Outline for Neuroscience Student Thesis Committee Progress Reports

Please use the Thesis Advisory Committee (TAC) Evaluation form, which can be found on the Sackler website. Fill out the first page prior to a meeting. Your progress report can simply be appended to the form pages rather than using the form text boxes. The following format is suggested for progress reports:

> Short introduction to the research topic (1-2 pages); this can be updated prior to each committee meeting.

> Specific Aims section listing and describing the specific aims of your research (1 page or less).

> Research Progress section describing the progress made towards each specific aim. Hypotheses should be stated. Methods and approaches should be mentioned but not described in detail. Figures (with legends) can be embedded in the text or appended at the end of the document. This section will grow in length as you complete experiments relevant for each aim (see example page below). Within this section, text describing research completed since the last committee meeting should be highlighted in some way (e.g., in italics or a different color font).

> Publications resulting from work (include those submitted or in preparation).

> Meetings attended (or which you plan to attend) during the current academic year.

> When you are close to finishing your thesis research, a timeline for completion of studies can be included in the progress report.

Progress reports ought to be emailed to committee members 1 week prior to the meeting. A short oral presentation (~30 min) should be prepared for the meeting that emphasizes progress since the last committee meeting.

Example of a “progress made” page for one specific aim (kindly provided by Ian Schmitt). This is only an example. You may choose to modify the format slightly depending on your research project. For example, you might wish to include a sentence summarizing the results shown in each figure.

Specific Aim 1: I will test the hypothesis that wakefulness increases synaptic adenosine in the hippocampus and cortex and that this increase depends on SNARE function in Astrocytes. While wakefulness-dependent changes in the level of adenosine have been measured in some brain regions using microdialysis based methods, this method has rather low temporal resolution and does not access synaptic adenosine. To overcome this problem, I will measure tonic A1 receptor-dependent inhibition at the CA3-CA1 synapse in hippocampal slices and use to quantify the level of adenosine at the synapse. I will then ask whether normal or enforced wakefulness increases synaptic adenosine and whether astrocytic dnSNARE expression prevents this increase. To obtain a corresponding measurement in vivo, I will measure the effect of pharmacological manipulation of A1 receptors receptors on slow oscillations in local field potential recordings in the intact organism during periods of high sleep pressure following normal or enforced wakefulness. The experiments for this aim are listed below:

A. Goal: Test whether normal or enforced wakefulness increases inhibition by extracellular adenosine at the Schaffer collateral synapse.

Method: I will obtain field recordings in acute slices taken at distinct time-points across the circadian period or following enforced wakefulness. To measure synaptic adenosine mediated inhibition, 200 nM 8-cyclopentyl-1,3-dimethylxanthine (CPT, an adenosine A1 receptor selective antagonist) will be applied for thirty minutes. The increase in field potential slope produced following relief of inhibition by this drug will be taken as a measure of adenosine tone: the steady-state level of synaptic adenosine acting on presynaptic, inhibitory A1 receptors.
B. Goal: Determine whether astrocytic glia mediate wakefulness-dependent changes in extracellular adenosine through a SNARE dependent mechanism.

Method: I will the adenosine tone assay described in (1) above in the dnSNARE transgenic mouse model. Measurements will be obtained from slices taken following either normal sleep or following enforced wakefulness.

Status: Complete, See Figures 2-3

C. Goal: Measure the effect of wakefulness-dependent increase in adenosine on cortical synaptic and network activity in the intact mouse.

Method: At either ZT 0, at the termination of the waking period, or ZT 4, following 4 hours of the normal sleep period, local field recordings will be obtained from WT mice under urethane anaesthesia. Mice will first undergo craniotomy surgery to allow placement of the local field potential electrode. The tungsten recording electrode will then be positioned in the somatosensory cortex, which shows robust signaling and which is responsible for the dominant components of EEG recording based markers of sleep pressure (low frequency Slow Wave Activity). Urethane will be employed to enhance slow wave activity in the cortex. Following acquisition of baseline frequency profile, CPT will be applied to the cortical surface and the resulting change will be taken as a measure of the adenosine acting on cortical synapses. This method has previously been employed in our laboratory.

Status: Essentially Complete, See Figure 3