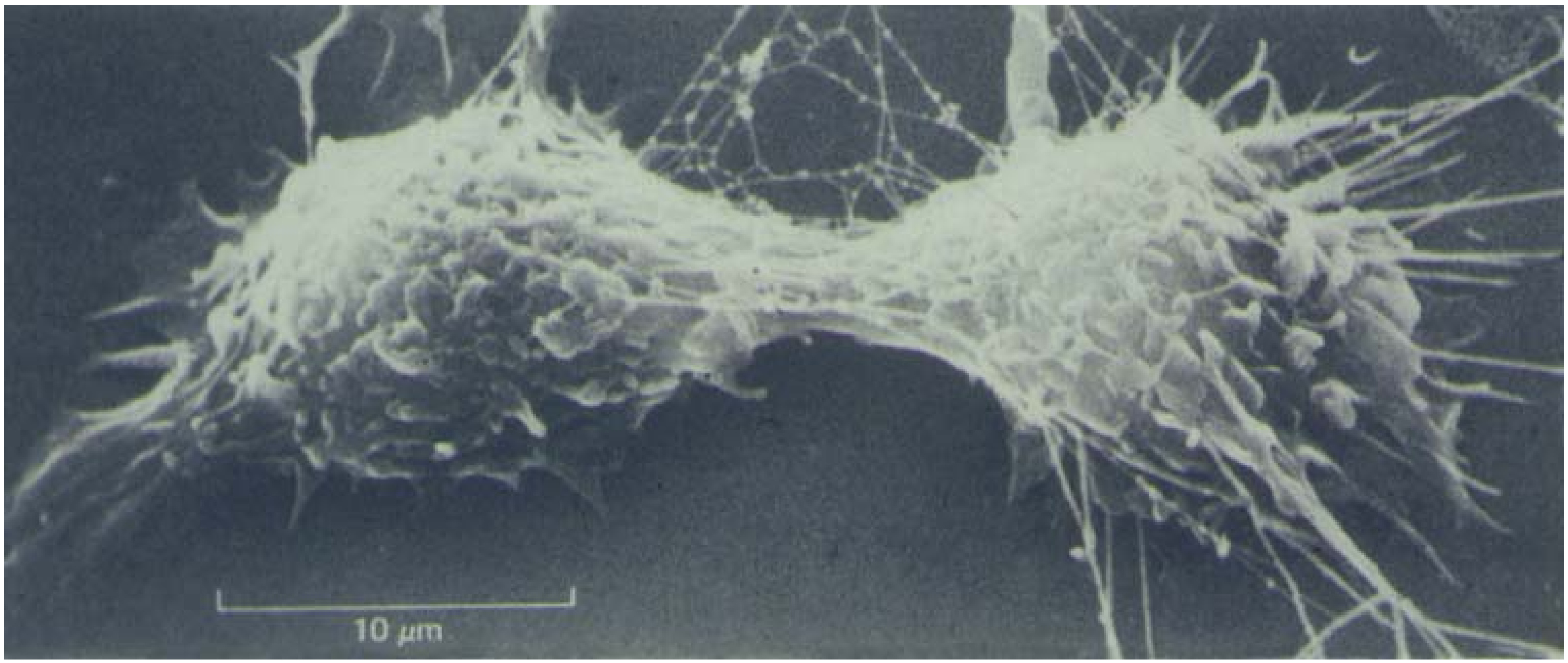
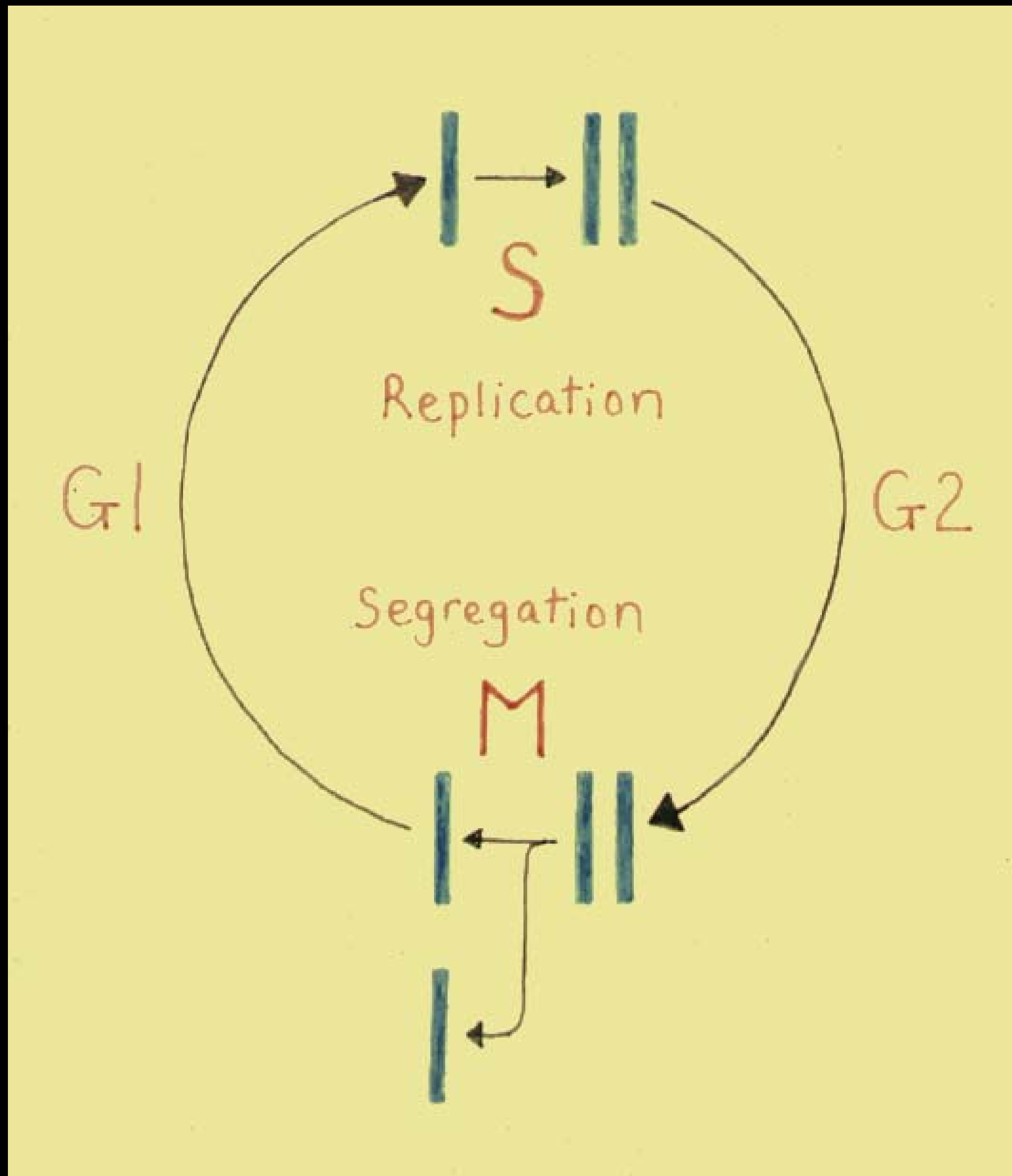
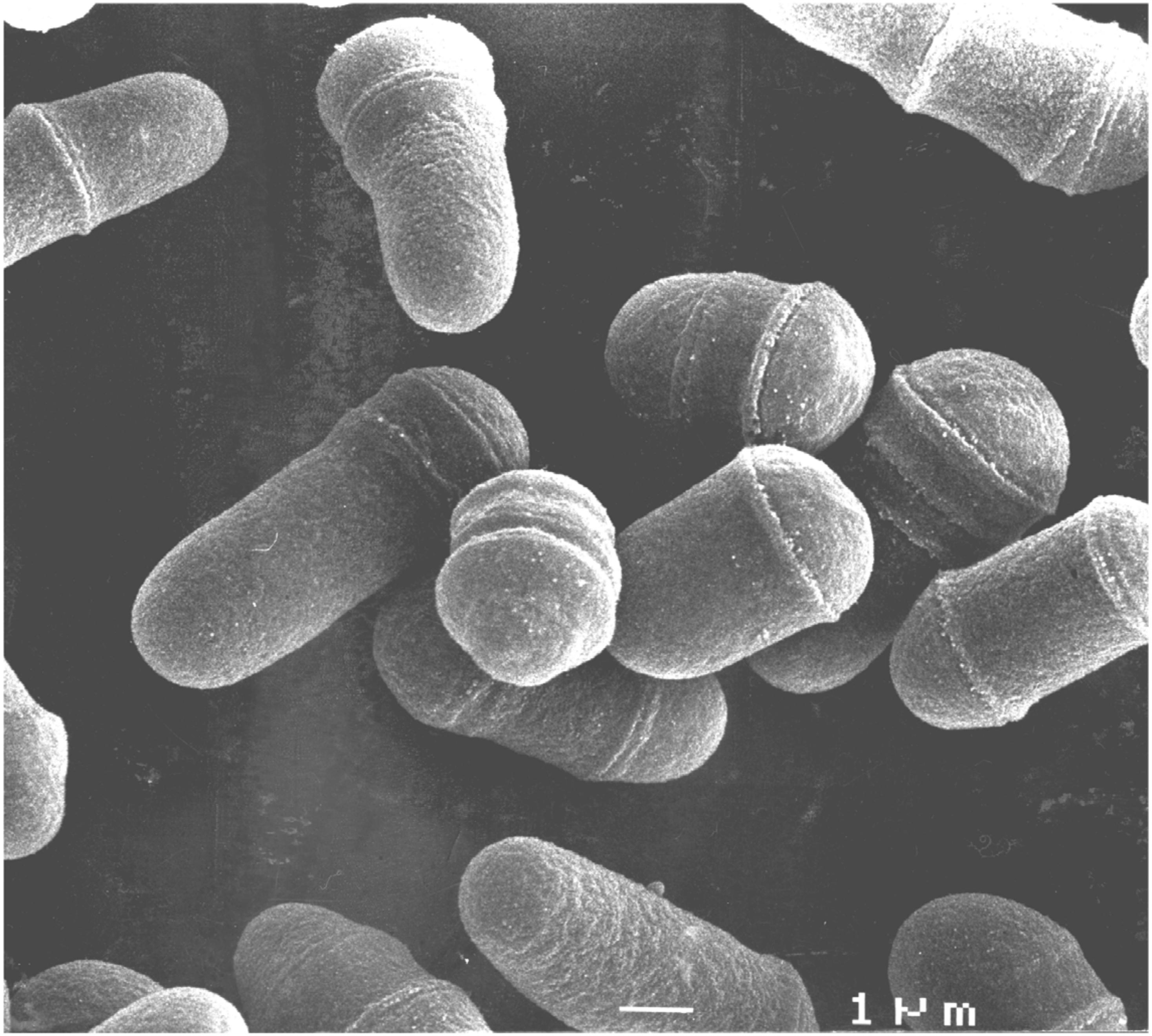

10 μm


S
Replication
G1
G2
Segregation
M


1 μm

Classical genetic analysis of the cell cycle in fission yeast
Identification of the CDK cdc2
Edinburgh, Zoology 1973-1980

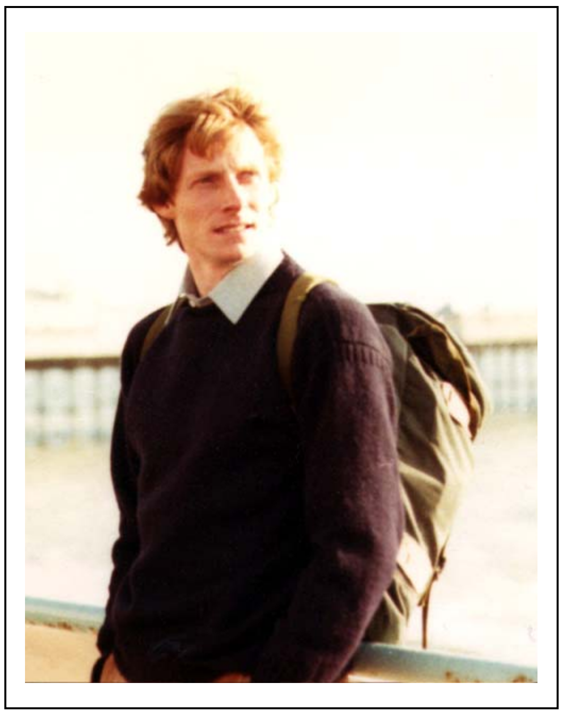
Murdoch Mitchison

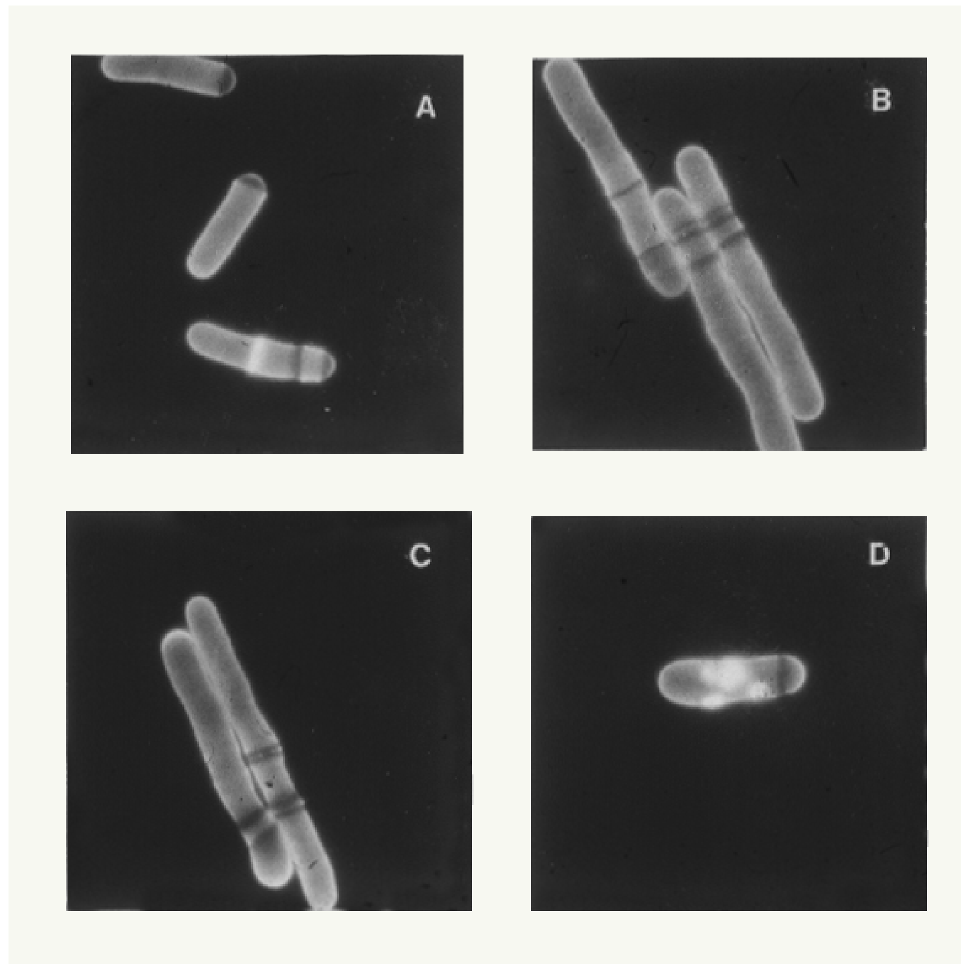
Urs Leupold

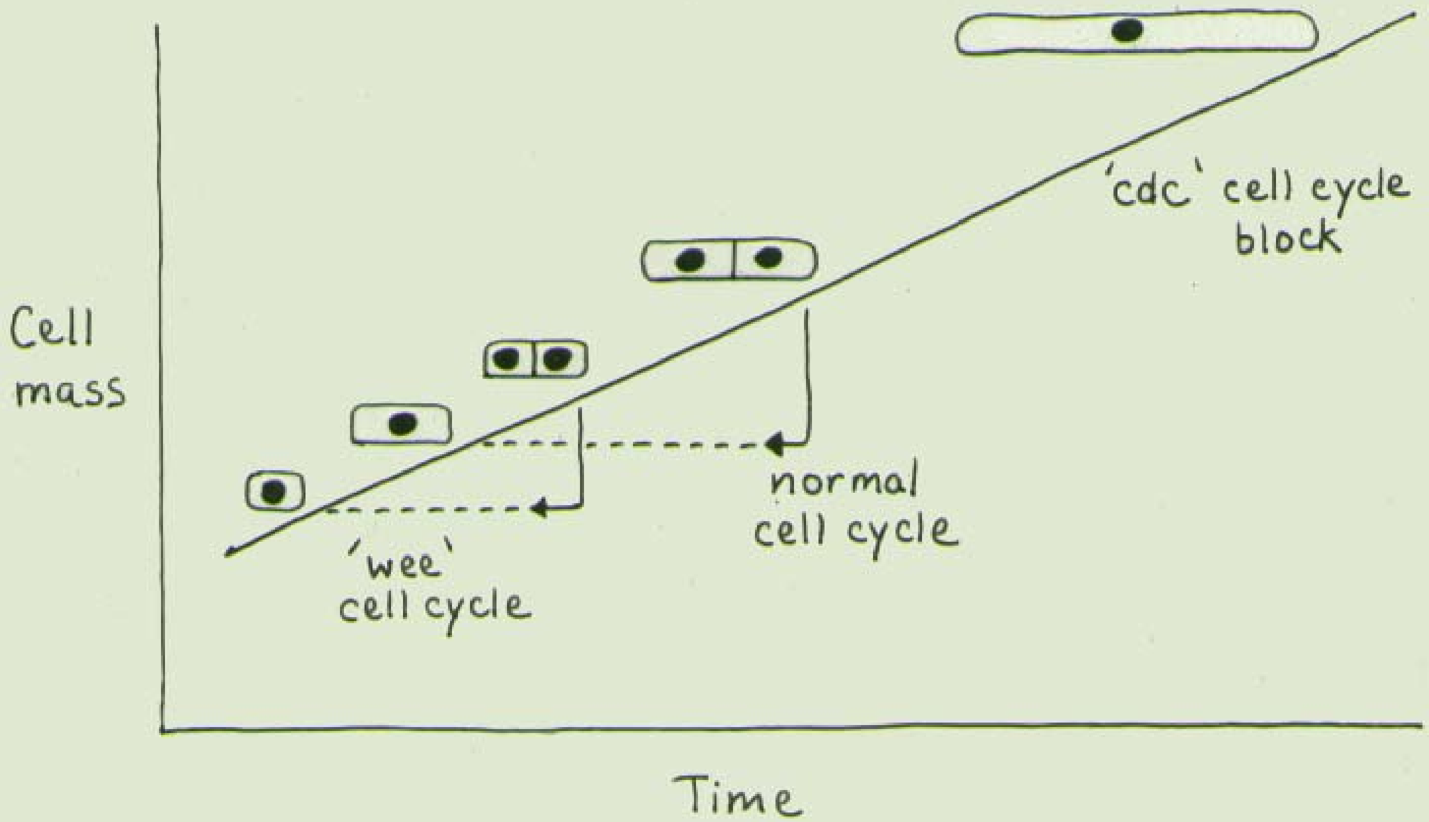
Molec. gen. Genet. 146, 167-178, March 18, 1976

Genetic Control of the Cell Division Cycle In the Fission Yeast *Schizosaccharomyces pombe*

Paul Nurse, Pierre Thuriaux and Kim Nasmyth
Department of Zoology, West Mains Road, Edinburgh EH9 3JT, UK.
Institut für Allgemeine Mikrobiologie, Universität Bern, Altenbergrain 21, CH 3013 Bern, Switzerland





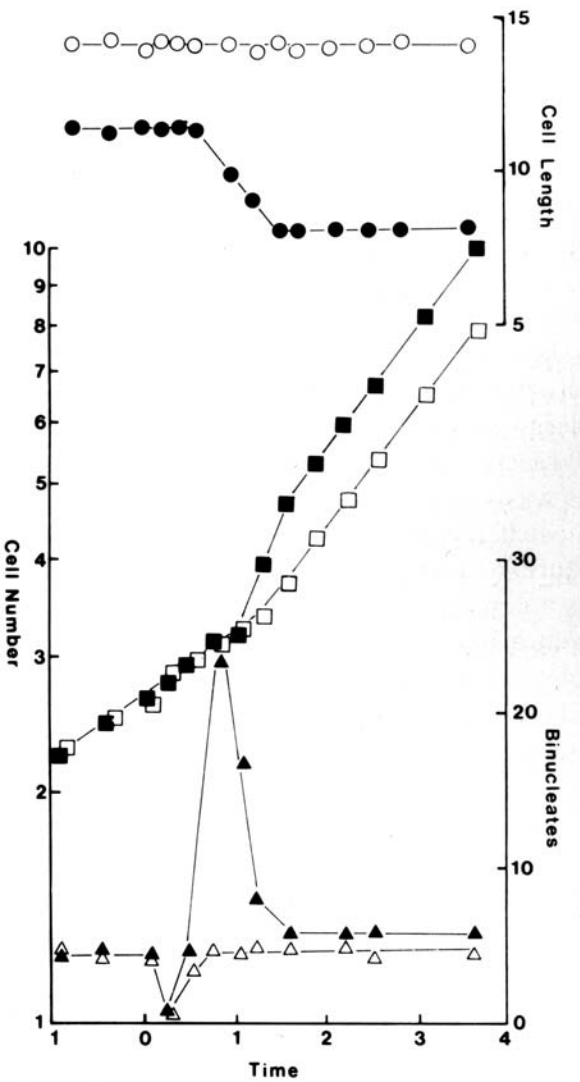


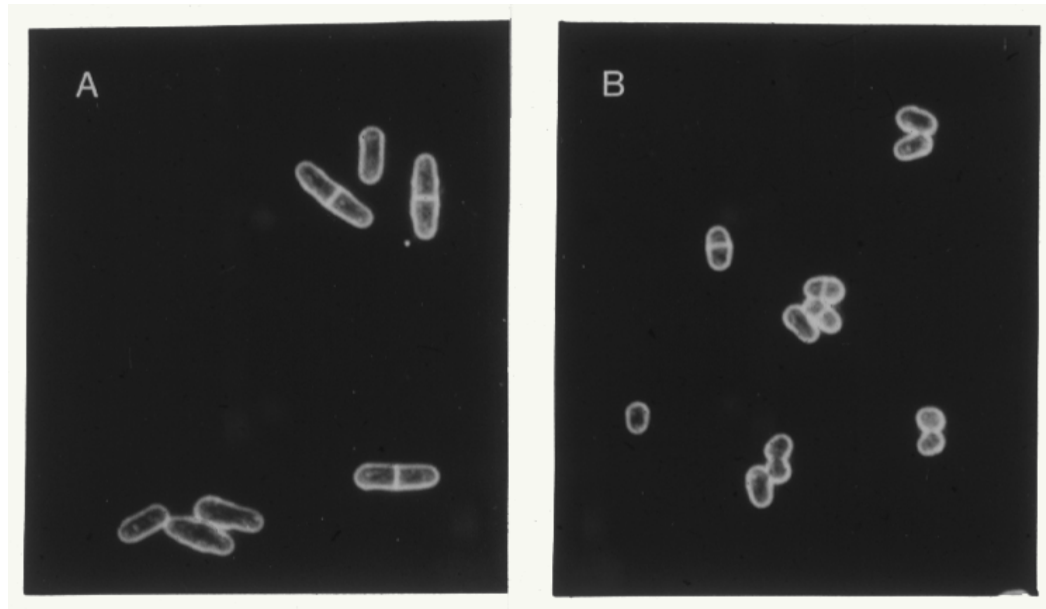
'wee' advanced through cell cycle
'cdc' delayed through cell cycle

Nature, Vol, 256, No. 5518, pp. 547-551, August 14, 1975

Genetic control of cell size at cell division in yeast

Paul Nurse
Department of Zoology, West Mains Road, Edinburgh EH9 3JT, UK





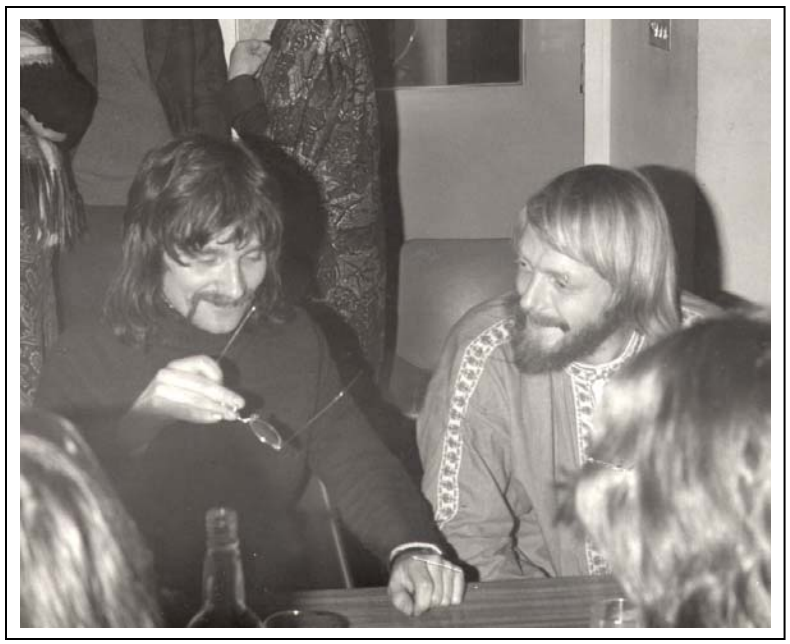
Peter Fantes

Genetics 96: 627-637, November, 1980

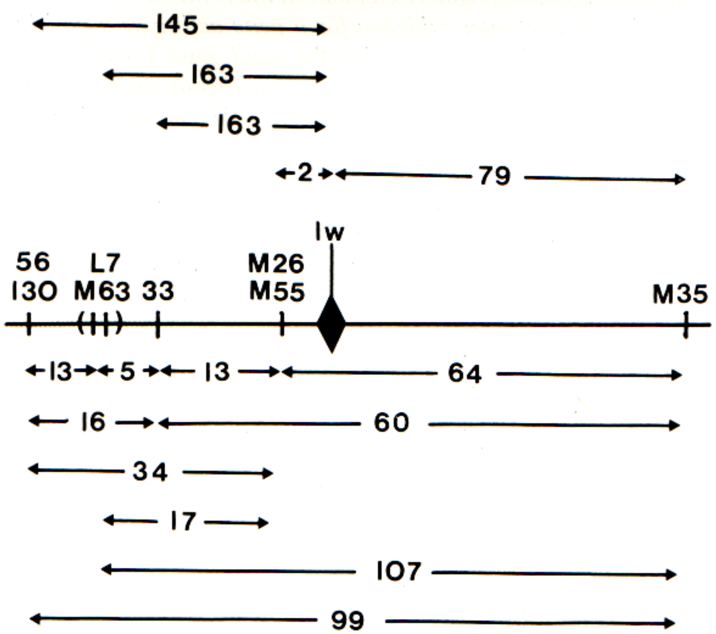
Regulatory genes controlling mitosis in the Fission Yeast *Schizosaccharomyces pombe*

Paul Nurse and Pierre Thuriaux

Strain	Cell length at septation μm	% *
wee1^{+} *sup3–5 ade6–704*	14.7	100
wee1–112 sup3^{+} *ade6–704*	7.5	51
wee1–112 sup3–5 ade6–704	13.1	89
wee1^{+} *sup*$^{+}$ *ade6–704*	15.0	102



Genetics 96: 627-637, November, 1980



cdc2⁻ allele tested	Cell length at septation in haploid strain grown at 25° µm	% *	Cell length at septation in heterozygous *cdc2⁺/cdc2⁻* diploid strain grown at 35° µm	% †
cde2–L7	14.6	112	26.8	112
cdc2–M26	13.8	106	26.3	110
cdc2–33	14.2	109	26.5	111
cdc2–M35	22.4	172	26.6	111
cdc2–M55	13.6	105	26.1	109
cdc2–56	10.2	79	25.5	107
cdc2M63	16.7	128	25.4	106
cdc2–M72	13.4	103	25.8	108
cdc2–M76	13.6	105	26.3	110
cdc2–130	10.0	77	25.4	106

Dominance relations of cdc2 *alleles when the mutant allele is active*

Strain	Temperature of growth	Cell length at septation µm	% *	Mean protein content per cell pg/cell	% *
cdc2+/cdc2+	35°	23.9	100	22.6	100
cdc2+/cdc2–1w	35°	15.6	65	15.8	70
cdc2–1w/cdc2–1w	35°	13.4	56	12.8	57
cdc2+/cdc2+	25°	20.3	100	—	—
cdc2+/cdc2–56	25°	16.6	82	—	—
cdc2+/cdc2–130	25°	16.9	83	—	—
cdc2–56/cdc2–56	25°	15.2	75	—	—
cdc2–130/cdc2–130	25°	15.8	78	—	—

Nature, Vol, 292, No. 5823, pp. 558-560, August 6, 1981

Gene required in G_1 for commitment to cell cycle and in G_2 for control of mitosis in fission yeast

Paul Nurse & Yvonne Bissett

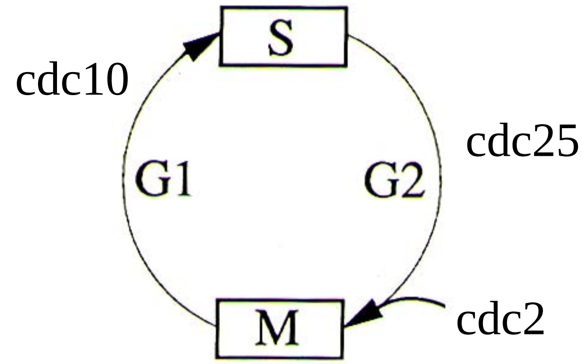
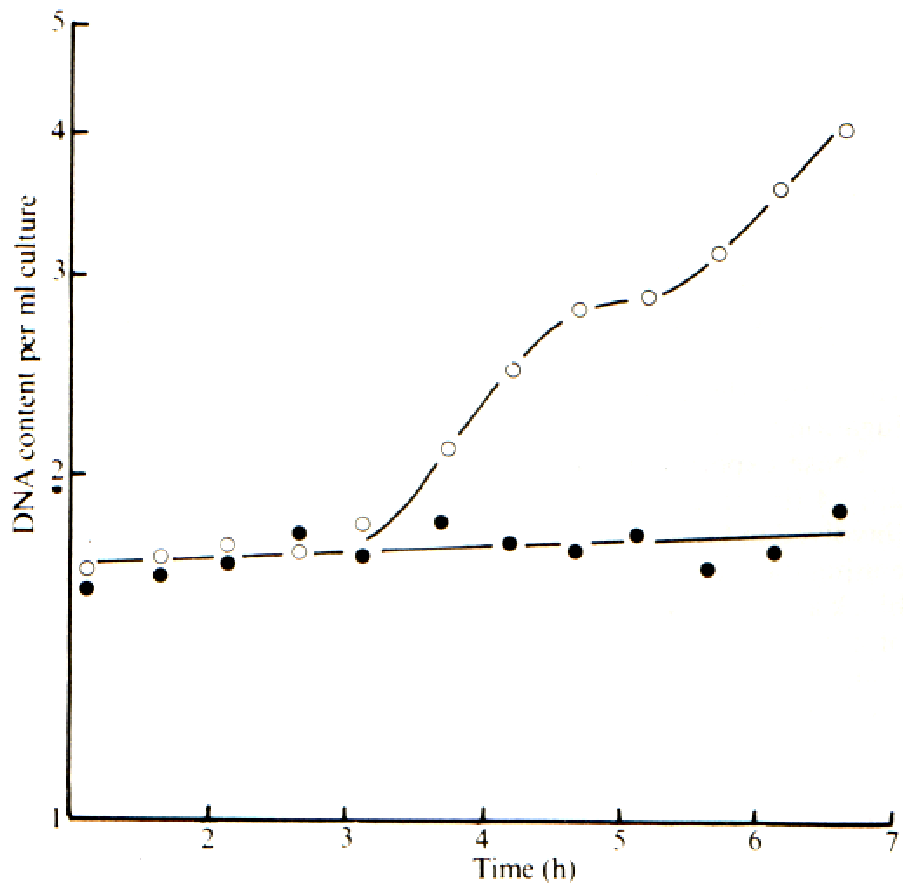
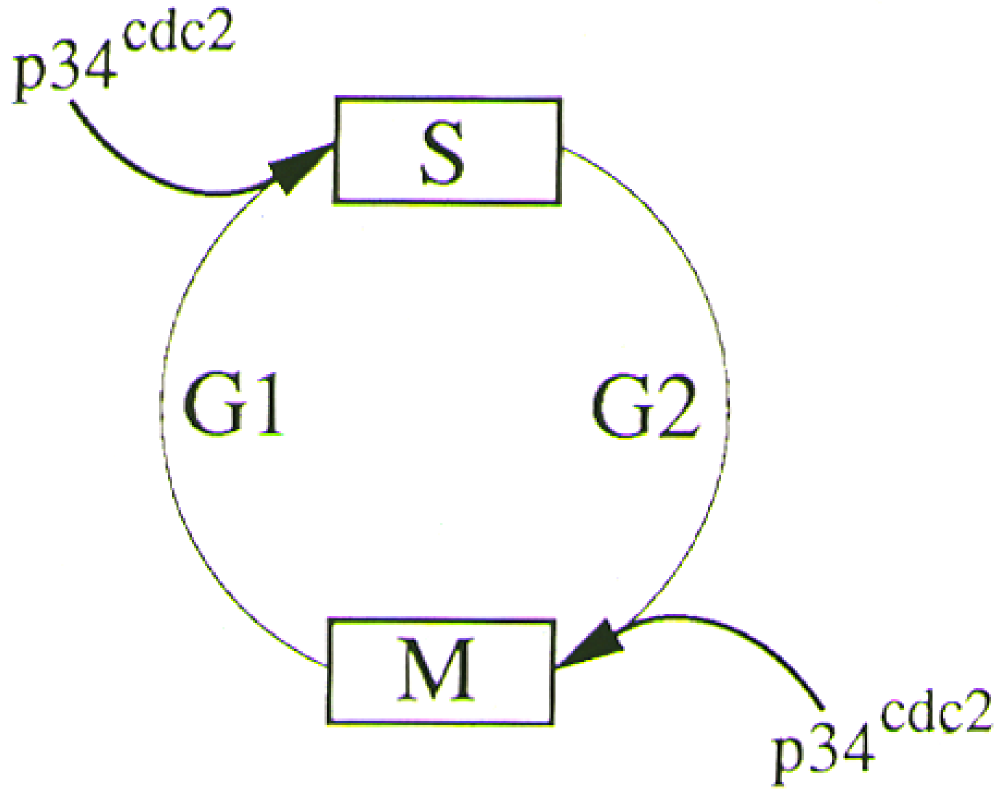


Table 1 % Conjugation for each temperature regime

cdc mutant	36/33 °C	25/25 °C	25/33 °C	% Viability	Can cells conjugate at this block?
cdc 1.7	0.046	76.2	10.4	47.6	No
cdc 2.33	30.9	106	105	97.1	Yes
cdc 2.M63	19.0	112	129	32.7	
cdc 6.23	3.09	52.6	37.4	20.8	No
cdc 10.129	138	94.6	88.2	78.1	Yes
cdc 10.K28	108	101	117	56.4	
cdc 13.117	0.205	60.3	33.5	59.4	No
cdc 17.K42	0.295	29.0	31.9	58.7	No
cdc 22.M45	4.44	51.2	42.8	87.3	No
cdc 23.M36	2.93	72.0	51.0	65.8	No
cdc 24.M38	2.83	80.3	119	19.2	No
cdc 25.22	0.086	36.7	14.0	57.6	No
cdc 27.K8	4.98	93.9	78.6	56.9	No





p34cdc2
S
G1
G2
M
p34cdc2

Molecular characterisation of the CDK cdc2 protein kinase

Sussex, Biology	1980-1984
ICRF, LIF London	1984-1988
Oxford, Biochemistry	1988-1993

David Beach
Barbara Durkacz
Kathy Gould
Jacky Hayles
Sergio Moreno
Paul Russell
Viesturs Simanis

Nature, Vol, 290, No. 5802, pp. 140-142, March 12, 1981

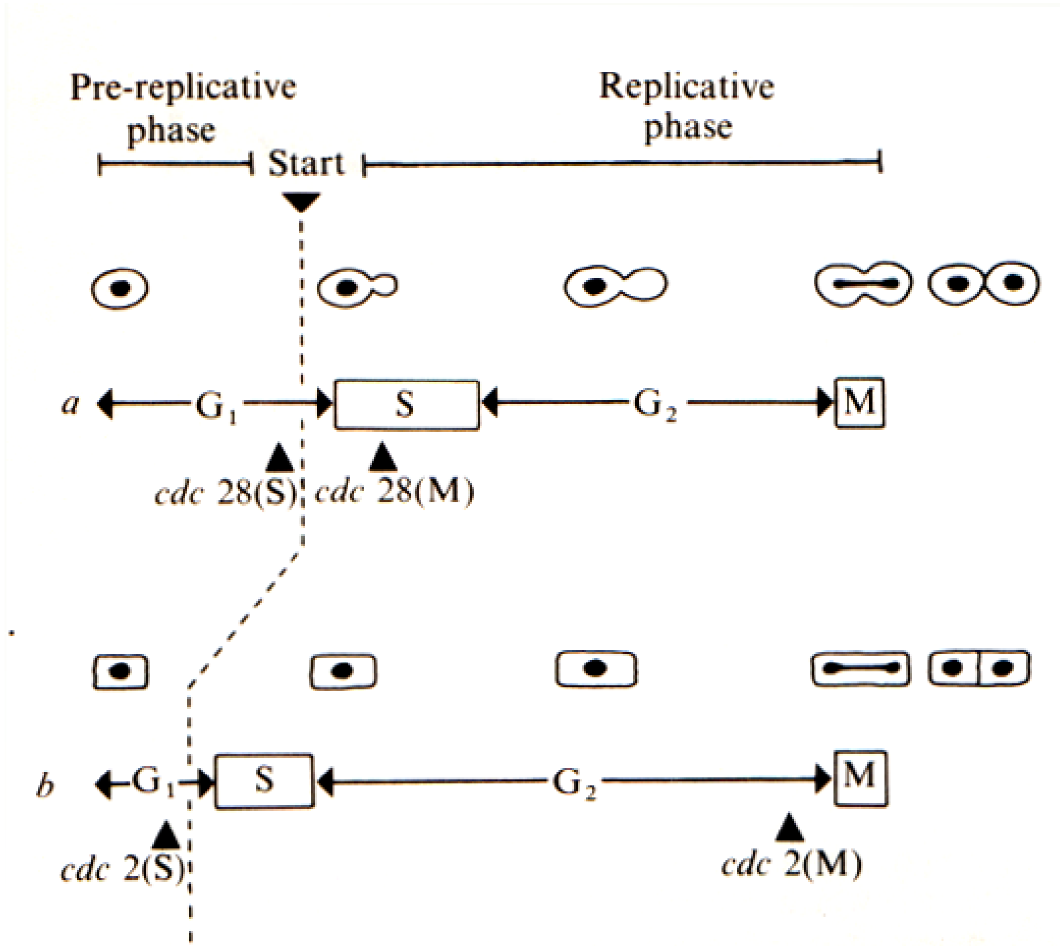
High-frequency transformation of the fission yeast *Schizosaccharomyces pombe*

David Beach & Paul Nurse

Nature, Vol, 300, No. 5894, pp. 706-709, December 22/30, 1982

Functionally homologous cell cycle Control genes in budding and fission yeast

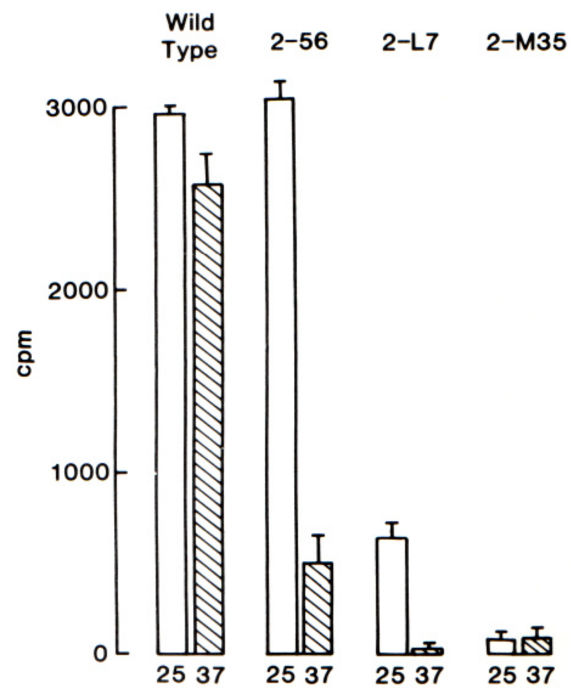
David Beach, Barbara Durkacz & Paul Nurse



Cell, Vol. 45: 261-268, April 25, 1986

The Cell Cycle Control Gene *cdc2*$^{+}$ of Fission Yeast Encodes a Protein Kinase Potentially Regulated by Phosphorylation

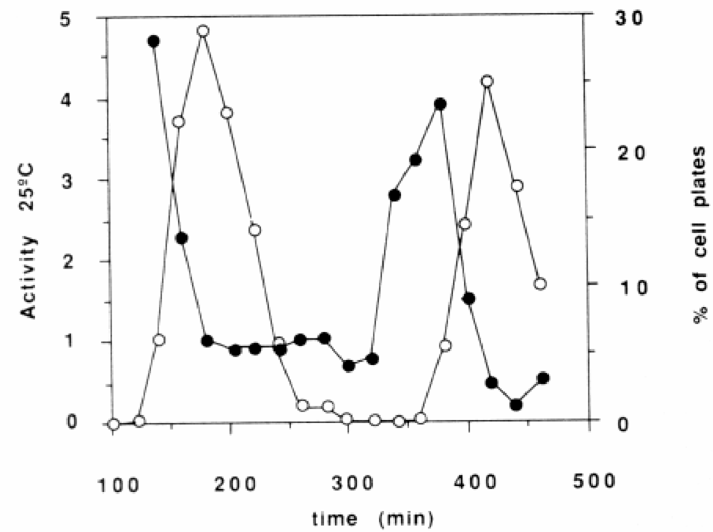
Viesturs Simanis and Paul Nurse
Cell Cycle Control Laboratory
Imperial Cancer Research Fund, P. O. Box 123
Lincoln's Inn Fields
London WC2A 3PX England



Cell, Vol. 58: 361-372, July 28, 1989

Regulation of p34^{cdc2} Protein Kinase during Mitosis

Sergio Moreno, Jacqueline Hayles, and Paul Nurse
ICRF Cell Cycle Control Group
Microbiology Unit, Department of Biochemistry
University of Oxford
Oxford OX1 3QU
England

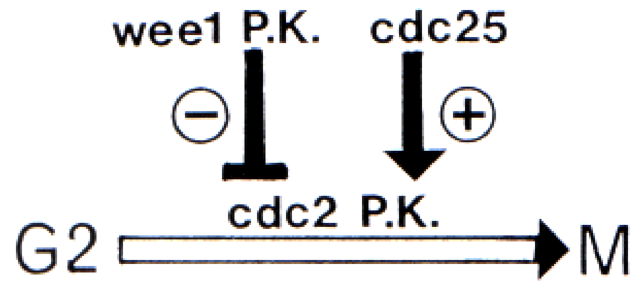


Sergio Moreno

Cell, Vol. 45: 145-153, April 11, 1986

cdc25+ Functions as an Inducer in the Mitotic Control of Fission Yeast

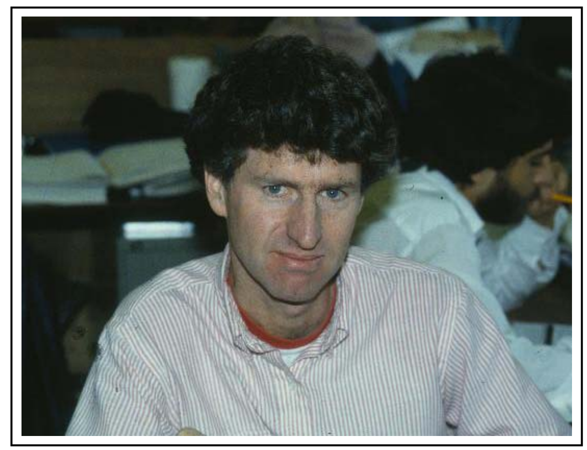
Paul Russell and Paul Nurse
Cell Cycle Control Laboratory
Imperial Cancer Research Fund
Lincoln's Inn Fields
London, WC2A 3PX, England



Cell, Vol. 49: 559-567, May 22, 1987

Negative Regulation of Mitosis by *wee1*+, a Gene Encoding a Protein Kinase Homolog

Paul Russell and Paul Nurse
Cell Cycle Control Laboratory
Imperial Cancer Research Fund
Lincoln's Inn Fields
London WC2A 3PX, England



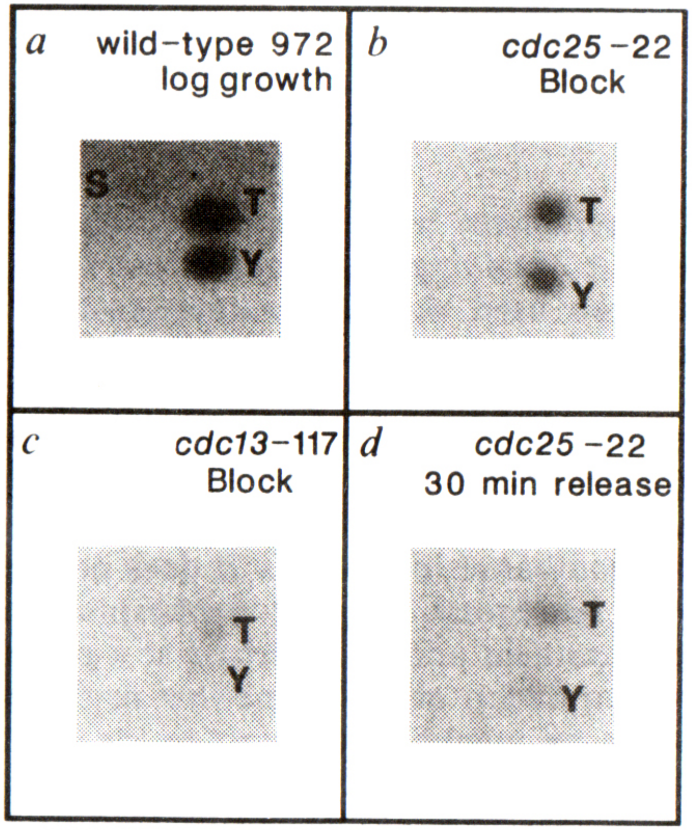
Paul Russell

Nature, Vol, 342, No. 6245, pp. 39-45, November 2, 1989

Tyrosine phosphorylation of the fission yeast *cdc2*[+] protein kinase regulates entry into mitosis

Kathleen L. Gould[*] & Paul Nurse

ICRF Cell Cycle Group, Microbiology Unit, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, UK



Kathy Gould

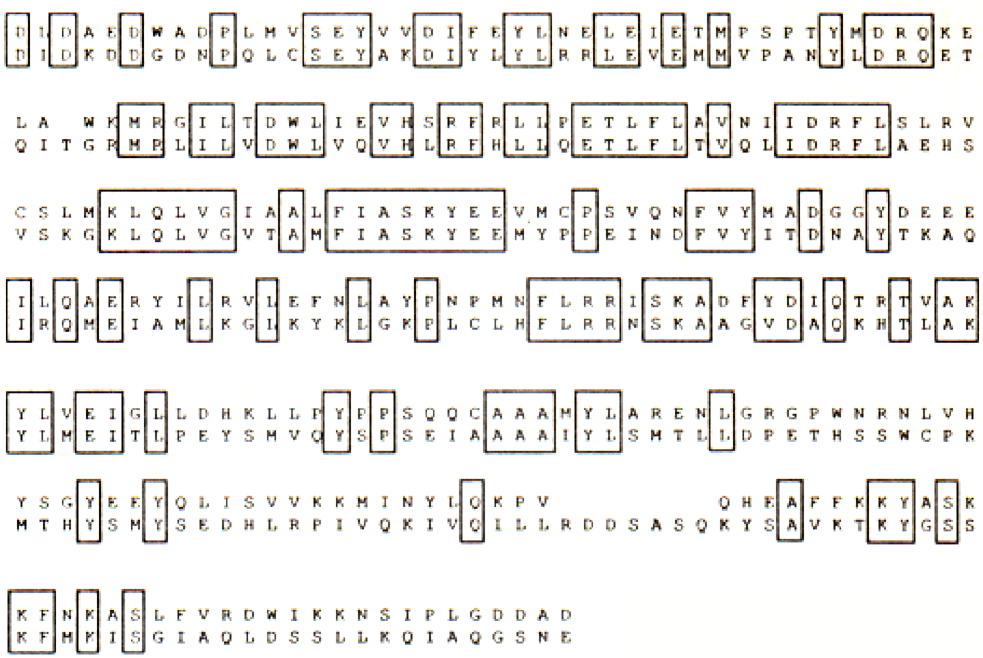
Journal of Cell Science, Vol, 91, 587-595, August 23, 1988

Cloning and sequencing of the cyclin-related *cdc13*$^{+}$ gene and a cytological study of its role in fission yeast mitosis

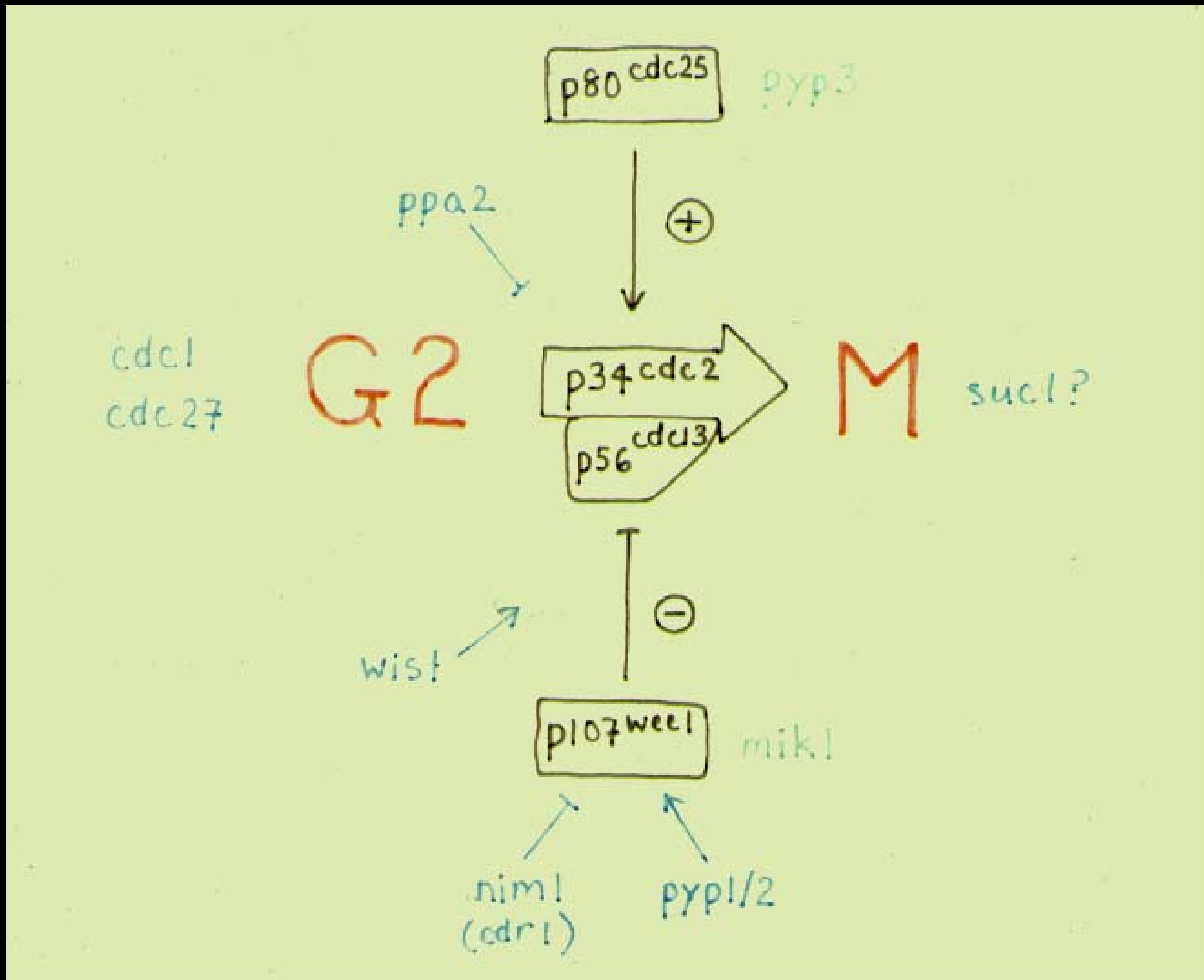
IAIN HAGAN, JACQUELINE HAYLES* and PAUL NURSE

ICRF Cell Cycle Control Laboratory, Microbiology Unit, Department of Biochemistry, University of Oxford, South Parks Road, Oxford, OX1 3QU

* Author for correspondence



Iain Hagan



p80 cdc25
pyp3
ppa2
+
cdc1
cdc27
G2
p34 cdc2
p56 cdc13
M
suc1?
−
wis1
p107 wee1
mik1
nim1
(cdr1)
pyp1/2

Cdc2 conserved in humans, starfish and frogs

ICRF, LIF London	1984-1988
Oxford, Biochemistry	1988-1993

Marcel Doree	Melanie Lee
Iain Hagan	Jim Maller
Jacky Hayles	Chris Norbury

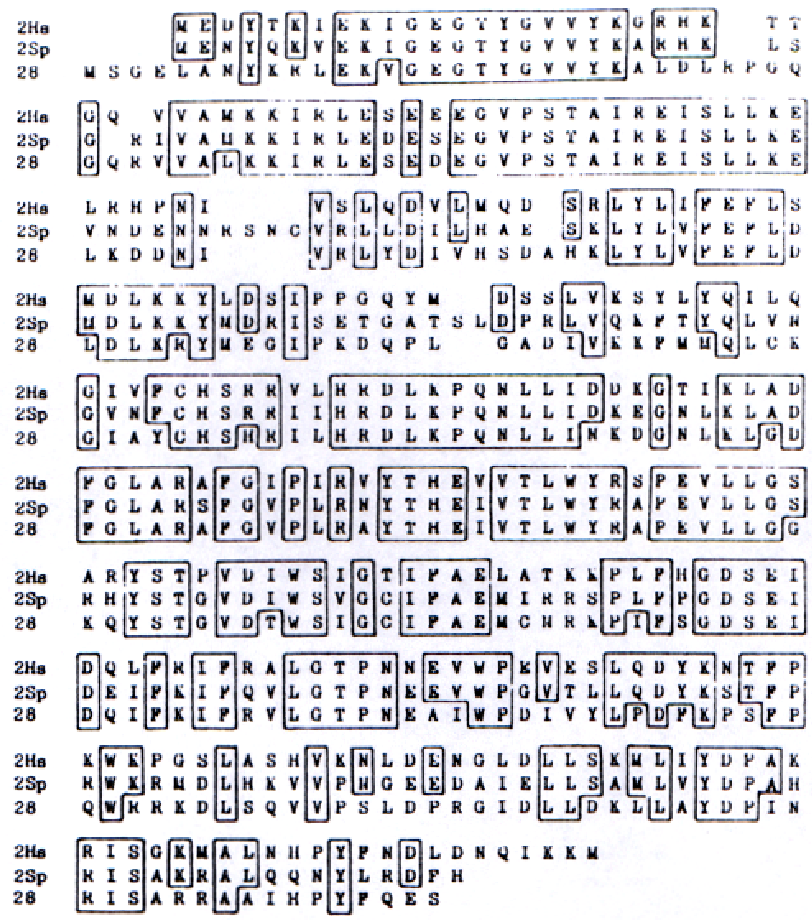
Nature, Vol, 327, No. 6117, pp. 31-35, May 7, 1987

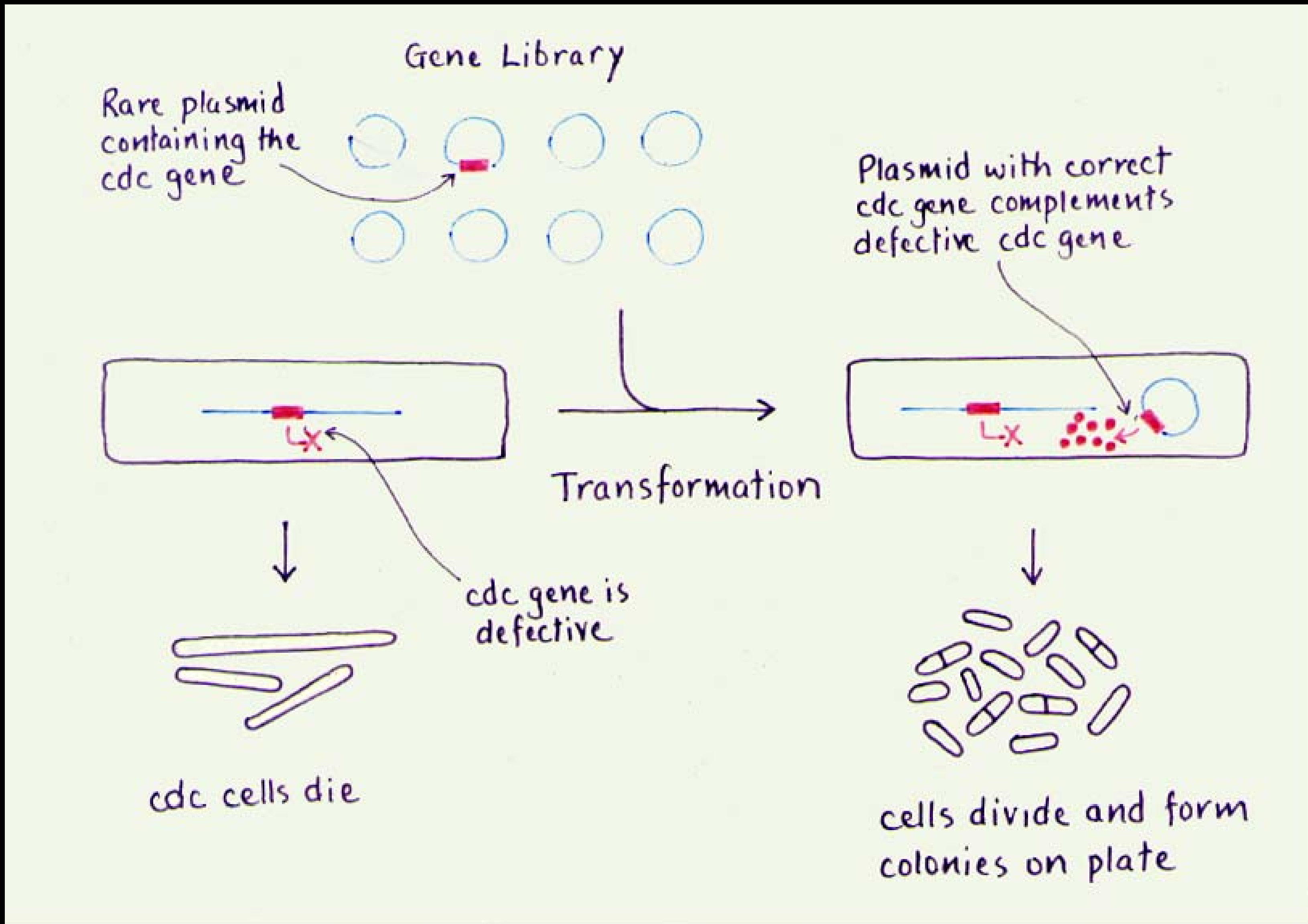
Complementation used to clone a human homologue of the fission yeast cell cycle control gene *cdc2*

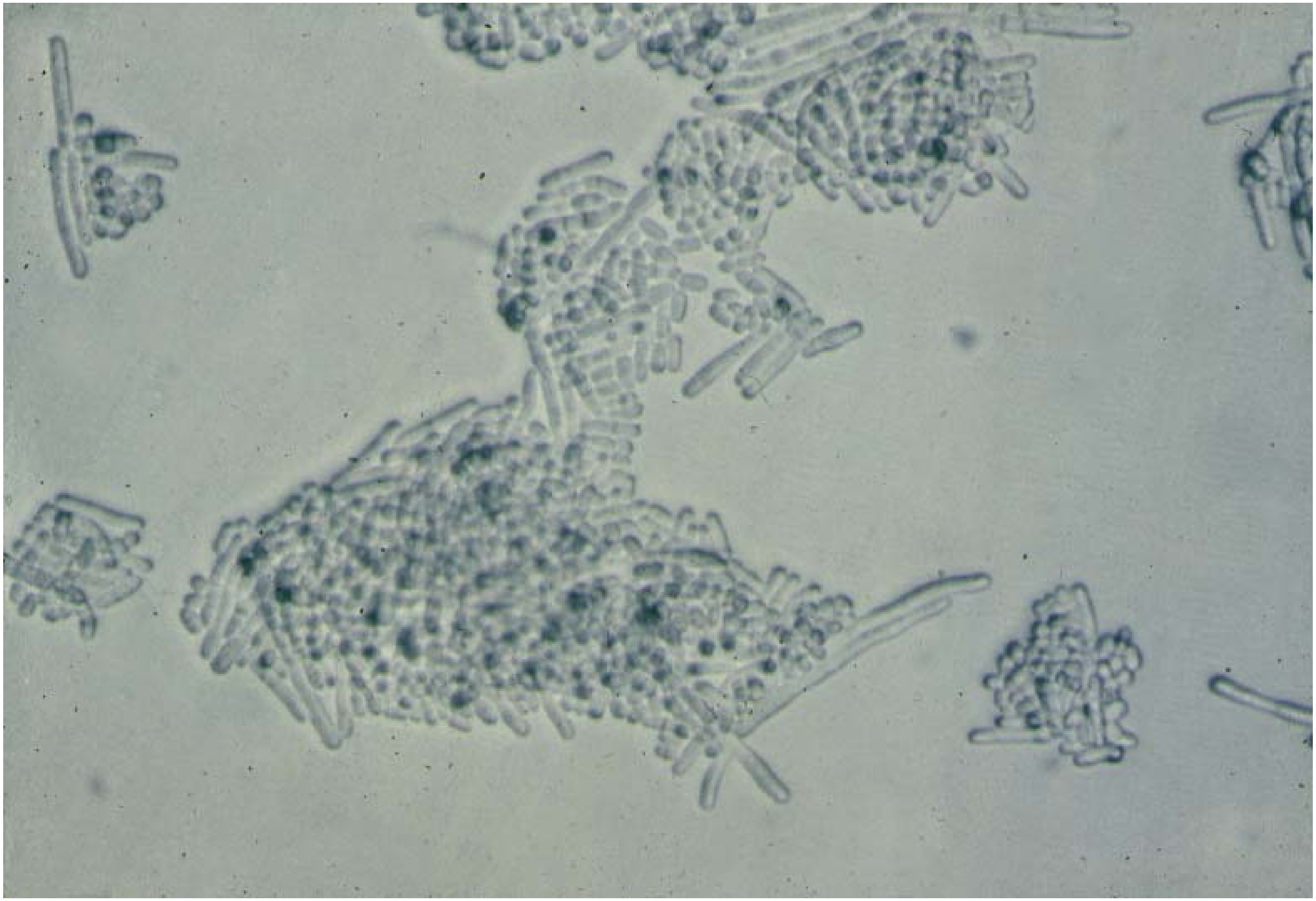
Melanie G. Lee & Paul Nurse

Cell Cycle Control Laboratory, Imperial Cancer Research Fund, Lincoln's Inn Fields, London, WC2A 3PX, UK

Melanie Lee




Gene Library
Rare plasmid containing the cdc gene
Plasmid with correct cdc gene complements defective cdc gene
Transformation
cdc gene is defective
cdc cells die
cells divide and form colonies on plate

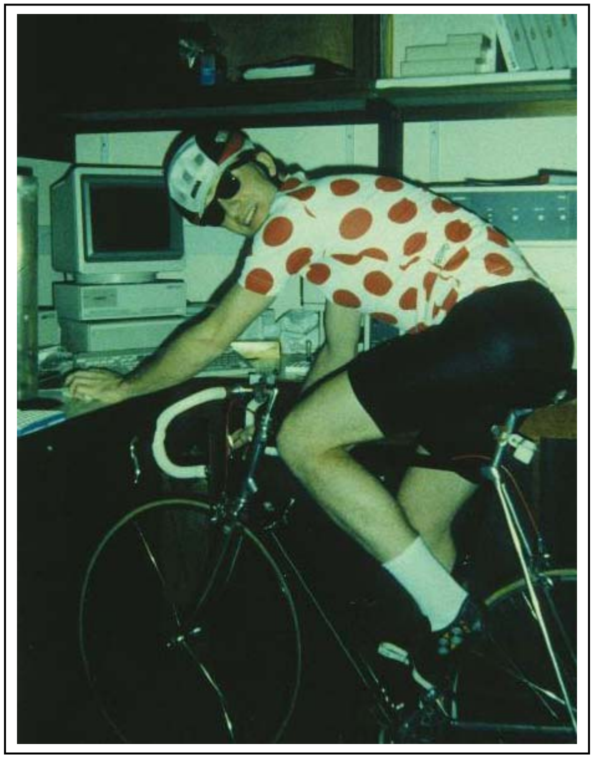


```
S. pombe          M  E  NYQKVEKIGEGTYGVVYKARHK  LSG RIVAMKKIRLEDESEGVPSTAIR
S. cerevisiae     MSGELANYKRLEKVGEGTYGVVYKALDLRPGQGQRVVALKKIRLESEDEGVPSTAIR
H.sapiens         M  E  DYTKIEKIGEGTYGVVYKGRHK  TTGQ VVAMKKIRLESEEEGVPSTAIR
M. musculus       M  E  DYIKIEKIGEGTYGVVYKGRHR  VTGQ IVAMKKIRLESEEEGVPSTAIR
G. gallus         M  E  DYTKIEKIGEGTYGVVYKGRHK  TTGQ VVAMKKIRLESEEEGVPSTAIR
D. melanogaster   M  E  DFEKIEKIGEGTYGVVYKGRNR  LTGQ IVAMKKIRLESDDEGVPSTAIR

S. pombe          EISLLKEVNDENNRSNCVRLLDILHAES KLYLVFEFLDMDLKKYMDRISETGATSL
S. cerevisiae     EISLLKELKDD     NIVRLYDIVHSDAHKLYLVFEFLDLDLKRYMEGIPKDQPLGA
H.sapiens         EISLLKELRHP     NIVSLQDVLMQDS RLYLIFEFLSMDLKKYLDSIPPGQYM
M. musculus       EISLLKELRHP     NIVSLQDVLMQDS RLYLIFEFLSMDLKKYLDSIPPGQFM
G. gallus         EISLLKELHHP     NIVCLQDVLMQDA RLYLIFEFLSMDLKKYLDTIPSGQYL
D. melanogaster   EISLLKELKHE     NIVCLEDVLMEE NRIYLIFEFLSMDLKKYMDSLPVDKHM

S. pombe          DPRLVQKFTYQLVNGVNFCHSRRIIHRDLKPQNLLIDKEGNLKLADFGLARSFGVPLR
S. cerevisiae     D  IVKKFMMQLCKGIAYCHSHRILHRDLKPQNLLINKDGNLKLGDFGLARAFGVPLR
H.sapiens         DSSLVKSYLYQILQGIVFCHSRRVLHRDLKPQNLLIDDKGTIKLADFGLARAFGIPIR
M. musculus       DSSTVKSYLHQIMQGIVFCHSRRVLHRDLKPQNLLIDDKGTIKLADFGLARAFGIPIR
G. gallus         DRSRVKSYLYQILQGIVFCHSRRVLHRDLKPQNLLIDDKGVIKLADFGLARAFGIPVR
D. melanogaster   KAELVRSYLYQITSAILFCHRRRVLHRDLKPQNLLIDKSGLIKVADFGLGRSFGIPVR

S. pombe          NYTHEIVTLWYRAPEVLLGSRHYSTGVDIWSVGCIFAEMIRRSPLFPGDSEIDEIFKI
S. cerevisiae     AYTHEIVTLWYRAPEVLLGGKQYSTGVDTWSIGCIFAEMCNRKPIFSGDSEIDQIFKI
H.sapiens         VYTHEVVTLWYRSPEVLLGSARYSTPVDIWSIGTIFAELATKKPLFHGDSEIDQLFRI
M. musculus       VYTHEVVTLWYRSPEVLLGSARYSTPVDIWSIGTIFAELATKKPLFHGDSEIDQLFRI
G. gallus         VYTHEVVTLWYRSPEVLLGSALYSTPVDIWSIGTIFAELATKKPLFHGDSEIDQLFRI
D. melanogaster   IYTHEIVTLWYRAPEVLLGSPRYSCPVDIWSIGCIFAEMATRKPLFQGDSEIDQLFRM

S. pombe          FQVLGTPNEEVWPGVTLLQDYKSTFPRWKRMDLHKVVPNGEEDAIELLSAMLVYDPAH
S. cerevisiae     FRVLGTPNEAIWPDIVYLPDFKPSFPQWRRKDLSQVVPSLDPRGIDLLDKLLAYDPIN
H.sapiens         FRALGTPNNEVWPEVESLQDYKNTFPKWKPGSLASHVKNLDENGLDLLSKMLIYDPAK
M. musculus       FRALGTPNNEVWPEVESLQDYKNTFPKWNPGSLASHVKNLDENCLDFLSKMLVYDPAK
G. gallus         FRALGTPNNDVWPDVESLQDYKNTFPKWKPGSLGTHVQNLDEDGLDLLSKMLIYDPAK
D. melanogaster   YRILKTPTEDIWPGVTSLPDYKNTFPCWSTNQLTNQLKNLDANGIDLIQKMLIYDPVH

S. pombe          RISAKRALQQNYLRDFH
S. cerevisiae     RISARRAAIHPYFQES
H.sapiens         RISGKMALNHPYFNDLDNQIKKM
M. musculus       RISGKMALKHPYFDDLDNQIKKM
G. gallus         RISGKMALNHPYFDDLDKSTLPANLIKKF
D. melanogaster   RISAKDILEHPYFNGFQSGLVRN
```

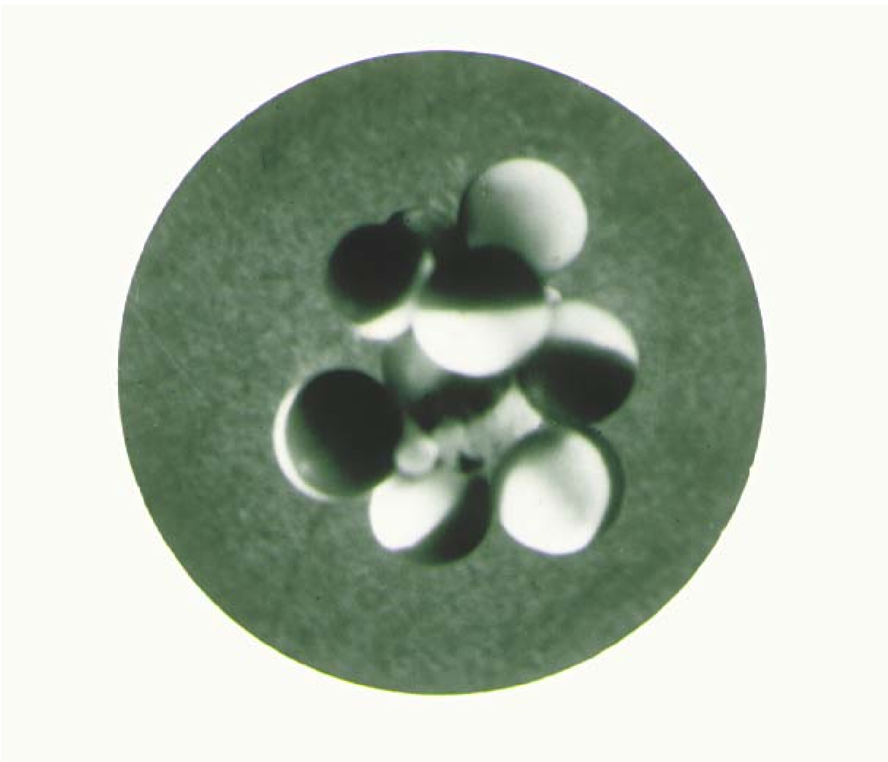
Cell, Vol. 54: 433-439, July 29, 1988

Purified Maturation-Promoting Factor Contains the Product of a Xenopus Homolog of the Fission Yeast Cell Cycle Control Gene *cdc2*$^+$

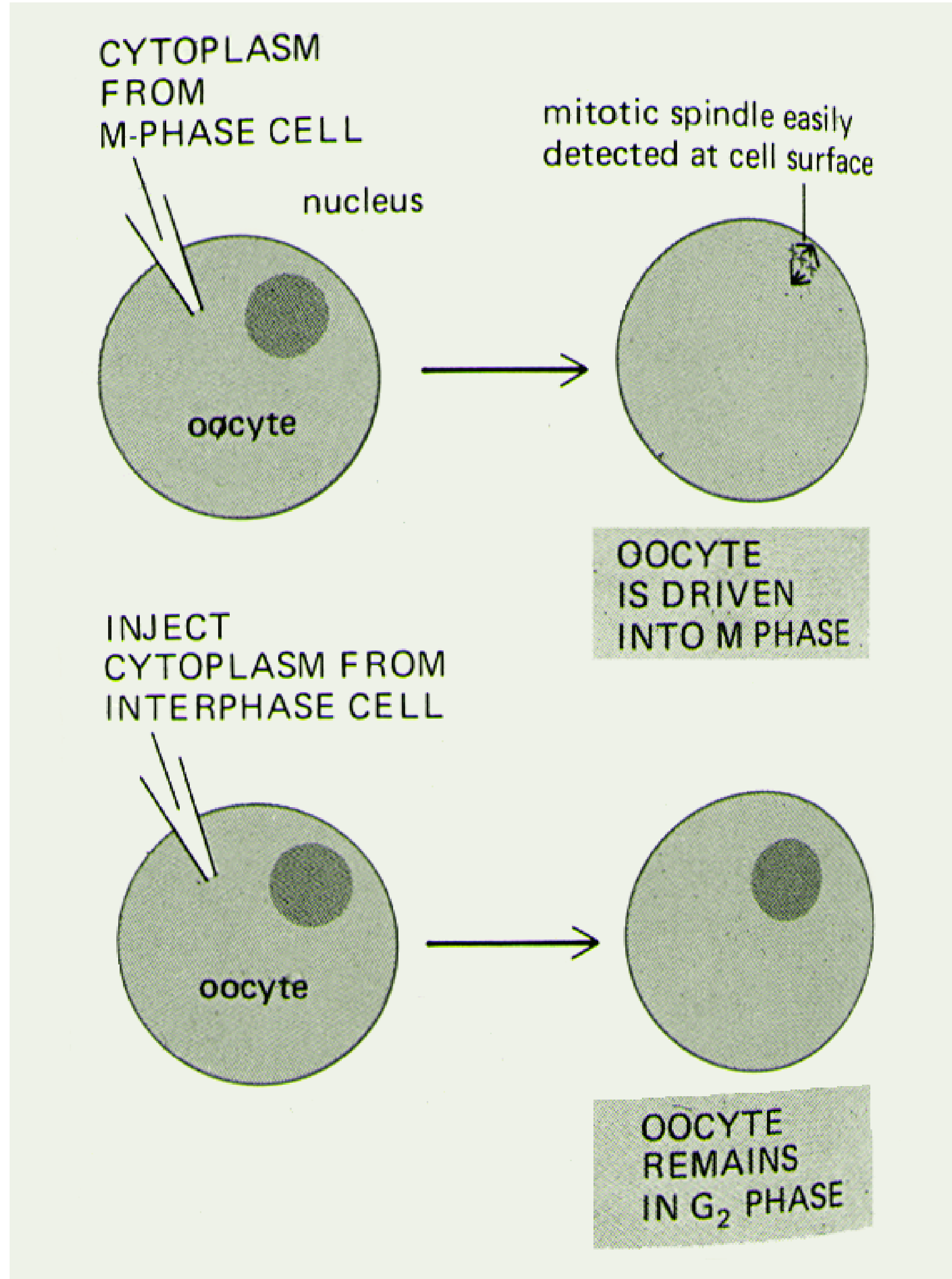
Jean Gautier,* Chris Norbury,† Manfred Lohka,* ‡ Paul Nurse,† and James Maller*
*Department of Pharmacology
University of Colorado School of Medicine
Denver, Colorado 80262
†ICRF Cell Cycle Control Laboratory
Microbiology Unit
Department of Biochemistry
University of Oxford
Oxford OX13QU, England



Chris Norbury

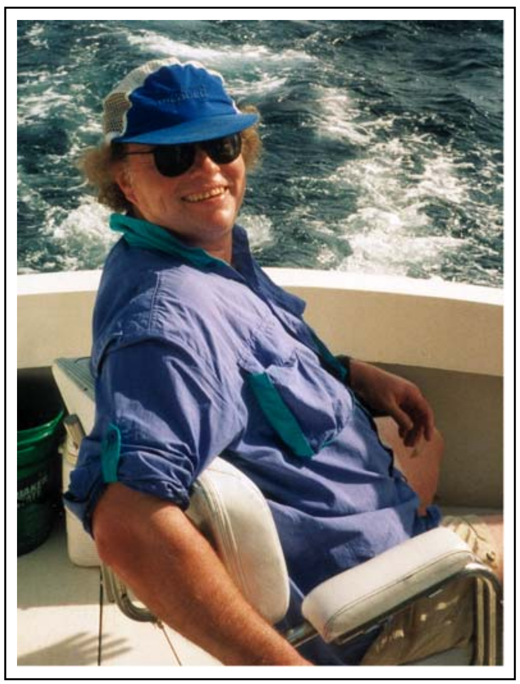


Yoshio Masui

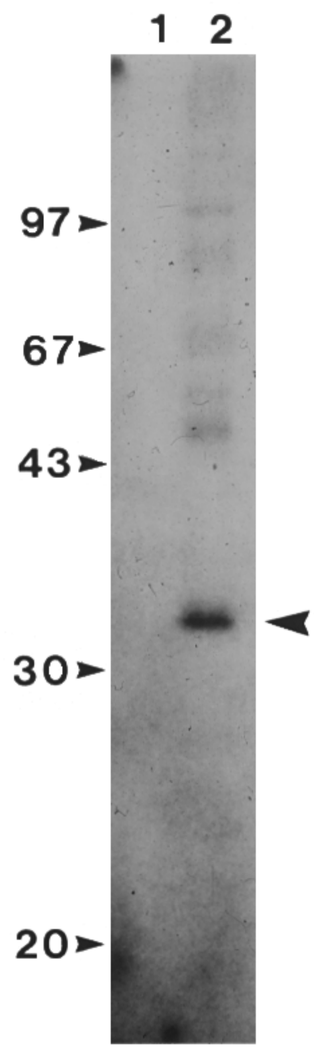


Purified Maturation-Promoting Factor Contains the Product of a Xenopus Homolog of the Fission Yeast Cell Cycle Control Gene *cdc2*+

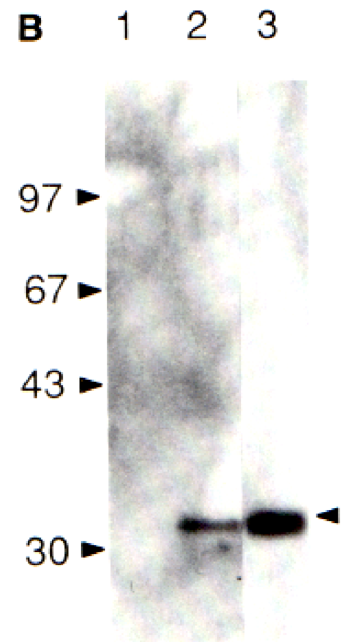
Jean Gautier,* Chris Norbury,† Manfred Lohka,* ‡ Paul Nurse,† and James Maller*
*Department of Pharmacology
University of Colorado School of Medicine
Denver, Colorado 80262
†ICRF Cell Cycle Control Laboratory
Microbiology Unit
Department of Biochemistry
University of Oxford
Oxford OX13QU, England



Jim Maller



IP



Western

Cell, Vol. 57: 253-263, April 21, 1989

Purification of MPF from Starfish: Identification as the H1 Histone Kinase p34cdc2 and a Possible Mechanism for Its Periodic Activation

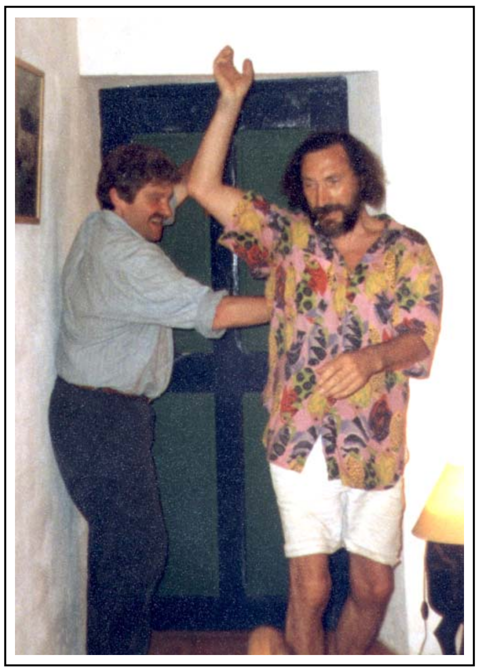
J. C. Labbe,* A. Picard,† G. Peaucellier,‡
J. C. Cavadore,* P. Nurse,§ and M. Doree*
*CNRS and INSERM
B.P. 5051
34033 Montpellier Cedex
France
†Laboratoire Arago
66650 Banyuls-sur-Mer
France
‡Station Biologique
29211 Roscoff
France
§ICRF Cell Cycle Control Laboratory
Microbiology Unit
Department of Biochemistry
South Parks Road
Oxford OX1 3QU
England

Nature, Vol, 335, No. 6187, pp. 251-254, September 15, 1988

Activation at M-phase of a protein kinase encoded by a starfish homologue of the cell cycle control gene *cdc2*⁺

J. C. Labbe*, M. G. Lee†, P. Nurse†,
A. Picard* & M. Doree*

* CNRS and INSERM, BP 5051, 34033 Montpellier, Cedex, France
† ICRF Cell Cycle Control Laboratory, Microbiology Unit,
Department of Biochemistry, University of Oxford,
South Parks Road, Oxford OX1 3QU, UK



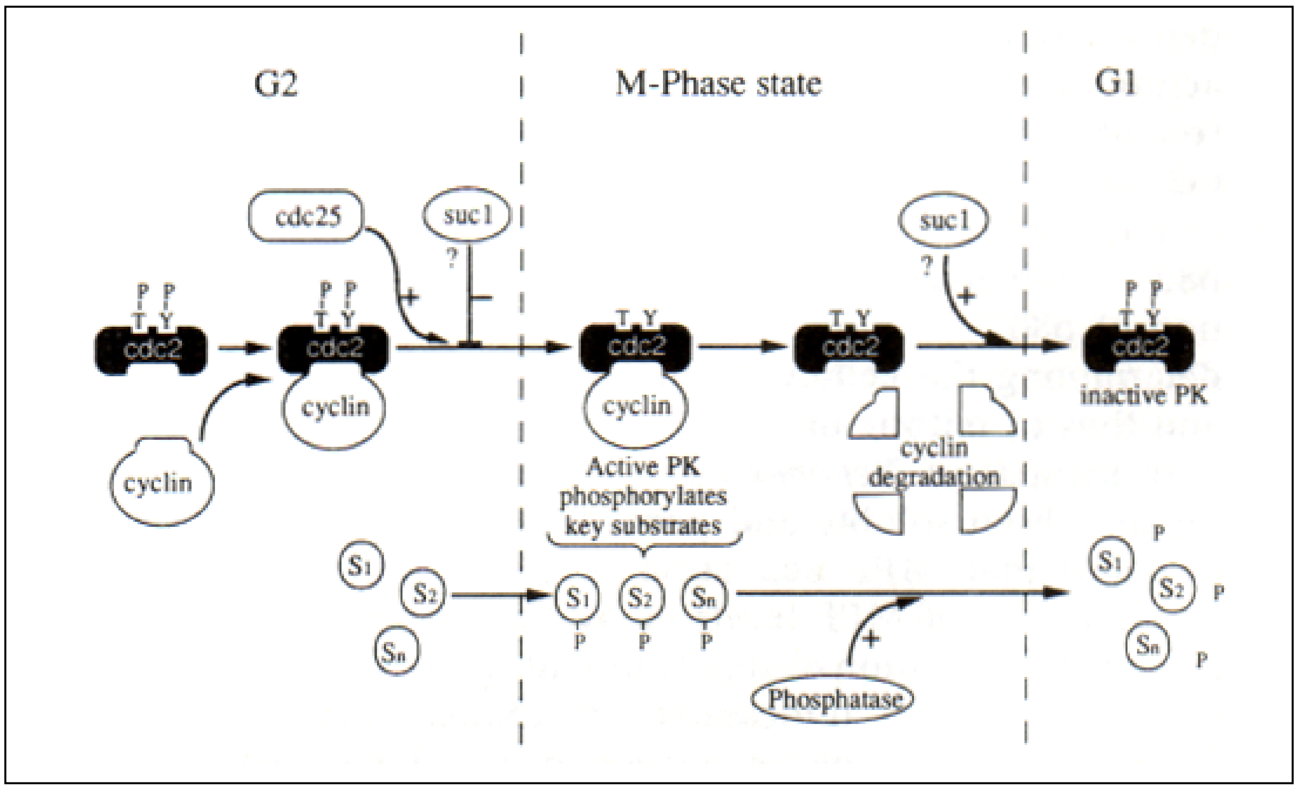
Marcel Doree

Nature, Vol, 344, No. 6266, pp. 503-508, April 5, 1990

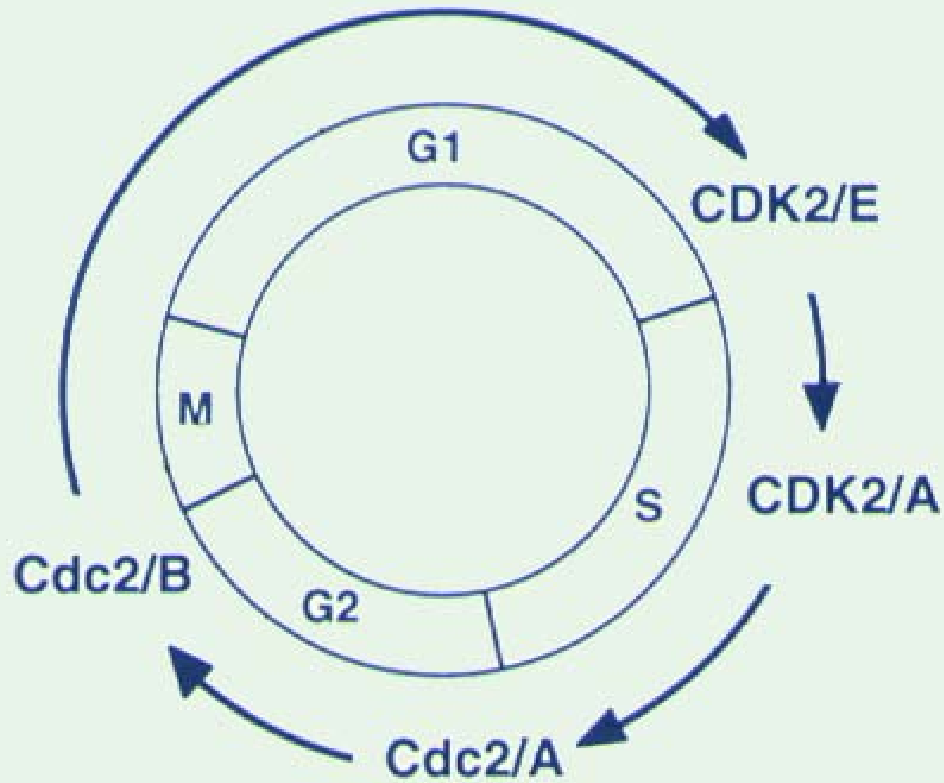
Universal control mechanism regulating onset of M-phase

Paul Nurse

The onset of M-phase is regulated by a mechanism common to all eukaryotic cells. Entry into M-phase is determined by activation of the p34^{cdc2} protein kinase which requires p34^{cdc2} dephosphorylation and association with cyclin.



the *essential* cell cycle



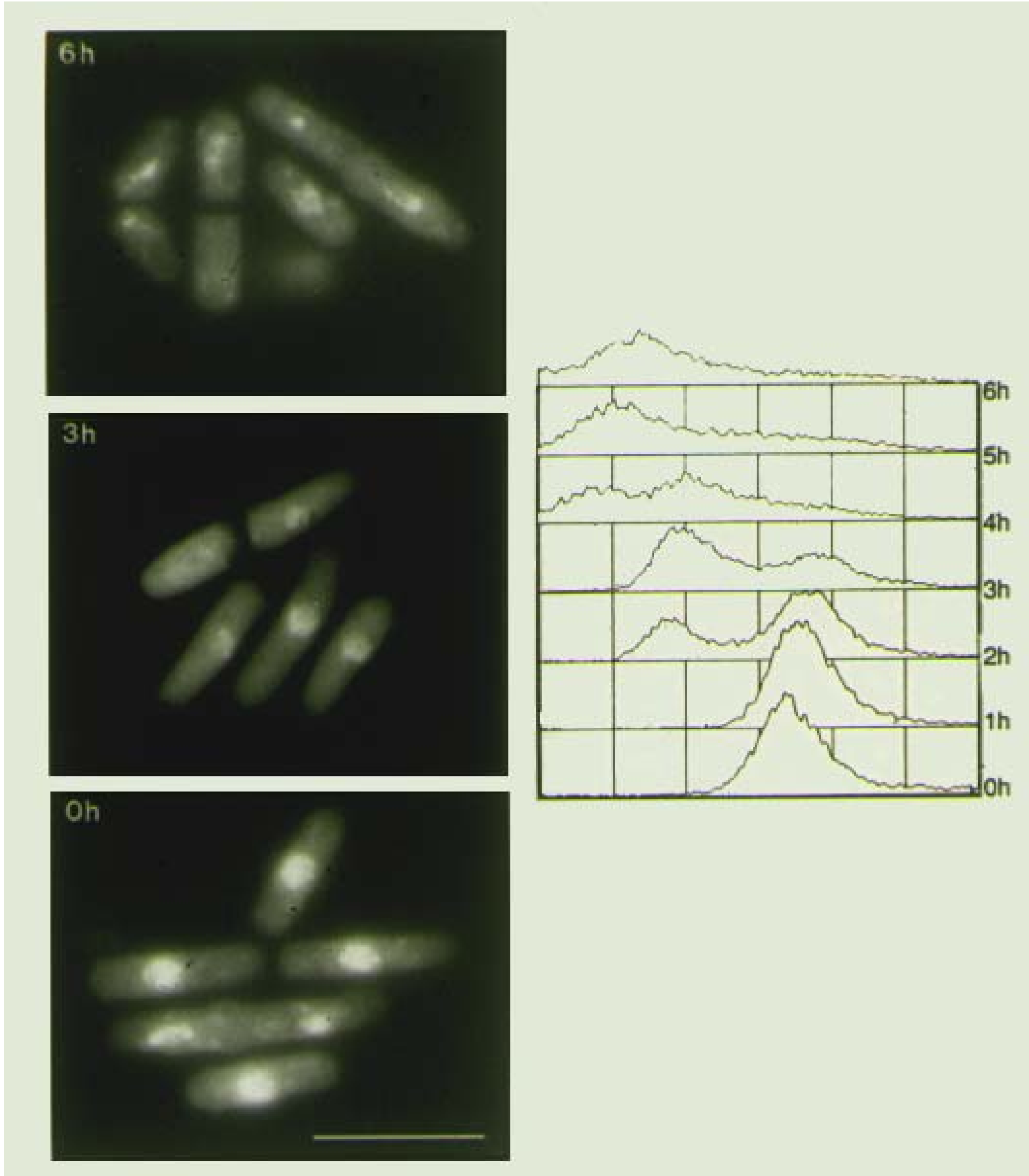
We have seen that all organisms are composed of essentially like parts, namely, of cells; that these cells are formed and grow in accordance with essentially the same laws; hence, that these processes must everywhere result from the operation of the same forces.

Schwann 1839

Further roles for cdc2

Oxford, Biochemistry	1988-1993
ICRF, LIF London	1993-2001

Tamar Enoch	Jacky Hayles
Daniel Brock	Sergio Morenó



6h
3h
0h
6h
5h
4h
3h
2h
1h
0h

Cell, Vol. 60: 665-673, February 23, 1990

Mutation of Fission Yeast Cell Cycle Control Genes Abolishes Dependence of Mitosis on DNA Replication

Tamar Enoch and Paul Nurse
ICRF Cell Cycle Group
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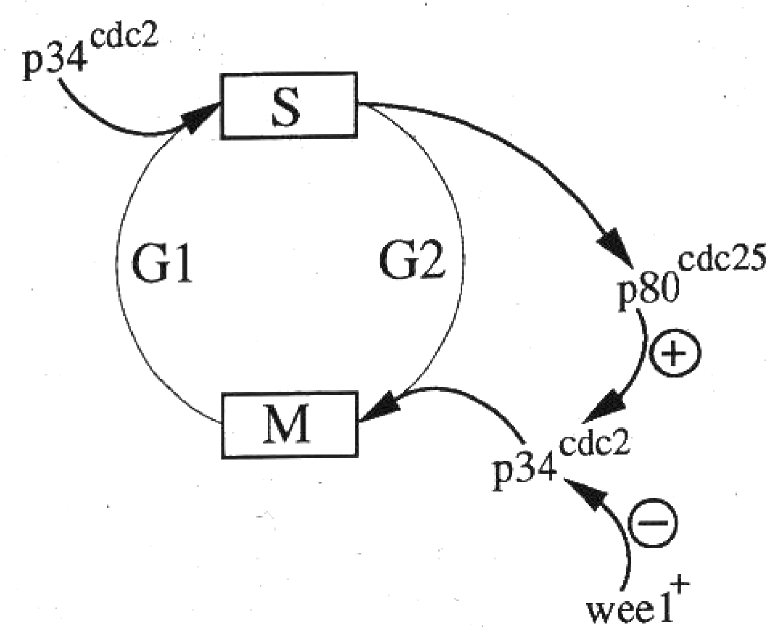
Oxford University
Oxford OX1 3QU
England

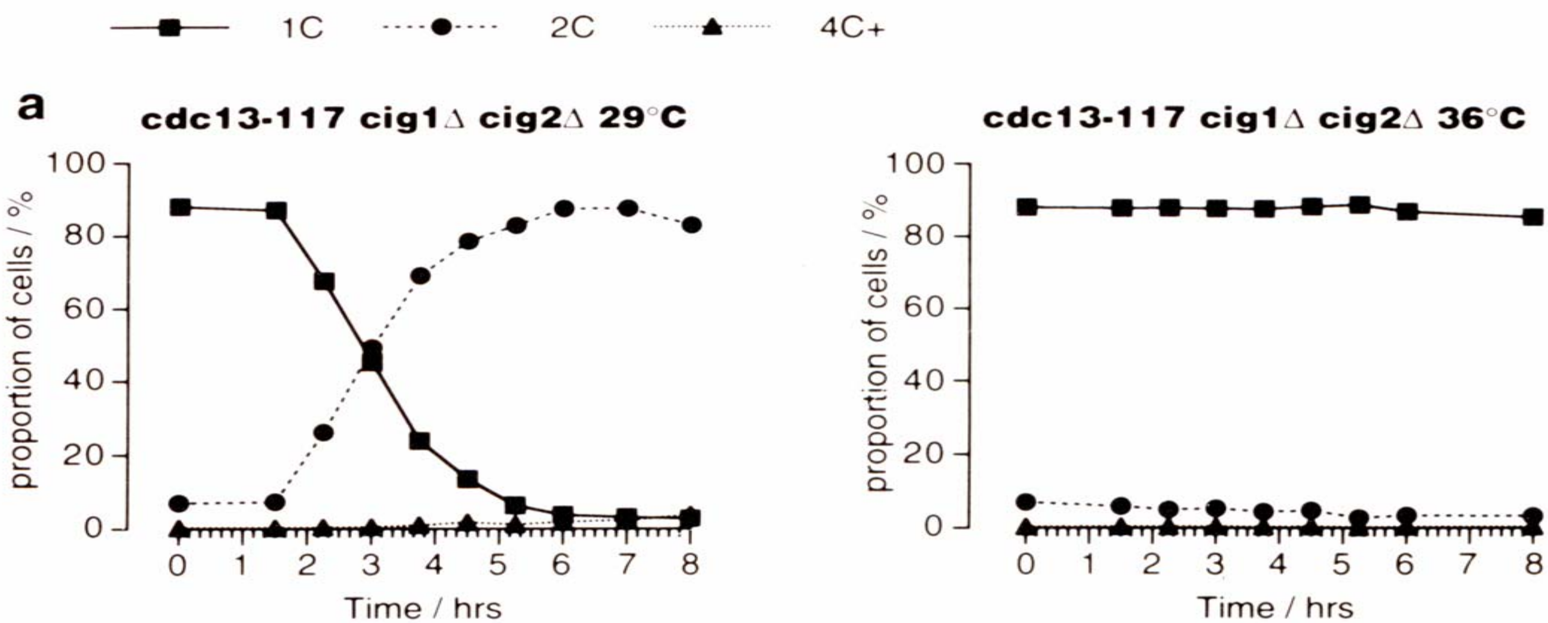
Tamar Enoch

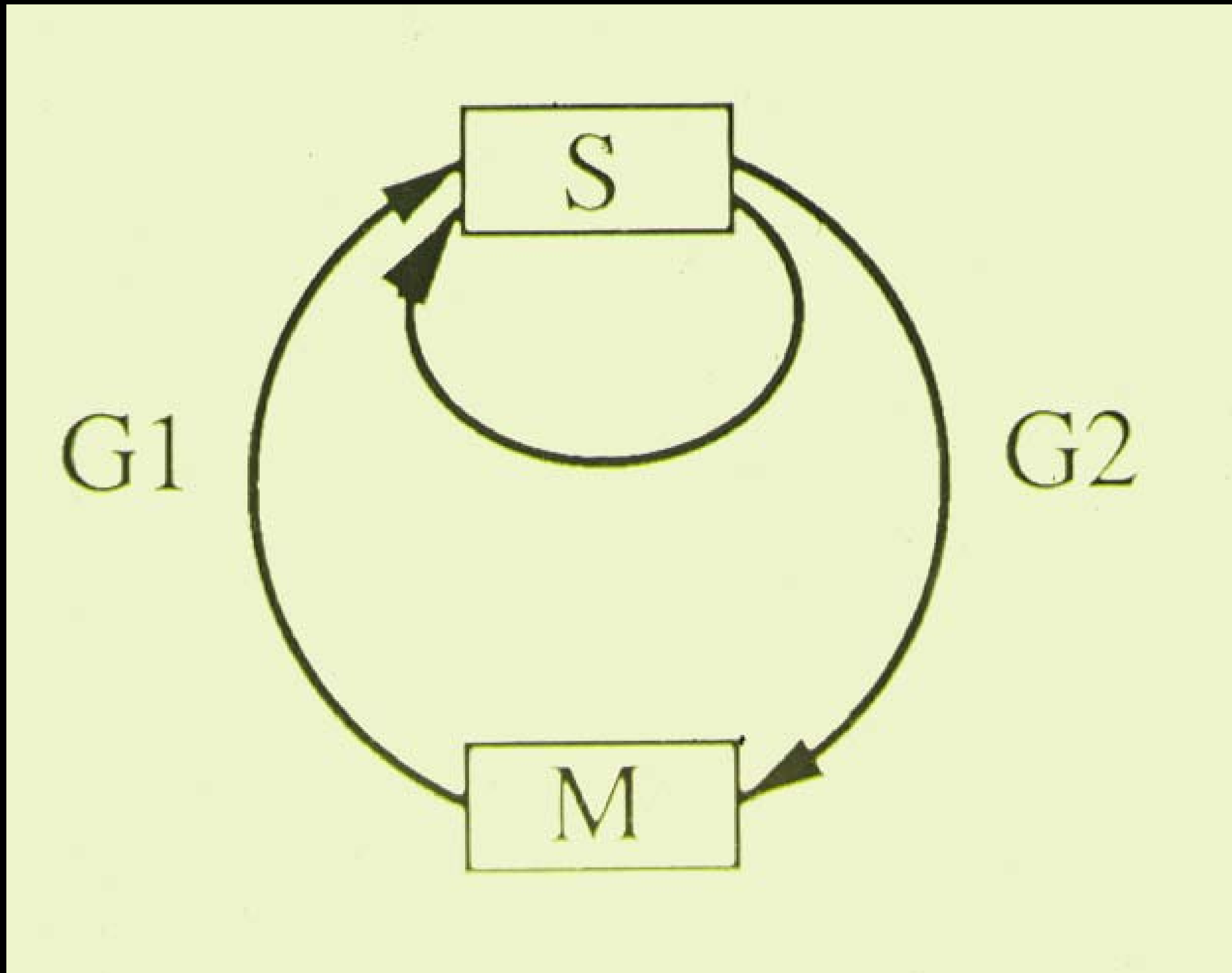


The EMBO Journal Vol 15, pp.850-860, 1996,

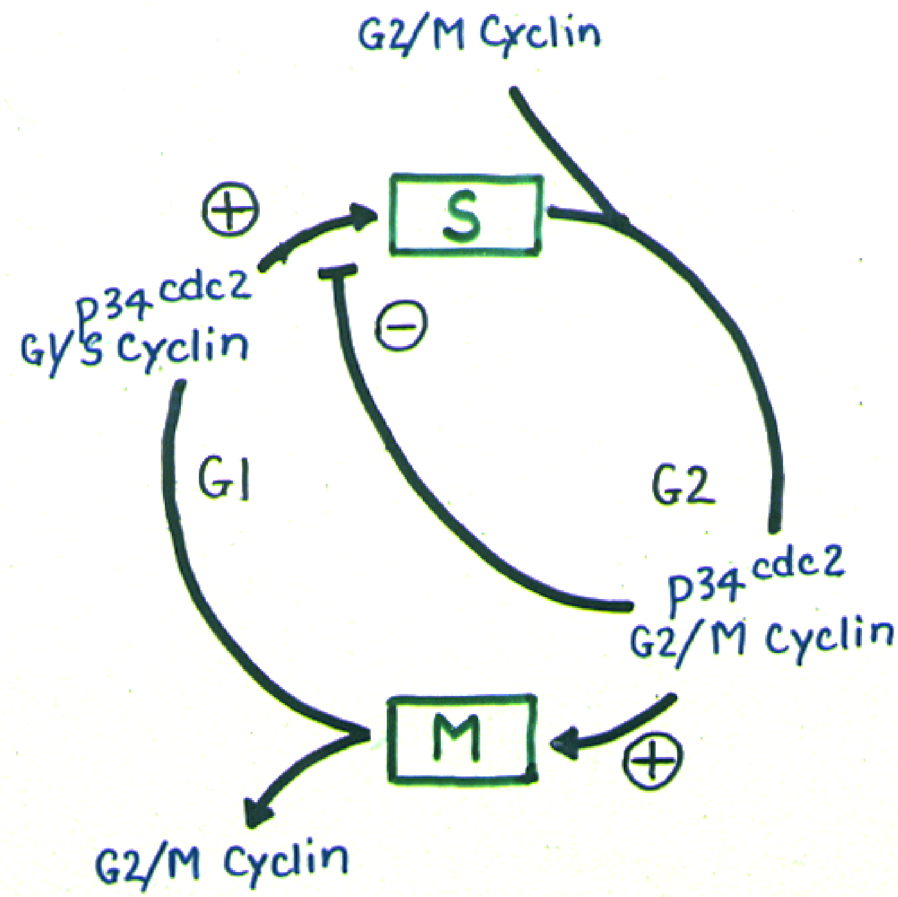
A single fission yeast mitotic cyclin B p34cdc2 kinase promotes both S- phase and mitosis in the absence of G1 cyclins

D.L.Fisher and P.Nurse
Cell Cycle Laboratory, Imperial Cancer Research Fund, London, UK.





S
G1
G2
M



Jacky Hayles

Cell, Vol. 78: 813-822, September 9, 1994

Temporal Order of S Phase and Mitosis in Fission Yeast Is Determined by the State of the p34^{cdc2}–Mitotic B Cyclin Complex

Jacqueline Hayles, Daniel Fisher, Alison Woollard, and Paul Nurse
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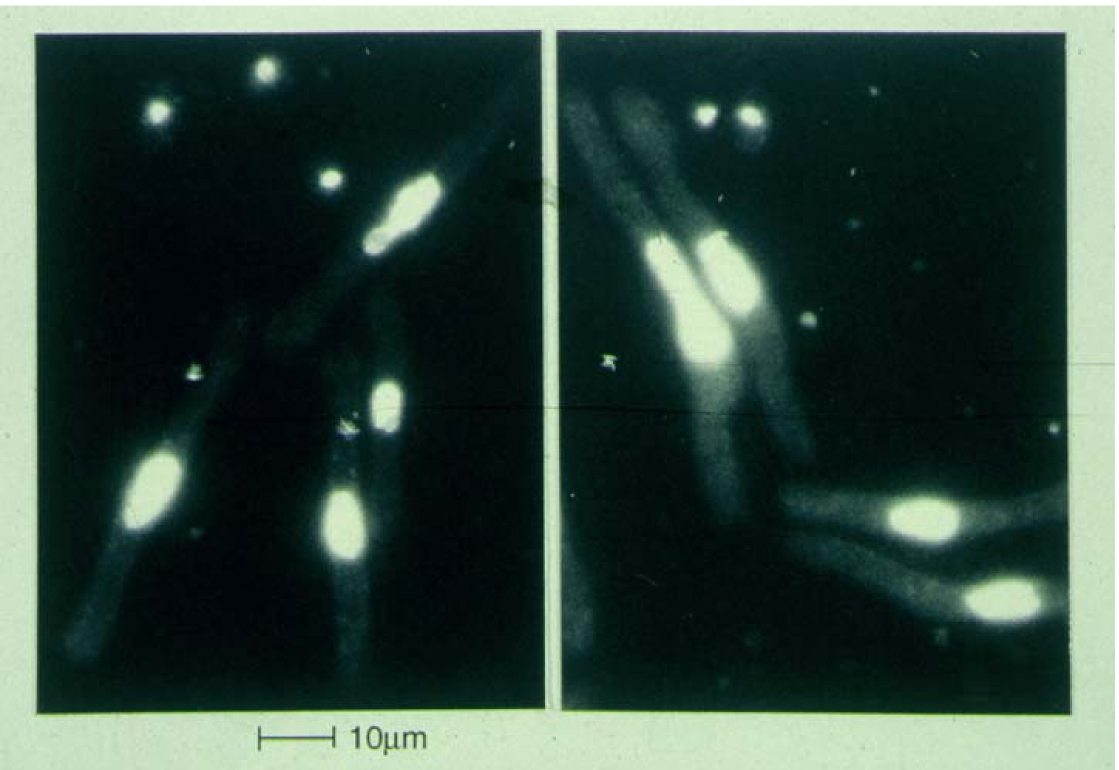
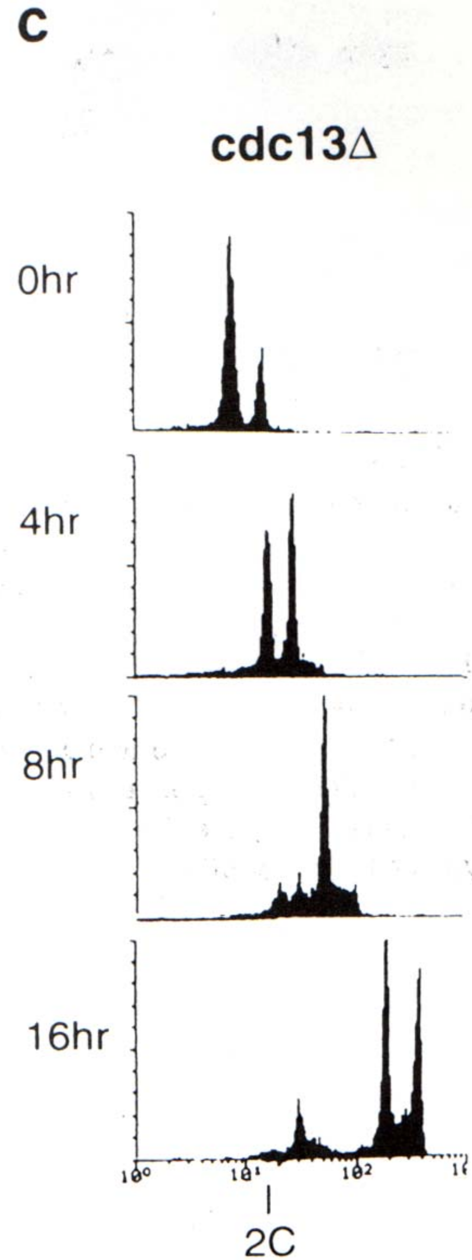
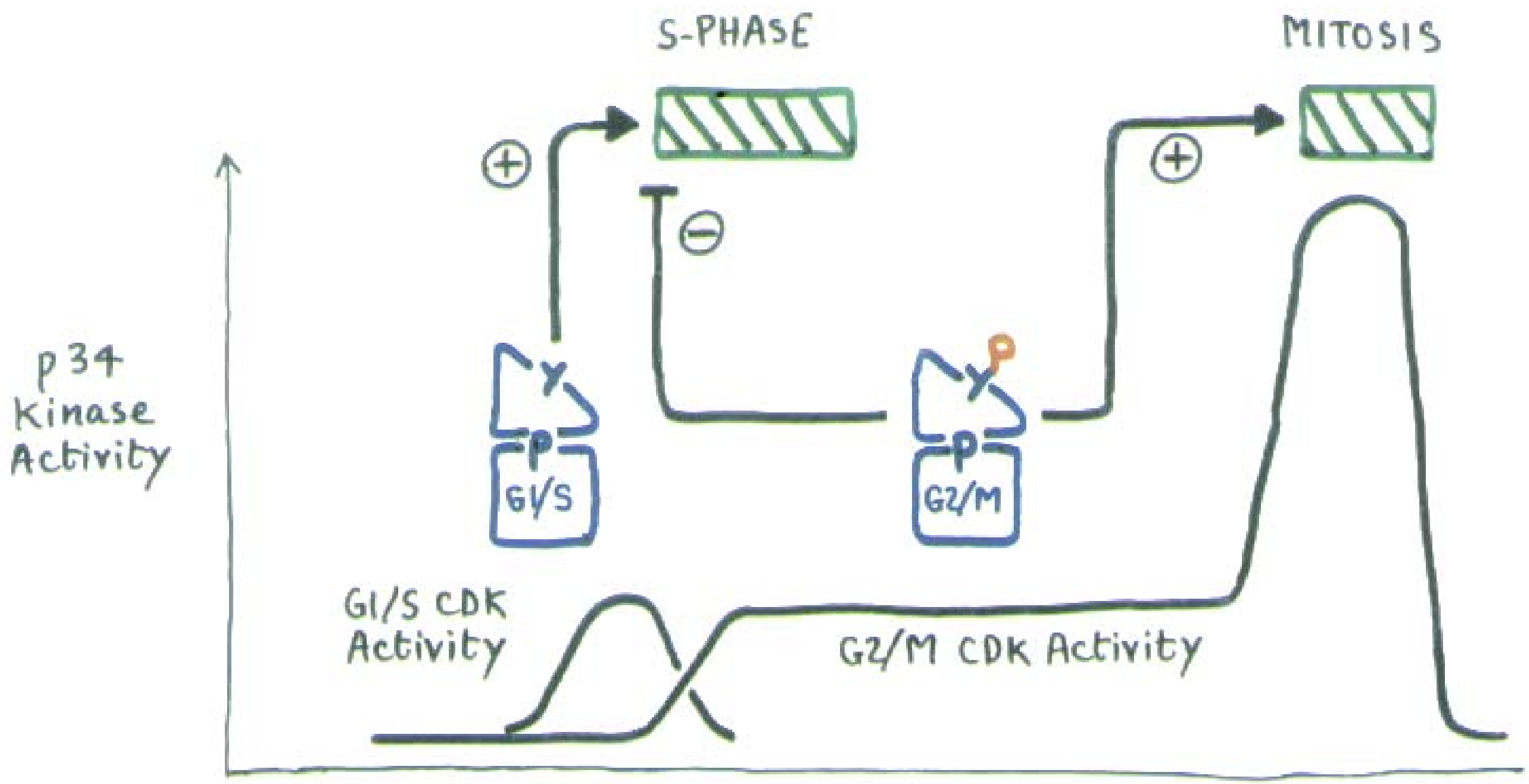
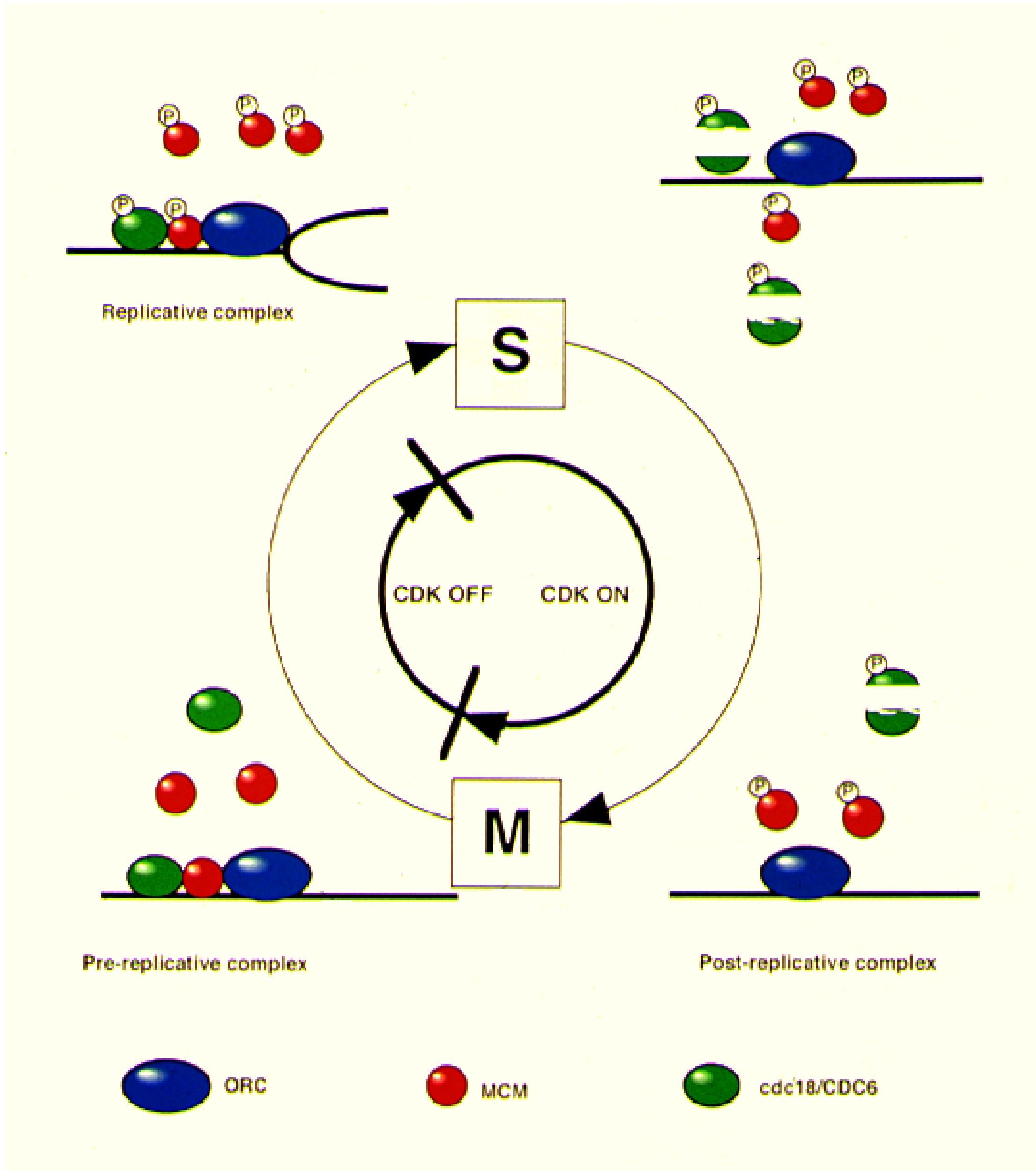
Imperial Cancer Research Fund
Lincoln's Inn Fields
London WC2A 3PX
England






S-PHASE
MITOSIS
p34
Kinase
Activity
G1/S
G2/M
G1/S CDK
Activity
G2/M CDK Activity



Replicative complex
S
CDK OFF
CDK ON
M
Pre-replicative complex
Post-replicative complex
ORC
MCM
cdc18/CDC6

Cell, Vol. 100: 71-78, January 7, 2000

A Long Twentieth Century of the Cell Cycle and Beyond

Paul Nurse
Cell Cycle Laboratory
Imperial Cancer Research Fund
44 Lincoln's Inn Fields
London WC2A 3PX
United Kingdom

1. CDKs and cell cycle events
2. Checkpoints
3. Meiotic cell cycles
4. Cell cycle and development
5. Cell cycle molecular machines
6. Spatial and temporal organisation

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