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Dr. Yves Brun Systems Biology/Microbiology Faculty Search Department of Biology Indiana University ybrun@bio.indiana.edu

October 28, 2005

Dear Prof. Brun:

It is my pleasure to recommend Dr. Li-Xia Yang for a Tenure-Track Faculty Position in Systems Biology/Microbiology in the Department of Biology and Biocomplexity Institute, Indiana University. I have known Dr. Yang since she first visited Kochi Medical School in Japan as a research collaborator in 1990. I worked at Kochi Medical School from 1987 to 1994 (as a faculty member for the last two years). I am a histology expert and neuroscientist. I published a histology book. An Atlas of Histology (Springer-Verlag, 1999, New York), which has been used as a textbook for many medical schools and colleges and translated into several foreign languages for publication. I am currently a principal investigator of the Spinal Cord Society Research Center in Fort Collins, CO, focusing on the treatment of chronic spinal cord injury with various approaches including cell transplantation. I have published many research papers in the field of spinal cord injury.

Dr. Yang majored in medicine in China and further obtained the Masters Degree in Medical Science from the graduate school with an emphasis on pathology/pathophysiology. From then on she, as a principal investigator, achieved remarkable accomplishments in studying the pathogenesis of cretinism, creating the rat animal model of endemic hypothyrioidism and cretinism. She extensively studied influence of iodine deficiency on the hearing ability of rats and humans. Using both physiological and morphological methods, she illustrated, for the first time, the mechanisms of deafness in endemic cretinism. Dr. Yang has substantially helped to pave the way for the further efforts to prevent and combat iodine-deficient disease and brain retardation diseases. Because of her outstanding achievement in research on endemic cretinism she was invited as a Cooperative Researcher to Kochi Medical School in Japan for study in developmental retardation of brain supported by Japanese government.

While in the graduate school for PhD in Japan, Dr. Yang made good contributions to the researches on gene regulation in the biosynthesis of steroid hormones and the hereditary diseases of steroid hormone deficiencies. Her achievements have provided immediate genetic evidence that the point mutation in P45011b gene completely abolishes the hydroxylase activity and causes the classic steroid 11b-hydroxylase deficiency in human. Her findings elucidate the molecular mechanisms of this hereditary disease and prove to be immensely potential of conducting prenatal diagnosis of the disease and developing new drugs or gene therapy to treat the disease. She also located an enhancer element in the region between -242 and -166 relative to the major cap site of the gene for human aromatase cytochrome P450 (CYP 19) and identified a nuclear factor specifically binding to the cisacting element between -2141 and -2115 of CYP 19 as NF-IL6.

During her research work in RIKEN (the largest research institute under the Japanese Ministry of Science and Technology), Dr. Yang discovered three novel isoforms of GDNF (glial cell line-derived neurotrophic factor) receptor alpha (GFRa1). Her discoveries of the soluble isoreceptors of GFRa1 provide the first in vivo evidence that GFRa1 can mediate the activation of the receptor tyrosine kinase Ret and NCAM-140 by GDNF not only in cis but also in trans to regulate the neuronal survival and neuron-target interactions in the nervous system.

As a research scientist at the National Institutes of Health in the United States, Dr. Yang has developed a new fluorescence double-labeling technique and discovered that GDNF, as a synaptotrophic modulator, regulates not only the presynaptic motor axon terminals but also the postsynaptic acetylcholine receptors insertion through the cell signal transduction and protein kinase phosphorylations. As an expert in the research field of spinal cord injury myself, I think these discoveries are great contributions to the understanding and applications of GDNF to the treatment of neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease and injuries of the nervous system.

As a faculty research scientist at the University of Pittsburgh Dr. Yang is making functional genomic study of human genetic diseases, such as diabetes, cardiovascular diseases, neurodegenerative diseases and autoimmune diseases. She also supervises the graduate students and technical staffs with her comprehensive knowledge and research experience in medical science. She has been an editorial reviewer contributing to the peer review process for the journal of NEUROSCIENCE.

I have been impressed by Dr. Yang's dedication, enthusiasm and creativity. She continuously worked harder than anyone I know on the research efforts, even on holidays. Dr. Yang is very respectful and considerate of others. Her extraordinary ability and achievements support my belief that she is a valuable scientist, performing work that will have a major impact on health welfare in this country. I strongly recommend and sincerely hope that she will be granted the opportunity to contribute her excellent research work and teaching in your department. Please feel free to contact me if you have any further questions. Sincerely yours,

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