
- 17 D.L. Frederick, M.T. Andrews
Cell cycle remodeling requires cell-cell interactions in developing Xenopus embryos
J. Exp. Zool., 270 (1994), pp. 410-416

- 18 W.V. Gerber, T.A. Yatskiewych, P.B. Antin, K.M. Correia, R.A. Conlon, P.A. Krieg
The RNA-binding protein gene, hermes, is expressed at high levels in the developing heart
Mech. Dev., 80 (1999), pp. 77-86
Article  PDF (2MB)
- 19 K.L. Gould, P. Nurse
Tyrosine phosphorylation of the fission yeast cdc2+ protein kinase regulates entry into mitosis
Nature, 342 (1989), pp. 39-45
- 20 B. Grallert, P. Nurse, T.E. Patterson
A study of integrative transformation in *Schizosaccharomyces pombe*
Mol. Gen. Genet., 238 (1993), pp. 26-32
- 21 C. Grimm, J. Kohli, J. Murray, K. Maundrell
Genetic engineering of *Schizosaccharomyces pombe*: A system for gene disruption and replacement using the ura4 gene as a selectable marker
Mol. Gen. Genet., 215 (1988), pp. 81-86
- 22 J. Grosshans, E. Wieschaus
A genetic link between morphogenesis and cell division during formation of the ventral furrow in *Drosophila*
Cell, 101 (2000), pp. 523-531
- 23 Z. Hardcastle, N. Papalopulu
Distinct effects of XBF-1 in regulating the cell cycle inhibitor p27 (XIC1) and imparting a neural fate
Development, 127 (2000), pp. 1303-1314
- 24 R.S. Hartley, R.E. Rempel, J.L. Maller
In vivo regulation of the early embryonic cell cycle in *Xenopus*
Dev. Biol., 173 (1996), pp. 408-419
Article  PDF (228KB)
- 25 R.S. Hartley, J.C. Sible, A.L. Lewellyn, J.L. Maller
A role for cyclin E/Cdk2 in the timing of the midblastula transition in *Xenopus* embryos
Dev. Biol., 188 (1997), pp. 312-321
Article  PDF (3MB)
- 26 R. Higuchi, B. Krummel, R.K. Saiki
A general method of in vitro preparation and specific mutagenesis of DNA fragments: Study of protein and DNA interactions
Nucleic Acids Res., 16 (1988), pp. 7351-7367
- 27 M.T. Hood, C.S. Stachow
Electroporation of *Schizosaccharomyces pombe*
Methods Mol. Biol., 47 (1995), pp. 273-278
- 28 J.A. Howe, M. Howell, T. Hunt, J.W. Newport
Identification of a developmental timer regulating the stability of embryonic cyclin A and a new somatic A-type cyclin at gastrulation
Genes Dev., 9 (1995), pp. 1164-1176
- 29 J.A. Howe, J.W. Newport
A developmental timer regulates degradation of cyclin E1 at the midblastula transition during *Xenopus* embryogenesis
Proc. Natl. Acad. Sci. USA, 93 (1996), pp. 2060-2064
- 30 M. Igarashi, A. Nagata, S. Jinno, K. Suto, H. Okayama
Wee1(+)-like gene in human cells
Nature, 353 (1991), pp. 80-83
- 31 M. Iwabuchi, K. Ohsumi, T.M. Yamamoto, W. Sawada, T. Kishimoto
Residual Cdc2 activity remaining at meiosis 1 exit is essential for meiotic M-M transition in *Xenopus* oocyte extracts
EMBO J., 19 (2000), pp. 4513-4523
- 32 L.A. Johnston
The trouble with tribbles

- 33 S.H. Kim, C. Li, J.L. Maller
A maternal form of the phosphatase Cdc25A regulates early embryonic cell cycles in *Xenopus laevis*
Dev. Biol., 212 (1999), pp. 381-391
Article  PDF (326KB)
- 34 C.R. Kintner, D.A. Melton
Expression of Xenopus N-CAM RNA in ectoderm is an early response to neural induction
Development, 99 (1987), pp. 311-325
- 35 A. Kumagai, W.G. Dunphy
Regulation of the cdc25 protein during the cell cycle in Xenopus extracts
Cell, 70 (1992), pp. 139-151
Article  PDF (2MB)
- 36 A. Kumagai, W.G. Dunphy
Control of the Cdc2/cyclin B complex in Xenopus egg extracts arrested at a G2/M checkpoint with DNA synthesis inhibitors
Mol. Biol. Cell, 6 (1995), pp. 199-213
- 37 D.J. Lew, S. Kornbluth
Regulatory roles of cyclin dependent kinase phosphorylation in cell cycle control
Curr. Opin. Cell Biol., 8 (1996), pp. 795-804
Article  PDF (955KB)
- 38 F. Liu, J.J. Stanton, Z. Wu, H. Piwnica-Worms
The human Myt1 kinase preferentially phosphorylates Cdc2 on threonine 14 and localizes to the endoplasmic reticulum and Golgi complex
Mol. Cell. Biol., 17 (1997), pp. 571-583
- 39 K. Lundgren, N. Walworth, R. Booher, M. Dembski, M. Kirschner, D. Beach
mik1 and wee1 cooperate in the inhibitory tyrosine phosphorylation of cdc2
Cell, 64 (1991), pp. 1111-1122
Article  PDF (3MB)
- 40 M.C. MacNicol, D. Pot, A.M. MacNicol
pXen, a utility vector for the expression of GST-fusion proteins in *Xenopus laevis* oocytes and embryos
Gene, 196 (1997), pp. 25-29
Article  PDF (296KB)
- 41 Y. Masui, P. Wang
Cell cycle transition in early embryonic development of *Xenopus laevis*
Biol. Cell, 90 (1998), pp. 537-548
Article  PDF (2MB)
- 42 J. Mata, S. Curado, A. Ephrussi, P. Rorth
Tribbles coordinates mitosis and morphogenesis in Drosophila by regulating string/CDC25 proteolysis
Cell, 101 (2000), pp. 511-522
Article  PDF (570KB)
- 43 K. Maundrell
Thiamine-repressible expression vectors pREP and pRIP for fission yeast
Gene, 123 (1993), pp. 127-130
Article  PDF (361KB)
- 44 S. Moreno, A. Klar, P. Nurse
Molecular genetic analysis of fission yeast *Schizosaccharomyces pombe*
Methods Enzymol., 194 (1991), pp. 795-823
Article  PDF (1MB)
- 45 D.O. Morgan
Cyclin-dependent kinases: Engines, clocks, and microprocessors

- 46 P.R. Mueller, T.R. Coleman, W.G. Dunphy
Cell cycle regulation of a *Xenopus* Wee1-like kinase
Mol. Biol. Cell, 6 (1995), pp. 119-134
- 47 P.R. Mueller, T.R. Coleman, A. Kumagai, W.G. Dunphy
Myt1: A membrane-associated inhibitory kinase that phosphorylates Cdc2 on both threonine-14 and tyrosine-15
Science, 270 (1995), pp. 86-90
- 48 P.R. Mueller, S.J. Salser, B. Wold
Constitutive and metal-inducible protein: DNA interactions at the mouse metallothionein I promoter examined by in vivo and in vitro footprinting
Genes Dev., 2 (1988), pp. 412-427
- 49 M.S. Murakami, T.D. Copeland, G.F. Vande Woude
Mos positively regulates Xe-Wee1 to lengthen the first mitotic cell cycle of *Xenopus*
Genes Dev., 13 (1999), pp. 620-631
- 50 M.S. Murakami, G.F. Vande Woude
Analysis of the early embryonic cell cycles of *Xenopus*: Regulation of cell cycle length by Xe-wee1 and Mos
Development, 125 (1998), pp. 237-248
- 51 N. Nakajo, S. Yoshitome, J. Iwashita, M. Iida, K. Uto, S. Ueno, K. Okamoto, N. Sagata
Absence of Wee1 ensures the meiotic cell cycle in *Xenopus* oocytes
Genes Dev., 14 (2000), pp. 328-338
- 52 M. Nakanishi, H. Ando, N. Watanabe, K. Kitamura, K. Ito, H. Okayama, T. Miyamoto, T. Agui, M. Sasaki
Identification and characterization of human Wee1B, a new member of the Wee1 family of Cdk-inhibitory kinases
Genes Cells, 5 (2000), pp. 839-847
- 53 M. Nemer, E.W. Stuebing
WEE1-like CDK tyrosine kinase mRNA level is regulated temporally and spatially in sea urchin embryos
Mech. Dev., 58 (1996), pp. 75-88
Article  PDF (3MB)
- 54 J. Newport, M. Dasso
On the coupling between DNA replication and mitosis
J. Cell Sci. Suppl., 12 (1989), pp. 149-160
- 55 J. Newport, M. Kirschner
A major developmental transition in early *Xenopus* embryos. I. Characterization and timing of cellular changes at the midblastula stage
Cell, 30 (1982), pp. 675-686
Article  PDF (6MB)
- 56 J. Newport, M. Kirschner
A major developmental transition in early *Xenopus* embryos. II. Control of the onset of transcription
Cell, 30 (1982), pp. 687-696
Article  PDF (2MB)
- 57 P.D. Nieuwkoop, J. Faber
Normal Table of *Xenopus laevis* (Daudin): A Systematical and Chronological Survey of the Development from the Fertilized Egg till the End of Metamorphosis, Garland Publishing, New York (1994)
- 58 S. Ohnuma, A. Philpott, K. Wang, C.E. Holt, W.A. Harris
p27Xic1, a Cdk inhibitor, promotes the determination of glial cells in *Xenopus* retina
Cell, 99 (1999), pp. 499-510
Article  PDF (624KB)
- 59 A. Palmer, A.R. Nebreda
The activation of MAP kinase and p34cdc2/cyclin B during the meiotic maturation of *Xenopus* oocytes
Prog. Cell Cycle Res., 4 (2000), pp. 131-143

- 60 K.D. Patterson, P.A. Krieg
Hox11-family genes XHox11 and XHox11L2 in xenopus: XHox11L2 expression is restricted to a subset of the primary sensory neurons
Dev. Dyn., 214 (1999), pp. 34-43
- 61 M. Pudney, M.G. Varma, C.J. Leake
Establishment of a cell line (XTC-2) from the South African clawed toad, *Xenopus laevis*
Experientia, 29 (1973), pp. 466-467
- 62 P. Russell, P. Nurse
Negative regulation of mitosis by wee1+, a gene encoding a protein kinase homolog
Cell, 49 (1987), pp. 559-567
Article  PDF (1MB)
- 63 Y. Saka, J.C. Smith
Spatial and temporal patterns of cell division during early Xenopus embryogenesis
Dev. Biol., 229 (2001), pp. 307-318
Article  PDF (2MB)
- 64 J. Sambrook, D.W. Russell
Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor (2001)
- 65 Y. Sasai, B. Lu, H. Steinbeisser, D. Geissert, L.K. Gont, E.M. De Robertis
Xenopus chordin: A novel dorsalizing factor activated by organizer-specific homeobox genes
Cell, 79 (1994), pp. 779-790
Article  PDF (18MB)
- 66 T.C. Seher, M. Leptin
Tribbles, a cell-cycle brake that coordinates proliferation and morphogenesis during Drosophila gastrulation
Curr. Biol., 10 (2000), pp. 623-629
Article  PDF (569KB)
- 67 H.L. Sive, R.M. Grainger, R.M. Harland
Early Development of *Xenopus laevis*: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor (2000)
- 68 J.H. Stack, J.W. Newport
Developmentally regulated activation of apoptosis early in Xenopus gastrulation results in cyclin A degradation during interphase of the cell cycle
Development, 124 (1997), pp. 3185-3195
- 69 D.L. Turner, H. Weintraub
Expression of achaete-scute homolog 3 in *Xenopus* embryos converts ectodermal cells to a neural fate
Genes Dev., 8 (1994), pp. 1434-1447
- 70 S.A. Walter, S.N. Guadagno, J.E. Ferrell Jr.
Activation of Wee1 by p42 MAPK in vitro and in cycling xenopus egg extracts
Mol. Biol. Cell, 11 (2000), pp. 887-896
- 71 N. Watanabe, M. Broome, T. Hunter
Regulation of the human WEE1Hu CDK tyrosine 15-kinase during the cell cycle
EMBO J., 14 (1995), pp. 1878-1891

¹ To whom correspondence should be addressed. Fax: (773) 702-4394. E-mail: pmueller@midway.uchicago.edu.



[About ScienceDirect](#) [Remote access](#) [Shopping cart](#) [Contact and support](#) [Terms and conditions](#) [Privacy policy](#)

Cookies are used by this site. For more information, visit the [cookies page](#).

Copyright © 2017 Elsevier B.V. or its licensors or contributors. ScienceDirect ® is a registered trademark of Elsevier B.V.

