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### **RESEARCH AREAS:**

1. Genetics/Molecular Biology of transcription control in *Escherichia coli*
2. Genetic Regulation by and of proteases in *E. coli*
3. Genetic regulation of mutagenesis in *Escherichia coli*

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### **RESEARCH INTERESTS:**

#### **Transcription control in *E.coli*:**

On the area of transcription control we have shown that the *fitA* and *fitB* genes earlier identified and very well characterized in *E.coli* in our laboratory are same as *pheS* and *pheT* genes of *E.coli*. This has led to the new finding that the productions of *pheS* and *pheT* genes namely phenylalanyl tRNA synthetase also functions as a transcription factor. By sequence analysis we have shown that the originally identified *fitA76* mutant has two lesions: a G293 → A293 transition in *pheS* locus and another mutation, designated as *fit95*. Very recently, based on molecular analysis we have shown that *fit95* defines an allele of the *pheT* locus. We have physically mapped the position of one of the earlier isolated *fit* mutation (*fitC4*), which was isolated as a suppressor of *fitA76\** mutant harboring *pheS4* and *fit95* mutations. Our physical mapping indicate that *fitC4* in all likelihood, could be duplicated copy of a *pheS4* mutation, which defines a G→C transversion at position 293 of *pheS* locus. Also our biochemical analyses indicate that neither *fit95*, nor *pheS5* mutations when present alone confer the phenotype characteristic of originally identified transcription mutant *fitA76* (*fit95 pheS5*). These results reinforce the conclusion that the phenylalanyl tRNA synthetase indeed functions as a transcription factor (Fit) and two mutations are needed to elicit the *fitA76* Ts phenotype (*pheS5 fit95*). Moreover we have clearly shown the *fitC4* suppresses the Ts phenotype due to various *fitA/B pheS/T* mutations in an allele specific manner. Also we have shown that the *fit* gene products do not function as global transcription factors but are involved in expression of only few classes of genes which might include genes for ribosomal proteins.

*Currently we are working in the following aspects:*

- a. Further substantiating the view that *fit95* and *pheS5* mutations are needed to elicit transcription defective phenotype characteristic of *fitA76* mutant by doing extensive biochemical analyses.
- b. Identification of the lesion present in the *fit95* mutant by PCR based amplification of *fit95* region and subsequent sequence analyses.

- c. Molecular characterization of the new alternate promoter that we have just recently identified in *pheST* operon of *E.coli* and finding its sigma dependence. Trying to identify transacting factors that potentially regulate the above alternate promoter.
- d. Isolating and characterizing several promoter *lacZ*<sup>+</sup> fusions which express beta galactosidase in *fit* dependent manner and analyzing such promoter sequences in order to know whether *fit* factors bind to specific sites on DNA to regulate transcription.

### **Proteolysis in *E.coli*:**

My collaborative research work with Dr. Susan Gottesman of National Cancer Institute, National Institute of Health, Bethesda, MD, USA, has led to the new finding that to elicit the originally proposed alternate Lon protease (Alp) proficient phenotype in *E.coli*, at least two proteases are needed. The Alp protease originally was named so because in Alp<sup>+</sup> strains the two substrates of Lon protease namely SulA and RcsA were expected to be degraded as like in a *lon*<sup>+</sup> strain. But now it is shown that SulA is degraded by ClpYQ protease but the other protease capable of RcsA is still not identified.

*Currently we are working in the following directions:*

- a) The *faa* mutation that we have identified and shown that it elicits Alp<sup>+</sup> phenotype has been shown to be a mutation at position 232 of *dnaJ* gene of *E.coli*. The Alp<sup>+</sup> phenotype becomes stronger when *ssrA* mutation is also present. The same Alp effect in a *lon*<sup>-</sup> strain is also seen in *ssrA* mutants which carry multicopy Kan<sup>R</sup> plasmid. In this area in the coming five years we would like to do the following.
- b) Identifying and characterizing mutations that restore RcsA function in *lon faa ssrA* mutant of *E.coli*. This will pave way to identify the actual gene coding for the protease responsible for RcsA decay. Later the protease activity can be demonstrated *in vitro* using purified proteases, if possible.
- c) Identifying the other phenotypic traits affected by both the above said *dnaJ* mutation as well as the mutation that we anticipate to get.
- d) Seeing the multicopy effect of *faa* mutation alone in a *lon* mutant strain.

### **PUBLICATIONS:**

1. Munavar, M.H. and Jayaraman, R. "Extragenic suppression of the temperature sensitivity of a temperature sensitive transcription mutant of *Escherichia coli*". Presented at the 55<sup>th</sup> annual meeting of the Society of Biological Chemists held at Trivandrum, India (December 15-17, 1986)
2. Munavar, M.H. and Jayaraman, R. Extragenic suppression of the temperature sensitivity of a *fitA* mutation by a *fitB* mutation in *Escherichia coli*: Possible interaction between *fitA* and *fitB* gene products in transcription control. *J.Genet.* 66:123-132, 1987
3. Munavar, M.H., Madhavi, K. and Jayaraman, R. Aberrant transcription in *fit* mutants of *Escherichia coli* and its alleviation by suppressor mutations. *J. Biosci.* 18:37-45, 1993

4. Munavar, M.H. and Jayaraman, R. Genetic evidence for the interaction between *fitA*, *fitB* and *rpoB* gene products and its implication in transcription control in *Escherichia coli* J. Genet. 72:21-33, 1993.
5. Sankaran, S., Munavar, M.H. and Jayaraman, R. "Phenylalanyl tRNA synthetase of *Escherichia coli* as an accessory transcription factor: analysis of *fitA76* and *pheS5* mutations". Presented at the meeting on "Molecular Genetics of bacteria and Phages" held at Cold Spring Harbour Laboratory, CSH, NY, USA (August 24-29, 1993).
6. Munavar, M.H. and Gottesman, S. "Isolation and characterization of mutations affecting ALP (Alternate Lon Protease) activity in *Escherichia coli*". Presented at the meeting on "Molecular Genetics of Bacteria and phages" held at the University of Wisconsin, Madison, WI, USA ( August 2-7, 1994).
7. Munavar, M.H. and Gottesman, S. "A chromosomal locus affecting Alternate lon-like protease (Alp) activity in *Escherichia coli*". presented at the 95<sup>th</sup> General Meeting of the American Society for Microbiology held at Washington DC. (May 21-25, 1995).
8. Ramalingam, S., Munavar, M.H., Sankaran, S. Rukmani, A. and Jayaraman , R. Elucidation of lesions present in the transcription defective *fitA76* mutant of *Escherichia coli*: Implication of phenylalanyl tRNA synthetase subunits as transcription factors J.Biosci. 1999 ,24;153-162
9. Sudha, S. Munavar, M.H. and Jayaraman, R. Synthesis versus stability of RNA in *fitA76* and *pheS* mutants of *Escherichia coli* and its implications Indian J.Microbiol. 2001, 41:123-127.
10. Hussain Munavar, YanNing Zhou. and Susan Gottesman (2005), Analysis of *Escherichia coli* Alp phenotype: Heat shock induction in *ssrA* mutants: J.Bacteriol. 187: 4739-4751
11. Vidya.S., Praveen Kamalakar.B., Hussain Munavar M., Satish Kumar, L and R. Jayaraman (2006). Allele-specific suppression of temperature sensitivity of *fitA/fitB* mutants of *E.coli* by a new mutation (*fitC4*); isolation, characterization its implications in transcription control. J.Biosci. 31: 31-45