CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE

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SCIENCES.TECHNOLOGIE.SANTÉ

Adaptation et pathogénie des micro-organismes
UMR 5163

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Grenoble 1

Grenoble, 19 octobre 2005

To whom it may concern

I met Jamie Bacher recently in July 2005 at the « Microbial Population Biology » Gordon Research Conference in Andover (New Hampshire). During this meeting, I presented data about the ecological and molecular mechanisms of bacterial adaptation during 20,000 generations of experimental evolution. This evolution strategy is the one set up by Richard Lenski in Michigan State University. We discovered several types of beneficial mutations, enhancing bacterial fitness. Some of them affect global regulatory networks, for example the bacterial response to nutritional stress, called the stringent response. We are now trying to understand the molecular mechanisms by which these mutations enhance organismal fitness.

Jamie Bacher suggested to me a very exciting perspective for some of the beneficial mutations, linked to his expertise. Hence, some of our mutations may affect translation rate and/or fidelity, which would be of great importance under our experimental evolution conditions. Jamie Bacher is a very enthusiastic young researcher, and we immediately decided to set up a collaboration. We already plan to exchange strains, making new constructs to check the hypothesis of a modified, enhanced translation process during 20,000 generations of evolution in *Escherichia coli*.

I am very interested in this new perspective and new collaboration with Jamie Bacher, and I offer you my strongest possible support for the applications of Dr. Jamie Bacher. Please contact me if I can provide you with any further information.

Yours Sincerely,

Prof. Dominique Schneider
Professor in Microbial Genetics

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TO WHOM IT MAY CONCERN

I confirm that I have strarted a research project in collaboration with Dr. Jamie Bacher, in the laboratory of Dr. Paul Schimmel, since the begining of this year.

The aim is to understand whether the aminoacids mis-incorporated into the proteins of an editing-defective tRNA synthetase mutant of *E.coli* (J.M.Bacher *et al.*(2005) *Proc.Natl.Acad.Sci.USA* **102**,1697-1701) trigger an increase in misfolded proteins, which would be detected and corrected by the protein quality control mechanisms mediated by chaperones, in particular HSP70 = DnaK.

An increase in misfolded proteins in Dr.J.Bacher ' s mutant should be accompanied by an increase in ribosome assembly defects, and both would be reversed by overexpression of DnaK (and/or other chaperones).

Yours Sincerely,

Jean - Hervé A L I X
Associate Professor at the University of Paris 7 - Denis Diderot

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