

Expansile Nanoparticles Chemotherapeutic Delivery Prolongs Survival of Human Malignant Pleural Mesothelioma in In vivo Model

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May 7, 2013, Minneapolis

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Disclosure

- None

Malignant Pleural Mesothelioma

Multimodality therapy includes surgery:

- Pleurectomy
- Extrapleural pneumonectomy

Overall survival for patients with MPM:

- Limited by a high incidence of local recurrence in the chest and/or abdomen

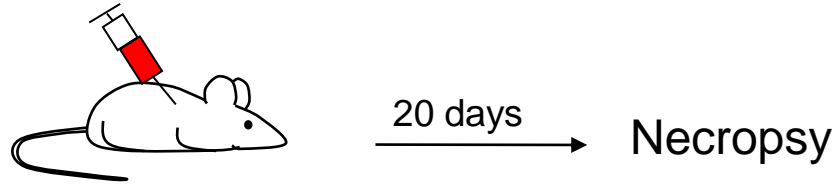
Intraoperative intracavitary hyperthermic chemotherapy

- Survival benefit in some patients
- Locoregional recurrence improved but persistent
- Risk of systemic toxicities limit dose

Goals

- Can we achieve prolonged deliver of chemotherapy in the treatment of pleural tumors?
- Can we improve the efficacy of drug delivery to pleural tumors using nanoparticles?

Human Intrathoracic Pleural Mesothelioma Xenograft Model



1×10^6 MSTO-211H-luc cells,
intrathoracic injection

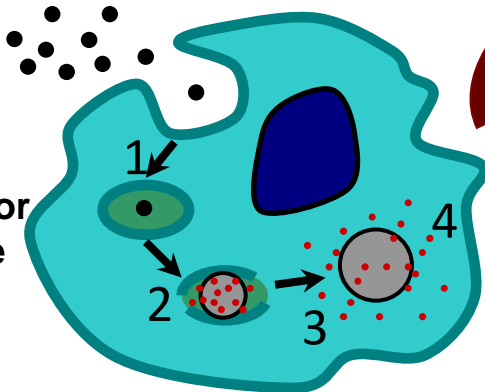


Gross disease at ~ 20 days. Mimics human disease.

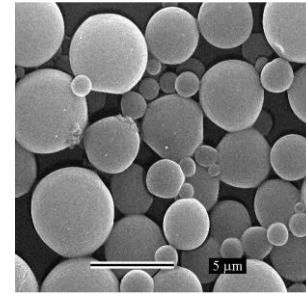
Can Nanoparticles Be Used to Treat Tumor in the Pleural Space?

Tumor affinity *in vivo*

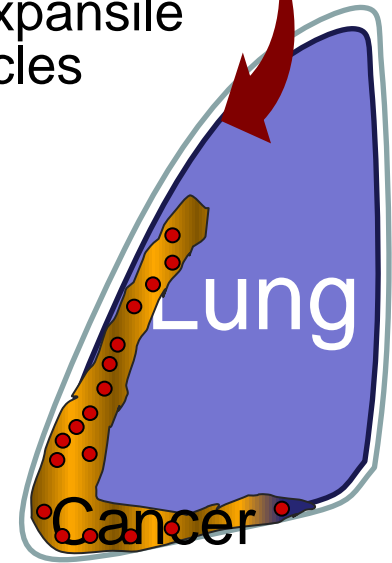
Enter tumor endosome



pH-triggered expansion and drug release



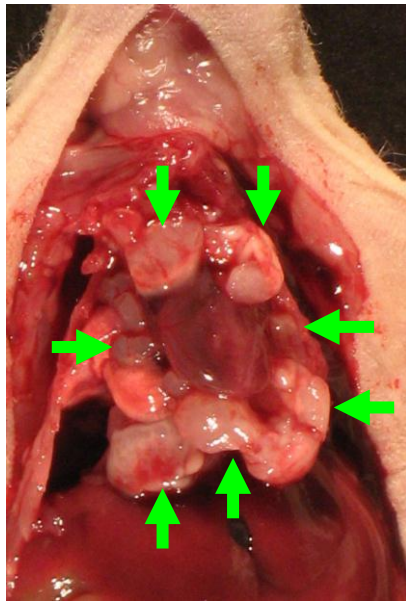
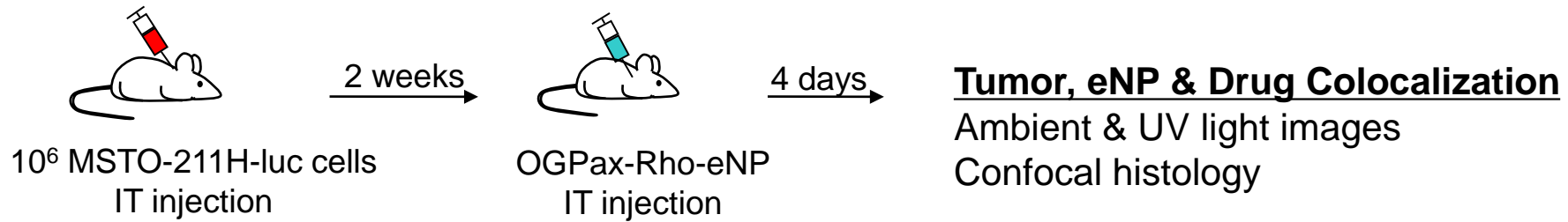
Drug-loaded expansile nanoparticles



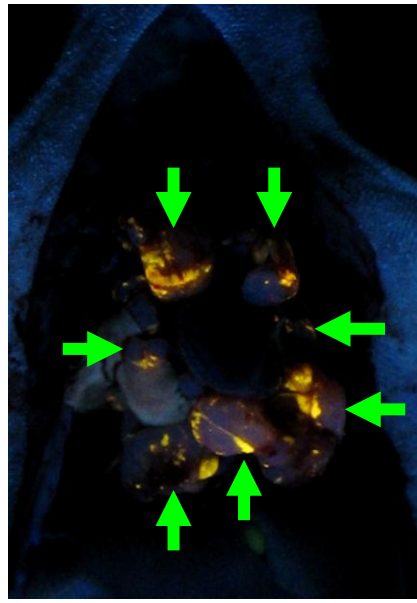
UNIQUE PROPERTIES of EXPANSILE NANOPARTICLES

- “Targeted” drug delivery to sites of tumor
- Prolonged high concentrations of local drug within tumor

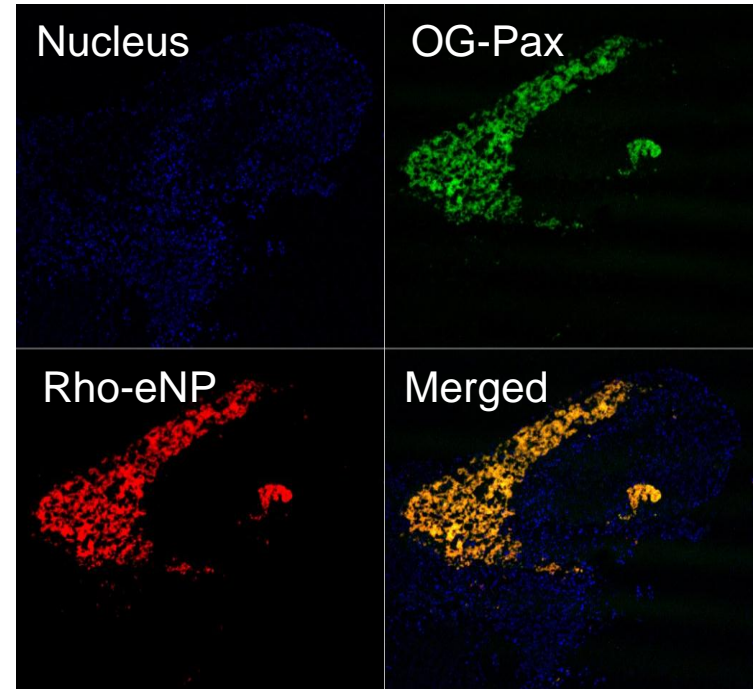
Colocalization of eNP, Drug, and Tumors



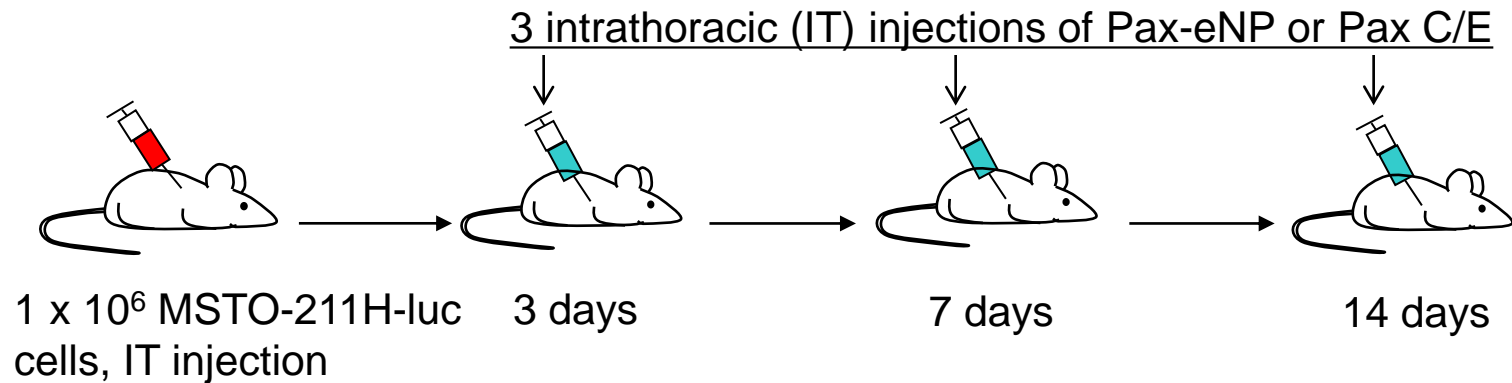
Ambient



UV

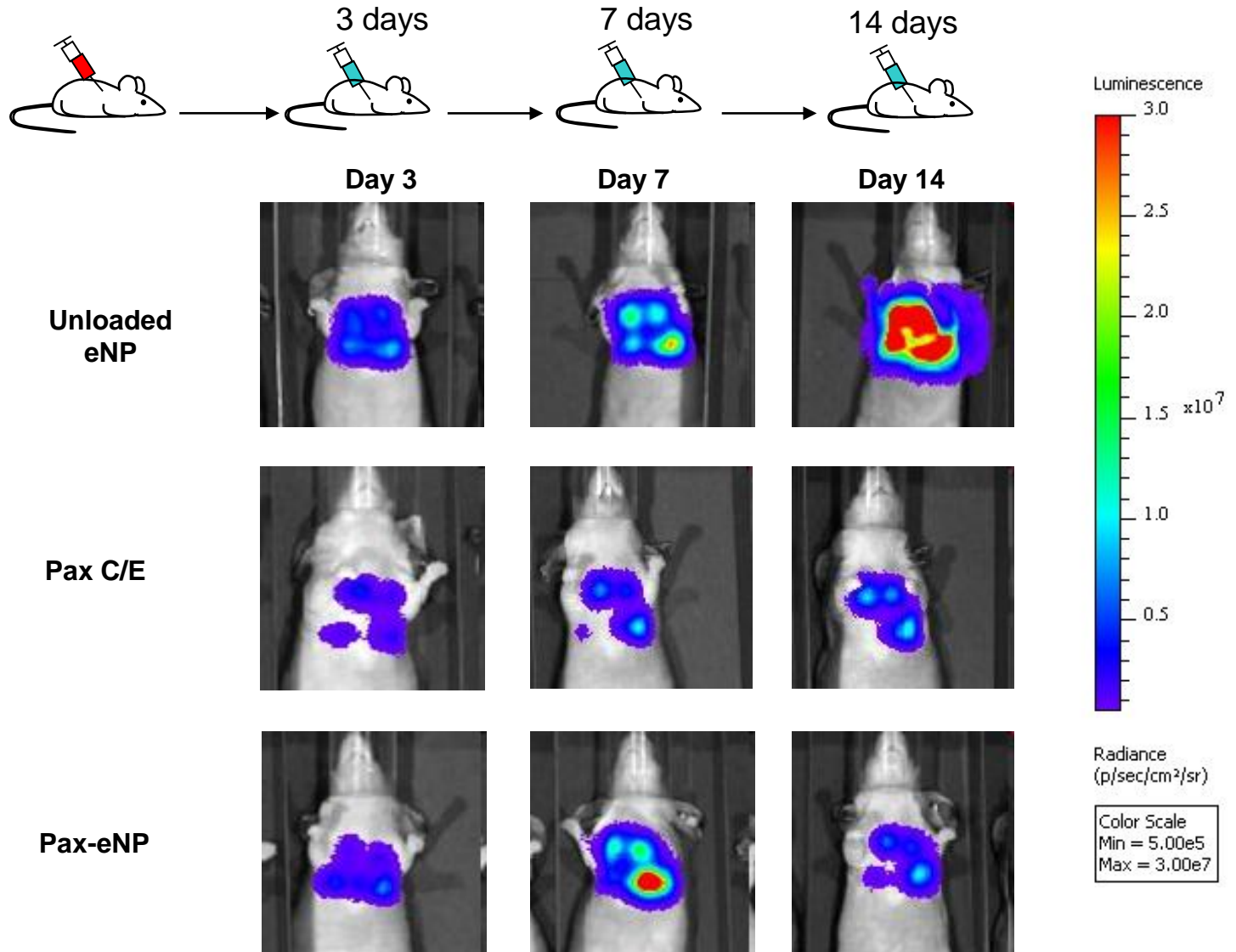


Pax-eNP vs Pax-C/E Treatment of Established IT Mesothelioma



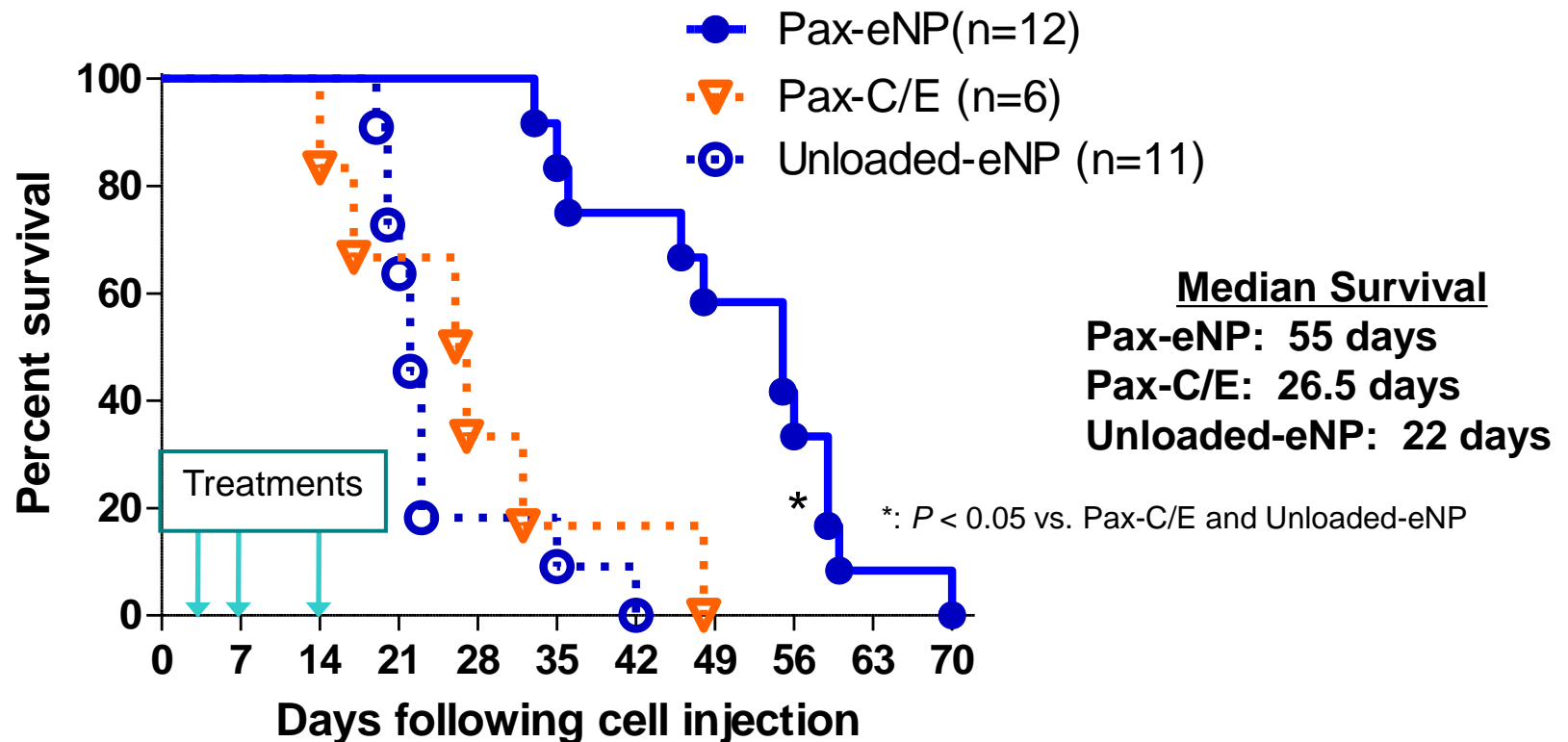
- ✓ Extent of disease and treatment response via bioluminescence
- ✓ Survival

In vivo response to Pax-eNP



As early as 14 days we see a decline in tumor burden in Pax-eNP animals

Pax-eNP Doubles Survival in Established IT Mesothelioma Model

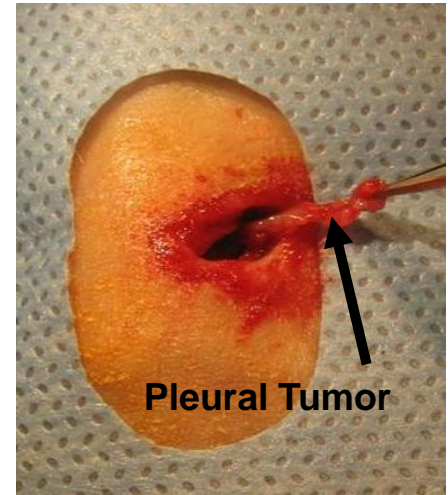


Conclusions

- A murine model of intrathoracic mesothelioma was developed in which tumor growth can be monitored using bioluminescent imaging
- Expansile NP demonstrate an *in vivo* affinity for sites of mesothelioma implants
- Intrathoracic Pax-eNP inhibits tumor growth and doubled survival in the established MPM model

Future Studies

- Assessment of treatment efficacy of eNP when used in a multimodality surgical model of intrathoracic mesothelioma
- Development of cisplatin and pemetrexed eNP delivery systems
- Study the mechanism of tumor affinity



Acknowledgements:

- Laboratories of Dr. Yolonda Colson at BWH and Dr. Mark Grinstaff at BU
- Mesothelioma Applied Research Foundation and IMP program at BWH.