

November 1, 2005

Dr. Jeremy Bennett
Faculty Search Coordinator
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Dear Dr. Bennett,

Dr. Guangnan Chen has asked me to send you a letter of recommendation on his behalf. Dr. Chen spent over two years in my lab a few years ago working as a postdoctoral fellow. He was a pretty good worker. Upon instruction from me he designed appropriate experiments, prepared the required materials, and performed all procedures efficiently, independently, and effectively. He interpreted his results correctly, however he required considerable help with some interpretations. He listened to my suggestions and consulted with others to learn the details of procedures he was not familiar with. He also exploited the literature effectively in his research. I felt that his capabilities were increasing appreciably with time. He is well prepared to make additional research contributions, and I am sure he would dedicate himself to this effort. He was a pleasant person to deal with, and is eager to continue performing original research. He obviously loves experimental science, which is why he is proposing to continue his career as a research scientist. I suspect he would not have exciting research opportunities if he returned to China, and this is why he appears to prefer to continue his research in the US.

While a member of my research group Dr. Chen discovered a very exciting example of translational regulation that affects tryptophan biosynthesis in *Bacillus subtilis*. He identified a short, 10 residue coding region, *rtpLP*, in the leader region of the *rtpA-ycbK (at)* operon of this organism. He showed that this uORF regulates translation of the *rtpA* coding region - the coding region for the Anti-TRAP regulatory protein, AT. The 10 codon *rtpLP* coding region has three consecutive tryptophan codons. He found that when there are adequate levels of charged tRNA^{Trp} in the cell, translation of *rtpLP* proceeds to completion, and the *rtpA* start codon is blocked by the ribosome that just completed translation of *rtpLP*. However, when cells are deficient in charged tRNA^{Trp}, the ribosome translating *rtpLP* stalls at one of its three Trp

codons. This stalling presumably exposes the *rtpA* Shine-Dalgarno region, which allows translation initiation at the *rtpA* start codon. Thus, a ribosome reaching the *rtpLP* stop codon would mask this Shine-Dalgarno sequence, blocking translation initiation, while a translating ribosome stalled at a Trp codon, would expose the Shine-Dalgarno region allowing AT synthesis. He showed that protein AT, when present in the cell in sufficient levels, binds to the TRAP regulatory protein, inactivating it, which turns on tryptophan biosynthesis. What makes Dr. Chen's findings so interesting, is that it was already known that the *at* operon was regulated by transcription attenuation in response to the accumulation of uncharged tRNA^{Trp}. Thus he has shown that a leader peptide coding region just upstream of the *rtpA* coding region of the *at* operon is also used to translationally sense uncharged tRNA^{Trp} and regulate AT synthesis. Thus tandem transcription and translation sensing of tRNA^{Trp} is used to regulate AT synthesis. Dr. Chen's exciting studies were published in *Science* and *Molecular Cell*. The structure of the AT protein has recently been determined by others, and is in press. A subsequent postdoc in my lab continued some of Dr. Chen's studies, and all of his findings supported Dr. Chen's findings and conclusions.

With regard to his general qualification as a research scientist I do not believe his prior scientific training was sufficiently broad to allow him to quickly cope with any new scientific problem. But he is dedicated, and does listen, and will do whatever is required to make progress on a research project. He had no difficulty learning new procedures in my laboratory or in adopting approaches he was not familiar with, in his own research. Thus although I do not view him as a team leader, I do believe he can plan and perform experiments in the areas of current research he becomes familiar with.

He was a creative and productive member of my small research group. If you have any questions about him please contact me.

Sincerely,

Charles Yanofsky