Nano-Enabled Drug Delivery: Exploring Cancer Treatment Opportunities

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and **Jing Ma**

Beijing Institute of Technology

- Mixed background
  - B.S. in Chemical Engineering (Caltech)
  - PhD in Engineering/Psychology (UCLA)
- Research focus
  - **Technology Intelligence, Forecasting & Assessment**
- Faculty – Georgia Tech (Professor Emeritus)
  - Industrial & Systems Engineering, and
  - Public Policy, and taught 10 years in
  - Management (Management of Technology – "**MOT**")
- Small Business – Search Technology
  - Decision aiding in complex environments since 1980
  - Since 1994, develop & apply text mining software (VantagePoint) focusing on Science, Technology & Innovation (ST&I)

Research Question(s)

Nanotechnology-Enabled Drug Delivery (NEDD) – which A) nano components are helping deliver which B) drugs to treat which C) cancers?

◦ Are certain B) treatments (drugs, gene therapies) concentrated on C) certain cancers?
◦ Are A) certain nano components concentrated on C) certain cancers?
◦ Are A) certain nano components concentrated on facilitating delivery of B) certain treatments?
◦ Are there some shifts over time in treatment applications?
◦ Might there be some underexplored combinations of A) nano enabling components with B) drugs, with C) cancer types?

Pointing toward further questions:
◦ How to facilitate discovery of such research opportunities?
◦ How might R&D policy/management better "connect" research in adjacent arenas?

But first, some background on our "tech mining" on NEDD

Simple schematic of the "NEDD dream"

Molecular imaging & therapy

Cancer diagnosed

Targeting medication

Homing on tumor

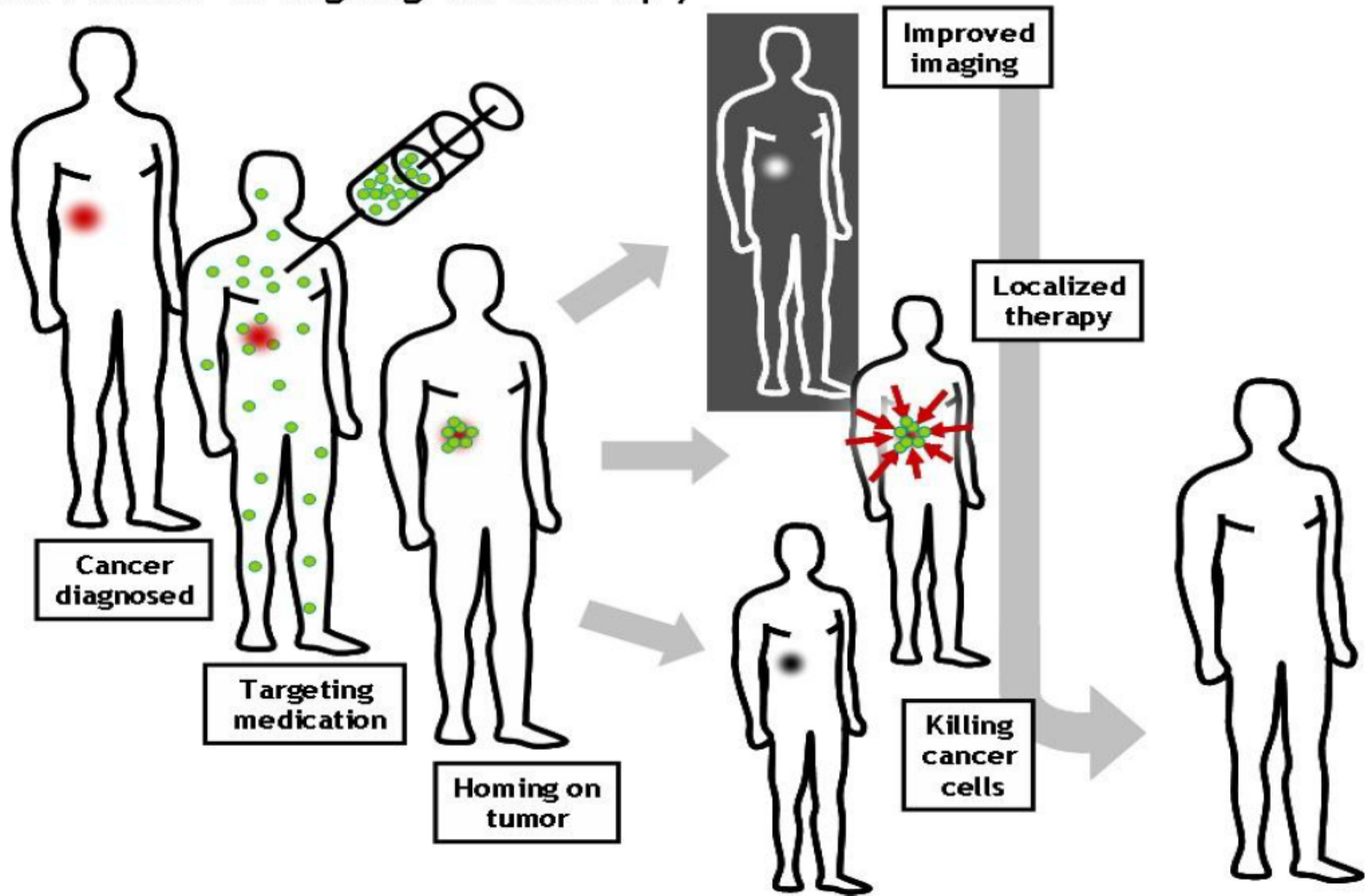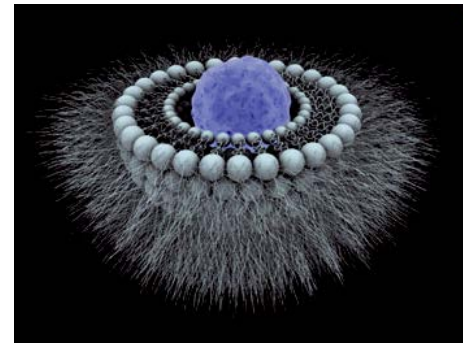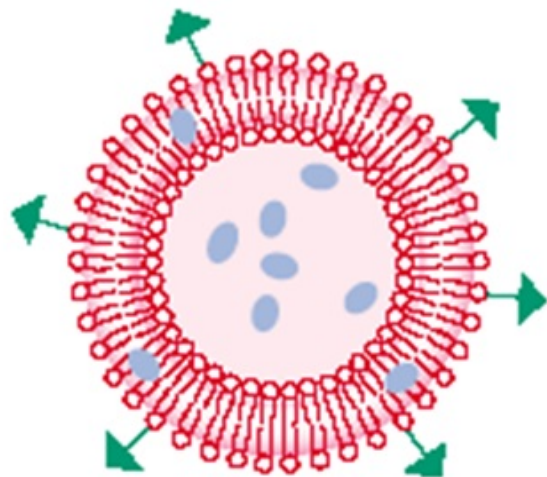Improved imaging

Localized therapy

Killing cancer cells

Fig.3: Nanoparticles used to treat cancer

Nano Promises for Drug Delivery

- Improve delivery of poorly soluble drugs

- Target delivery (get enough drug where you want it, and minimum drug where you don't want it)

- Deliver large macromolecular drugs into cells (getting them through the natural barriers of cell walls)

- Co-deliver two or more drugs

- See where drugs go through incorporating tags

- Perform "theranostics"
(if diagnostics can be added to the therapeutics)

Douglas K. R. Robinson. TEQNODE Limited, Paris, France

Different Kinds of Nanoparticles

Liposome
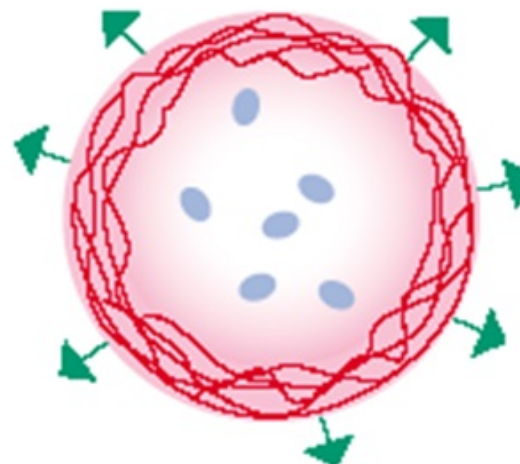
Polymeric nanoparticle

Block copolymer micelle

Dendrimer

Drug ⬤   Ligand ⬅

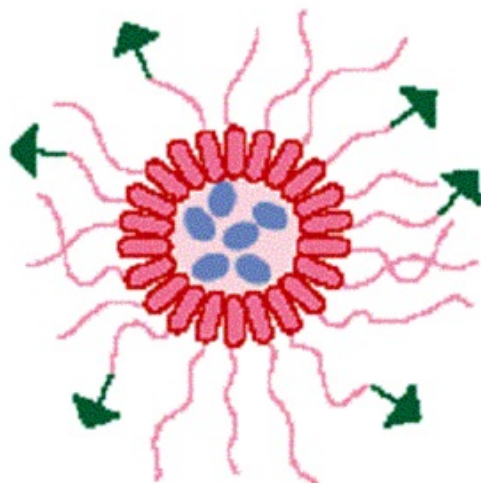# How do "nano" components work to treat diseases like cancer?
[deriving mainly from analyses of the NEDD patents]
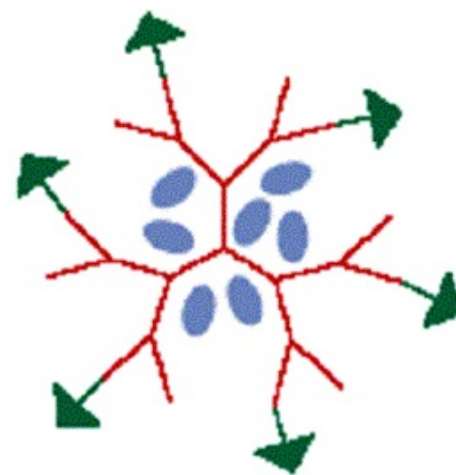
NEDD Search Strategy

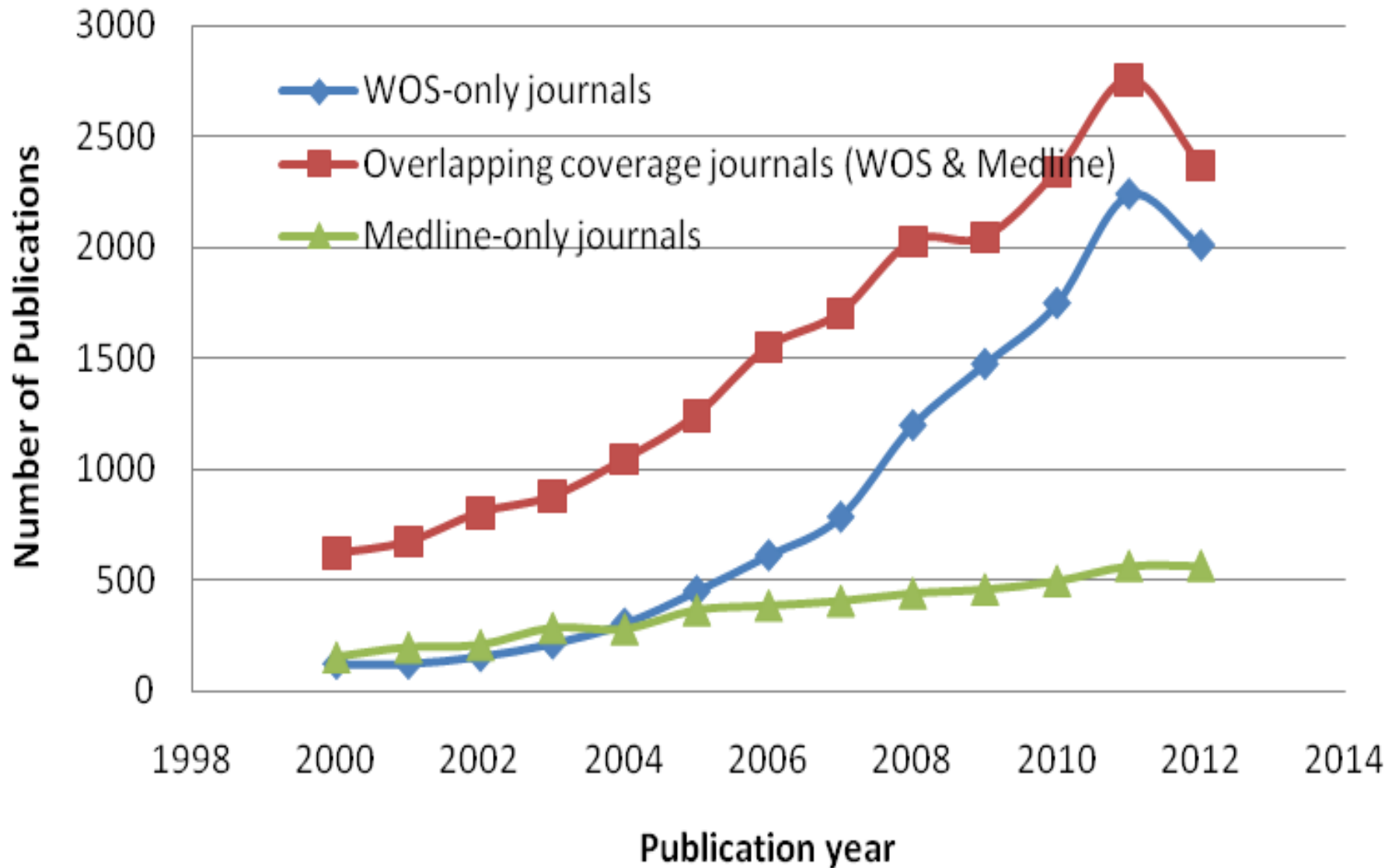| No.	Category	Keywords
1	B (biological processes)	(bioavailab*or biodistrib* or biocompatib* or cytotox* or biodegradab*)
2	I (imaging)	Image* or imaging
3	T (target)	(Cancer or tumor* or tumour* or "RNA interference" or RNAi)
4	H (helpers)	("polyethylene glycol" or pegylate or PEG or molecule* or polymer* or polyethylenimine or PEI or polyspermine or polypropylenimine or "poly lactic-co-glycolic acid" or PLGA or cyclodextrin or dendrimer* or chitosan* or atelocollagen* or "hyaluronic acid" or polypeptid* or peptid* or lipid* or ligand* or or Micelle* or Liposom* or conjugat* or Viral* OR Virus* or nonvira* or non-vira*)
5	P(pharmaceutical)	(1) (agent* or Drug* or pharmac* or formulation*) (2) (siRNA or "short interfering RNA") (3) microRNA (4) DNA or gene (5) (Dox or Doxorubicin*) (6) actives or adjuvant
6	D(delivery approach)	(1) (deliver* or vehicle* or carrier* or vector*) (2) (treat* or therap*) (3)("control* releas*" or transduct* or transfect* or transport* or translocat*)
7	N(nano-delivery vehicle)	This category means GT nano Database or some approximation of its search terms; also consider viral or virus or dendrimer or colloid

Zhou, X., Porter, A.L., Robinson, D.K.R., Zhang, Y., and Guo, Y. (to appear), Nano–enabled drug delivery: Recent trends, emerging issues, and future directions, in Islam, N. (ed.), *Nanotechnology: Recent Trends, Emerging Issues and Future Directions*, Nova Science Publishers, Hauppauge, NY.

Data & Analyses

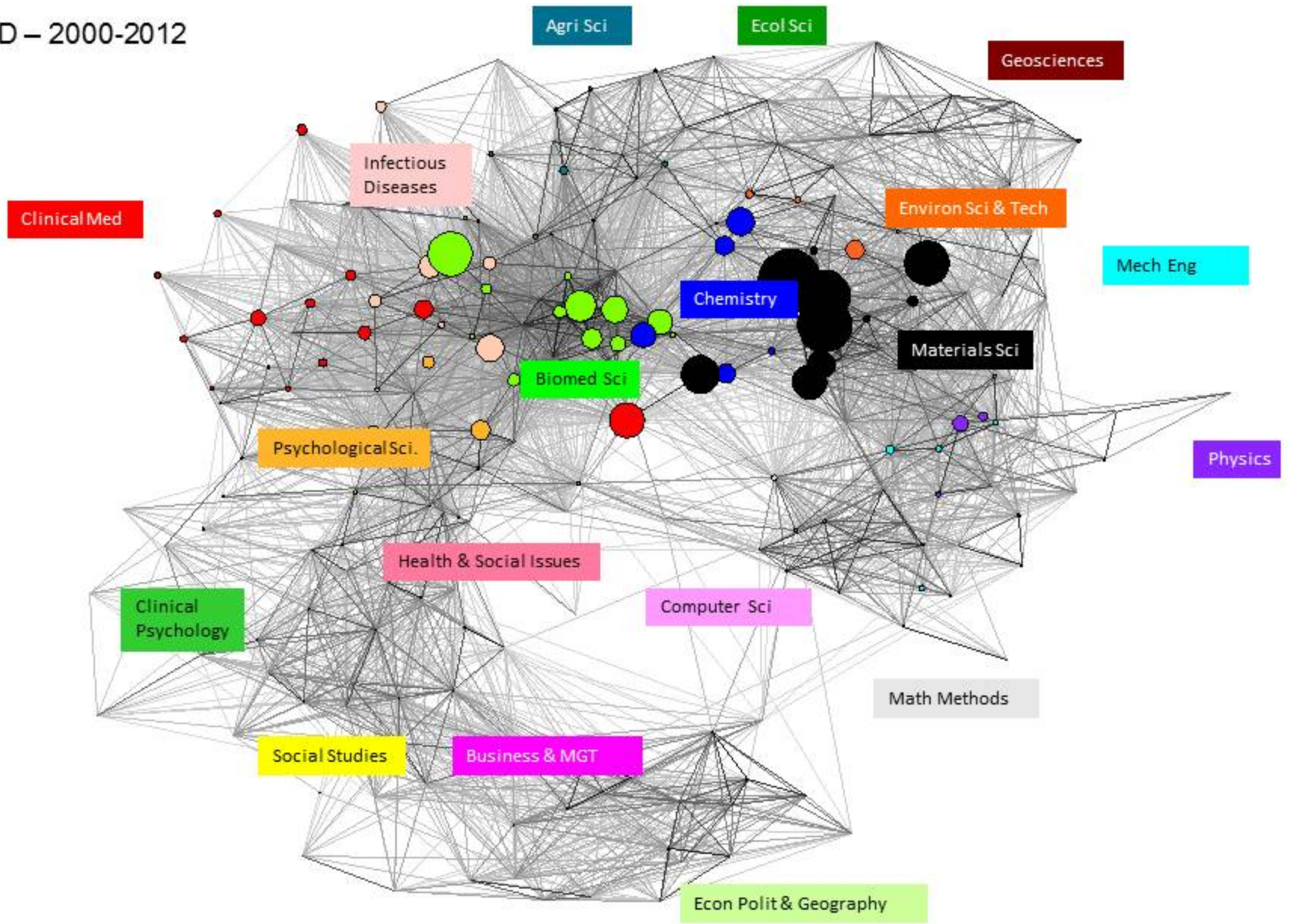Multi-part Boolean search to retrieve NEDD data

➢ ~60,000 Web of Science publication abstracts

➢ ~8,000 Derwent Innovation Index abstracts

➢ **~50,000 MEDLINE publication abstracts**

NEDD research publication trends by Database Journal Coverage

Global Map of Science, 2010 update
224 Web of Science Categories

NEDD – 2000-2012

Agri Sci

Ecol Sci

Geosciences

Infectious Diseases

Clinical Med

Environ Sci & Tech

Mech Eng

Chemistry

Materials Sci

Biomed Sci

Physics

Psychological Sci.

Health & Social Issues

Clinical Psychology

Computer Sci

Math Methods

Social Studies

Business & MGT

Econ Polit & Geography

Method from Rafols, Porter and Leydesdorff (2009)

Developmental Pathways, Locating the 13 NEDD Topics of NEDD
[based mainly on the patent topical analyses]
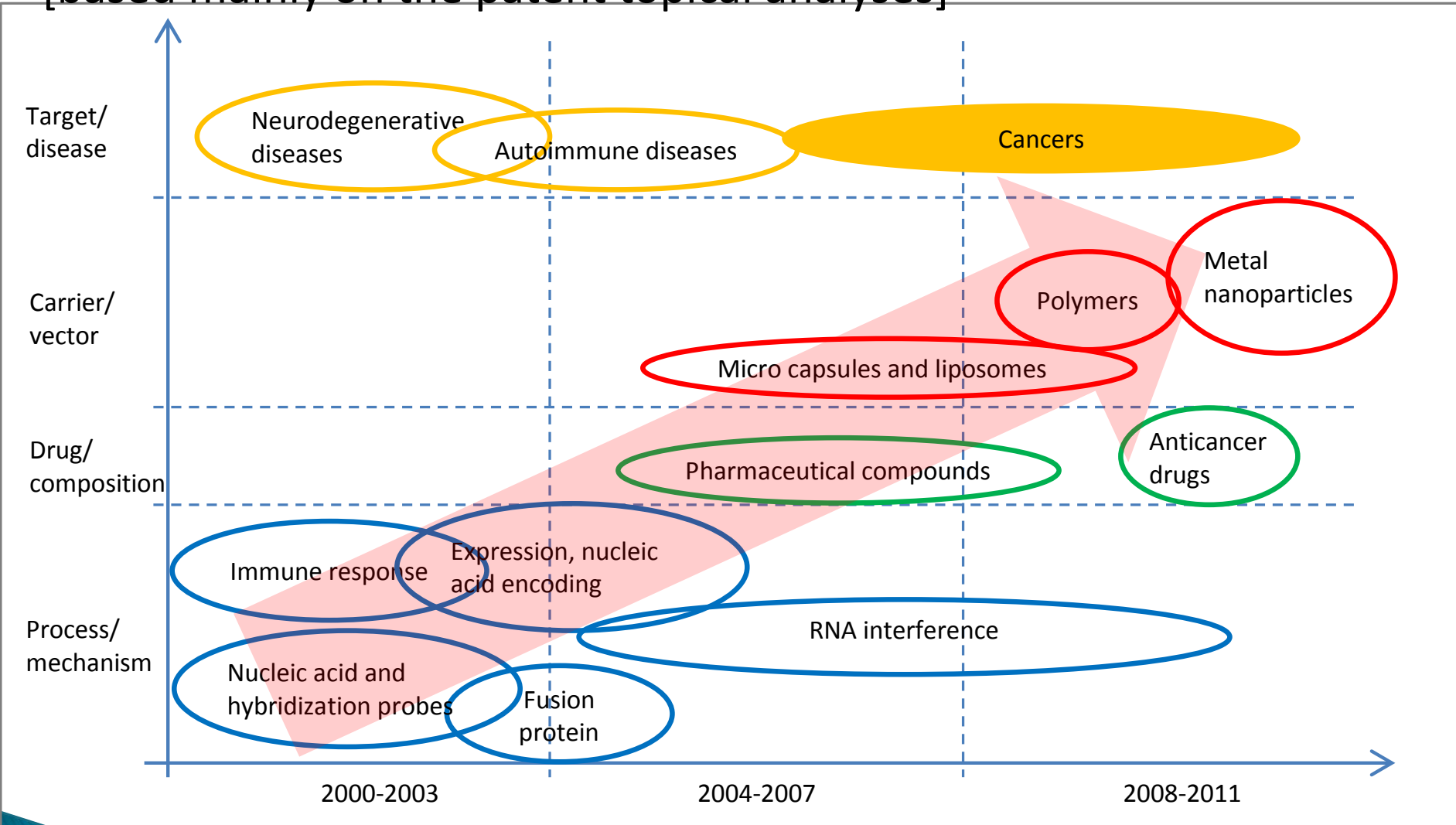
Feedback on the Empirical Research Profiling

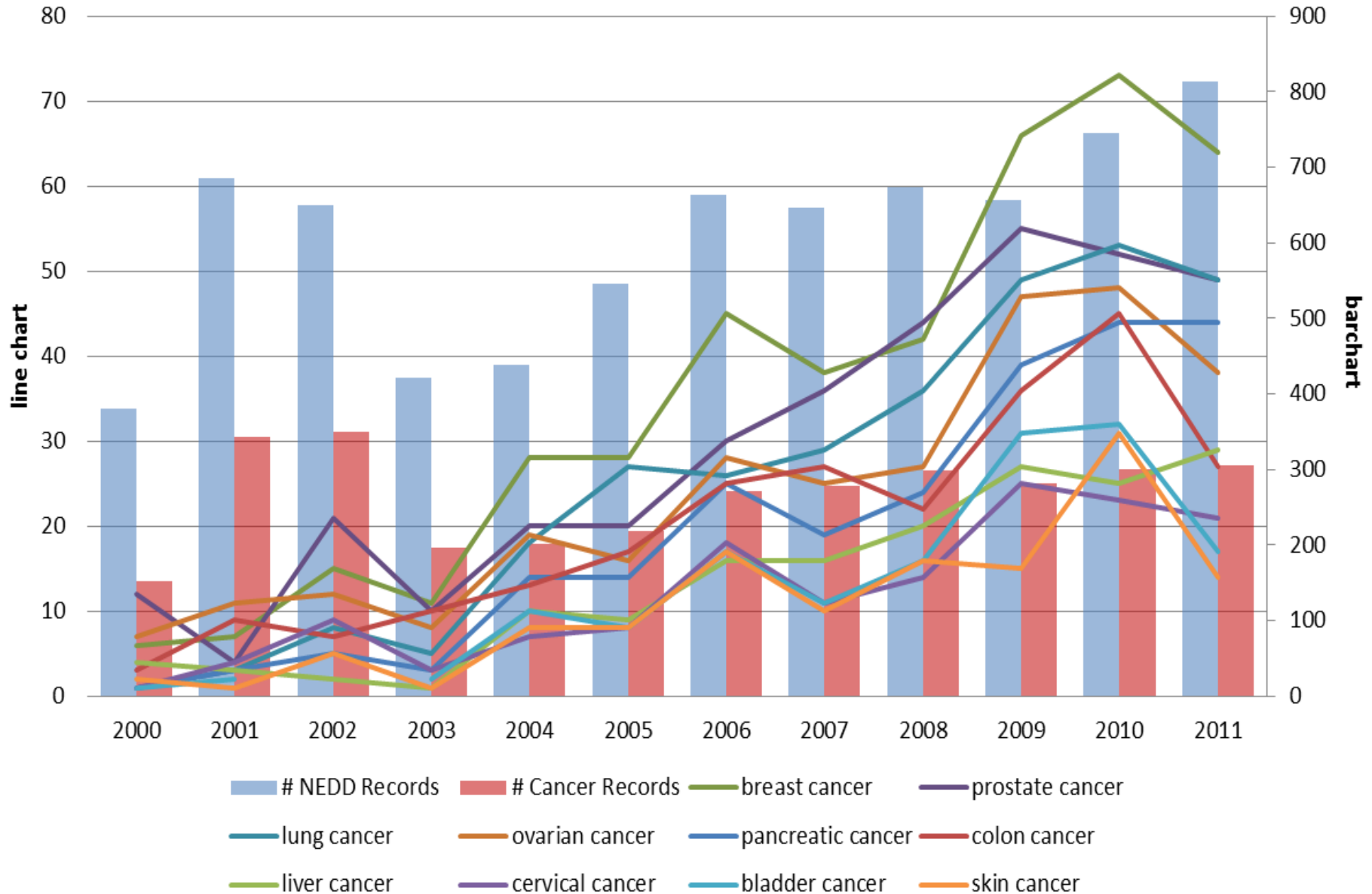Workshop with bio-medical & science policy colleagues at Georgia Tech (and 2d workshop at a Novel Drug Delivery Systems conference) – payoff will come from **focusing on particular nano components and/or targets**

- ➤ One path: comparing NEDD for brain applications – Alzheimer's Disease and brain cancer
- ➤ **Second path (today's focus) – NEDD for cancer treatments**

Focus on Cancers [patenting patterns]

Nanoparticle Topical Emergence in the Cancer Patent Dataset

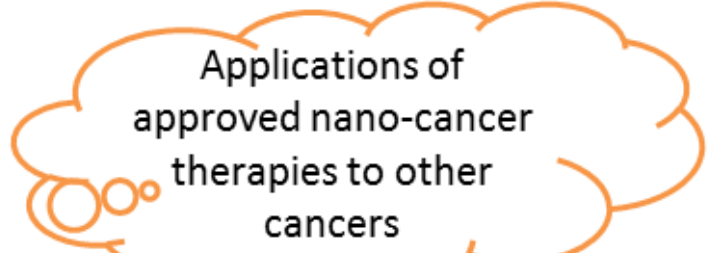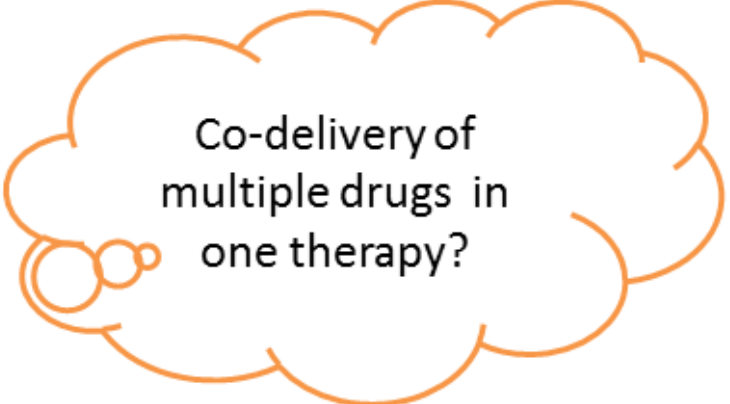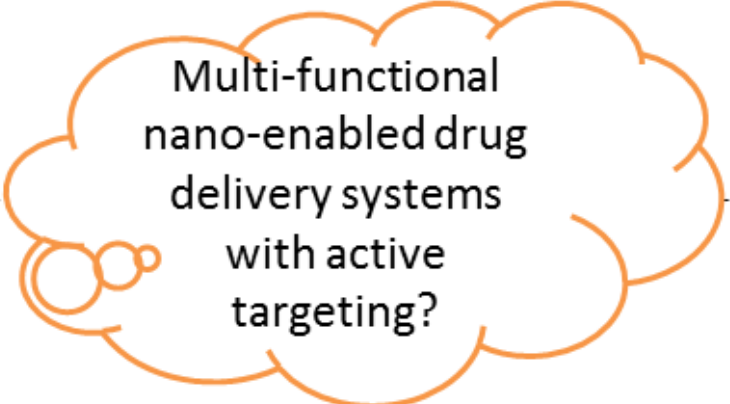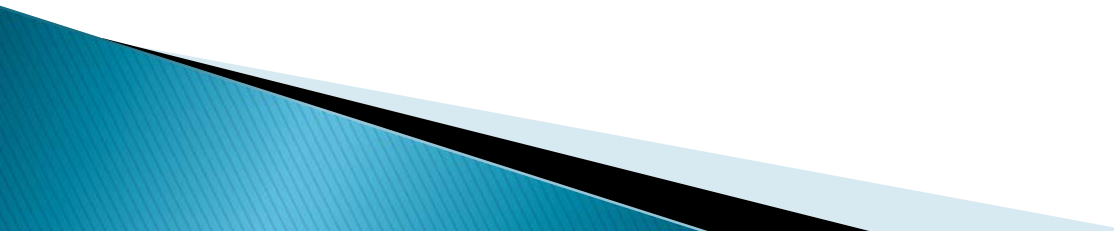|		TODAY	TOMORROW?
COMMERCIAL-ISATION	**Approved on Market**	Doxil/Caelyx (Breat cancer / leukemia) Abraxane (Breast cancer) Myocet (Ovarian cancer) DaunoXome (Karposi's sarcoma) Genexol-PM (lung and breast cancer (KOREA) Depocyte (neoplast meningitis)	Applications of approved nano-cancer therapies to other cancers
EFFICACY & TOXICITY TESTS	**Clincial Trials**	S-CKD602 / PEGyl. Liposome – Alza Corp. CRLX101 / Cyclodextrin – Cerulean Pharma CPX-1 / Liposomal irinotecan – Celator Pharma LE-SN28 Liposoma SN38 – Neopharm NC-6004 / Cisplatin – NanoCarrier Co. ALN-VSP / lipid nanoparticle of siRNA – Alnylam OSI-211 / Liposomeal lurtotecan / OSI Pharma BIND-014 / polymeric NPdocetaxel – BIND Bioscience MBP-426 / Transferrin targetd oxaliplatin – Mebiopharm CALAA-01 / cyclodextrin and siRNA – Calando Pharma SGT53-01 / Liposome with p53 gene – SynerGene Therap.	Co-delivery of multiple drugs in one therapy?
RESEARCH & DEVELOPMENT	**Vector + drug R&D**	Liposomes Phospholipids PluronicR Poly (L-aminoacid) with oligonucleotides Polyester micelles Nanoemulsions Drug nanocrystals	Multi-functional nano-enabled drug delivery systems with active targeting?
	Nano-vector research	Polymer-based nanoparticles Lipid-based nanoparticles Ceramic-based nanoparticles Albumin nanoparticles Nanogels Dendrimers	

NEDD + Cancers

#	Search Strategy (Web of Knowledge's MEDLINE –– 2000–2013, performed 7/24/14)	NO. of records
#1	MeSH HEADING:exp: (Neoplasms OR Antineoplastic Agents) AND (Drug carriers OR Micelles)	8715
#2	((MeSH HEADING:exp: (Neoplasms OR Antineoplastic Agents) AND Nanostructures) NOT #1) AND MeSH HEADING: (Drug Delivery Systems OR RNA Small Interfering OR Gene Transfer Techniques OR Delayed–Action Preparations OR RNA Interference OR Pharmaceutical Vehicles OR Genetic Vectors OR Transfection OR Polyglycolic Acid)	1517
#3	(((((MeSH HEADING:exp: (Neoplasms OR Antineoplastic Agents) AND Nanostructures) NOT #1) AND MeSH HEADING: (Doxorubicin OR Polyethylene Glycols OR Paclitaxel)) NOT #2) AND ABSTRACT/TITLE: deliver*	122
#4	Total	10354

- National Library of Medicine colleagues reviewed the search strategy, suggesting some enhancements
  - Focus on Medical Subject Headings (**MeSH)** is a good way to go
  - Add some cancer terms
- MeSH "Qualifiers" offer good categorization (MeSH assignment based on human indexer review of full articles)
- Current dataset of **10,354 MEDLINE** abstract records

- Use VantagePoint desktop software (www.theVantagePoint.com) to separate ~3334 primary MeSH terms and 73 Qualifiers in those 10,354 abstract records
- Focus on top **200 primary MeSH terms** and **73 Qualifiers** = matrix
- SPSS Hierarchical Clustering to consolidate those 200 MeSH terms into 7 clusters
  - Method – techniques, procedures, and programs
  - Drug – drugs and formulas
  - Component – nanoparticles and accompanied materials
  - Cancer – different cancer types
  - Effect – effects of treatment
  - Interface – receptors and metabolism
  - Antibody – antibodies and antigens

Resulting MeSH Clusters (partial)

Method	Drug	Component	Cancer	Cancer (combined)	Effect	Interface	Antibody
Drug Delivery Systems	Antineoplastic Agents	Drug Carriers	~~Neoplasms~~	Breast Neoplasms	Apoptosis	Receptor, Epidermal Growth Factor	Cancer Vaccines
Genetic Therapy	Doxorubicin	Nanoparticles	Breast Neoplasms	Brain and Nerve Neoplasms	Drug Resistance, Neoplasm	Carrier Proteins	Antigens, Neoplasm
Gene Transfer Techniques	Antibiotics, Antineoplastic	Liposomes	Lung Neoplasms	Liver Neoplasms	RNA Interference	Receptor, erbB–2	Dendritic Cells
Transfection	Antineoplastic Agents, Phytogenic	Polyethylene Glycols	Brain Neoplasms	Lung Neoplasms	Cell Proliferation	Receptors, Cell Surface	Antibodies
Nanomedicine	Paclitaxel	Polymers	Liver Neoplasms	Skin Neoplasms	Drug Resistance, Multiple	Macrophages	

Happy Hunting Grounds!

- Explore co-occurrences
- 3 key relationships to explore:
  - **Cancers (20) by Drugs (50)**
  - **Cancers (20) by Nano components (62)**
  - **Drugs (50) by Nano components (62)**
- But really more than 2-D – additional dimensions to explore:
  - Density [intensity of research publication]
  - What? + Who? Where? When?
  - Other 4 of the 7 MeSH Qualifier clusters: methods, effects, interfaces, antibodies

Co-occurrence of 20 Cancers by 50 Drugs: Concentrations of R&D Activity

Show Values >= 1 and <= 142

Cooccurrence # of Records

MeSH Terms (Primary) (1): MeSH headings	# Records	13 Photosensitizing Agents	14 Radiopharmaceuticals	15 Taxoids	16 Camptothecin	17 Antimetabolites, Antineoplastic	18 Antibodies, Monoclonal	19 Fluorouracil	20 Prodrugs	21 Angiogenesis Inhibitors	22 Genetic Vectors	23 Daunorubicin	24 Methotrexate	25 Cytarabine	26 Organoplatinum Compounds	27 Porphyrins	28 Vincristine	29 Peptide Fragments	30 Antineoplastic Agents, Alkylating	31 Organometallic Compounds	32 Oligonucleotides, Antisense	33 Amphotericin B
# Records		162	55	176	273	272	172	172	139	133	108	102	100	90	86	63	61	56	55	55	106	54
1 Breast Neoplasms	627	10	4	14	4	7	22	3	5	8	5	4	5	2		1	5	3	1	4	15	
2 Brain and Nerve Neoplasms	490	3	2	3	11	9	11	3	2	6	5	2	4	7	1			4	14		10	
3 Liver Neoplasms	397	1	2	9	9	17	7	18		2	8	1	3		2	1	2	1	1		5	1
4 Lung Neoplasms	376	3		4	13	8	2	2	2	3	6	1		1	2	3		3	1	1	8	2
5 Skin Neoplasms	356	11	2	2	6	3	3	7	2	8	1		1	2	1	5	3	4	4	3	3	
6 Colorectal Neoplasms	269	9	4	1	16	9	7	12	1	5	1		1		10	4				4	6	
7 Ovarian Neoplasms	237	1		3	5		4			2	2							3	1		3	
8 Prostatic Neoplasms	208	7	1	5	3	3	4	1	3	2	1					2		3		1	3	
9 Adenocarcinoma	133	8	1	2	5	6	4	3		1	4		1			2				1	3	
10 Leukemia	131				11	1		1				26	2	21		10				2		13
11 Pancreatic Neoplasms	122				4	9	5	1	2	3	1								1			
12 Carcinoma, Squamous Cell	114	6	3		1	1	1	3			2		1			1	3		2	1	3	
13 Stomach Neoplasms	79	2	1	6	3	5	4	6	1		1	1				1					2	
14 Bone Neoplasms	67	1	1		1			1	1			1				1						
15 Head and Neck Neoplasms	59	2	1					1					1			2				1	3	
16 Urinary Bladder Neoplasms	53	2		1		1														1		
17 Peritoneal Neoplasms	51		1	1	4	2		2	1				1		3					1		
18 Uterine Cervical Neoplasms	38	1	1	1																		
19 Lymphoma	37				1	2							7								1	1
20 Sarcoma	35	1		1	1	1				1							1				1	1

# Records	3879 Col Sum	704	580	248	224	89	319	238	224	23
	# Records	2697	1476	713	430	212	864	761	290	42
# Records	CANCERS \ AGENTS	Antineopla	Doxorubici	Paclitaxel	RNA, Sma	DNA	Antibiotics,	Antineopla	Antineopla	Adjuvants, P
1	627 Breast Neoplasms	0.79	1.51	1.37	0.83	0.42	1.34	0.94	1.52	0.27
2	490 Brain and Nerve Neoplasms	1.02	0.78	1.12	0.85	1.16	0.77	1.00	0.53	0.69
3	397 Liver Neoplasms	0.96	1.43	0.59	1.00	1.76	1.72	0.86	0.26	0.85
4	376 Lung Neoplasms	1.10	0.80	1.33	1.70	1.16	0.81	1.30	0.88	0.90
5	356 Skin Neoplasms	1.05	0.83	0.53	0.78	1.59	0.75	0.96	0.34	3.32
6	269 Colorectal Neoplasms	1.09	0.72	0.70	0.52	0.32	0.54	1.33	0.71	1.25
7	237 Ovarian Neoplasms	1.05	1.50	2.11	1.46	0.55	1.74	1.31	2.41	0.00
8	208 Prostatic Neoplasms	0.90	0.71	0.38	2.41	1.26	0.47	0.63	0.50	0.81
9	133 Adenocarcinoma	0.91	0.75	0.82	0.65	1.31	0.82	0.74	1.82	1.27
10	131 Leukemia	0.72	0.36	0.12	0.13	0.33	1.58	1.00	2.51	0.00
11	122 Pancreatic Neoplasms	1.45	0.22	0.77	0.71	2.14	0.20	0.94	1.28	0.00
12	114 Carcinoma, Squamous Cell	0.77	0.47	0.69	0.61	0.76	0.43	0.71	1.37	0.00
13	79 Stomach Neoplasms	0.91	0.25	1.78	1.10	0.55	0.62	1.86	1.10	0.00
14	67 Bone Neoplasms	1.40	1.90	0.47	1.29	0.65	0.73	0.00	1.29	0.00
15	59 Head and Neck Neoplasms	1.21	1.13	0.27	0.88	0.00	1.03	0.00	1.17	0.00
16	53 Urinary Bladder Neoplasms	1.04	0.76	2.95	1.63	0.00	1.38	1.85	0.00	3.18
17	51 Peritoneal Neoplasms	1.94	0.92	1.23	0.00	0.85	0.72	1.60	0.34	0.00
18	38 Uterine Cervical Neoplasms	0.87	0.70	1.65	1.37	3.44	0.64	0.86	0.91	8.88
19	37 Lymphoma	0.74	0.90	0.00	0.47	0.00	0.66	0.88	0.00	4.56
20	35 Sarcoma	1.57	2.87	0.45	0.00	1.25	1.39	0.47	1.98	4.82

a) Column (agent) proportion – of 580 Doxorubicin (DOX) hits (as Primary MeSH for these 20 cancers), what proportion are directed at each cancer type?

b) Row (cancer) Proportion – what proportion of these are bone neoplasm studies?

(etc.)

Divide a/b to look at relative research concentrations (cells)

# Records	CANCERS \ AGENTS	Antineopl	Doxorubici	Paclitaxel	RNA, Sma	DNA	Antibiotics,	Antineopla	Antineopla	Adjuvants, P
3879	Col Sum	704	580	248	224	89	319	238	224	23
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3	397 Liver Neoplasms	0.96	1.43	0.59	1.00	1.76	1.72	0.86	0.26	0.85
4	376 Lung Neoplasms	1.10	0.80	1.33	1.70	1.16	0.81	1.30	0.88	0.90
5	356 Skin Neoplasms	1.05	0.83	0.53	0.78	1.59	0.75	0.96	0.34	3.32
6	269 Colorectal Neoplasms	1.09	0.72	0.70	0.52	0.32	0.54	1.33	0.71	1.25
7	237 Ovarian Neoplasms	1.05	1.50	2.11	1.46	0.55	1.74	1.31	2.41	0.00
8	208 Prostatic Neoplasms	0.90	0.71	0.38	2.41	1.26	0.47	0.63	0.50	0.81
9	133 Adenocarcinoma	0.91	0.75	0.82	0.65	1.31	0.82	0.74	1.82	1.27
10	131 Leukemia	0.72	0.36	0.12	0.13	0.33	1.58	1.00	2.51	0.00
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19	37 Lymphoma	0.74	0.90	0.00	0.47	0.00	0.66	0.88	0.00	4.56
20	35 Sarcoma	1.57	2.87	0.45	0.00	1.25	1.39	0.47	1.98	4.82

Agent profiling: DOX –– Used for all 20; sarcoma & bone neoplasm most: Paclitaxel used for all but one (lymphoma) – why not?

Cancer profiling: Leukemia – 5 drugs overwhelmingly used to treat this – see earlier matrix

Agent for Cancer; Explore the zeroes with biomedical scientists

# Records	CANCERS \ AGENTS	Antineopla	Doxorubici	Paclitaxel	RNA, Sma	DNA	Antibiotics	Etoposide
3879	Col Sum	704	580	248	224	89	319	7
	# Records	2697	1476	713	430	212	864	45
627	Breast Neoplasms	0.79	1.51	1.37	0.83	0.42	1.34	0.88
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397	Liver Neoplasms	0.96	1.43	0.59	1.00	1.76	1.72	0.00
376	Lung Neoplasms	1.10	0.80	1.33	1.70	1.16	0.81	2.95
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133	Adenocarcinoma	0.91	0.75	0.82	0.65	1.31	0.82	0.00
131	Leukemia	0.72	0.36	0.12	0.13	0.33	1.58	0.00
122	Pancreatic Neoplasms	1.45	0.22	0.77	0.71	2.14	0.20	0.00
114	Carcinoma, Squamous Cell	0.77	0.47	0.69	0.61	0.76	0.43	0.00
79	Stomach Neoplasms	0.91	0.25	1.78	1.10	0.55	0.62	0.00
67	Bone Neoplasms	1.40	1.90	0.47	1.29	0.65	0.73	0.00
59	Head and Neck Neoplasms	1.21	1.13	0.27	0.88	0.00	1.03	0.00
53	Urinary Bladder Neoplasms	1.04	0.76	2.95	1.63	0.00	1.38	0.00
51	Peritoneal Neoplasms	1.94	0.92	1.23	0.00	0.85	0.72	0.00
38	Uterine Cervical Neoplasms	0.87	0.70	1.65	1.37	3.44	0.64	0.00
37	Lymphoma	0.74	0.90	0.00	0.47	0.00	0.66	29.95
35	Sarcoma	1.57	2.87	0.45	0.00	1.25	1.39	0.00

Examine **groups** of agents or cancers: genetic treatments [RNAi & DNA] – notably widely used.

Crosswalk: explore why RNAi is not showing for peritoneal neoplasms, but DNA is? Also, DNA is prominent for uterine cervical, why less so RNAi?

Look at **narrowly targeted** agents; might they hold potential for others?

20 Cancers by 50 Drugs: Added Dimensions Ex. 29 articles on RNAi for Prostate

File Edit View Sheets Fields Groups Tools Scripts Window Help

cancer-drug

Title

29 Titles, 1 Selected

- Enhanced docetaxel-mediated ...
- A non-covalent peptide-based...
- Anisamide-targeted cyclodext...
- Atu027, a liposomal small inte...
- Cover story. RNA interference (...
- Delivery of multiple siRNAs usi...
- Efficient delivery of small inter...
- Efficient delivery of sticky siRN...
- Inhibitory effect of silencing S...
- Intracellular siRNA delivery sys...
- Lipid nanoparticle siRNA syste...
- Local and systemic delivery of ...
- PAMAM dendrimers mediate s...
- PEG conjugated VEGF siRNA fo...
- Plasmid-based Stat3 siRNA de...
- Polymeric nanoparticles for su...
- Prostate cancer cell death pro...
- Prostate-targeted biodegrada...
- PSA-responsive and PSMA-me...
- Redox-active polymer microca...
- Reducible poly(amido ethyleni...
- RNA interference in the mouse...
- siRNA transfection with calciu...
- Solid lipid-PEI hybrid nanocarr...
- Systemic delivery of RafsiRNA f...
- Systemic delivery of therapeut...
- Targeting ECM-integrin intera...
- Therapeutic delivery of siRNA ...
- Well-defined degradable cati...

MeSH Terms (Primary) (1):

Show Values >= 5 and <= 142

Cooccurrence # of Records

	# Records	MeSH Terms	1 Antineoplastic Agents	2 Doxorubicin	3 Paclitaxel	4 RNA, Small Interfering	5 DNA	6 Antibiotics, Antineoplastic	7 Antineoplastic Agents, Phytogenic	8 Antineoplastic Combined Chemotherapy Prot	9 Adjuvants, Immunologic	10 Plasmids	11 Cisplatin	12 Curcumin	13 Photosensitizing Agents	16	17	18	19	20	22	23	26
	# Records		2697	1476	713	430	212	864	761	290	42	73	233	110	162	273	272	172	172	139	133		
1	627	Breast Neoplasms	90	142	55	30	6	69	36	55		5		5	10								
2	490	Brain and Nerve Neoplasms	91	57	35	24	13	31	30	15													
3	397	Liver Neoplasms	69	85	15	23	16	56	21	6		6	9										
4	376	Lung Neoplasms	75	45	32	37	10	25	30	19			16	7		13	8		6				
5	356	Skin Neoplasms	68	44	12	16	13	22	21	7	7	5		11		6		7		8			
6	269	Colorectal Neoplasms	53	29	12	8		12	22	11			7	9		16	9	7	12		5		10
7	237	Ovarian Neoplasms	45	53	32	20		34	19	33			24			5							
8	208	Prostatic Neoplasms	34	22	5	29	6	8	8	6				7	5								
9	133	Adenocarcinoma	22	15	7	5		9	6	14				8		5	6						
10	131	Leukemia	17	7				17	8	19						11					26	21	10
11	122	Pancreatic Neoplasms	32		6	5	6		7	9			6			9	5						
12	114	Carcinoma, Squamous Cell	16	8	5			5	9			7		6									
13	79	Stomach Neoplasms	13		9	5		9	5					6		5		6					
14	67	Bone Neoplasms	17	19		5			5														
15	59	Head and Neck Neoplasms	13	10			5																
16	53	Urinary Bladder Neoplasms	10	6	10	5		6	6														
17	51	Peritoneal Neoplasms	18	7					5														
18	38	Uterine Cervical Neoplasms	6																				
19	37	Lymphoma	5	5																			
20	35	Sarcoma	10	15																			

cancer-drug | drug-component | cancer-component | cancer-method | co
NEDD ca...

Publication Year

2005 2006 2007 2008 2009 2010 2011 2012 2013

Nano Components 62

6		Nanoparticles
3		Nanocapsules
3		Polyethylene Glycols
2		Lipids
2	↑↑	Polyethyleneimine
1		Aptamers, Nucleotide
1		beta-Cyclodextrins
1	↑	Cell-Penetrating Peptid
1	↑	Coated Materials, Bioco
1		Dendrimers
1		Liposomes
1		Oligopeptides
1		Peptides
1		Polyamines

Cancers (20)

29	↑↑↑	Prostatic Neoplasms
2	↑↑	Bone Neoplasms
1		Pancreatic Neoplasms

Agents (drugs) 50

29	↑↑↑	RNA, Small Interfering
1		Antibiotics, Antineoplastic
1	↓↓↓	Antineoplastic Agents
1	↓	Doxorubicin
1		Taxoids

Hot!

Using which nano components?

+ other cancers?

+ other drugs (multi-drug delivery?)

50 Agents (Drugs) by 62 Nano Components

Address 4958 of the 10,354 articles; spotlighted a row (one agent) – 430 articles on "RNA, small interfering"

20 Cancers by 62 Nano Components

Spotlight on skin neoplasms with its most prominent nano delivery component, liposomes (55 articles)

Other Cuts on the Multiple Dimensions

- Agent by Agent – how much "combo" treatment?

  [multiple drug delivery via NEDD]

- Nano component by Nano component – in conjunction?

- Explore the other 4 clusters – methods, effects, etc.

- Pursue "who, what, where, when" elements on subsets of interest – e.g., leading journals, leading researchers, etc.

▶ Text mining software:
http://www.theVantagePoint.com

▶ Global Tech Mining Conference, in conjunction with the S&T Indicators Conference, 2-5 Sep., 2014, Leiden, The Netherlands
*www.gtm**conference**.org*

▶ Future-oriented Technology Analysis Conference, 27-28 November, 2014, Brussels, Belgium
//forera.jrc.ec.europa.eu/

Select References

- Porter, A.L., and Cunningham, S.W. (2005), *Tech Mining: Exploiting New Technologies for Competitive Advantage*, Wiley, New York.

- Zhou, X., Porter, A.L., Robinson, D.K.R., Zhang, Y., and Guo, Y. (2014), Nano-enabled drug delivery: Recent trends, emerging issues, and future directions, in Islam, N. (ed.), *Nanotechnology: Recent Trends, Emerging Issues and Future Directions*, Nova Science Publishers, Hauppauge, NY., 25-44.

- Ma, J., and Porter, A.L., (2014), Analyzing patent topical information to identify technology pathways and potential opportunities, Scientometrics. http://link.springer.com/article/10.1007/s11192-014-1392-6/fulltext.html

- Porter, A.L., Ma, J., and Robinson, D.K.R., (2014), Forecasting Nano-Enabled Drug Delivery (NEDD) Innovation Pathways, Pharmaceutics & Novel Drug Delivery Systems, San Antonio, TX (March) – presentation & workshop.

Discussion??

Can we "discover" opportunities via such tech mining?

➢ Research gap analyses – could nano component X also facilitate delivery of treatment Y, for disease Z?

❖ Could such R&D profiling/parsing help in your studies?

➢ Could we boost research proposals by incorporating such nano R&D profiling to explore "connections"?

❖ How do you learn about "one step removed" research findings, methods, applications, etc.?

➢ Could you help us interpret NEDD relationships?

Nano grafted on current pharma TDS (illustrated for cancer] — **Co–development of NEDD with drug** — **Multi–functional nanotherapies**

COMMERCIAL–ISATION

Approved on Market

- Six approved therapies
- Therapeutic families
- Wider variety of nano platforms
- Co-delivery
- Active targeted therapies

EFFICACY & TOXICITY TESTS

Clinical Trials

- Liposome dominance
- Nanoparticulate drugs
- NEDD with imaging
- ?
- NEDD with RNAi
- Prominance of NEDD with ligands
- ?

RESEARCH & DEVELOPMENT

Vector + drug R&D

- Liposomes
- ?
- Holistic development of therapies
- Proliferation of NEDD platforms

Nano-vector research

- Passive targeting
- Active targeting
- ?

TODAY — NEAR-TERM — MID-TERM

Regulator

Consumer

R&D

Trialer

Provider

Marketer

2) Market

7) Market

8) Feeling on acceptability

8) New protocol discussions

9) Protocol approval

9) Confid proce fina

ader discussion reased awareness s health

11) Trial extension to include MED patients through organic causes

for cau

6) Expertise and help

6) Excitement being involved with something new

Legitimacy

recruitment and ipation

3) Info on new approach to MED

questionnaire)

2) New trial design possible, Questionnaire generation: Discovery Push

1) Trial results

1) Experience of side-effect profile

2) Feeling on whether can design a new trial A pre

A web of regulatory landscapes?

Pharma –regulation is clear but what about
Nanomaterial regulation for a
drug delivery system? Drug or device
or biomaterial?

Orphan Diseases?

NEDD's potetnial for orpha diseases? Who develops What are the business models? Beyond the Blockbuster model?

From single firms to networks?

The more complex the NEDD system, the more disciplines, expertise and facilities.
Where will R&D be housed? Will nanoenabled therapies be created by networks of public and private R&D firms?

What does this mean for IP management? Also what does it mean for development contracts?

Costly and time-consuming trials

The more complex the NEDD therapy, the greater the challenge of understanding toxcity and saefty. This may pressure already itime and resopurce intensive clinical trial processes

Is the bottleneck of current clinical trial procedure compunded by more complex therpies? Will this shape wha NEDDs will be invested in (less risky?)

Is the success of NEDD therapy options dependent on innovations in the clinical trial procedure?

co-inventor on the 'Viagra' patents (Drug Discovery Today), January 2009)