Investigation of a Molecular Mechanism of Anesthetic Preconditioning
Amanda MacAvoy ’14, Bonnie Hawkins ’15, Emily Flynn ’14, Jamila Barger ’16 Scott D. Edmands, PhD, and Adam C. Hall, PhD
Department of Biological Sciences, Neuroscience Program, Smith College, Northampton, MA 01063

Introduction
Stroke is the third leading cause of death in the US with approximately 87% of such events being ischemic (National Stroke Association, 2010). Researchers have estimated that 8.7% of strokes occur post-operatively, with a higher incidence in patients with cardiovascular problems (Kelley, 2001). Anesthetic preconditioning (AP) is a budding preventative treatment for patients undergoing surgery that are at risk for post-operative ischemic stroke damage. AP is a phenomenon by which tissues are pre-treated with clinical concentrations of a general anesthetic, resulting in the upregulation of endogenous protective measures that can protect against subsequent more extreme insults (e.g. stroke). Our lab proposes that increases intracellular concentrations of free zinc due to anesthetic exposure causes zinc to bind to MTF-1 and translocate to the nucleus. In the nucleus, MTF-1 acts as a transcription factor and upregulates the production of apothionein, which buffers divalent cations, such as zinc, and radical species (Figure 1).

Methods
• To confirm the translocation of MTF-1 to the nucleus in response to general anesthetics in primary neuronal cultures, immunofluorescent staining of MTF-1 was used to assess nuclear and cytoplasmic levels of MTF-1 before and after zinc (200mmol) or isoflurane (2.5%) exposure.
• Immunofluorescent staining using MTF-1 antibody and goat-antirabbit Alexafluor secondary antibody was conducted 1 and 2 hours following Zinc exposure and 2 and 6 hours following isoflurane exposure. Dapi and hoechst staining was used to stain cell nuclei.

Results
• Preliminary results have demonstrated that neurons exposed to zinc or isoflurane (Fig 5 and 6) have elevated levels of nuclear MTF-1 in comparison to control cells.

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References

Figure 1: Proposed mechanism of anesthetic preconditioning (Hall and Edmands).