

September 05, 2005

Yves Brun Systems Biology/Microbiology Faculty Search Department of Biology Indiana University Jordan Hall 142 1001 E 3rd St Bloomington, IN 47405

Reference:

Faculty Position, 73583

Dear Dr. Yves Brun:

With reference to your advertisement in Nature jobs, August 26, 2005 regarding the opening of a faculty position in the Department of System Biology/Microbiology, I would like to offer myself as a candidate.

Currently, I am working as a Senior Lecturer in Division of Science at University of Luton, UK. I am teaching courses related to biomedical and biological sciences. I am also involved in research and have been working on in vitro and in vivo models of brain injury, neuronal survival, memory impairment, programmed cell death (apoptosis) and gene therapy for about ten years.

I did my Ph.D. in 1997 from Kagawa Medical University, Japan. My Ph.D thesis was related to brain injury and long term potentiation. I then moved to USA and did my postdoctorate from Baylor College of Medicine, Houston Texas and Auburn University, Alabama. My research project at Baylor College of Medicine was to study the regulation and developmental differences of Bcl-2, Bax and Bcl-xl in kainate induced seizure in rat brain. While at Auburn University I worked on novel peptide ligands for targeted delivery to brain and immunostimulation of microglia by CpG oligoneucleotide. I then moved to UK and joined University College London (UCL). My research project at UCL was to determine the role of certain genes in axonal regeneration following brain injury, using Cre-loxP recombination system. I made the adeno-associated and lentiviral vectors expressing Cre and successfully delivered Cre recombinase to a mammalian cell line in vitro and to cells in the brain of reporter mice (paper has been published in BMC Neuroscience). Furthermore, using my viruses, I have succeeded in deleting the floxed gene in floxed mice (paper is in process). I have also shown the retrograde labelling in facial nucleus following facial nerve crush in floxed mice after the AAV-Cre and LV-Cre delivery at different time interval (paper is in process).

My training and experiences in teaching and research has helped me to develop following skills, which make me suitable for the available position.

- I have shown during my course and whilst at work the ability to plan, analyze, prioritize and solve problems effectively to complete tasks under pressure and easily able to become an active team member.
- I am motivated, coordinated, take responsibility for a team or project and work effectively in teams or independently and can adjust to different roles accordingly.
- I am self-disciplined, time keeping and deal different matter simultaneously. I have worked with many collaborators in Europe, North America, Pakistan and in Japan and have developed very good communication skills. Moreover, my publications and the presentations of research papers in the international and



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national meetings/conferences have provided me experience to communicate with a wide range of people. This has also given me confidence in my ability to speak in public and has taught me the importance of good preparation.

• Living in different countries, juggling to get scholarships and fellowships, and managing to gain a Ph.D. degree with award have involved a high level of planning, dedication and hardship. In order to make sure that my experiments, thesis writing and research articles have been on time I have had to be self-disciplined and committed.

Having wide experience in immunohistochemistry, in situ hybridization, confocal microscopy, molecular & cellular biology, cDNA cloning, cell culture and transfection techniques is advantageous and reinforces my value to the available post where I will be required to teach these techniques.

• I have willingness and ability to learn and incorporate new skills and knowledge and am flexible in approach to work.

I feel confident that I can contribute a great deal towards the teaching and research programmes in your department. I have attached my resume, research and teaching statements. I am very much looking forward to meet you to discuss your requirements in depth and my own background in more detail.

Thank you very much for your kind consideration.

Many best regards,

Sincerely yours,

Bushra Ahmed
Senior Lecturer
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University of Luton
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Statement of Research and Teaching Interests

My training in teaching and research makes me a suitable candidate to apply for the available faculty position, where I will utilize my training in teaching and research by advancing my technical knowledge and expertise. Research experiences in fields like neurology, molecular and cellular biology, gene expression, protein biochemistry, histopathology, and cell culture and receptor biochemistry also reinforces my value for the available post. These all techniques have led to remarkable advances in the understanding of the genetics and molecular pathogenesis of many diseases. Basic and clinical studies utilizing gene products as "gene therapy" are providing the means for manipulating cellular processes to alter the course of diseases regardless of whether the disease is genetic or acquired. Such studies offer great potential for therapy for many diseases.

Since 1994, I have been working on in vitro and in vivo models of gene therapy, brain injury, neuronal survival, memory impairment and programmed cell death (apoptosis). In the Indiana University, I will design the system and develop all applications, procedures and training programs using molecular, cellular, functional and structural approaches. I am well prepared for such a challenge by my previous experiences.

My research interests are primarily focused in two areas. The first area of interest is centered on the conditional inactivation of genes using Cre recombinase system and gene therapy technology. Inactivating genes in vivo is an important technique for establishing their function in the adult nervous system. Unfortunately, conventional knockout mice suffer from several limitations including embryonic or perinatal lethality and the compensatory regulation of other genes. One approach to producing conditional inactivation of genes involves the use of Cre recombinase system in which the gene under investigation is bracketed by loxP recognition sites and activated by focal delivery of an enzyme (Cre recombinase). I have made the adeno-associated (AAV) and lentiviral (LV) vectors expressing Cre and have successfully delivered Cre recombinase to a mammalian cell line in vitro and to cells in the brain of reporter mice (see Ahmed et al., BMC Neuroscience, 2004). In addition, using my viruses, I have succeeded in deleting the floxed gene CAP-23 in CAP-23 floxed mice (paper is in process). I have also shown the retrograde labeling in facial nucleus of floxed mice following facial nerve crush after the viral delivery at different time interval (paper is in process).

The second area of my research interest is to understand the role of RNA binding protein (s) in regulation of cytoskeletal genes in brain. RNA binding proteins play an important role in developmental control of several neural gene expression. The stability of mRNA, its transport, localization and translation in the cytoplasm is an essential mechanism for regulation of gene expression. I am keenly interested in understanding the role of RNA binding protein under both normal and over expressed conditions utilizing viral vectors to transfer the gene of interest to non-dividing cells.

Currently, I am in a process of writing the grant application related to RNA binding protein and cytoskeletal genes. The main goal of this project is to define the regulatory mechanisms by which the RNA binding protein controls the expression of cytoskeletal genes. The long term goal is to characterize the cellular and molecular

mechanisms of the regulation of cytoskeletal genes by RNA binding protein. The elucidation of regulatory mechanisms by which the RNA binding proteins control the expression of cytoskeletal genes have potential application for the treatment of neurodegenrative and neurodevelopmental disorders and spinal cord injury. Furthermore, the results from this project may also provide a feasible route to study function of target genes delivered into selected regions of the brain using gene therapy approaches.

Collaboration is the key ingredient of modern research. Fortunately, I have worked with many collaborators in Europe, North America and Japan. I would like to have collaboration with appropriate laboratories in future if possible.

Teaching in the sciences is always a dynamic process. As a teacher, I try to motivate students to understand the material, present information in a clear and concise manner, determine the level of students understanding and adjust my approach as needed. It is also important to know when students have been lost in the course of explanation. The primary objective of my teaching is to provide a stimulating learning environment to the students. I promote active learning among students by giving examples to illustrate complex scientific information given to them.

Teaching is a challenging endeavour, as an instructor, one must be up to date on all the latest developments in the field. Application to current events should encourage students to understand concepts. This can be achieved by (i) using current literature in scientific journals that is based on class lecture and (ii) modifying the teaching strategy utilizing technological advancements. My goals for continuous improvement in my teaching practices are to incorporate use of multimedia including on-line, web based applications and use of computer software to enhance the learning experiences of the students.

I look forward to applying my skills, energy and enthusiasm to the challenge of the advanced teaching and research at Indiana University. I feel sure you will find my teaching and research experiences definitely applicable to your needs.