

- **Project Title:** Characterization of new genes mediating exchange of DNA between chromosomes

Investigator: Kevin L. Lewis

Department: Chemistry and Biochemistry Department

Project Summary:

This REP grant was funded to pursue two major Aims, involving application of DNA repair assays developed in my lab to identify new genes required to fix broken chromosomes during normal cell growth and also in meiosis. Two graduate students, Rachel Roberts and Jennifer Summers, with some assistance from undergraduate Jasmine Joseph, performed these experiments and many more during this past year. They screened over 100 genetic mutants that we previously found to be sensitive to killing by gamma radiation and chemical DNA damaging agents to identify which of them were specifically defective in DNA double-strand break repair.

Rachel used the plasmid: chromosome homologous recombination assay described in the proposal (after a lot of work to make it more efficient) plus a new assay for sensitivity to in vivo expression of the DNA endonuclease HO. This nuclease creates a break in yeast chromosome III at a single site that cannot be repaired if cells are defective in intrachromosomal DNA recombination. She identified 10 previously unrecognized genes that cause cells to become hypersensitive to HO endonuclease expression. Two of these genes also had strong defects in her plasmid: chromosome recombination assay.

Jennifer screened the same set of over 100 mutants looking for those that died when a different endonuclease, EcoRI, was expressed in vivo. EcoRI has many recognition sites and breaks chromosomes at many places inside the cell. She found 33 new mutants that were EcoRI-sensitive. She subsequently showed that 14 of these genes were also essential for resistance to the chemicals bleomycin and MMS. These 14 genes had not previously been linked to DNA double-strand repair. These and many other results were all performed after receipt of this REP award in spring 2007.

Publications:

1.) Lewis, K.P. & Smith, R.J. (2008) Issues of allometry in the scaling of the human brain. *American Journal of Physical Anthropology*, 135, S46.

2.) Lewis, K.P. and Smith, R.J. (IN PREP) Scaling of regions of interest in the human brain: New statistical considerations.

Presentations:

Lewis, K.P. & Smith, R.J. Issues of allometry in the scaling of the human brain. 77th Annual Meeting of the American Association of Physical Anthropologists, Columbus, Ohio, April 9-12th 2008.

Student Number: 1