NanOlogy

January 2019

Targeted Submicron Particle Chemoimmunotherapy

- Submicron particles of pure paclitaxel or docetaxel
- Locally delivered to the site of disease
- Sustained drug release

Targeted Therapy

- High, sustained concentration of drug in the tumor
- Prolonged tumor kill
- Minimal systemic side effects

Powerful and Safe

- Increased cellular debris
- Large amounts of exposed tumor-specific antigens
- Strong immune response

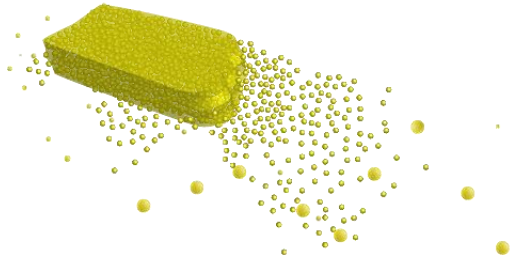
Immune Stimulation

Submicron Particles

NanoPac® or NanoDoce® Submicron Particle

- Each submicron particle of pure drug contains 2-3 billion drug molecules.
- Local delivery of large dose.
- Entrapped at the disease site.

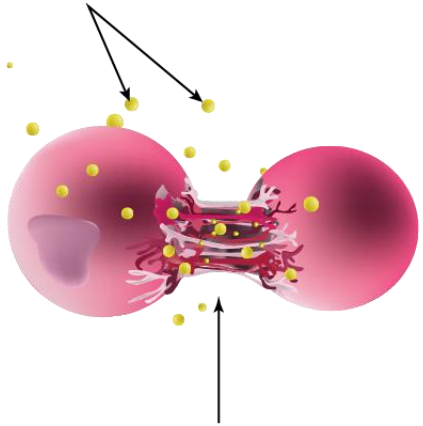
Submicron Particle Release



- Continual release of active drug over several weeks.
- Gradual clearance at subtoxic levels.
- Minimal systemic adverse effects.

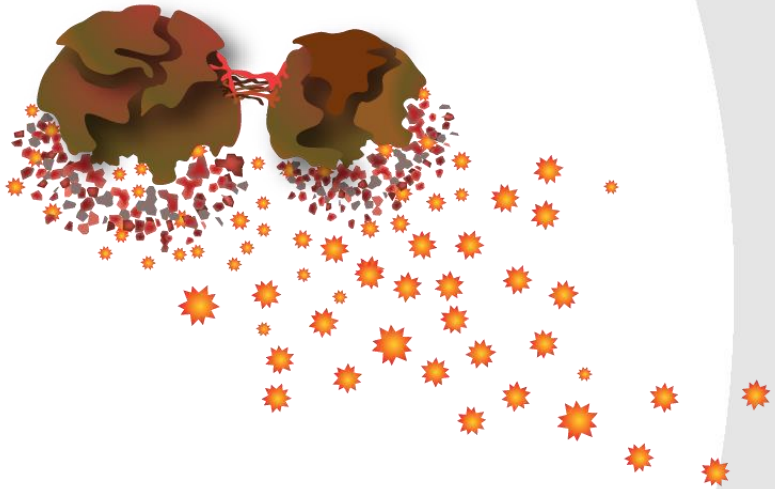
Cancer Cell Dividing

Taxanes are active against dividing cancer cells.



Taxanes stabilize microtubules which inhibits mitosis, causing cancer cell death.

Destruction of dividing cancer cells



Prolonged cancer cell death occurs within the tumor's micro-environment:

- Creating a large amount of cellular debris
- Exposing vast amounts of tumor specific antigens

Patented particles characterized by their size, surface area, density, and dissolution

Observations and hypotheses have not been evaluated by US FDA.

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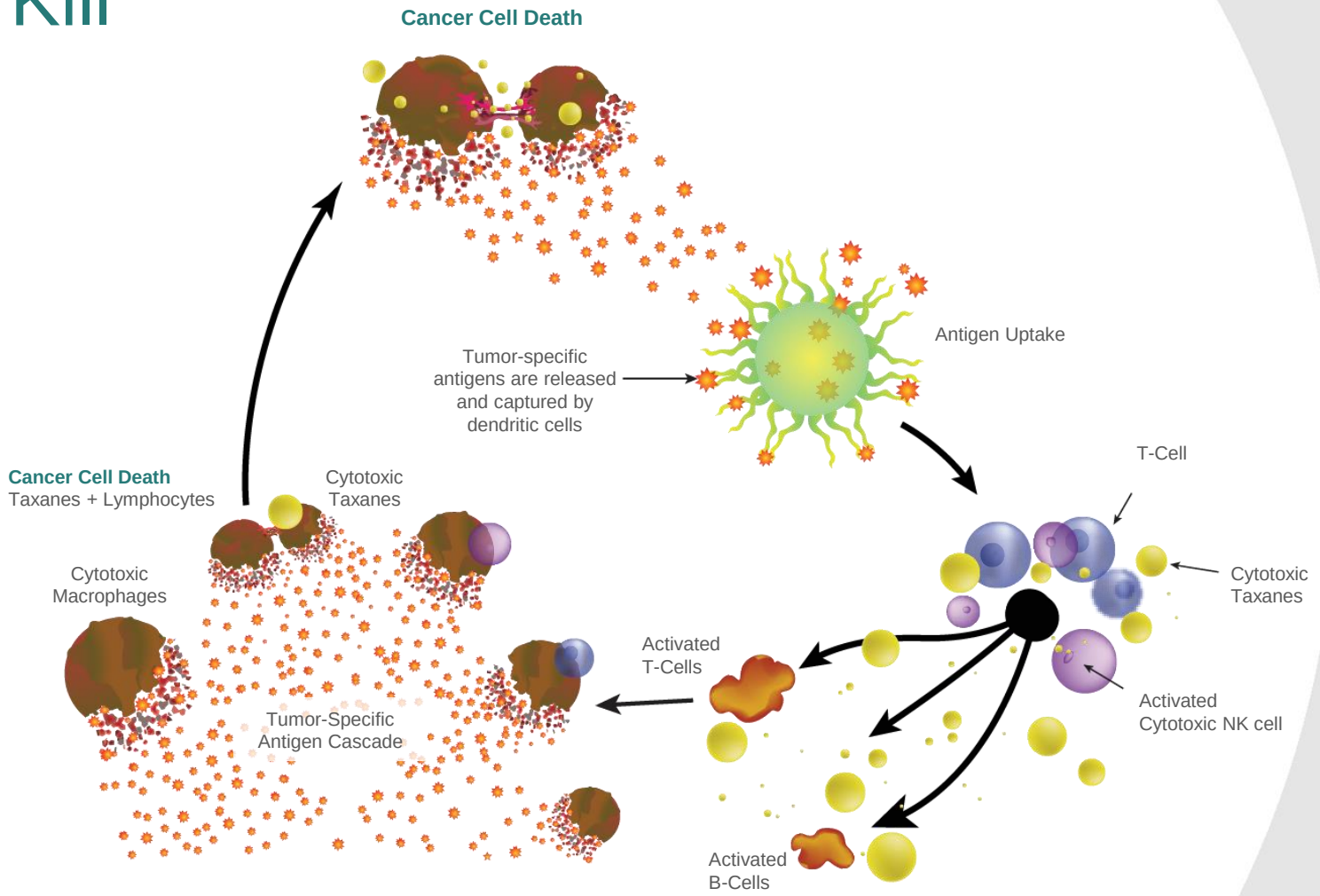
Two Modes of Tumor Kill

1. Prolonged Direct Tumor Kill
2. Immune-Mediated Tumor Kill
   - Observed sites of increased immune response
     - Lung
     - Renal
     - Bladder
     - Breast
     - Prostate
   - Immune response significantly greater than IV comparator



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Evidence of Increased Immune Response

Ideal Companion with IO Therapy

- Preclinical (versus IV comparator) and clinical IHC data
  - NSCLC
  - Bladder
  - Renal
  - Breast
  - Prostate (human single-arm clinical trial)
- Fully characterizing dual mode of action of our technology:
  - Direct tumor cell death via inhibition of cell division
  - Indirect immune-mediated cell death
- Syngeneic mouse study in process with NanoDoce® to evaluate effect on distant metastases and gain flow cytometry to quantify immune response
- Publications on IHC in progress

Dual Therapeutic Approaches

Early Stage Disease

- Treat local (non-metastatic) tumor
- Primary goals:
  - Delay or prevent disease progression, which often leads to organ removal as the only curative option
    - Examples include prostate, bladder, renal, lung, pancreas
  - Otherwise treat the tumor alone or in combination before it spreads

Late Stage Disease

- Additive to standard of care (SOC) in metastatic disease
  - IO therapy
    - Enhanced immune stimulation without adding to systemic side effects
  - Other SOC
    - Enhance effectiveness without adding to systemic side effects

NanOlogy Value Proposition

Therapeutic Potential for Both Early and Late Disease

Broad Therapeutic Applications

De-risked Regulatory Pathway

Extensive Global IP Portfolio

NanOlogy Overcomes Systemic Taxane Limitations

Weaknesses of Systemic Taxanes on the Market or in Development

- Short half life
- Tumor kill is limited to a single cell cycle requiring multiple administrations
- Only a small fraction of the administered dose reaches the disease site
- Not bioavailable at all for certain tumors
- Bone marrow suppression offsets immune response
- Severe systemic side effects additive to IO side effects

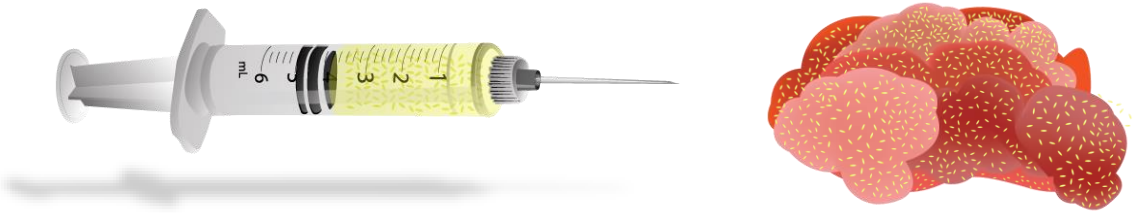
Particles versus Solution

Tumor Site

IV Paclitaxel Solution

- Paclitaxel and co-solvent in solution
- If injected into tumor, drug leaks out by simple diffusion
- Rapidly cleared in 1 to 2 days

Intratumoral NanoPac® Suspension

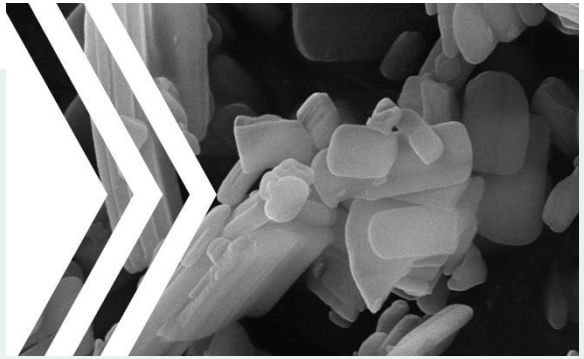


- Submicron particles of pure paclitaxel in suspension
- High, sustained dose entrapped within tumor, releasing drug at therapeutic levels over several weeks
- Gradually cleared at subtoxic levels

It would take up to 1000 times the IV paclitaxel dose to deliver one intratumoral dose of NanoPac

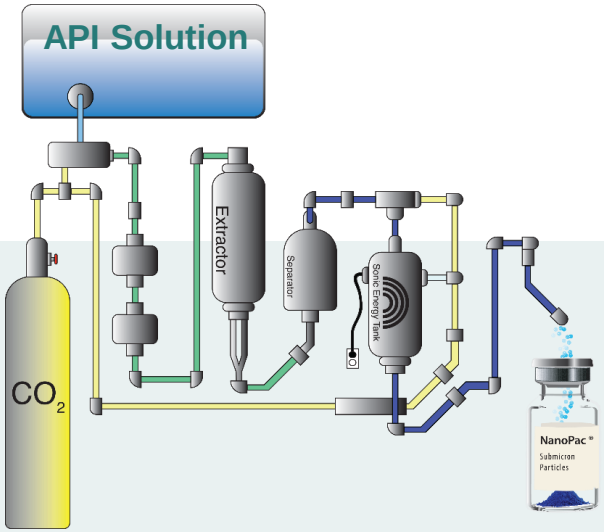
NanOlogy Submicron Particle Production Technology

API Crystals



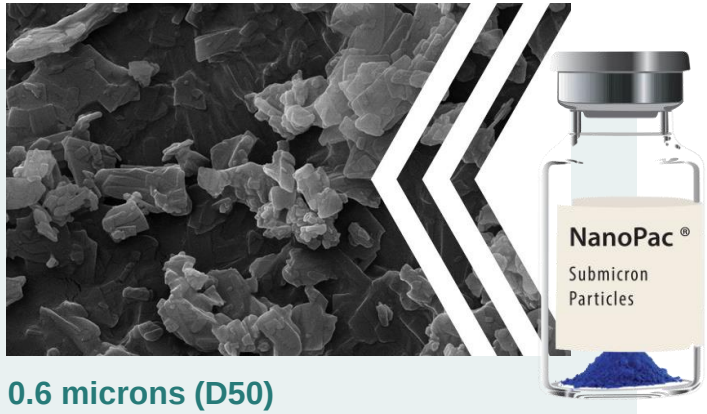
20-100 microns

- ✓ API Crystals are too large
- ✓ Cannot suspend or inject
- ✓ Insufficient drug release



- ✓ Supercritical fluid CO_2
- ✓ Sonic energy
- ✓ Imparts no static charge to particles
- ✓ Particles remain free-flowing

Submicron Particles



0.6 microns (D50)

- ✓ Can be suspended, locally delivered
- ✓ Particles entrapped at disease site, increasing residence time
- ✓ Increased particle surface area allows for sustained therapeutic API release

Products in Development

Local Injection

Nebulized Inhalation

Topical

Pipeline

Therapeutic Area	Product	Indication	Delivery	Preclinical	Phase 1	Phase 2	Phase 3
Ovarian Cancer/Peritoneal Malignancies	NanoPac® for Suspension Sterile Submicron Particle Paclitaxel	Ovarian Cancer	Intraperitoneal	→	→	→	
Gastrointestinal Oncology		Pancreatic Cancer	Intratumoral	→	→	→	
		Pancreatic Cyst	Intracystic	→	→	→	
Genitourinary		Prostate Cancer	Intratumoral	→	→	→	
	NanoDoce® for Suspension Sterile Submicron Particle Docetaxel	Renal Cancer	Intratumoral	→			
		Bladder Cancer	Direct Injection Intravesical Instillation	→	→		
Non-Small Cell Lung Cancer	NanoPac® for Nebulized Inhalation Submicron Particle Paclitaxel	Non-Small Cell Lung Cancer	Nebulized Inhalation	→			
Dermal Oncology	NanoPac® Topical (SOR007) Submicron Particle Paclitaxel Ointment	Cutaneous Metastases	Topical	→	→	→	
		Actinic Keratosis	Topical	→	→	→	

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Regulatory Strategy

Multiple pathways for expedited approval

- 505(b)(2)
  - FDA approved all programs to follow 505(b)(2) regulatory program
  - Use of published data for docetaxel and paclitaxel
  - Expedites NDA approval
  - Cost-efficient
- Breakthrough therapy designation
  - Serious condition
  - Unmet medical need
  - Intensive FDA interaction and support
  - Accelerated approval with surrogate endpoints
  - Submissions planned for prostate, pancreas, bladder, renal, lung, cutaneous metastases

Growing Global IP Portfolio
Advantages Like a New Molecular Entity

Aspect	Status
Composition of Matter	• US 9,814,685 • Expires June 2036 • 13 ROW patents pending • Covers size, surface area, dissolution, density • Forms proposed regulatory specifications
Process	64 issued or pending patents
Formulation	14 pending patents
Use/Indications	40 issued or pending patents
Therapeutic Combinations	1 pending patent
Orphan Drug Designation	1 granted (ovarian cancer)

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