INDO SWISS JOINT RESEARCH PROGRAMME (ISJRP)

RESEARCH FELLOWSHIPS

EXCHANGE GRANT REPORT

Grant No.: RF19

Part 1 - General Information

Project Title: Cellular mechanisms of temporal lobe epilepsy: *in vitro* studies in the human brain and animal models.
Start date: 4th October 2010
Duration: 6 months

Part 2 - Exchange Participant(s) Details

VISITING SCIENTIST

**Mr. Deepak Subramanian**
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HOSTING SCIENTIST

**Dr. Ron Stoop**
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3.1 Purpose of visit

The purpose of this visit was to acquire detailed knowledge in setting up and troubleshooting an electrophysiology setup for neuronal cell recordings. Major part of the visit was focussed towards understanding the practical aspects of patch-clamping and field potential recording in a modified in vitro rodent brain preparation.

3.2 Short description of work carried out during the visit

Over 30% of patients suffering from temporal lobe epilepsy (TLE), the most common form of epilepsy, fail to respond to pharmacological interventions. Termed as “Intractable” epilepsy, the last resort for such patients is to undergo resective surgery to remove the epileptic foci, which in almost 90% of cases lies in the hippocampus and the amygdala. Extensive research on TLE focus on pathological changes in the hippocampus, while the amygdala has received less attention. Our hypothesis is that the amygdala plays a pivotal role in temporal lobe epileptogenesis and its sensitivity to electrical stimulation could render it an ideal candidate for deep brain stimulation, a procedure considered highly efficient for treating movement disorders (for e.g. Parkinson’s disease) and recently psychiatric conditions.

Prof. Stoop has done extensive research in this field and has defined a novel rat brain slice preparation which includes both the hippocampus and amygdala in a single slice, opening a new window to study interaction between these key structures during epileptogenesis. The primary aim during this fellowship was to master the technique of rodent and human brain slices preparations that include these 2 key regions. Also, emphasis was paid in understanding the functioning and troubleshooting of patch clamp recording technique, which would be crucial to
understand the complex changes underlying drug-resistance and effectiveness of DBS as a possible treatment.

The initial part of my fellowship focused on learning how to prepare the brain slices, how to identify the structures of interest and to familiarize with the functioning of the electro physiology unit (for field potential reading). Parallel to this, intricate details on artificial cerebrospinal fluid (ACSF) preparation, temperature and other conditions required to induce epileptic bursts in brain slices using Bicuculline methiodide, a GABA\textsubscript{A} antagonist, was studied.

The second half of my training focussed on patching single neurons and recording their activity by using Cell attached and Whole cell patch clamp configurations. Identification of different types of neurons based on their electrical characteristics is crucial for this study to understand differential changes occurring during epileptogenesis on different types of neurons in the amygdala. Training for processing of human brain tissue for \textit{in vitro} analysis at a single neuronal level was also obtained.

Special emphasis was given to troubleshooting field recording and patch-clamping units and highly specific parameters that have to be satisfied to obtain healthy brain slices.
3.3 Outcomes

Considering the purpose of the visit, the main objective was to learn to setup, operate and troubleshoot an electrophysiology setup and to be able to record and analyse both single neuronal activity and field potentials. This training will enable us to implement these techniques in the Neurophysiology laboratory at Christian Medical College, Vellore, where we have access to both animal and human tissue to study epileptogenesis.

3.4 Future collaboration with host institution

There is an ongoing collaborative project between my supervisor Prof. K. Srinivasa Babu and with the host scientist Prof. Ron Stoop (Indo Swiss PPP Pilot Programme, Joint Bilateral Market-Oriented R&D Projects). Considering the number of studies conducted on human brain tissue parallel to animal model of epilepsy, this collaboration is of great significance. It would also be crucial to exchange results and expertise to maximize the output. Also, more such visits would be crucial to periodically update and if necessary, alter the course of the study.

3.5 Various comments

I would like immensely thank Prof. Ron Stoop for allowing me to work in his lab and for guiding me patiently throughout the research fellowship period. It was a fantastic experience working with him and his group, where I had the opportunity to not only learn various electrophysiological techniques but also was able to interact with other laboratories through regular seminars and journal clubs. I also would like to extend my thanks to Prof. Roy Daniel (CHUV,Lausanne), Dr. Etienne Pralong (CHUV,Lausanne), Prof. Ari Chacko (CMC,Vellore) and Prof. Srinivasa Babu (CMC,Vellore) for their constant support and interesting interactions during the visit.
I sincerely thank DST and EPFL for giving us this excellent opportunity to visit new laboratories and update ourselves with recent advances in our respective fields. The six month time period was just right for learning cutting edge technology. Programs such as these are very important and would be of immense help for students like us.

3.6 Projected publications/articles resulting or to result from the exchange

The current study is of very high potential and likely to get published on reputed journals. But, since the study is at its initial stage, this would require more time for publications.