

P068 Bim regulation in seizure-induced neuronal death and epilepsy
Sachiko Shinoda,^{1,2} Clara K. Schindler,¹ Robert Meller,¹
Norman K. So,³ Tomohiro Araki,^{1,2} Akitaka Yamamoto,^{1,2}
Jing-Quan Lan,¹ Waro Taki,² Roger P. Simon¹ and
David C. Henshall^{1,4}

¹Robert S. Dow Neurobiology Laboratories, Legacy Research,
Portland, OR, USA ²Department of Neurosurgery, Mie University
School of Medicine, Tsu, Mie, Japan ³Oregon Comprehensive
Epilepsy Program, Neurological Sciences Center, Portland, OR,
USA

⁴Department of Physiology, Royal College of Surgeons in
Ireland, Dublin, Ireland

Programmed (apoptotic) cell death pathways may contribute to seizure-induced neurodegeneration. While Bcl-2 family proteins regulate the initiation and progression of these pathways their significance remains poorly defined in this setting. We examined the role of the pro-apoptotic Bim pathway in experimental seizure models and hippocampal resections from patients with intractable temporal lobe epilepsy. A short period of status epilepticus in rats that damaged the hippocampus activated the transcription factors FKHR/FKHRL-1 and induced a significant increase in expression of Bim. Blocking FKHR/FKHRL-1 dephosphorylation after seizures improved hippocampal neuronal survival *in vivo*, and Bim antisense oligonucleotides were neuroprotective against seizures *in vitro*. Analysis of hippocampi from patients with intractable epilepsy revealed that Bim levels were significantly lower than in controls and FKHR was inhibited; we were able to reproduce these results experimentally in rats by evoking multiple brief, electroshock seizures. We conclude that Bim expression may be a critical determinant of whether seizures damage the brain, and that its control may be neuroprotective in status epilepticus.