STRADEFY

IMPROVED INTRAPERITONEAL DELIVERY OF CHEMO FOR PERITONEAL CARCINOMATOSIS

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IMPROVED INTRAPERITONEAL DELIVERY OF CHEMO FOR METASTATIC ABDOMINAL CANCERS

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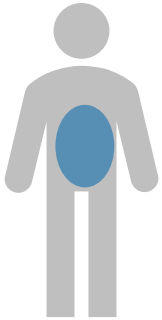
PERITONEAL CARCINOMATOSIS (PC)

Late Stage Manifestation Of GI+GYN Cancer



- Fast disease progression + poor prognosis
- **Systemic chemotherapy not effective** due to poor intraperitoneal penetrance
- Current approach uses **surgical removal** of primary tumor and **hyperthermic intraperitoneal chemotherapy**

Primary Malignancy	Incidence	Outcome
Colorectal	39.4/100K	Poor
Gastric	~10/100K	Poor
Epithelial Ovarian	~10/100K women	For stage III -> 15-20% 5-year survival
Peritoneum	0.6/100K	Median survival <2-years

IP CHEMOTHERAPY IS EFFECTIVE, BUT CURRENT METHODS ARE TOXIC AND NOT EASILY TOLERATED

IP/IV therapy improve overall survival 15.9 months
Only 42% of patients in IP/IV therapy group completed 6 cycles of therapy due to toxicity, and QoL was significantly worse
N Engl J Med 2006;354:34-43.

Effective Ovarian Cancer Treatment Is Underused, Study Finds
Denise Grady, Aug 2015

16-month survival benefit with IP/IV chemo
Between 2003 and 2012, fewer than 50% of eligible patients received this method of treatment
J Clin Oncol 2015 33:2841

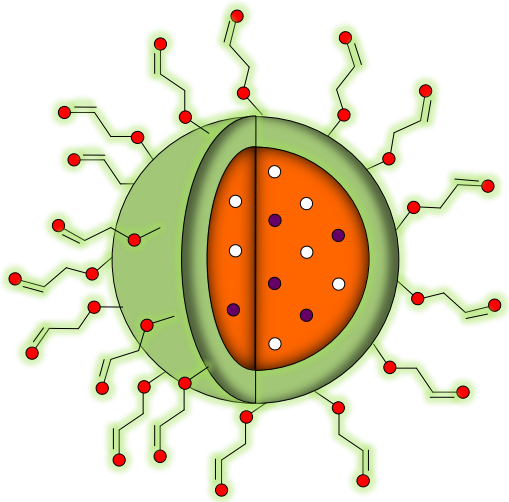
TOXICITY OF IP CHEMOTHERAPY IS A MAJOR HURDLE FOR COMPLIANCE

Optimization of Intraperitoneal Chemotherapy Administration is Needed

BIODEGRADABLE BIOADHESIVE NANOPARTICLE (BNP) DRUG-DELIVERY PLATFORM

MAJOR COMPETITIVE ADVANTAGES:

Biodegradable poly-lactic acid (PLA) encapsulation of hydrophobic bio-actives, hydrophilic hyperbranched polyglycerols (HPG) surface that permits covalent bonding to proteins:



A. **SAFER, LOCALIZED TREATMENT: non-surgical, non-XRT, alternative treatment that eliminates systemic toxicity concerns.**

B. **CONTROLLED DRUG RELEASE: tunable, local pharmacokinetics improves efficacy vs drug alone.**

C. **RETENTION IN TUMOR MATRIX: with increased uptake by tumor cells, and decrease clearance rate.**

Technology currently licensed to Nanosive for sunscreen application

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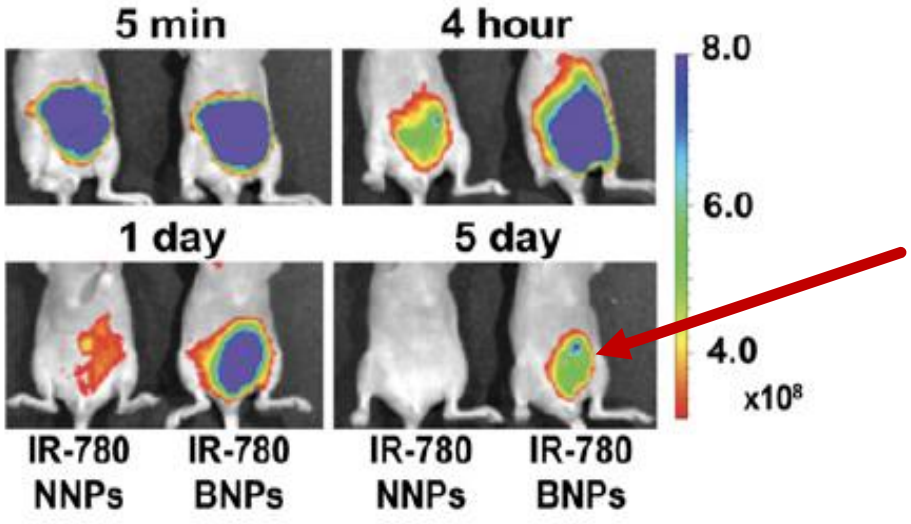
BNP RETENTION IN THE PERITONEAL SPACE

Nanoparticles were loaded with IR Imaging agents to compare NNP and BNP retention in the peritoneum



BNPS STILL VISIBLE 5 DAYS POST IP ADMINISTRATION

BNPS COULD DELIVER MORE SUSTAINED DOSE OF CHEMOTHERAPY VIA DECREASE CLEARANCE AND INCREASED UPTAKE INTO CANCER CELLS

PNAS *Improved i.p. drug delivery with bioadhesive nanoparticles* Yang Deng *et al.* Vol 113. no. 41, 11453011458

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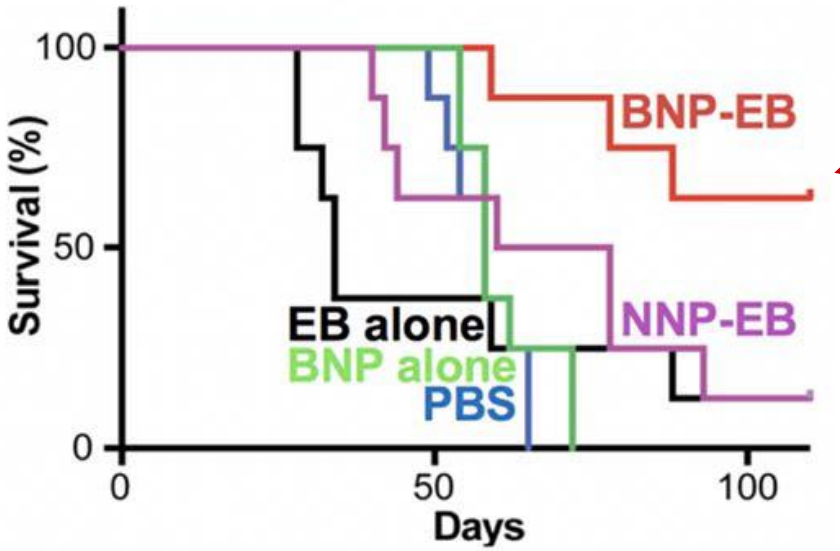
TREATMENT UTERINE SEROUS CARCINOMA MOUSE MODEL

Intraperitoneal xenograft mouse model derived from the primary USC cell line, USC-ARK-2



IP administration of BNP encapsulated epothilone B (BNP-EB) significantly improves survival

IP ADMINISTRATION OF BNP-EB ENHANCES SURVIVAL IN MICE

Improved i.p. drug delivery with bioadhesive nanoparticles Yang Deng *et al.* Vol 113. no. 41, 11453011458

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KEY VALUE INFLECTION POINTS OF THE BIOADHESIVE TECHNOLOGY

- **2016: Won YCCI ($50,000) and CBIF ($30,000) Awards**
  - Formulation development; Pilot clinical trial
- **2017: Blavatnik Development Award of $140,000**
  - Key Milestone:
    - Develop manufacturing process at CRO (Particle Science)
- **2018: Leveraged into $2.6M Melanoma Prevention Grant from NCI**

Blavatnik Success Story: Utilized Blavatnik Funds to de-risk technology attracting a €3M Series A investment from Truffle Capital to found Nanosive, a start-up employing BNPs for adhesive sunscreen and cosmetic applications

VENTURE SEED FUNDING

DEVELOPMENT OF A LOCALIZED BNP-BASED THERAPY FOR UTERINE CANCER

Goal: Utilize BNPs for retention of chemotherapy within the peritoneum to prevent metastasis

***In Vitro* SCREENING**	***2 months*** *(Yale)*	Controlled release and efficacy studies in cell lines; final selection of active(s)	**$50K**
Pilot MANUFACTURING and QA Testing	***4 months*** *(CRO: Particle Sciences)*	Adapt manufacturing processes developed from sunscreen scale-up	**$50K**
***In Vivo* Pre-clinical PK Studies**	***4 months*** *(CRO: Biomodels)*	Assessment of BNP and cargo PK, dose response. and toxicity	**$50K**
***In Vivo* Pre-clinical EFFICACY**	***4 months*** *(CRO: Biomodels)*	Models in Uterine, Colon and Ovarian Cancer	**$150K**

FUTURE DIRECTIONS

- Co-delivery of chemotherapeutic and immuno-stimulatory BNPs
- Other models (e.g. cutaneous lymphoma, glioblastoma)

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APPENDIX

PIVOTAL TRIALS FOR IP CHEMOTHERAPY – OVARIAN CANCER

Study	Control Arm	Experimental Arm	Median Survival (IP)	Median Survival (IV)	Benefit
GOG 104	Cisplatin 100 mg/m^2 IV, Cyclophosphamide 600 mg/m^2 IV, Every 3 wks, 6X	Cisplatin 100 mg/m^2 IP, Cyclophosphamide 600 mg/m^2 IV, Every 3 wks, 6X	*Overall Survival* 49 months	*Overall Survival* 41 months	**+8 months (P = 0.02)**
GOG 114	Cisplatin 75 mg/m^2 IV, Paclitaxel 135 mg/m^2 (24-h) IV, Every 3 wks, 6X	Carboplatin (AUC 9) IV, every 28 days x 2, Cisplatin 100 mg/m^2 IP, Paclitaxel 135 mg/m^2 (24-h) IV, Every 3 wks, 6X	*Overall Survival* 62 months	*Overall Survival* 53 months	**+9 months (P = 0.05)**
GOG 172	Cisplatin 75 mg/m^2 IV, paclitaxel 135 mg/m^2 (24-h) IV, Every 3 wks, 6X	Paclitaxel 135 mg/m^2 (24-h) IV, Cisplatin 100 mg/m^2 IP, Paclitaxel 60 mg/m^2 IP on day 8, Every 3 weeks, 6X	*Overall Survival* 65 months	*Overall Survival* 49 months	**+16 months (P = 0.03)**
GOG 252	Paclitaxel 80 mg/m^2 weekly IV, Carboplatin (AUC 6) IV, Bevacizumab 15 mg/kg IV, Bevacizumab every 3 weeks (maintenance)	1. Paclitaxel 80 mg/m^2 weekly IV, Carboplatin (AUC 6) IP., Bevacizumab 15 mg/kg IV, Bevacizumab every 3 weeks (maintenance) 2. Paclitaxel 135 mg/m^2 day 1 IV. (24-h); Cisplatin 75 mg/m^2 day 2 IP.; Paclitaxel 60 mg/m2 day 8 IP.; Bevacizumab 15 mg/kg IV, Bevacizumab every 3 weeks (maintenance)	*Progression Free Survival* 1. 27.3 months 2. 26.0 months	*Progression Free Survival* 24.9 months	No observed benefit