MICHIGAN STATE
UNIVERSITY

10/6/03

Curt Lively
Microbial Ecology/Evolution Search
Department of Biology
Indiana University
1001 E. Third Street
Bloomington, IN 47405-3700

Dear Dr. Lively,

It is my pleasure to recommend **Gregory Velicer** for a tenure-track faculty position in your department. Greg is an outstanding young scientist. I think his idea to use a social bacterium, *Myxococcus xanthus*, to study the evolution and ecology of cell-cell interactions, has proven to be brilliant. Greg's current and proposed research will lead to important new insights about the evolution of social interactions between bacteria in the environment. His broad training, his high level of energy and creativity, and his commitment to excellence in research and teaching, make Greg a strong candidate for addition to your faculty.

Greg did his dissertation research in the laboratory of Richard Lenski here at Michigan State University. Rich is widely recognized as a leader in the use of bacteria to study evolution experimentally. Greg used bacteria that degrade and metabolize the herbicide 2,4-D as a model system to ask whether a genetic tradeoff exists between maximal growth rate and nutrient affinity. One approach involved comparing the maximal growth rate and nutrient affinity of natural isolates to look for evidence of a tradeoff. Another approach involved evolving strains that were well-adapted to growth in high 2,4-D, or low 2,4-D, then comparing the maximal growth rate and nutrient affinity of the evolved and ancestral strains under defined conditions. The short generation of bacteria allowed strains to be evolved for hundreds of generations in a fairly short time. Greg's results clearly demonstrate that the tradeoff hypothesis is incorrect, at least in its simplest form. More complex models are required to explain the evolutionary behavior that was observed. From his doctoral research, Greg has a book chapter that has been published, first-author manuscripts that appeared in *Ecology* and in *Microbial Ecology*, and a sole-author manuscript that appeared in *Applied and Environmental Microbiology*.

DEPARTMENT OF
BIOCHEMISTRY AND MOLECULAR BIOLOGY
Michigan State University
Biochemistry Building
East Lansing, MI
48824-1319
FAX: 517/353-9334

While still a graduate student, Greg was inspired by a seminar presented by Dale Kaiser to conceive the idea of using *Myxococcus xanthus* to study the evolution and ecology of social behaviors. As you may know, *M. xanthus* is a well-characterized soil bacterium that exhibits cooperative feeding, movement, and developmental behaviors. In particular, the motility and the cell-cell interactions that coordinate development have been characterized at the molecular level, so numerous biochemical and genetic approaches are available for analysis of this model organism. On his own initiative, Greg attended the Myxobacteria meeting in 1995. Shortly thereafter, he began evolving *M. xanthus* lines for maximal growth rate in liquid culture.

After finishing his Ph.D. in the Spring of 1997, Greg continued his *M. xanthus* evolution studies as a postdoc mentored jointly by Rich Lenski and I. My lab studies developmental gene regulation in *M. xanthus* and *Bacillus subtilis*. The unique proximity of groups working on bacterial evolution and *M. xanthus* attracted Greg to remain at Michigan State University for his postdoctoral studies. He wrote proposals that were funded by the Biotechnology Research Center and by the Intramural Research Grant Program here on campus to support part of his postdoctoral work.

Greg's evolution experiment in liquid culture yielded interesting results. During growth in liquid, *M. xanthus* rapidly lost social motility and the ability to develop, though the phenotypes after 1000 generations were somewhat different for 12 replicate populations. Greg gave an excellent seminar describing his results at the 1997 Myxobacteria meeting and his first paper on this topic was published in the *Proceedings of the National Academy of Science.*

Greg went on to show that some strains evolved in liquid had become developmental cheaters. The cheater strains sporulate more efficiently than wild-type cells in mixtures of the two, unless the cheater is too abundant in the initial population. Certain defined mutants defective in cell-cell signaling also exhibit cheating behavior. Greg's results were the first demonstration of cheating behavior among bacteria and were published in *Nature.*

Greg also performed a molecular analysis of his liquid-evolved lines. He showed that the loss of social motility in most of the lines is due to mutations in the *pil* locus involved in the production of pili. His results demonstrate that a tradeoff exists between maximal growth rate and pili production. In one case, he has identified a mutation in an evolved strain that appears to be responsible for the loss of social motility and can partially account for the increased growth rate of the strain. This illustrates the power of the *M. xanthus* system Greg has developed, offering the possibility to rapidly progress from experimental evolution to molecular explanations. This work was published in the *Journal of Bacteriology.*

To gain additional experience with the molecular analysis of *M. xanthus*, Greg worked on several projects related to our interest in developmental gene expression in this organism. First, he applied a diagnostic PCR technique to analyze the DNA structure of *M. xanthus* recombinants, which has greatly speeded our analysis. Second, he constructed plasmids and introduced them into *M. xanthus* to test specific hypotheses about mechanisms of gene regulation. Third, he used PCR to make mutations in a suspected promoter element and tested them *in vivo*. A manuscript resulting from this work was published in the *Journal of Bacteriology* with Greg as a co-author.

This first-hand experience with molecular biology and genetics trained Greg for truly interdisciplinary research, building on a strong foundation in experimental evolution at the population level and equipping Greg to think and perform experiments at the molecular level.

As a group leader at the Max-Planck Institute for Developmental Biology in Tubingen, Germany, Greg is building an impressive track record. He is guiding experimental evolution approaches with *M. xanthus* to study social motility, predation, and development, as well as ecological studies of natural *M. xanthus* isolates and molecular phylogenetic comparisons of key genes in different myxobacteria. Recently, Greg's lab demonstrated the evolution of a novel swarming behavior, which was published in *Nature*. His lab also published a follow-up study on cheating behavior in *Proceedings of the Royal Society, London*. As an independent scientist, Greg has authored review articles in *Trends in Micribiology* and *Antonie van Leeuwenhoek*. Also, he is receiving frequent invitations to speak at symposia and conferences. The importance of interactions between microbes in soil ecosystems is beginning to be appreciated. Greg's research is bringing fundamental insights into the evolution and ecology of cell-cell interactions.

Greg far exceeds most of his peers in terms of intellectual independence and creativity. He has tremendous breadth of scientific knowledge. He is a rigorous, clear thinker, with excellent verbal and written communication skills. There is no doubt that he will be an outstanding teacher and mentor (he is already mentoring 3 Ph.D. students). He is certainly the best postdoc I have mentored and I believe he compares favorably with the best postdocs I observed when I was a graduate student at Stanford and a Helen Hay Whitney Fellow at Harvard.

In summary, Greg is a gifted young scientist with brilliant ideas for building on his past experience and opening up rich areas of investigation. I recommend him for the faculty position in your department with utmost enthusiasm.

Sincerely,

Lee Kroos

Lee Kroos
Professor and Associate Chair
phone: 517-355-9726