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

September 26, 2005

Dear Prof. Yves Brun:

I am writing to apply for a Tenure-Track Faculty Position in Systems Biology/Microbiology in the Department of Biology and Biocomplexity Institute, Indiana University. I have the research program investigating the function and mechanisms of signal transduction of glia cell line-derived neurotrophic factor (GDNF) and its receptors, particularly related to the molecular mechanisms of development, gene regulation, cell differentiation and cell excitability in the nervous system, neural injury and repair, and treatment of neurodegenerative diseases. I have included my detailed Curriculum Vitae and other documents for your perusal. I was born in a teacher's family and my father was a biologist (Prof.). I am an amateur of art and sports, speaking English, Japanese as well as Chinese. I have worked and been extensively trained for medical research in the medical school in China, 8 years in Japan and 6 years in the United States. I have been a member of the Society for Neuroscience in America since 1998. I am now working in the Department of Human Genetics at the University of Pittsburgh. I would like to take a new step for my research career in your department to pursue the high-level research.

Recently I have published a full paper of GDNF effect on neuromuscular synapse as the first and the corresponding author. I especially have had many novel discoveries in the study of structure and characterization of the gene for GDNF receptor (GFRα1, a membrane glycolipid linked ligand-binding receptor component as the co-receptor of c-Ret receptor tyrosine kinase as well as the NCAM-140). I have deposited 14 items (Accession Numbers), 17,000 bp novel cDNA and genomic DNA sequences in the GenBank (I haven't released them yet). My discoveries in the novel isoforms and alternative splicing of GFRα1 are unprecedented (see SFN Abstracts), which attracted attentions of the scientists from other research institutions who research in the same field and did not get those novel results. In 1999 I wanted to come to the United States early and then changed my research project in the new labs. In fact the groups in Washington University and the Karolinska Institute in Sweden (they had different opinions in the Neuron papers in 2000 & 2001) used the artificial or putative soluble GDNF receptor GFRα1 (cut off the GPI-linker from the classical ones at the level of protein or cDNA), but only I who discovered and obtained the new gene clones for the novel

soluble GDNF receptor GFRα1 from human and mouse cDNA libraries and genomes. I have several data sets (unpublished novel research done by myself, I worked a double time everyday in Japan) and plasmids of GDNF receptors. I have concrete ideas and ready techniques to finish and publish several good papers in the first class journal (Cell or Neuron) with only a few experiments added in the near future. At first, while setting up the lab I will finish the following papers within two to three years to attract extramural research funding:

1. **Li-Xia Yang**, et al.: Detection of the Alternative Splicing of Novel Exon 1B for the Heterogeneity in 5'-Untranslated Region of Mouse GFRα-1 Gene
2. **Li-Xia Yang**, et al.: Molecular Cloning and Characterization of GFRα1 Promoter in Mouse
3. **Li-Xia Yang**, et al.: Identification of a Novel Isoreceptor of GFRα1 with an Insertion of 10 Amino Acids Derived from Alternative Spliced Exon 4A in Mouse GFRα1 Gene
4. **Li-Xia Yang**, et al.: Cloning and Identification of the Endogenous Soluble Receptors for Glia Cell Line-Derived Neurotrophic Factor, GFRα1d and GFRα1e in Mouse and Human

In addition, according to my previous study, in GFRα1 promoter that I have cloned and sequenced there are binding sites for p53, estrogen receptor and NF-IL6, etc. related with neoplastic, sexual development and neuroprotective signaling pathways in the neuro-immuno-endocrine systems interactions during development or aging. For the long term studies I can expand these research discoveries and perform multidisciplinary research with the advanced technology of imaging, molecular genetics, biochemistry and cell biology to investigate the role of neurotrophic factors and their receptors in development and adult plasticity of the nervous system, the cell signal transduction pathways of GDNF family of ligands exerting neuroprotection/regeneration against neurodegenerative diseases and neural injury.

I am energetic and good at making several experiments at once by organizing them overall. I can well apply any new technique to my research according to the necessity and I also like to make some modifications for it. I have the strong background & broad expertise in molecular biology/genetics, biochemistry, cell biology, neurobiology as well as developmental biology. In addition I am a pathologist originally with a lot of neuroanatomical and histochemical methods. I have studied the developmental retardation of brain and inner ear in hypothyroidism and cretinism, the regulatory mechanisms of human aromatase cytochrome P450 gene expression, molecular genetic analysis of steroid 11β//c18-hydroxylase (cytochrome P450s) deficiencies in humans and functional genomic studies of human genetic diseases, the regulation of insulin on lipoprotein lipase gene

expression and DNA–protein interactions. I have much experience in molecular cloning, DNA mutagenesis, analysis and characterization of gene structure and regulation of gene expression, molecular imaging, the regulation of proteins by phosphorylations, the dopaminergic system, PKC, PKA, colinergic receptors, receptor-ligand coupling mechanisms and the signaling transduction. I have the capability of inter-disciplinary research which is very important to the success of a lab and certainly complement the research interests of your department. I will make high-level creative research to get new discoveries in cellular and molecular biology and genetics.

I am good at supervising graduate students and technicians with my lots of ideas and hands-on techniques. I have experience in teaching pathology to the medical students and I can teach molecular and cell biology here.

Please do not hesitate to contact me if you have any questions concerning the information I have sent you and thanks for your consideration in advance.

Sincerely yours,

Li-Xia Yang, MD/PhD
Department of Human Genetics
University of Pittsburgh

CURRICULUM VITAE

Name: Li-Xia Yang **Birth Place:** Mudanjiang City, China
Citizenship: China; Resident of US, Green Card pending with approved Employment Authorization.

Present Address:

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Education and Research Experience:

1977—July 1982:

Passed the strict national entrance examinations, entered Jiamusi University School of Medicine

(former Jiamusi Medical College), majored in Medicine with 30 courses and practices, graduated with the **Medical Degree** (No. **77118**) and Qualified Medical Doctor, China.

Aug. 1982—July 1984:

Promoted as faculty **Assistant Professor** by the professors committee of Alma Mater through many strict examinations including oral presentation as Teacher in Medicine. Teaching/Research and pathological diagnosis in the Dept. of Pathology, Jiamusi University School of Medicine, China.

Aug. 1984—July 1987:

Assistant Professor with graduate study in **Pathology/Pathophysiology**. Passed the national entrance examinations including Advanced Immunology for Graduate School and studied in the pathogenesis of endemic cretinism, development of brain and the mechanisms of deafness in cretinism using both physiological (BSRA: Brain Stem Response Audiometry, and DANAC-7E computerized ERA system for objective hearing) and morphological (transmission and scanning electron microscopy) methods. Successfully created the animal model of endemic hypothyroidism and cretinism (internationally confirmed) and studied in the influence of iodine deficiency and hypothyroidism on the morphogenesis of brain, thyroid and inner ear synaptogenesis in rats. Graduated with the **Masters Degree of Medical Science** (No. **87002**), Jiamusi University School of Medicine, Graduate School, China.

Aug. 1987—Sep. 1991:

Lecturer of Pathology and **Principle Investigator**. Teaching/Research. Dept. of Pathology, Jiamusi University School of Medicine, China. As principle investigator with my research grants I was responsible for the research on developmental retardation of brain and inner ear and their synaptogenesis. Using the animal model of iodine-deficient rat pups born in Jixian (an area of severe iodine deficiency and 11.04% incidence of endemic cretinism) I studied the postnatal development of Corti's organ and the mechanisms of deafness in cretinism. I found that iodine deficiency led to sluggish development of the cochlear structures in the developing rats with delayed formation of the inner spiral sulcus and abnormal persistence of synaptic bodies, kinocilia and the junctional complexes. In the 60-day-old iodine-deficient rats the Corti's organ and spiral ganglion neurons were underdeveloped and accompanied by degenerative changes. The major lesion sites of cretinous deafness are found to be the peripheral sensory apparatus and the spiral ganglia neurons (the first neurons in the auditory pathways) leading to irreversible hearing dysfunction with dramatically elevated hearing threshold, increased wave I latency and slightly delayed I-IV interpeak interval. I participated in collaborative research with Kochi Medical School (a top national university in Japan) on the clinical study of endemic cretinism (our patients). The work was published in the title of "Thyroid Stimulating Hormone in The Endemic Cretinism". I became a Cooperative Researcher on the Pathological Study in Developmental Retardation of Brain supported by the Ministry of Education, Science and Culture (Monbusho) of Japan. I had given more than 300 hours lectures of pathology to the medical students (200 students/year).

Oct. 1991—Jan. 1993:

Research Scholar of Monbusho in the First Department of Pathology, Kochi Medical School, Japan. **Neuropathology and Surgical Pathology**. I passed the written and oral entrance examinations in English and entered the Graduate School of Medicine for Ph.D. in April 1992. I continued and expanded the research work in China on developmental retardation of brain and Corti's organ by

creating animal models of hydrocephalus, microcephaly, and cretinism in rats, such as "Immunological localization of glial fibrillary acidic protein and synaptophysin in the cerebellum of experimental cretinism rat" and "Number of Synapses in the Cerebellar Glomeruli of Experimental Cretinism Rat--An Electron Microscopic Analysis with Phosphotungstic Acid Stain". Completion of 30hr Radiation Safety License Course and obtained the license in July 1992, Kochi Medical School, Japan.

Feb. 1993—July 1993:

Monbusho Scholar/Graduate Student, Dept of Immunology, Kochi Med Schl., Japan. **Immunology and Cell biology**. Study in tumor immunology, cytotoxic T lymphocyte therapy of cancer and mechanisms of the cytotoxicity of CTL and macrophage to tumor cells with immuno-electronmicroscopy as well as scanning electron microscope. Study in apoptosis and the neuro-immune-endocrine networks in mice.

Aug. 1993—Sep. 1996:

Monbusho Scholar/Graduate Student and Research Fellow, Department of Medical Chemistry, Kochi Medical School, Japan. **Biochemistry and Molecular Biology/Genetics**. Study in gene regulation in the biosynthesis of steroid hormone and molecular genetic analysis of steroid 11β/c18-hydroxylase (cytochrome P450s) deficiencies in humans. Under the supervision of Prof. Yutaka Shizuta who had worked with the Nobel Prize laureate, Dr. Edwin Krebs I analyzed the gene expressions of *CYP11B1* and *CYP11B2* in human fetal organs including the brain and examined the transcriptional regulation of *CYP11B1* and *CYP11B2* in NCI H-295, the human adrenocortical carcinoma cells. I demonstrated that the classic 11β-hydroxylase deficiency is caused by a point mutation in exon 7 of the gene for $P450_{11\beta}$ (*CYP11B1*) and that the mutant protein of $P450_{11\beta}$ lacks the hydroxylase activity *in vitro* by transfecting the full-length cDNA corresponded to the *CYP11B1* of the patient into COS-7 cells and measuring steroid 11β-hydroxylase activity in the solubilized mitochondria. I 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 *cis*-acting element between 2141 and 2115 of *CYP 19* as NF-IL6 that participate in TPA-mediated transcriptional enhancement of *CYP 19* gene expression. I also worked on "CMO Deficiencies Are Caused by Mutations in The Gene *CYP11B2* Encoding Steroid 18-Hydroxylase (P-450c18)", "Cloning and Structural Characterization of the Human Endothelial Nitric-Oxide-Synthase Gene", "Genetic Variation in the Triploids of Japanese Fasciola Species and Relationships with Other Species in the Genus", and "Mitochondrial DNA Differentiation of Japanese Diploid and Triploid Paragoniums Westermani". Graduated in March 1996 with **Ph.D. in Medical Science,** Doctorate Number: HAKU-KOU **167**. I obtained job offers for a Postdoc position in the USA but failed to get the J-1 visa and abandoned that position.

Oct. 1996— Sep. 1999:

Research Fellow, Lab for Genes of Motor Systems, Institute of Physical and Chemical Research (RIKEN), Japan. **Molecular Neurobiology**. Study in the dopaminergic motor systems, neurotrophic factors, GDNF/receptor families, and study in the structure and characterization of the genes for GDNF receptor alpha 1 (GFRα1) and its homologues. I cloned the cDNA for GFRα1 from the mouse midbrain, screened out several genomic clones of the GFRα1 gene from a Lambda FIX II mouse

genomic library, and devised a PCR approach and genomic walking for locating all the exon-intron boundaries and the promoter region. By performing 5'- and 3'-RACE, studies of the genomic structure and Southern blot analysis in parallel, I clarified that the 446 bp sequence of the 5'-end cDNA designated as exon 1A is located downstream of TATA box in the promoter region, the heterogeneity in 5'-UTR is generated by alternative RNA splicing of the 263-bp exon 1B locating downstream of exon 1A, and the initiation codon ATG is located in exon 2. I obtained the cDNA clones showing that 7 kinds of transcripts exist in mouse brain encoding five isoforms of GFRα1and resulted from alternative splicing in exon 1, 4, 5 and 9 of the gene that comprises 14 exons. I have cloned out the full-length cDNAs encoding three novel isoreceptors of GFRα1 named GFRα1c, GFRα1d and GFRα1e. They are splice variants from the single gene, *GFRα1*. The cDNA encoding GFRα1c contains a 30-bp insertion in coding region, resulting in a single long open reading frame encoding a protein of 478 amino acids. The insertion of 30 bp in cDNA derives from a novel exon named exon 4A according to its upstream location of exon 4B in the genomic DNA. The novel soluble isoreceptors GFRα1d and GFRα1e consist of 425 and 420 amino acids, respectively. They have different C-terminals from the former isoforms and their stop codons are located in the novel spliced exon 9B that I newly found. I have analyzed their mRNA expression patterns in developing mouse brains, various embryo and adult mouse tissues. I have also cloned out the full-length cDNAs encoding human GFRα1d and GFRα1e consisted of 416 and 411 amino acids, respectively. I have constructed the full-length cDNA clones of the 5 isoreceptors for functional assay. By genomic walking I have obtained the 2.4 kb promoter region of this gene showing two typical TATA boxes and many other cis-elements. I have deposited 14 items (Accession Numbers), 17,000 bp novel cDNA and genomic DNA sequences in the GenBank. The novel discoveries have been published on the International Conferences, the Annual Meetings of the Society for Neuroscience in 1998 and 1999, respectively, in the US. I also worked on "Functional analyses of mammalian protein kinase C isozymes in budding yeast and mammalian fibroblasts", "Distribution of RGS4 mRNA in mouse brain shown by in situ hybridization", "Molecular Cloning and Expression Analysis of GFRα3, a Novel cDNA Related to GDNFRα and NTNRα", and "Expression analysis of GFRα3, a glial cell line-derived neurotrophic factor family receptor" in 1997 and 1998, respectively.

Oct. 1999—Dec. 2002:

Postdoctoral Research Fellow, Lab of Developmental Neurobiology, NICHD, NIH, USA. **Molecular/Cellular and Developmental Neurobiology**. Study in Hebb activity-dependent synapse elimination, synaptogenesis, synaptic plasticity and the molecular mechanisms of Autism. With an in vitro model of neuromuscular junction and the methods of eletrophysiological (twitch assay), morphological (immunocytochemistry), molecular biology and biochemistry I studied the role and molecular mechanisms of PKC theta in synaptogenesis and plasticity in neuromuscular junction using PKC-θ knockout mice, acetylcholine receptor phosphorylations by protein kinases, pre-and post-synaptic regulations by neurotrophic factors and the effects of GDNF on neuromuscular synapse. With a computerized image analysis system I have developed a new fluorescence double-labeling technique and simultaneously quantitated both the insertion of clustered AchRs into muscle surface membrane and the degradation of pre-existing AchR aggregates. Treatment of the primary nerve-muscle co-cultures with GDNF results in a prompt increase of the insertion rate at muscle surface AchR aggregates but AchR degradation is not much influenced by GDNF. Using biochemical methods of cold blocking the pre-existed AchRs with unlabeled bungarotoxin and

biotinylation/precipitation of the newly inserted membrane AchRs, I demonstrate that GDNF increases the insertion of AChRs into the surface membrane of muscle cells. Imaging and Immunocytochemical analysis show that GDNF promotes the neurites outgrowth and increases the number of synaptic buttons. My findings demonstrate that in addition to its classic functions, GDNF regulates not only the presynaptic differentiation in motor axon terminals but also the postsynaptic AchR insertion in muscles. I have also studied the molecular and cellular mechanisms of the effects of GDNF as a synaptotrophic modulator. With Western blotting, Northern blotting, RT-PCR and sequence analysis I find that both GDNF receptor subunits, Ret and GFRα-1 are expressed in skeletal muscles and motoneurons. By immunoprecipitation and Western blot I show that Src protein-tyrosine kinase binds to the AchR of skeletal muscle. GDNF treatment of the primary cultures induces Src kinase phosphorylations differentially in primary myotubes and nerve-muscle co-cultures with a time course dependence that is slower than CREB phosphorylation. These data suggest that GDNF selectively activates Ret and NCAM-140 pathways through CREB and Src to promote the insertion and stabilization of AchRs at the endplate. As an endogenous factor GDNF may play an autocrine and retrograde roles in/from muscles, an anterograde transport from motoneuron and the paracrine role from Schwann's cells at neuromuscular junction, inducing both short- and long-term synaptic changes in presynaptic inputs and postsynaptic apparatus, thereby strengthening the functional and structural connections and plasticity of neuromuscular synapses.

Dec. 2002—Jul. 2003: Intramural Research Fellow, Molecular Imaging Lab, Clinical Center, NIH, USA. **Molecular/Cellular Pathology.** Using laser capture microdissection, confocal microscopy, pathology, genomics and proteomics, etc. image guided tissue analysis to identify novel endothelial molecular targets for imaging and treatment of angiogenesis associated with cancer and autoimmune diseases. This FTE position together with others was cut off because of the Iraq War and NIH budget cut down.

Aug. 2003—Present: Faculty Research Associate. Department of Human Genetics, University of Pittsburgh, USA. **Functional genomic research** on human genetic diseases, such as diabetes, cardiovascular diseases, neurodegenerative diseases and autoimmune diseases. training/mentoring graduate students and lab technicians. In addition to setting up a platform of molecular and cellular biology for the functional genomic studies, I work on the functional analysis of a putative Insulin Response Element (IRE) located in non-coding exon 10 of the human lipoprotein lipase (LPL) gene. By competitive gel shift assay I have found that a nuclear protein binds to the putative IRE in a sequence-specific manner and the novel 5-bp deletion mutation in exon 10 can influence the affinity of this binding. Antibody supershift assay confirmed that transcription factor Elk-1 specifically binds to the putative IRE in LPL gene. I have transfected the mutant and wild type cDNA expression plasmids into human muscle cells/COS-1 cells, followed by TaqMan real-time RT-PCR to quantitatively measure the changes of LPL gene expression in response to insulin. I am also performing Western blot analysis to determine if the mutation affects LPL gene expression at the translational or post translational (phosphorylation) level.

Practical Experience and Techniques:

Pathology/Pathophysiology and Neurobiology:

Autopsy and diagnosis of surgical pathology. Study in the development of brain and the synaptogenesis in Corti's Organ and auditory cortex in rats, isolation of synaptosomal fractions. Animal surgery, dissections of different brain regions of rodents including striatum and hippocampus, obtaining the heads and whole brains from fetus of E10.5, E13 and E15 mice. Histochemistry, immunocytochemistry, immuno-electronmicroscopy, scanning and transmission electronmicroscopy including sample preparations of rodent cochlear and locating the hair cells in inner ear; electrophysiology (Brain Stem Response Audiometry and DANAC-7E computerized ERA system for objective hearing). Creating animal models of hydrocephalus, microcephaly, and cretinism in rats. Molecular and cellular study of synapse elimination and synaptic plasticity using an in vitro model of neuromuscular junction. Fluorescence-double labeling and imaging, and intensity quantitation of acetylcholine receptor aggregates and the innervations by motor neurons of mouse spinal cord, 3-Demensional reconstruction of synapses, twitch assay for synaptic efficacy.

Molecular Biology/Genetics:

Extraction and purification of DNA and RNA, genomic restriction mapping, long PCR, PCR-SSCP, Quantitative Real-time RT-PCR, Northern blot and Southern blot including semi-dry blotting, RFLP analysis, genomic Southern blot, DNA sequencing (ABI, A.L.F. sequencing and ^{32}P-sequencing) and Bioinformatics. Construction of cDNA library; Detection of alternative splicing. Molecular cloning, 3'-and 5'-RACE, Primer extension, obtaining the promoter region quickly through genomic walking and finding all the exon/intron organization and boundaries in a gene, mouse and human genomics. Site-directed mutagenesis, construction of mutant cDNA expression vector and recombinant viral vector, transfection of the gene into mammalian cells by electroporation or Lipofectamine methods and gene expression, CAT assay, luciferase assay, ribonuclease protection assay, RNA differential display, DNA Microarrays, foot-printing analysis, electrophoretic mobility shift assay, antibody supershift assay, in vitro trancription and translation, in situ hybridization, Two Hybrid Selection, Imaging Analyzer Bas-2000, Molecular Imager System GS-525 and TaqMan 7900.

Biochemistry:

Protein extraction and purification from mammalian cultures and tissues, BCA protein assay, β-galactosidase assay, ECL Western blotting and quantitation, immunoprecipitation, protein phosphorylation, Protein kinase assy. protein arrays, Living cell membrane protein biotinylation and precipitation, Assay for membrane receptor insertion and internalization; Preparations of mitochondria, nuclear, cytosol and membrane fractions; measurement of steroid hydroxylase activity with tritium-labeled reverse-phase HPLC system. Chromatin Immunoprecipitation, Transcrpition factor assay, Proteomics, Liquid Scintillation Analyzer and STORM-860.

Immunology/Cell Biology:

Cellular immunology, mammalian cell line and primary cultures including stem cells, motoneurons, muscles, glia, fibroblasts and fat cells, T lymphocytes, Aorta smooth muscle cells, COS cells and tumor cells, NCI-H295, cloning of specific cytotoxic T cell to the tumor cells, animal models of cancer, tumor immunotherapy, flow cytometry, cell-sorter-EPICS 752. Ultrastructural study of the cell-cell interactions between the cytotoxic T lymphocyte, tumor cell and macrophage. Laser capture microdissection, fluorescence and confocal microscopy, 3-Demensional imaging. Measurement of cytokine and enzyme by ELISA; Radioimmunoassay, CTL assay and TNF assay, and preparing McAb.

Awards:

1. "The Fist Prize for Research Article of Excellence" awarded by the Association for Science and Technology of Jiamusi (Influence of Iodine Deficiency on Audition of Rats), China, 1991.
2. Award for "Contributions to the Advancement of Science and Technology" in research on Endemic Cretinism, by the Education Commission of Heilongjiang Province, China, 1996.
3. "Young Investigator Award, for Recognition of Outstanding Neuropeptide Research", 22nd Annual Winter Neuropeptide Conference, Breckenridge, Colorado, USA. February 4, 2001.
4. "NIH Fellows Award for Research Excellence" In Recognition of Excellence in Biomedical Research, 2002 awarded by the National Institutes of Health, USA.

Scholarships:

1. April 1990--Mar.1992: Cooperative Researcher on the Pathological Study in Developmental Retardation of Brain supported by Grants-in-Aid for International Scientific Research # 02045029 from the Ministry of Education, Science and Culture (Monbusho) of Japan.
2. Oct. 1991--Mar.1996: Japanese Government (Monbusho) Scholarship in Medical Science.

Professional Memberships:

2005—present: American Association for the Advancement of Science (AAAS).
2003—present: American Society of Human Genetics (ASHG).
1998—present: the Society for Neuroscience (SFN of USA).
1997—1999: The Molecular Biology Society of Japan.
1994—1999: The Japanese Biochemical Society.
1990—1993: The Japanese Society of Pathology, Member ID # 006510.
1982—present: The Chinese Society of Medicine.

Professional Experience:

Aug. 1982—Dec. 1986:	Assistant Professor, Dept of Pathology, Jiamusi University School of Medicine.
Jan. 1987—Aug. 1994:	Board Certified Lecturer of Pathology and Principle Investigator, Dept of Pathology, Jiamusi Univ. School of Medicine, China.
Sep. 1994—Oct. 1996:	Board Certified Associate Professor of Pathology, Jiamusi Univ. Schl.of Medicine. Qualification Certificate #A060111979 Issued by Personnel Department of Heilongjiang Province and registered in the Ministry of Education, China.
Oct. 1996—Sep.1999:	Postdoctoral Research Fellow, Laboratory for Genes of Motor Systems, Institute of Physical and Chemical Research (RIKEN), Japan.
Oct.1999—Dec. 2002:	Postdoctoral Research Fellow, Laboratory of Developmental Neurobiology, NICHD, NIH, USA.
Dec. 2002—Jul. 2003:	Intramural Research Fellow, Molecular Imaging Lab, Clinical Center, NIH, USA.
2000—2003:	Licensed as Authorized User of Radioactive Materials at NIH (# 039246), USA.

Aug. 2003—Present: Faculty Research Associate, Department of Human Genetics, University of Pittsburgh, USA.

Other Medical and Professional Certificates:

1992: Radiation Safety License Course 30 hr and obtained the License in July 1992, Kochi Medical School, Japan.

1999: The novel nucleotide sequence data of 17000 bp deposited in the DDBJ/EMBL/GenBank nucleotide sequence databases with 14 accession numbers certified.

2000: Satisfactorily Completed the Training Program Two Hybrid Selection: Identification and Characterization of Protein-Protein Interactions.

2000: NIH Radiation Safety Course for Authorized Users.

2000: Completion of the Short Course for DNA Microarrays: The New Frontier in Gene Discovery and Gene Expression Analysis, SFN 2000.

2000: NIH Using FileMaker Pro on the Web-Real World Examples Computer Training Program.

2001: NIH Sequence Alignment and Modeling System Computer Training Program.

2002: NIH Using Photoshop for Acquiring Scientific Images Computer Training Program.

2003—2005: At the University of Pittsburgh:

Completion of the Environmental Health and Safety Training, Bloodborne Pathogens Training; Research Integrity Module, Human Subjects Research module, HIPAA Researchers Privacy Requirements Module, Conflict of Interest Module, HIPAA Physician Security Training Module and Use of Laboratory Animals in Research & Education Module, etc. associated with the Education and Certification Program in Research & Practice Fundamentals.

Manuscript Reviews for the International Publications

1. Editorial reviewer for the journal of NEUROSCIENCE

1) Research Paper NSC-04-645: "Age related changes of various markers of astrocytes in the hippocampus of senescence accelerated mouse" (Reviewer 1)

2) Research Paper NSC-05-1021: "INTERLEUKIN-18 mRNA EXPRESSION IN THE RAT PITUITARY" (Reviewer 1)

2. Scientific Judge in Neuroscience--Cellular and Molecular Study Section (20 reviewing, ranking and judgments) for the NIH Fellows Award for Research Excellence 2003 Competition.

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Published Papers:

1. **Lixia Yang** (1987): Proceedings of Research in the Deafness of Endemic Cretinism. *Journal of Jiamusi Medical College* **Suppl.**: 82-85.
2. **Lixia Yang,** Y. Yan, L. Leng, C. Guan, and J. Li (1990): Influence of Iodine Deficiency on Audition of Rats. *Chinese Journal of Endemiology* **9** (3):133-136 and the cover pages, ISSN 1000-4955.
3. Yamane, T., Moriyama, Y., F-S., **Lixia Yang,** Li , S. and Hara, H. (1991): Thyroid Stimulating Hormone in The Endemic Cretinism. *Rep. Pub. Hlth. Kochi.* **37**, 79-81.

4. Yamane, T., Moriki, T., Hiroi, M., Kubo, T., Ouchi, T., **Lixia Yang** and Hara, H. (1991): Tissue anomalies in the cerebellum in trisomy 13. *Rep. Pub. Hlth. Kochi.* **37**, 63-72.
5. Hiroi, M., Moriki, T., **Lixia Yang,** Yamane, T. and Hara, H. (1991): Effect of ethylnitrosrea on the rat cerebellum. *Medicine and Biology* **122** (5): 199-203.
6. Togo, M., Hiroi, M., Tao, F-S., **Lixia Yang** and Hara, H. (1991): Alteration of GABA receptors in mouse cerebellum after transplacental administration of methylnitrosourea. *Medicine and Biology* **122** (6): 233-236.
7. Hara, H., Kiyoku, H., Tao, F-S., **Lixia Yang** and Yamane, T. (1991): Immunohistochemical localization of glial fibrillary acidic protein and synaptophysin in the cerebellum of experimental cretinism rat. *Medicine and Biology* **122** (5): 171-174.
8. Hara, H., Kiyoku, H., Hiroi, M., Tao, F-S., **Lixia Yang** and Yamane, T. (1991): Number of Synapses in the Cerebellar Glomeruli of Experimental Cretinism Rat--An Electron Microscopic Analysis with Phosphotungstic Acid Stain. *Medicine and Biology* **123** (1): 43-45.
9. **Lixia Yang,** H. Yao and H. Hara (1992): Effects of Iodine Deficiency on the Structural Development of the Organ of Corti in Rat. *Medicine and Biology* **124** (3): 119-122.
10. H. Yao, **Lixia Yang,** Tanioka, F., Yamane, T. and Hara, H. (1992): Ultrastructural Changes of nerve fibers of the Organ of Corti in the Developing Rat on Iodine Deficient Diet. *Medicine and Biology* **125** (3): 99-102.
11. X. Zhang, **L. Yang,** Y. Zhang, H. Li, Y. Zheng, F. Tao, W. Hao, L. Tao, J. Tao, Y. Zhong, R.Jiang, and Z. Zhang (1992): Sudden Death of Coronary Artery Disease Without Clinical Symptom: A Pathological Study of 6 Cases. *Journal of Jiamusi Medical College* **15** (2): 11-13.
12. T. Agatsuma, K. Terasaki, **L. Yang,** and D. Blair (1994): Genetic Variation in the Triploids of Japanese Fasciola Species, and Relationships with Other Species in the Genus. *Journal of Helminthology* **68**, 181-186.
13. T. Agatsuma, **L. Yang,** D. Kim, and H. Yonekawa (1994): Mitochondrial DNA Differentiation of Japanese Diploid and Triploid Paragoniums Westermani. *Journal of Helminthology* **68**, 7-11.
14. Yui, Y., Miyahara, K., Sase, K., Kawamoto, T., Toda, K., Doi, Y., Ogoshi, S., Hattori, R., Aoyama, T., Yamamoto, Y., Doi, Y., Ogoshi, S., Hashimoto, K., **Li-Xia Yang,** Kawai, C., Sasayama, S., and Shizuta, Y. (**1994**): Molecular Biology of Nitric Oxide Synthase and Structure of Endothelial Nitric Oxide Synthase Gene. *Endothelium-Derived Factors and Vascular Functions.* T. Masaki, ed. Elsevier Science B.V., 21-27.
15. Miyahara, K., Kawamoto, T., Sase, K., Yui, Y., Toda, K., **Li-Xia Yang,** Hattori, R., Aoyama, T., Yamamoto, Y., Doi, Y., Ogoshi, S., Hashimoto, K., Kawai, C., Sasayama, S. and Shizuta, Y. (1994): Cloning and Structural Characterization of the Human Endothelial Nitric-Oxide-Synthase Gene. *Eur. J. Biochem.* **223**, 719-726.
16. Katsumi Toda, **Li-Xia Yang** and Yutaka Shizuta (1995): Transcriptional Regulation of the Human Aromatase Cytochrome P-450 Gene Expression in Human Placental Cells. *J. Steroid. Biochem. Molec. Biol.* **53** (1-6): 181-190.
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