Mark J. Dvorscak

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Mark J. Dvorscak

Date

(630) 252-2349

E-mail: mark.dvorscak@ch.doe.gov

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Final Report

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ANALYSIS OF GENE TARGETING AND NONHOMOLOGOUS END-JOINING

We have published the following papers related to this grant:

Lee, S.E., J.K. Moore, A. Holmes, K. Umez, R.D. Kolodner and J.E. Haber (1998) Role of yeast Ku, Mre11/Rad50 and RPA proteins in adaptation to DNA damage-induced G2/M arrest. *Cell* **94**: 399-409.

Pâques, F. and J.E. Haber (1999) Mechanisms of double-strand break repair in *Saccharomyces* (review). *Mol. Biol. Microbiol. Rev.* **63**: 349-404.

Le, S., J.K. Moore, J.E. Haber and C. Greider (1999) *RAD50* and *RAD51* define two independent pathways that collaborate to maintain telomeres in the absence of telomerase. *Genetics* **152**: 143-152.

Lee, S.E., F. Pâques, J. Sylvan and J.E. Haber (1999) Role of yeast SIR proteins and mating type in directing DNA double-strand breaks to homologous or nonhomologous repair routes. *Curr. Biol.* **9**: 767-770.

Haber, J.E. (1999) Sir-Ku-itous routes to make ends meet. *Cell* **97**: 829-832.

Haber, J.E. 2000. Lucky breaks: analysis of recombination in *Saccharomyces*. *Mutat Res* **451**: 53-69.

Haber, J.E. (2000) Partners and Pathways in Repairing a Double-Strand Break. *Trends Genet.* **16**: 259-264.

Demeter, J., S.E. Lee, J.E. Haber and T. Stearns (2000) The DNA-damage checkpoint signal in budding yeast is nuclear-limited. *Mol. Cell.* **6**: 487-492.

Lee, S.E., A. Pelliccioli, J. Demeter, M. Vaze, A.P. Gasch, A. Malkova, P. Brown, T. Stearns, M. Foiani and J.E. Haber. (2002) Arrest, adaptation and recovery following a chromosome double-strand break in *Saccharomyces cerevisiae*. *Cold Spring Harbor Symp. Quant. Biol.* **65**: 303-314.

Pelliccioli, A., S.E. Lee, C. Lucca, M. Foiani and J.E. Haber (2001) Regulation of *Saccharomyces* Rad53 checkpoint kinase during adaptation from G2/M arrest. *Mol. Cell* **7**: 293-300.

Kraus, E., Leung, W.-Y. and J.E. Haber (2001) Break-induced replication: a review and an example in budding yeast. *Proc. Natl. Acad. Sci. USA* **98**: 8255-8262.

Lee, S.E., A. Pelliccioli, A. Malkova, M. Foiani, and J.E. Haber (2001) The *Saccharomyces* recombination protein Tid1p is required for adaptation from G2/M arrest induced by a double-strand break. *Curr. Biol.* **11**: 1053-1057.

Valencia, M., M. Bentele, M.B. Vaze, G. Herrmann, E. Kraus, S.E. Lee, P. Schar, and J.E. Haber. 2001. *NEJ1* controls non-homologous end joining in *Saccharomyces cerevisiae*. *Nature* **414**: 666-9.

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Lee, S.E., D.A. Bressan, J.H.J. Petrini, and J.E. Haber. 2002. Complementation between N-terminal *Saccharomyces cerevisiae mre11* alleles in DNA repair and telomere length maintenance. *DNA Repair* 1: 27-40.

Vaze, M., A. Pellicioli, S.E. Lee, G. Ira, G. Liberi, A. Arbel-Eden, M. Foiani and J.E. Haber. (2002) Recovery from checkpoint-mediated arrest after repair of a double-strand break requires Srs2 helicase. *Mol. Cell.* 10: 373-385

Overall, we identified a number of new proteins that participate in nonhomologous end-joining and also in telomere addition to the ends of broken chromosomes. We showed that NHEJ is severely reduced in cells expressing both yeast mating-type genes and then went on to identify the NEJ1 gene that was under this control. We showed the epistasis relations among a set of mutations that impair telomere addition and we showed that there are in fact two pathways to repair broken chromosomes in the absence of telomerase. We characterized the DNA damage checkpoint pathway in response to a single broken chromosome and characterized especially the adaptation of cells arrested by an unrepaired DSB. We demonstrated that the DNA damage response is nuclear-limited. We showed adaptation defects for Tid1 and Srs2 proteins and showed that Srs2 was also recovery-defective, even when DNA was repaired.