Curriculum Vitae

Leonard R. Duncan

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Educational History

Graduate Education
September 1989-June 1996
Department of Molecular and Cellular Biology
Harvard University
Cambridge, MA 02138
Laboratory: Professor R. Losick
Degree: Ph.D.
Thesis Title: "Biochemical studies of a regulatory pathway governing cell-type-specific transcription in *Bacillus subtilis*"

Undergraduate Education
August 1984-May 1987/August 1988-May 1989
Department of Biochemistry
University of Iowa, Iowa City, IA
Degree: B.S. with honors and with highest distinction

September 1987-June 1988
Visiting student, Part 1B Natural Sciences
Christ's College, University of Cambridge, Cambridge, England

Fellowships

Jane Coffin Childs Postdoctoral Fellow 1997-2000
Howard Hughes Medical Institute Predoctoral Fellow 1989-1994
Rotary Foundation Scholar to the University of Cambridge 1987-1988

Awards

Nat L. Sternberg Thesis Prize (co-winner) 1996
University of Iowa Collegiate Scholar 1989
Christ's College Scholar (Honorary) 1988
Christ's College "College" Prize in Biological Natural Sciences 1988
Christ's College Haddon Prize in Biological Natural Sciences 1988

Previous Research

1. Scientist, Cumbre, Inc.
April 2002-present
The mission of Cumbre, Inc. is to discover and develop new antibacterial agents using two different research platforms. The goal of the first platform is to identify novel compounds that have superior activity against bacteria living within biofilms. The second platform utilizes panels of efflux-deficient bacterial strains to identify anti-bacterial agents that would have been missed in conventional screens using efflux-competent bacteria.

I have contributed to the progress and success of a number of different projects in both research platforms. My experiences with these projects, which have involved complex biochemical assays, protein purification, bacterial molecular genetics, mammalian cell culture cytotoxicity assays and robotics, have tremendously broadened my skill-set. Although I manage the work of other researches, I also conduct active research "at the bench." Finally, and of particular importance, I was involved in writing several grants, and was the sole author of an SBIR grant that received a fundable score (see below).

2. Post-doctoral fellow in Dr. David Kirk's laboratory at Washington University, St. Louis
August 1997-April 2002
This work is described in the accompanying document "Research Interests."

3. Post-doctoral fellow in Dr. Greg Petsko's laboratory at Brandeis University, Waltham, MA
July 1996-July 1997.
This "mini-post-doc" involved over-expression, purification and crystallization trials of the SpoIIAB anti-sigma factor.

4. Graduate Research in Dr. Richard Losick's Laboratory at Harvard University
Bacillus subtilis is a bacterium that activates the σ^F transcription factor in only one of two juxtaposed cell types during the developmental process of sporulation. My graduate work uncovered the biochemical basis by which three proteins (SpoIIE, SpoIIAA and SpoIIAB) control the activity of σ^F and generate its cell-type specific activity. Specifically, I showed that SpoIIAB is an anti-sigma factor that binds to and inhibits the activity of σ^F. Colleagues and I also demonstrated that SpoIIAB forms an alternative long-lived complex with SpoIIAA. Dr. M. Yudkin's group concurrently demonstrated that SpoIIAB is also a protein kinase that phosphorylates SpoIIAA, and I was the first to show that this phosphorylation leads to the inactivation of SpoIIAA. Finally, I discovered that SpoIIE, which localizes to the membrane that separates the two developing cells, is a protein phosphatase that de-phosphorylates SpoIIAA-P and that de-phosphorylated SpoIIAA liberates active σ^F from SpoIIAB-σ^F complexes. From this work, I proposed a model for the cell-type specific activation of σ^F that is based on the different topologies of the two cell types (see reference 8). I note that since my graduate work, numerous homologous regulatory systems have been discovered in other bacterial species, and where investigated, the protein components in these systems have been shown to possess regulatory activities similar to those that I first elucidated.

References

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2. Dr. David Kirk
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3. Dr. Gregory Petsko
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4. Dr. Jim Umen
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Publication List

1. **Duncan, L.**, Nishii, I., Howard, A., Kirk, D. and S.M. Miller. (submitted) Orthologs and paralogs of *regA*, a master cell-type regulatory gene in *Volvox carteri.*

2. **Duncan, L.**, Bouckaert, K., Yeh, F. and D. Kirk (2002) *kangaroo*, a mobile element from *Volvox carteri*, is a

member of a newly discovered class of retrotransposons. *Genetics* 162: 1617-1630.

3. Garsin, D.A., **Duncan, L.**, Paskowitz, D.M. and R. Losick. (1998) The kinase activity of the antisigma factor SpoIIAB is required for activation as well as inhibition of transcription factor σ^F during sporulation in *Bacillus subtilis. J. Mol. Biol.* 284: 569-578.

4. Garsin, D.A., Paskowitz, D.M., **Duncan, L.** and R. Losick. (1998) Evidence for common sites of contact between the antisigma factor SpoIIAB and its partners SpoIIAA and the developmental transcription factor σ^F in *Bacillus subtilis. J. Mol. Biol.* 284: 557-568.

5. **Duncan, L.**, Alper, S. and R. Losick. (1996) SpoIIAA governs the release of the cell-type specific transcription factor σ^F from its anti-sigma factor SpoIIAB. *J. Mol. Biol.* **260**: 147-164.

6. Alper, S., Dufour, A., Garsin, D. A., **Duncan, L.** and R. Losick. (1996) Role of adenosine nucleotides in the regulation of a stress response transcription factor in *Bacillus subtilis. J. Mol. Biol.* **260**: 165-177.

7. Arigoni, F., **Duncan, L.**, Alper, S., Losick, R. and P. Stragier. (1996) SpoIIE governs the phosphorylation state of a protein regulating transcription factor σ^F during sporulation in *Bacillus subtilis. Proc. Natl. Acad. Sci. USA* **93**: 3238-3242.

8. **Duncan, L.**, Alper, S., Arigoni, F., Losick, R. and P. Stragier. (1995) Activation of cell-specific transcription by a serine phosphatase at the site of asymmetric division. *Science* **270**: 641-644.

9. **Duncan, L.**, Alper, S. and R. Losick. (1994) Establishment of cell type specific gene transcription during sporulation in *Bacillus subtilis. Curr. Opin. Genet. Dev.* **4**: 630-636.

10. Alper, S., **Duncan, L.** and R. Losick. (1994) An adenosine nucleotide switch controlling the activity of a cell type-specific transcription factor in *B. subtilis. Cell* **77**: 195-205.

11. **Duncan, L.** and R. Losick. (1993) SpoIIAB is an anti-sigma factor that binds to and inhibits transcription by regulatory protein σ^F from *Bacillus subtilis. Proc. Natl. Acad. Sci. USA* **90**: 2325-2329.

12. **Duncan, L. R.**, Gay, L. S. and J. E. Donelson. (1991) African trypanosomes express an immunogenic protein with a repeating epitope of 24 amino acids. *Mol. Biochem. Parasitol.* **48**: 11-16.

13. Schmidt, R., Margolis, P., **Duncan, L.**, Coppolecchia, R., Moran Jr., C.P. and R. Losick. (1990) Control of developmental transcription factor σ^F by sporulation regulatory proteins SpoIIAA and SpoIIAB in *Bacillus subtilis. Proc. Natl. Acad. Sci. USA* **87**: 9221-9225.

Recent Posters

1. **Duncan, L.**, Doyle, T., Du, Q., Ehrhardt, J., Lynch, A. S., Mdluli, K. & Robertson, G. T. (2004). Construction of a Novel *Pseudomonas aeruginosa* Strain Panel Deficient in Fifty-Two Potential Drug Efflux Systems. *ICAAC Abstracts* 44, F-1532.

Grantsmanship: I recently authored a Small Business Innovative Research (SBIR) Phase I grant entitled "A novel peptide-based assay for FtsZ polymerization." This grant received a fundable score, but changes in business ownership subsequently disqualified Cumbre, Inc. as a "small business" before the grant could be activated.