NANOONCOLOGY:

DRUG DELIVERY IN
NEUROLOGICAL CANCERS

By Ian Kanterman
BME281

Introduction

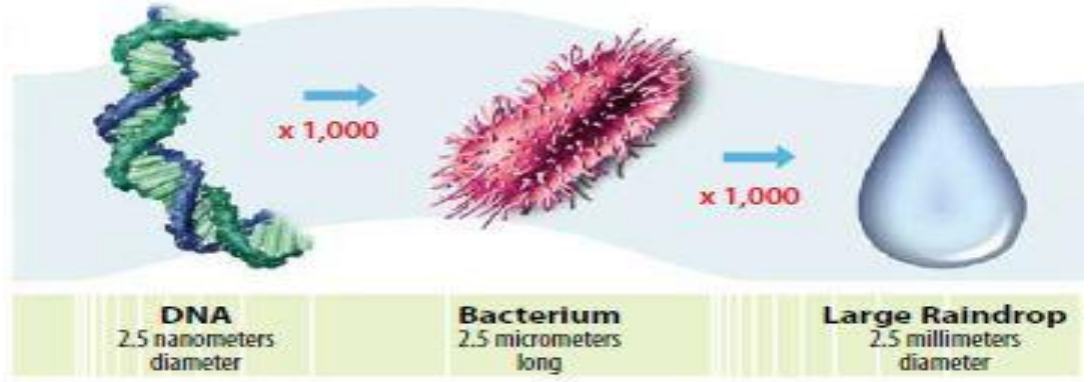
- Nanooncology is the application of Nanomedicine to cancer diagnosis and treatment.
- Has the potential to alter clinical oncology for a multitude of different cancers
- Has the ability to create novel drug delivery systems that can specifically target the tumor sites.

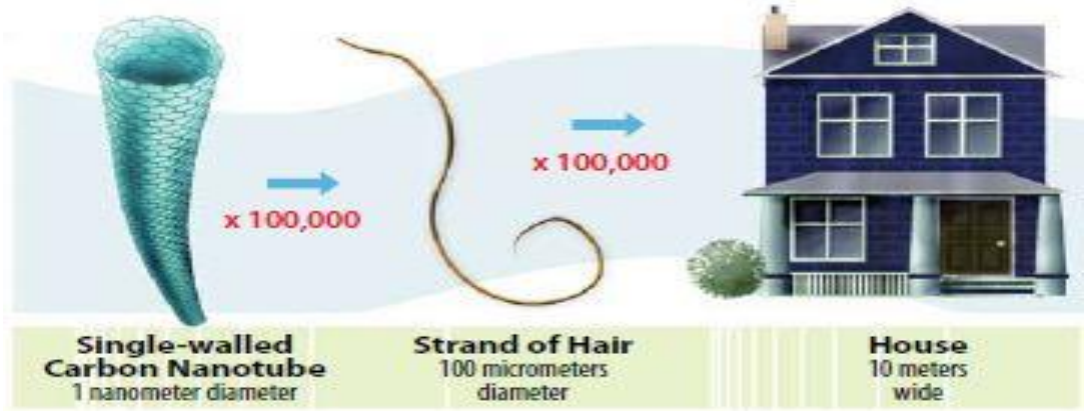
Introduction

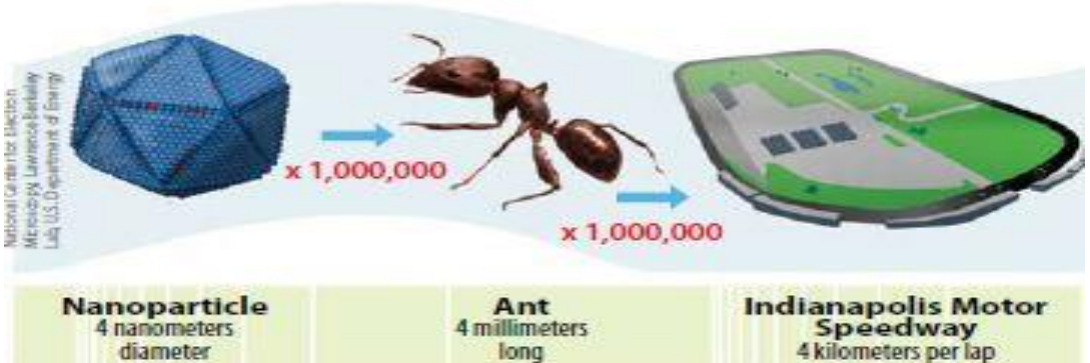
- Nanooncology/nanomedicine is a branch of nanotechnology.

- Nanotechnology is the design of small devices on the nanometer scale (nm), from 1 to 100 nm.
  - This miniscule scale allows these devices to reach places in the body that conventional treatment methods cannot.

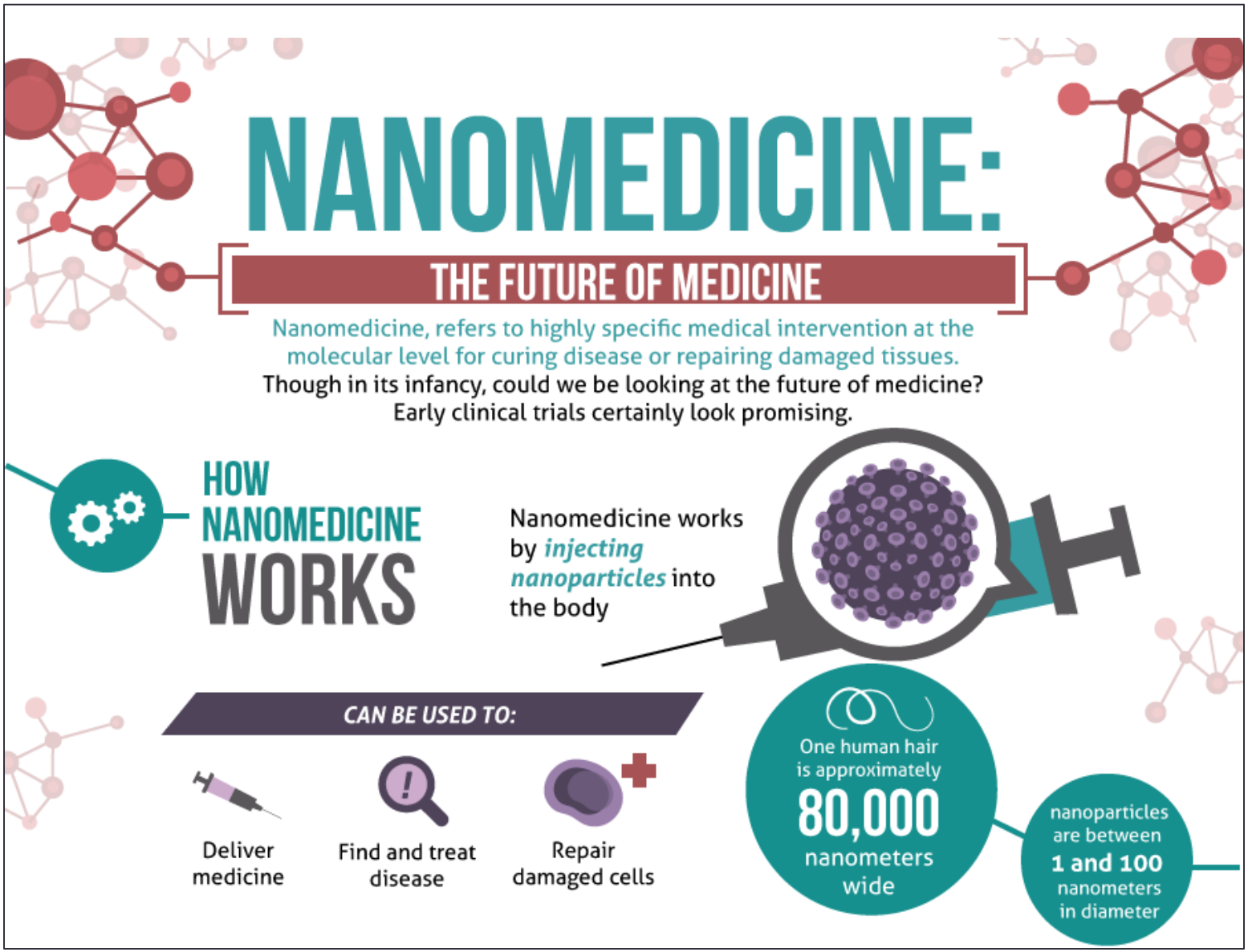
Introduction – How Small Is "nanometer"







Understanding nanomedicine



Understanding nanomedicine

APPLICATIONS OF NANOMEDICINE

Nanotechnology is already commonly used in sunscreen and to make **tennis balls more bouncy**

DRUG DELIVERY

Using nanotechnology to deliver medicine, diabetic rats kept stable blood sugar levels for 10 days after injection

CANCER DIAGNOSIS AND TREATMENT

- Using microRNA from a patient's blood plasma and nanotechnology:

Medical professionals can determine if lung cancer is present...

and begin treatment the same day

- Using Nano-Therm therapy to overheat brain cancer cells helps to destroy them:

In clinical trials, those with recurrent glioblastoma survived a median of 13 months

More than double the survival rate of those who did not receive Nano-Therm therapy

FLU TESTING

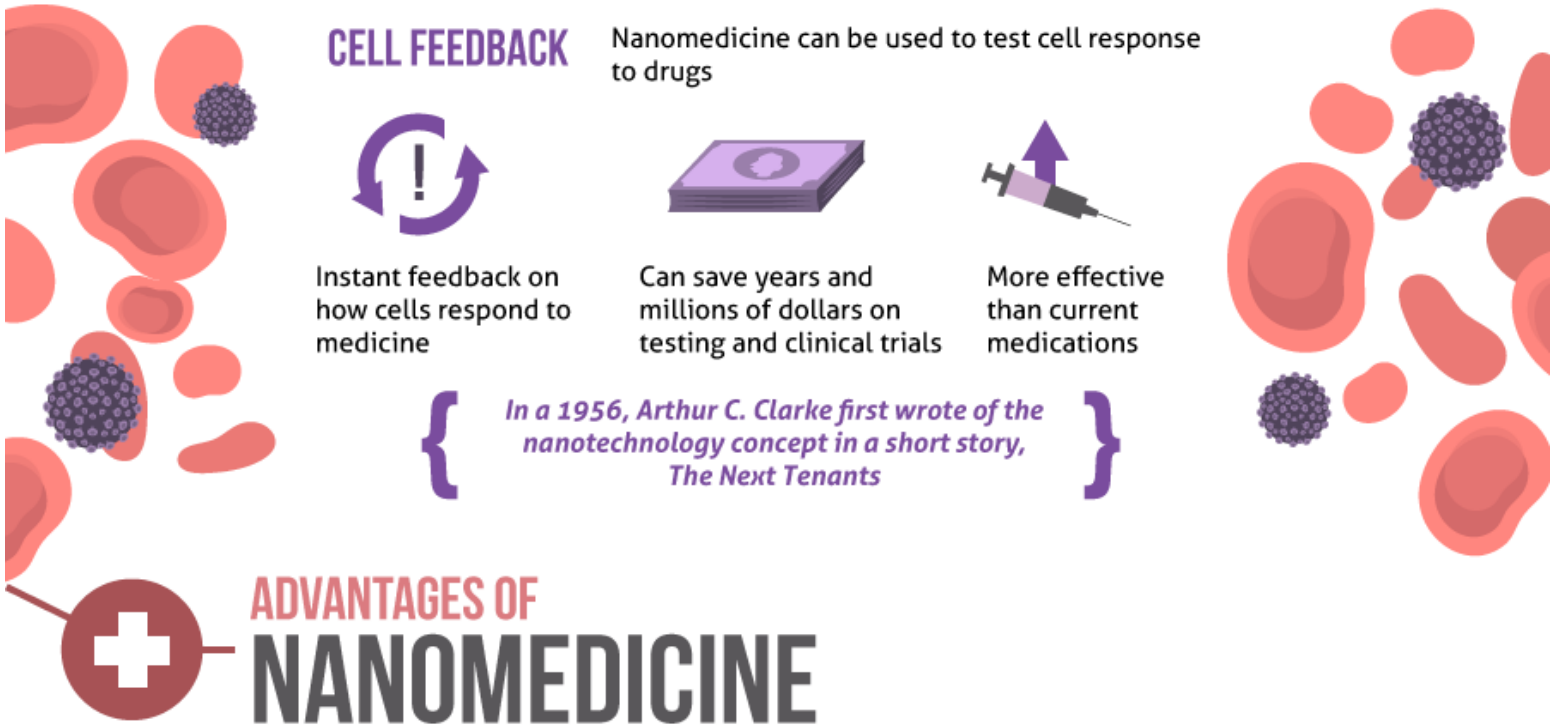
Today's flu tests are:

- ✖ Time consuming
- ✖ Inaccurate

NANOMEDICINE GOLD FLU TESTING:

- ✔ Instant results
- ✔ Immediate treatment to prevent spreading to others
- ✔ commercial nanotech testing no more than 5 years away

Understanding nanomedicine



Neurological Cancers

- Central nervous system (CNS) tumor malignancies have a high mortality and morbidity rate.
  - Five year survival rate is at around 35%.
  - An excess of 50% of patients with CNS tumors in 2013 were expected to die.
    - Median survival rate of one year.
- For example, Glioblastoma Multiforme (GBM) is a primary brain tumor and a major challenge for neurosurgery and oncology.
  - Lack of knowledge of pathophysiology of GBM.
  - Limited access of chemotherapeutic agents at the tumor site.

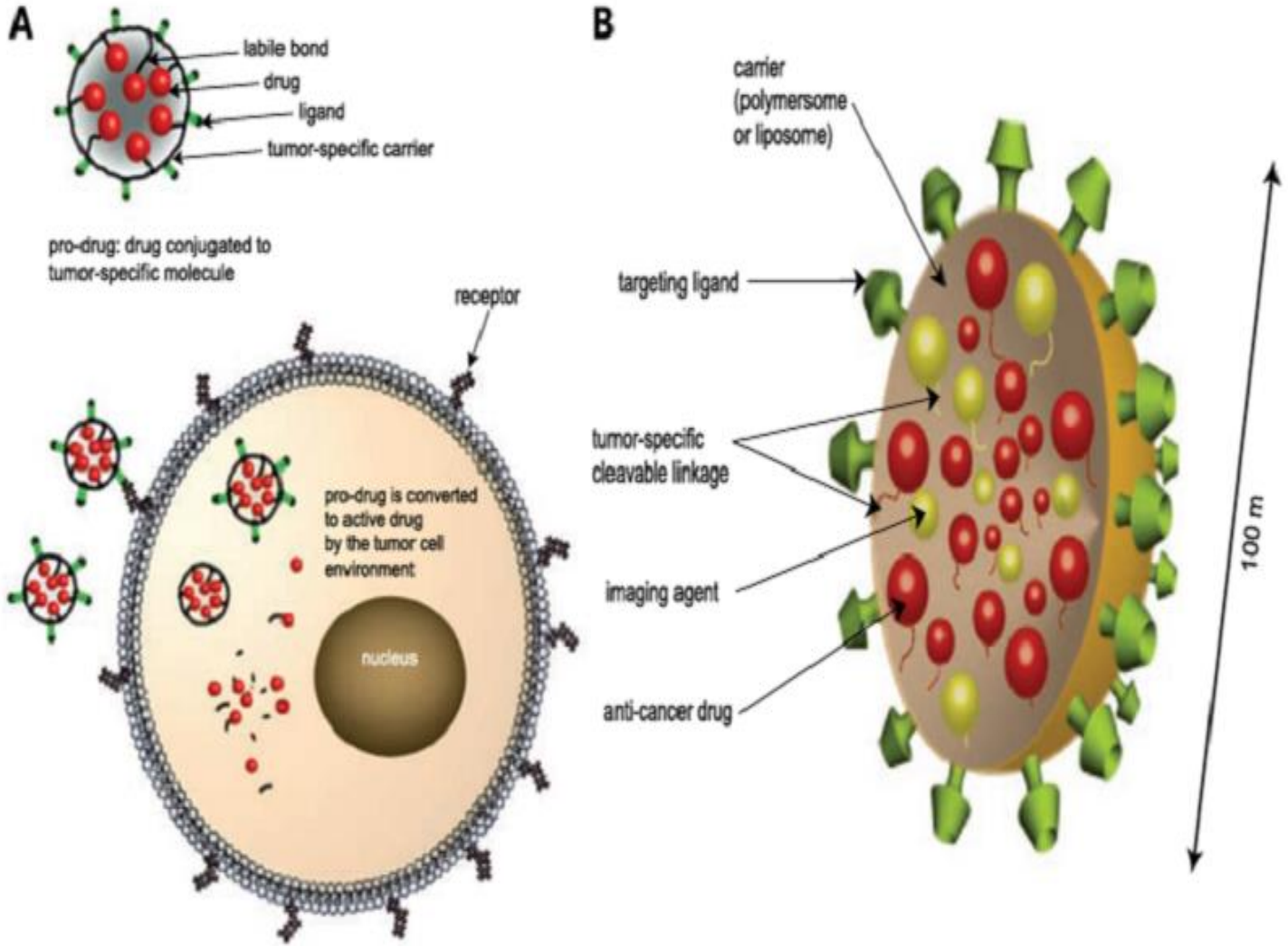
How is nanooncology helping treat GBM?

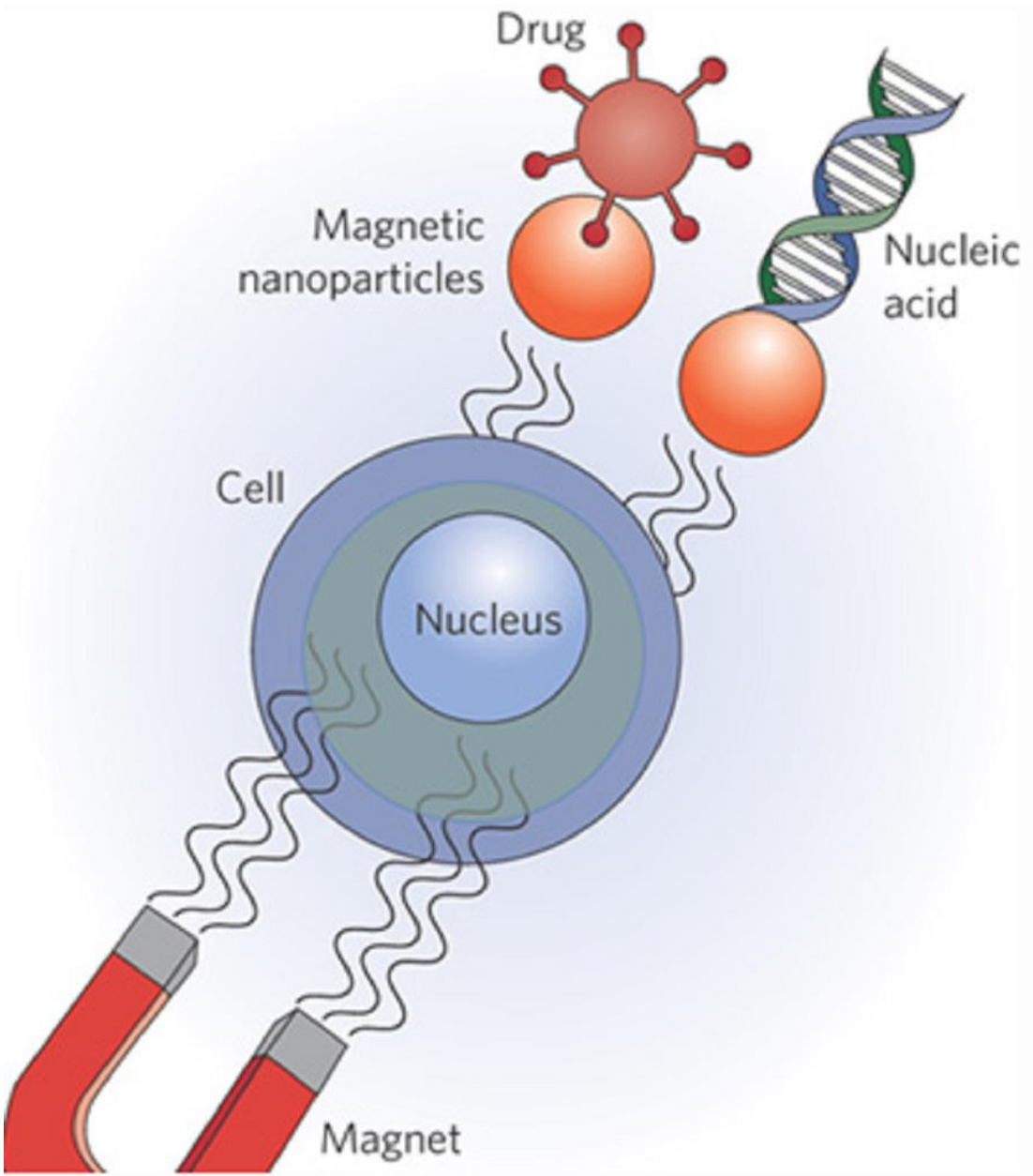
- New innovations in nanooncology allow for a more precise target of the tumor due to:
  - The nanoparticle's has the ability to pass the blood brain barrier (BBB)
    - Via optimization of elemental processes in engineering, physics, biology, chemistry and pharmacology.
- Hone in on the specific tumor site
  - No leakage of anti-cancer drug
  - Spares healthy tissue of cytotoxicity in the drugs.

GBM Treatment via MNPs

- MNPs or Magnetic Nanoparticles, are used in “Nano-therm” treatment methods.
  - These nanoparticles can induce hyperthermia via alternating magnetic fields (AMFs)
- Hyperthermia induction in the tumor tissue leads to:
  - Protein denaturation, DNA cross linking w/ nucleus → apoptosis
  - Rising oxygenation levels are cause for more susceptibility to chemoagents.

GBM Treatment via MNPs




Drug
Magnetic nanoparticles
Nucleic acid
Cell
Nucleus
Magnet

Drawbacks

- Nanomedicine/nanooncology faces many obstacles:
  - Safety of nanoparticle's usage in the body
    - Biodegradable shells and easy distribution to the tumor site
    - No "lost" particles in healthy tissue/organs
    - Possible undesirable toxic properties in other parts of body.
  - Improvement of "targeting efficacy" of nano-vectors to specific cancerous microenvironments.
  - Development of effective triggers for release of drug agents.
  - More physiological barriers including:
  - The Blood-Brain Barrier, drug resistance, etc.

Future Direction

- Development of a multifunctional nanoparticle that can carry:
  - 1) one or more drugs
  - 2) specific targeting moiety
  - 3) an imaging agent
  - 4) cell-penetrating agent
  - 5) a stimulus-sensitive element for controlled release
  - 6) Stabilizing polymer for biocompatibility

- European Union recognized the importance of research in nanomedicine and established the “Nanosafety Network” that:
  - brings in additional reports for additional knowledge on nanosafety.
  - will eventually lead to newer nanomedicine products for healthcare.

Table 1. Examples of Nanoparticles Used in Cancer Therapy

TRADE NAME	DESCRIPTION OF NANOPARTICLE	CANCER TARGETED BY THE NANOPARTICLE	PHASE OF DEVELOPMENT
Abraxane	Albumin-bound paclitaxel	Metastatic breast cancer[24]	Approved
Doxil	Liposomal doxorubicin	HIV-related Kaposi sarcoma, metastatic breast and ovarian cancer[25]	Approved
DaunoXome	Liposomal daunorubicin	HIV-related Kaposi sarcoma[26, 27]	Approved
Myocet	Liposomal doxorubicin	EGFR2-positive metastatic breast cancer[28]	Approved
DepoCyt	Liposomal cytarabine	Intrathecal lymphomatous meningitis[29]	Approved
Marqibo	Liposomal vincristine sulphate	Acute lymphoblastic leukemia[30, 31]	Approved
Oncaspar	Polymeric PEG-L-asparaginase	Acute lymphoblastic leukemia[32]	Approved
Zinostatin stimalamer	Copolymer styrene maleic acid-conjugated neocarzinostatin	Unresectable hepatocellular carcinoma[33, 34]	Approved
Resovist	Carboxydextran-coated SPIO	MRI contrast agent for imaging hepatocellular carcinoma[35]	Approved
Genexol-PM	Polymeric methoxy-PEG-poly(D,L-lactide) paclitaxel	Metastatic breast cancer[36]	Approved
NanoTherm	Aminosilane-coated SPIO	Local ablation of glioblastoma multiform[37, 38]	Approved
Xyotax	Poly-L-glutamic acid (poliglumex) conjugate with paclitaxel	Ovarian cancer and NSCLC[39]	Phase 3
NKTR-102	PEG micelle with irinotecan	Breast and colorectal cancer[40]	Phase 3
Mepact	Liposomal muramyl tripeptide phosphatidyl ethanolamine	Nonmetastatic resectable osteosarcoma[41]	Phase 3
ThermoDox	Liposomal nanoparticle with thermal release of doxorubicin	Hepatocellular carcinoma[42]	Phase 3

References

- Jacob A, Chakravarthy K (2014-04-06 14:52:34 UTC) Engineering Magnetic Nanoparticles for Thermo-Ablation and Drug Delivery in Neurological Cancers. Cureus 6(4): e170. doi:10.7759/cureus.170
- “Nanobiotix: nanomedicine for cancer treatment” <https://www.youtube.com/watch?v=vg4b7WztpmQ>
- Thakor, A. S. and Gambhir, S. S. (2013), Nanooncology: The future of cancer diagnosis and therapy. CA: A Cancer Journal for Clinicians, 63: 395–418. doi: 10.3322/caac.21199
- Cristina Riggio et al. “Nano-Oncology: Clinical Application for Cancer Therapy and Future Perspectives,” Journal of Nanomaterials, vol. 2011, Article ID 164506, 10 pages, 2011. doi:10.1155/2011/164506
- Apatow et al. (2013) *Nanomaterials: Cancer Treatment and Imaging*, University of Rhode Island
- “Nanomedicine: Application of Nanotechnology in Medicine: Great Infographic”, http://internetmedicine.com/2014/01/01/22575/