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Office of the Dean

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To Whom It May Concern:

I have sought to make basic and translational research into epilepsy a primary focus of my research. Towards this end I have sought to populate my research labs, including my previous lab that I shared with Paul Carney (MD) at the University of Florida, with bright, energetic graduate students and postdoctoral fellows that are focused on this area. I have sought extremely bright people from all fields and made it my mission to complement their training in a variety of the physical and biophysical sciences with hands on training in neuroscience and Neural engineering as it relates to epilepsy. Dr. Talathi is a prime example of the type of person we need to attract to this field in order to speed up the ongoing progress of providing innovative and effective new treatments. His background in physics as well as theoretical and computational neuroscience acquired during his graduate work at UCSD forms a strong foundation for his research.

Thus it is with pleasure that I can recommend Dr. Sachin Talathi. Sachin has been a postdoctoral fellow under both Paul Carney (University of Florida) and myself since August 2006 and is currently an Assistant Professor in the Department of Neurology at the University of Florida. In the five years that I have been working with him I have found him to be one of the most promising and hard working postdoctoral fellows that I have encountered. He has mastered very complex animal experiments while continuing to mature as a computational neuroscientist/neuroengineer. His combination of *in vivo* animal work with computational neuroscience has positioned him very well to start up his own laboratory combing both experimental and theoretical work. Currently he is working on the dynamics of the transition to seizures in animal models and humans. Over the course of this relatively new project we have accumulated and are analyzing tremendous amounts of data (over 50TB of microwire in vivo recordings, video and MRI imagery so far with much more to come) and are broadening our research to now include real time electrical stimulation for the control of seizures. As you might imagine, the skill set to be successful in developing and transitioning such techniques requires rare individuals that can be cross trained to performed animal surgery and develop animal models, program, and develop real time signal analyses, while applying a deep knowledge of neuroscience towards the understanding and ultimate mastery of epilepsy. This type of cross training has resulted recently paid off as Sachin has made a profound discovery about the evolution of the development of epilepsy in a temporal lobe epilepsy animal model. This discovery concerns quantitative measures of the dynamical course of the fine balance between neuronal excitation and inhibition that governs the physiological state of the brain. It has been hypothesized that when this balance is lost as a result of excessive excitation or reduced inhibition, pathological states such as epilepsy emerge. Decades of investigation have shown this to be true in vitro. However, *in vivo* evidence of the emerging imbalance during the latent period between the initiation of injury and the expression of the first spontaneous behavioral seizure has not been demonstrated. Sachin's work provides the first demonstration of this emerging imbalance between excitation and inhibition in vivo by employing long term, high temporal resolution, and continuous local field recordings from microelectrode arrays implanted in an animal model of limbic epilepsy. He was able to detect and track both the inhibitory and excitatory neuronal populations during the entire latent period from the time of injury to the occurrence of

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the first spontaneous epileptic seizure. During this latent period we observe a sustained increase in the firing rate of the excitatory neuronal populations, paired with a subsequent decrease in the firing rate of the inhibitory neuronal populations within the CA1 region of the hippocampus. The really surprising and completely unexpected result was that the firing rates of both excitatory and inhibitory CA1 field potentials followed a circadian like rhythm, which is locked near in-phase in controls and near anti-phase during the latent period. We think that these observed changes are implicated in the occurrence of spontaneous seizure onset following injury. Sachin's work has now opened a new path towards the control of seizures, a path that we are just now beginning to explore. Basically the control approach involves changing the phase relationship between different neuronal populations with respect to the circadian rhythm to bring the imbalance between excitation and inhibition under control. Indeed, in order to make the transition from lab to clinic faster I have been working with Sachin (along with Paul Carney) to patent and ultimately commercialize this approach.

Personally, Sachin is one of those rare individuals that are driven, self-motivated, brilliant and hard working with a willingness to become cross-trained in biology, medicine and engineering. He is starting to become known in the community and was a recent recipient of a prestigious one-year Epilepsy fellowship from the Epilepsy Foundation. This is a very competitive fellowship and he faced intense competition. I honestly think that he has the most potential, at this stage in his career, as any postdoctoral fellow or young scientist I have ever encountered over my entire career at Emory, Georgia Tech, University of Florida and at ASU. While I could go on for a while in this letter in support of his application let me just conclude by saying that Sachin receives my highest recommendation. Please do not hesitate to contact me if you need further information.

Regards,

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