Supporting Online Material for

An Oncogene-Induced DNA Damage Model for Cancer Development

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References
Supporting References Grouped by Section

DNA DSBs in Cells Expressing Activated Oncogenes and in Human Precancerous Lesions and Cancers


Genomic instability in MycER-activated Rat1A-MycER cells. 

S29. Felsher DW, Bishop JM. 
Transient excess of MYC activity can elicit genomic instability and tumorigenesis. 

S30. Berkovich E, Ginsberg D. 
ATM is a target for positive regulation by E2F-1. 

Defective double-strand DNA break repair and chromosomal translocations by MYC overexpression. 

S32. Woo RA, Poon RY. 
Activated oncogenes promote and cooperate with chromosomal instability for neoplastic transformation. 

S33. Frame FM, Rogoff HA, Pickering MT, Cress WD, Kowalik TF. 
E2F1 induces MRN foci formation and a cell cycle checkpoint response in human fibroblasts. 

MYC can induce DNA breaks in vivo and in vitro independent of reactive oxygen species. 

Ras induces chromosome instability and abrogation of the DNA damage response. 

**A Tumorigenesis Barrier in Human Precancerous Lesions**

S36. Kuerbitz SJ, Plunkett BS, Walsh WV, Kastan MB. 
Wild-type p53 is a cell cycle checkpoint determinant following irradiation. 

S37. Clarke AR, Purdie CA, Harrison DJ, Morris RG, Bird CC, Hooper ML, Wyllie AH. 
Thymocyte apoptosis induced by p53-dependent and independent pathways. 

S38. Lowe SW, Schmitt EM, Smith SW, Osborne BA, Jacks T. 
p53 is required for radiation-induced apoptosis in mouse thymocytes. 
DNA damage triggers a prolonged p53-dependent G1 arrest and long-term induction of Cip1 in normal human fibroblasts.

S40. te Poele RH, Okorokov AL, Jardine L, Cummings J, Joel SP.
DNA damage is able to induce senescence in tumor cells in vitro and in vivo.

S41. Sharpless NE, DePinho RA.
Cancer: crime and punishment.

BRAFE600-associated senescence-like cell cycle arrest of human naevi.

S43. Evan GI, Vousden KH.
Proliferation, cell cycle and apoptosis in cancer.

The DNA Damage Checkpoint as an Important Mediator of the Tumorigenesis Barrier

[See also refs. S36 to S42.]

Tumour biology: senescence in premalignant tumours.

Crucial role of p53-dependent cellular senescence in suppression of Pten-deficient tumorigenesis.

Oncogene-induced senescence as an initial barrier in lymphoma development.

S47. Kemp CJ, Donehower LA, Bradley A, Balmain A.
Reduction of p53 gene dosage does not increase initiation or promotion but enhances malignant progression of chemically induced skin tumors.


S57. Powers JT, Hong S, Mayhew CN, Rogers PM, Knudsen ES, Johnson DG.
E2F1 uses the ATM signaling pathway to induce p53 and Chk2 phosphorylation and apoptosis.

S58. Pauklin S, Kristjuhan A, Maimets T, Jaks V.
ARF and ATM/ATR cooperate in p53-mediated apoptosis upon oncogenic stress.

S59. Frame FM, Rogoff HA, Pickering MT, Cress WD, Kowalik TF.
E2F1 induces MRN foci formation and a cell cycle checkpoint response in human fibroblasts.

Ras triggers ataxia-telangiectasia-mutated and Rad-3-related activation and apoptosis through sustained mitogenic signaling.

ATM promotes apoptosis and suppresses tumorigenesis in response to Myc.
Proc Natl Acad Sci USA 2006; 103: 1446-51.

S62. Hong S, Pusapati RV, Powers JT, Johnson DG.
Oncogenes and the DNA damage response: Myc and E2F1 engage the ATM signaling pathway to activate p53 and induce apoptosis.
Cell Cycle 2006; 5: 801-3.

S63. Maclean KH, Kastan MB, Cleveland JL.
Atm deficiency affects both apoptosis and proliferation to augment Myc-induced lymphomagenesis.

S64. Mallette FA, Gaumont-Leclerc MF, Ferbeyre G.
The DNA damage signaling pathway is a critical mediator of oncogene-induced senescence.

Tip60 is a haplo-insufficient tumour suppressor required for an oncogene-induced DNA damage response.

Atm-deficient mice: a paradigm of ataxia telangiectasia.
Cell 1996; 86: 159-71.
Pleiotropic defects in ataxia-telangiectasia protein-deficient mice.

S68. Xu Y, Ashley T, Brainerd EE, Bronson RT, Meyn MS, Baltimore D.
Targeted disruption of ATM leads to growth retardation, chromosomal fragmentation during meiosis, immune defects, and thymic lymphoma.

Chk2 is a tumor suppressor that regulates apoptosis in both an ataxia telangiectasia mutated (ATM)-dependent and an ATM-independent manner.

S70. Chao C, Herr D, Chun J, Xu Y.
Ser18 and 23 phosphorylation is required for p53-dependent apoptosis and tumor suppression.

S71. Canadillas JM, Tidow H, Freund SM, Rutherford TJ, Ang HC, Fersht AR.
Solution structure of p53 core domain: structural basis for its instability.
Proc Natl Acad Sci USA 2006; 103: 2109-14.

S72. Milner J, Medcalf EA.
Cotranslation of activated mutant p53 with wild type drives the wild-type p53 protein into the mutant conformation.

S73. Bargonetti J, Reynisdottir I, Friedman PN, Prives C.
Site-specific binding of wild-type p53 to cellular DNA is inhibited by SV40 T antigen and mutant p53.

S74. Xu Y, Yang EM, Brugarolas J, Jacks T, Baltimore D.
Involvement of p53 and p21 in cellular defects and tumorigenesis in Atm-/- mice.

Chromosomally unstable mouse tumours have genomic alterations similar to diverse human cancers.


**DNA Replication Stress Underlies DNA DSB Formation and Genomic Instability in Human Precancerous Lesions**

[See also refs. S5 to S27.]
S85. Bishop JM.
The molecular genetics of cancer.
Science 1987; 235: 305-11.

S86. Tanaka S, Diffley JF.
Deregulated G1-cyclin expression induces genomic instability by preventing efficient pre-RC formation.

Mol Cell 2003; 11: 997-1008.

S88. Deb-Basu D, Aleem E, Kaldis P, Felsher DW.
CDK2 is required by MYC to induce apoptosis.

S89. Desany BA, Alcasabas AA, Bachant JB, Elledge SJ.
Recovery from DNA replicational stress is the essential function of the S-phase checkpoint pathway.

S90. Osborn AJ, Elledge SJ, Zou L.
Checking on the fork: the DNA-replication stress-response pathway.

S91. Tourriere H, Pasero P.
Maintenance of fork integrity at damaged DNA and natural pause sites.

S92. Branzei D, Foiani M.
Interplay of replication checkpoints and repair proteins at stalled replication forks.
DNA Repair 2007; 6: 994-1003.

S93. Tercero JA, Diffley JF.
Regulation of DNA replication fork progression through damaged DNA by the Mec1/Rad53 checkpoint.

The DNA replication checkpoint response stabilizes stalled replication forks.

S95. Cobb JA, Schleker T, Rojas V, Bjergbaek L, Tercero JA, Gasser SM.
Replisome instability, fork collapse, and gross chromosomal rearrangements arise synergistically from Mec1 kinase and RecQ helicase mutations.

S96. Casper AM, Durkin SG, Arlt MF, Glover TW.
Chromosomal instability at common fragile sites in Seckel syndrome.

S97. Casper AM, Nghiem P, Arlt MF, Glover TW.
ATR regulates fragile site stability.

Gross chromosomal rearrangements and elevated recombination at an inducible site-specific replication fork barrier.

Replication stress induces tumor-like microdeletions in FHit/FRA3B.
Proc Natl Acad Sci USA 2007; Epub ahead of print.

Oncogene-induced replication stress preferentially targets common fragile sites in preneoplastic lesions. A genome-wide study.
Oncogene 2007; Epub ahead of print.

Mutations of mitotic checkpoint genes in human cancers.

Securin is required for chromosomal stability in human cells.

Inactivation of hCDC4 can cause chromosomal instability.

Three classes of genes mutated in colorectal cancers with chromosomal instability.
Cancer Res 2004; 64: 2998-3001.


