Drug Loading of Nanodiamonds for Highly Efficient Drug Delivery and Disease Treatment

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Overview

Motivations
- 1/5 of patient deaths caused by breast cancer are attributed to triple-negative breast cancer, which has few treatment options.
- Administering proper drug dosages is difficult over sustained periods of time.
- A sudden influx of drugs exposes healthy cells in addition to targeted cells.

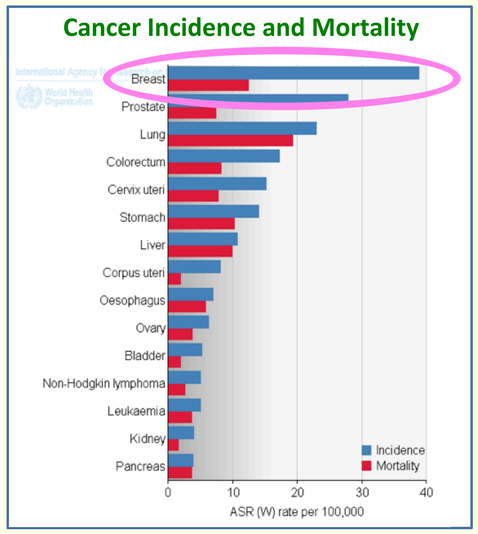
Methods
- Select drugs to reduce tumor growth and subsequent cancer proliferation.
- Nanodiamonds offer a revolutionary approach through prolonged drug release.

Results
- With nanodiamonds, drugs are slow-released to eliminate cancerous cells while minimizing impact on healthy cells.

Introduction

Breast Cancer Statistics

Cancer Incidence and Mortality



Source: GLOBOCAN project by International Agency for Research on Cancer, 2008.

Over 1 million patients diagnosed annually.

Over 450,000 deaths in year 2008.

Globally, in women
- most frequently diagnosed cancer
- most common invasive cancer
- second-most common cause of cancer deaths

Challenges

Most Types of Breast Cancer
- overexpress three key receptors:
  - estrogen receptor
  - progesterone receptor
  - Her2/neu receptor

Triple-Negative Breast Cancer (TNBC) Cells
- do not overexpress these three receptors
- do not respond to traditional receptor-targeted therapies

Methods

Drug Treatment

Targeted Inhibition by Drugs
- doxorubicin – prevents DNA replication via intercalation and biosynthesis inhibition
- mitoxantrone – disrupts DNA synthesis and DNA repair via intercalation

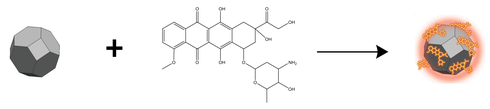
Drug Delivery Methods
- unmodified drug treatment – drugs applied directly to cell cultures *in vitro*
- drug-loaded nanodiamonds – drugs or drug combinations loaded onto nanodiamonds for later release once within cells

Drug-Loaded Nanodiamonds

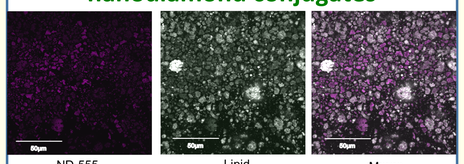
Characteristics
- individual nanodiamonds – truncated octahedrons, 2-6 nm in diameter
- aggregated clusters of nanodiamonds – 50-100 nm in diameter

Advantages
- penetrate targeted cell membranes with load for slow-release
- can functionalized to carry drugs, DNA, and other molecules
- can be coupled with fluorophores

Nanodiamond synthesis schematic

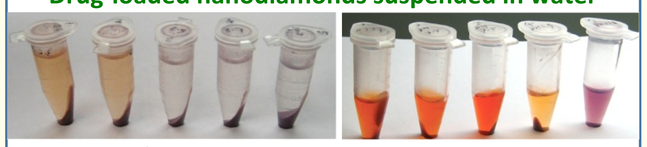


Liposomes encapsulate nanodiamond conjugates



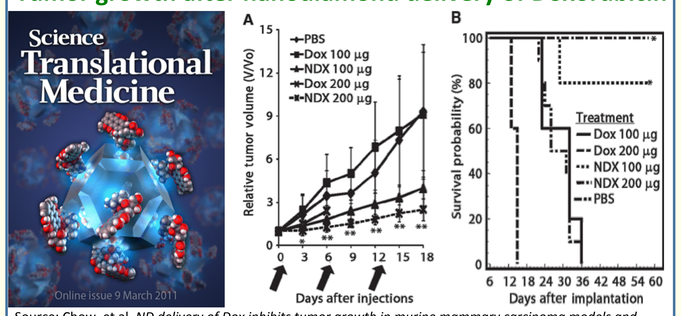
Source: Moore, et al. *Diamond-Lipid Hybrids Enhance Chemotherapeutic Tolerance and Mediate Tumor Regression*. Advanced Materials. 2013.

Drug-loaded nanodiamonds suspended in water



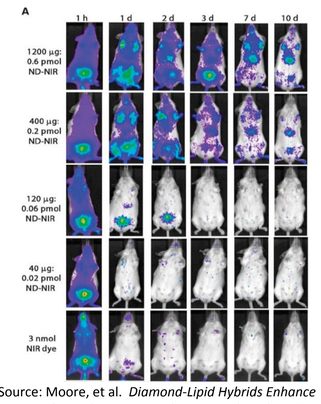
Source: *Applications of Nanodiamonds Toward Medicine*. www.n-base.org

Tumor growth after nanodiamond delivery of Doxorubicin



Source: Chow, et al. *ND delivery of Dox inhibits tumor growth in murine mammary carcinoma models and facilitates delivery of more therapeutic agent*. Science Translational Medicine. 2011.

Nanodiamonds promote retention of near-infrared fluorescence in mice, fluorophores help track nanodiamond biodistribution



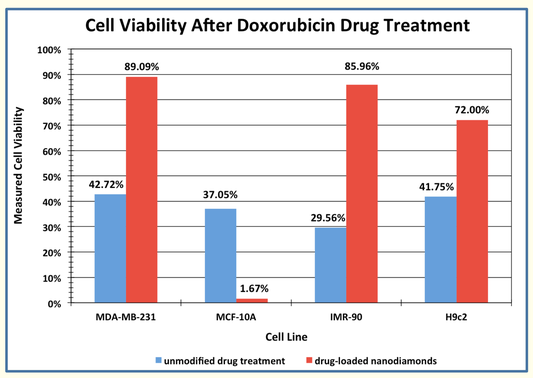
Source: Moore, et al. *Diamond-Lipid Hybrids Enhance Chemotherapeutic Tolerance and Mediate Tumor Regression*. Advanced Materials. 2013.

Results

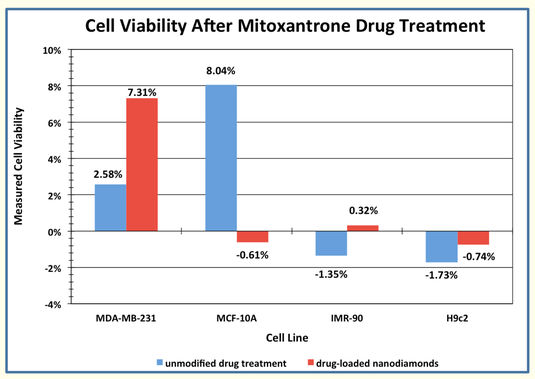
***In vitro* cell viability studies were conducted for triple-negative breast cancer and multiple control cell lines (breast, lung, heart).**

- MDA-MB-231 – TNBC cells
- MCF-10A – normal epithelial breast cells
- IMR-90 – normal lung fibroblasts
- H9c2 – normal heart mybolasts

Cell Viability After Doxorubicin Drug Treatment



Cell Viability After Mitoxantrone Drug Treatment



Discussion

Doxorubicin
- unmodified drug treatment – no significant difference in cell viability between cancerous and healthy cells
- drug-loaded nanodiamonds – slow-release of drugs in cancerous cells, equivalent healthy breast cells are killed, minimal effect on other healthy cell types

Mitoxantrone
- unmodified drug treatment – more cancerous cells are dying than equivalent healthy breast cells
- drug-loaded nanodiamonds – slow-release of drugs in cancerous cells, while all healthy cells are killed

Conclusions

Nanodiamonds revolutionize drug treatment.
- Nanodiamonds slow-release loaded drugs into cancerous cells, rather than overwhelming cells with an influx of drugs.

Drugs effectively reduce tumor growth.
- Target pathways to prevent cancer proliferation.
- Eliminate the need for receptor-targeted therapies that are ineffective for TNBC tumors.

Future Work

Broader drug search
- Treat more cancers and diseases.
- Screen large drug libraries

Advanced drug treatment
- Test drugs at different concentrations.
- Drugs at lower dosage levels can reduce the potential side effects and toxicity caused by high concentrations.

Drug efficacy measurements
- Analyze drug-induced damage through fluorescence and confocal microscopy.
- Evaluate structural morphologies over time.
- Track cell displacement and speed throughout treatment.

Incorporation into existing biochemical platforms
- Since nanodiamonds are soluble and biocompatible, they can be fluidly integrated into other biotechnologies.

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