nuclear sequestration of HMGB1. Cisplatin treated mice were protected from liver injury after I/R (Table). Serum ALT and tissue IL-6 and TNF levels were reduced in cisplatin treated mice compared to controls. This protection was associated with increased nuclear retention of HMGB1 in hepatocytes and decreased circulating HMGB1 levels.

<table>
<thead>
<tr>
<th>Method</th>
<th>Sham-NSS</th>
<th>Sham-Cis (0.1mg/kg)</th>
<th>IR-NSS</th>
<th>IR-Cis (0.1mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortogram</td>
<td>218 ± 89</td>
<td>245 ± 100</td>
<td>2226 ± 218</td>
<td>799 ± 85*</td>
</tr>
<tr>
<td>Histology</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>

(Data are mean ± SEM, n=6 per group, * indicates p<0.05 vs NSS)

**CONCLUSIONS:** Cisplatin pretreatment is protective in a murine model of hepatic I/R. The mechanism of this protective effect appears to involve sequestration of HMGB1 within the nucleus of ischemic cells. Strategies to inhibit HMGB1-mediated inflammation using platinating agents may be protective in a variety of ischemic settings.

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**Paralysis and cell death from thoracic aortic stenting ameliorated by peroxynitrite decomposition catalyst**

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**INTRODUCTION:** Endovascular treatment of thoracic aortic pathology carries a significant paralysis risk. Our lab has previously shown that administration of INO-4885, a peroxynitrite decomposition catalyst, promotes neurological recovery in a novel animal model of thoracic aortic stenting. This study is designed to further evaluate the spinal cord salvage mechanism of this drug.

**METHODS:** Rabbits were treated with aortography, thoracic stent, or thoracic stent with administration of INO-4885 preoperatively and postoperatively. Postoperatively, each animal was scored by the Tarlov scale which rates hind-limb function on a scale from 0 (no movement) to 5 (normal hop). Histological analysis of the spinal cord was performed and viability index (viable neurons / total neurons) was calculated. Terminal transferase and biotin-16-dUTP staining (TUNEL staining) was performed to assess cell apoptosis. Data are expressed as mean ± standard error.

**RESULTS:** Ischemia time and contrast volumes were not significantly different. Both paralysis score and viability index of animals treated with stent alone were significantly lower than aortogram animals, indicative of severe neurological injury. Treatment with INO-4885 attenuated motor injury, and TUNEL staining showed a significant decrease in apoptosis compared to the stent group. Histologic exam demonstrated a lack of inflammatory cells in all groups (Table, * p < 0.05 versus aortogram, † p < 0.05 versus stent).

**METRONOMIC RAPAMYCIN IS ANTI-ANGIOGENIC IN EWING’S SARCOMA**

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**INTRODUCTION:** Low, continuous dosing (metronomic) of chemotherapeutic agents is thought to target tumor angiogenesis. Rapamycin, an immunosuppressant, has been shown to suppress tumor growth. We hypothesized that metronomic dosing of rapamycin, as compared to cytotoxic dosing, would target the endothelial cells (anti-angiogenesis) rather than the native tumor cells and result in tumor suppression.

**METHODS:** XTT of in-vitro Ewing’s sarcoma (ES) cells with rapamycin, an immunosuppressant, has been shown to suppress tumor growth. We hypothesized that metronomic dosing of rapamycin, as compared to cytotoxic dosing, would target the endothelial cells (anti-angiogenesis) rather than the native tumor cells and result in tumor suppression.

**RESULTS:** Mean tumor weights were significantly reduced in the treated groups (4.1g±0.81SEM, control; 0.9g±0.15SEM, low-dose (p<0.0001); 1.0g±0.22SEM high-dose (p=0.0002). Grossly, tumors in the low-dose group were pale and avascular when compared to the high-dose and control groups. Lectin angiography and immunostaining for endothelial cell markers (PECAM, ASMA, collagen-4) and mammalian target of rapamycin (mTOR) pathway proteins (Akt, p70s6k) and TUNEL assays were performed. Tumor weights were compared with Kruskal-Wallis analysis.

**CONCLUSIONS:** Metronomic rapamycin effectively blocks angiogenesis in ES as compared to cytotoxic dosing, which targets native