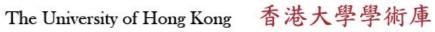
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Title	Melatonin protects against focal cerebral ischemia in rats via inhibition of ischemia-induced overproduction of nitric oxide
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#### S-NU-1

## A Cell Culture Model for Amyotrophic Lateral Sclerosis (ALS): Mutations of Human Superoxide Dismutase Gene are Induced in Neuroblastoma Exposed to Mutagen

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**Background:** Amyotrophic Lateral Sclerosis (ALS) is a fatal neuromuscular disease characterized by progressive muscle weakness resulting in paralysis with specific nerve cell death in the brain and spinal cord. 50% of ALS patients die within 18 months after diagnosis. Only 20% of patients survive 5 years. One type of ALS is familial ALS and is hereditary, which showed mutations in super oxide dismutase (SOD1) gene from patients. There is no cure for ALS now. Although a great deal of promising research is on it, the cause of this neurotransmitter problem remains a mystery.

**Method:** Human breast carcinoma, MCF7, and neuroblastoma, SH-SY5Y, cells, were treated with mutagen and total RNA was extracted. RT-PCR amplified SOD1 gene was subclone to TA cloning vector and sequenced.

**Results:** SOD1 gene mutations were induced from SH-SY5Y but not from MCF7 cells after exposing to mutagen. One mutation was as same as reported from ALS patient.

**Conclusion:** Mutations of Human SOD1 gene can be induced by mutagen and the neurobkastoma treated by mutagen can be used to study the mechanism of ALS.

### S-NU-2

# Melatonin Protects Against Focal Cerebral Ischemia in Rats via Inhibition of Ischemia-Induced Overproduction of Nitric Oxide

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**Background:** Melatonin is a neurohormone secreted from the pineal gland. Our previous results have showed that pretreatment with melatonin protected against focal cerebral ischemia in rats. The purpose of the present study was to determine whether giving melatonin after onset of ischemia is effective and to explore its neuroprotective mechanisms in rat MCAO model.

**Methods:** Adult male Sprague-Dawley rats were anaesthetized with sodium pentobarbital (60mg/kg, I.P.) to undergo reversible endovascular MCAO for 3 hours. Three days after MCAO, the rats were killed by decapitation. The brains were cut into 2-mm coronal slices for staining with 2% tetrazolium chloride to reveal the infarction. The NO concentration was measured using NO trapping reagents and electron paramagnetic resonance spectroscopy. The integrity of the blood brain barrier (BBB) was revealed by extravasation of Evans Blue.

**Results:** In single-dose study, relative infarct volumes were, in mean  $\pm$  SEM,  $27.0 \pm 4.6\%$  (7 rats) with vehicle and  $20.1 \pm 4.1\%$  (8 rats) and  $19.8 \pm 3.2\%$  (8 rats) with 5 mg/kg melatonin given at 0 and 60 min after onset of ischemia, respectively ( $P \ge 0.05$ ). In repeated-dose study, Relative infarct volumes were, in mean  $\pm$  SEM,  $31.46 \pm 5.30\%$  (10 rats) with vehicle and  $13.48 \pm 1.46$ (9 rats; P = 0.05) 23.88  $\pm 4.99$  (8 rats P = 0.05) with the first of 3 repeated Doses of melatonin (5mg/kg) given at 2 hours and 3 hours after onset of ischemia, respectively; the second and third dose melatonin given at 24 and 48 hours after onset of ischemia. The relative NO concentration was  $132.64 \pm 7.96\%$  (mean  $\pm 5.56\%$ ; 1.59%;

**Conclusion:** Treatment with repeated doses of melatonin is neuroprotective even at 2 hours after onset of ischemia. Melatonin may protect against focal cerebral ischemia via lowering the tissue NO concentration.