- **PROJECT-4 : Spontaneous mutations in nondividing cells**

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In order to address the intriguing question of whether spontaneous mutations can occur in nondividing cells (apart from their known occurrence during replication of the genetic material associated with cell division), we have developed and exploited a novel conditional-lethal strategy *(1)*. Briefly, the parental population of cells is able to grow under both permissive ($30^0$C) and restrictive ($42^0$C) growth conditions whereas mutants at a particular target locus grow only at $30^0$C and are killed at $42^0$C. Thus, by growing the parental strain to stationary phase at $42^0$C, one gets a population in which all spontaneous mutants at the target-locus that arose during cell replication have been killed; by shifting the population subsequently to $30^0$C, one can now score for new mutants that arise in the nondividing cell population. We have used newly isolated $Kan^r$ (Ts) and *galE* (Ts) mutations to study reversion of *lacZ* mutations in nondividing cells, and have shown that such events indeed occur *(1)*. The current interests in this project are (i) to employ the *galE*(Ts) strategy to study the spectrum of forward mutations in the *lacI* repressor gene in nondividing cells; and (ii) to isolate and characterize mutators and antimutators that affect mutation frequencies in nondividing cells. The conditional-lethal strategy developed by us has also been patented *(2)* for use in the identification of agents that increase or decrease mutation rates in nondividing cells.


1. Reddy, M., and J. Gowrishankar. 1997. A genetic strategy to demonstrate the occurrence of spontaneous mutations in nondividing cells within colonies of *Escherichia coli*. Genetics **147**: 991-1001.

2. Reddy, M., J. Gowrishankar, and S.M. Bharatan. Process for identifying mutagens and antimutagens. United States Patent 5,981,191 issued on 9 November, 1999.


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