Global Alliance for NanoBioElectronic
A European Union and USA program Project

Babak Kateb, MD

Chairman of the Board of Directors

Society for Brain Mapping & Therapeutics (SBMT) , CA

President and Scientific Director of Brain Mapping Foundation

Director of National Center for Nano-Bio-Electronics (NCNBE),

Director of Brain Technology and Innovation Park (BTIP)

Chairman CEO, Smart Microscopy Inc.

Mission of SBMT:

….improve the diagnosis, treatment and rehabilitation of patients afflicted with neurological disorders.

Approach Of SBMT

…multi-disciplinary collaborations with government agencies, patient advocacy groups, educational institutes and private sectors (industry) as well as philanthropic organizations.

www.WorldBrainMapping.Org

SBMT Annual Meetings and Symposia
















World Congresses Held at:

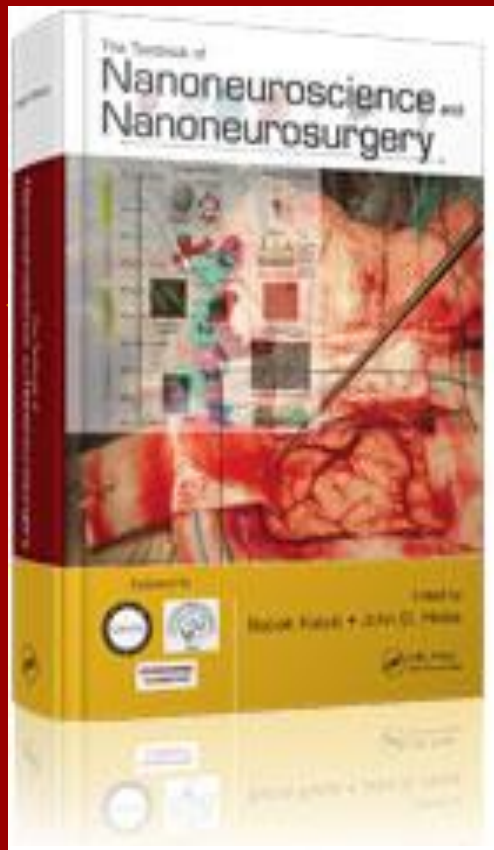
1.USC-Keck School of Medicine, Los Angeles, CA-2004
2.University of Auvergne Clermont Ferrand-France-2006
3.The West in Pasadena Hotel, Pasadena, CA-2005
4.The Washington Plaza Hotel-2007
5.California NanoScience Institute-UCLA Auditorium-2008
6.Harvard Medical School, Conference Center, Boston, MA-2009
7.USUHS, Conference Center, Baltimore, MD, 2010
8.UCSF School of Medicine Conference Centre, 2011
9.Toronto Metro Convention Center, 2012
10.Baltimore Convention Center, 2013
11.Sydney Australia (March 17-19, 2014)
12.Los Angeles Convention Center (March 6-8, 2015)
13.Miami Florida, 2016
14.Silicon Valley , CA 2017 (March 30-April 1st 2017)

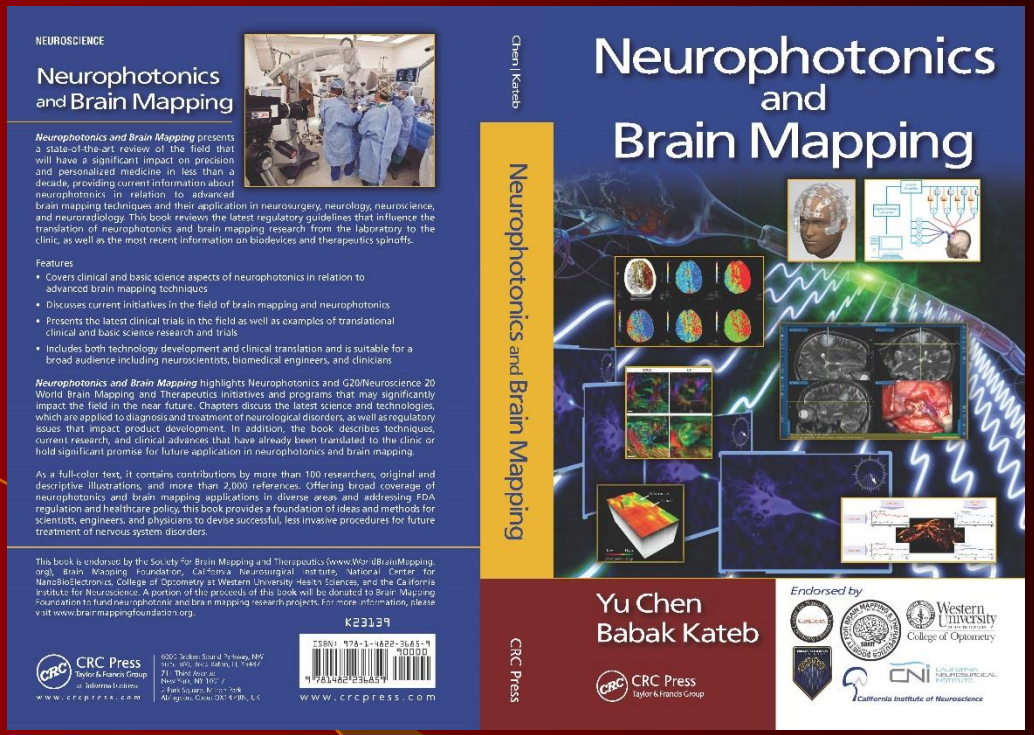
Satellite Symposium Held at:

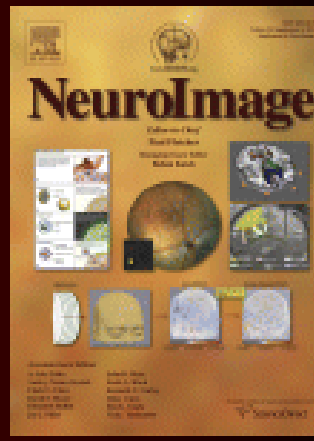
2012 satellite Symposium-France & 2015 In DC

WORLD BRAIN MAPPING & THERAPEUTICS INITIATIVE G20+/N20+

WWW.WORLDBRAINMAPPING.Org







THE WHITE HOUSE
WASHINGTON

November 21, 2013

Dr. Babak Kateb
West Hollywood, California

Dear Dr. Kateb:

This is just a quick note to thank you for your kind gift. Each day, I am moved and inspired by the generosity of the American people, and I appreciate your thoughtful gesture.

Thank you again for your wonderful gift. I wish you all the best.

Sincerely,

Global Brain Policy and Advocacy:

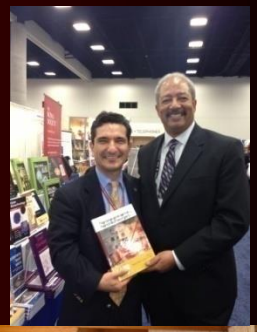
From scientist to: The President, Congress, Senate, Parliament, supreme Court justices, Ministers, Military leaders, ambassadors and Consul Generals, advocacy groups, Hollywood Stars and international coalitions















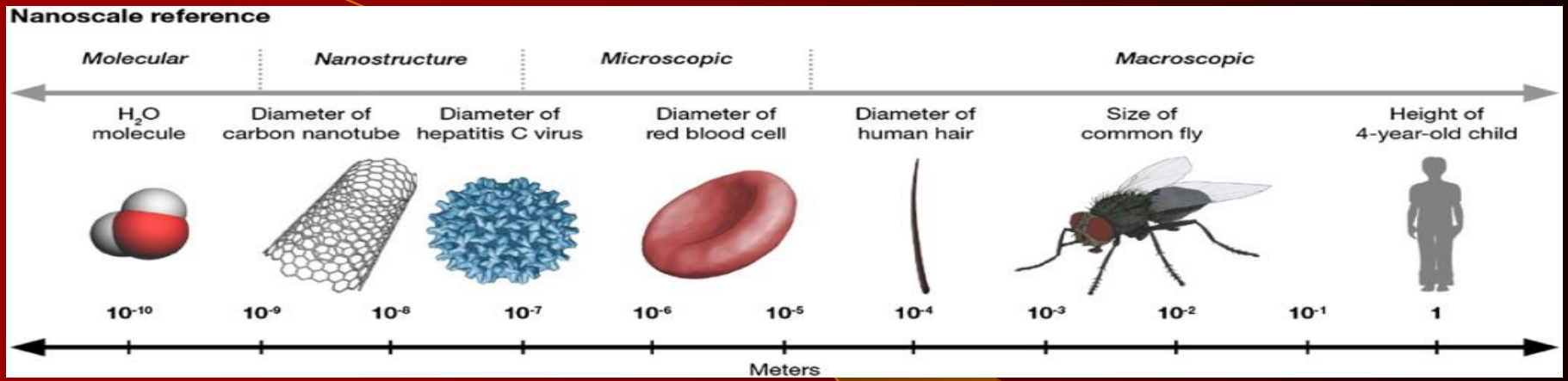







•**What is the Definition of Brain Mapping?** http://vimeo.com/vc1/review/89547242/827ac5b02

The study of the anatomy and function of the brain and spinal cord through the use of imaging (including intraoperative, microscopic, endoscopies and multi-modality imaging), immunohistochemicistry, molecular and optogenetics, stem cell and cellular biology, engineering (Material, Electrical and biomedical), neurophysiology and nanotechnology.



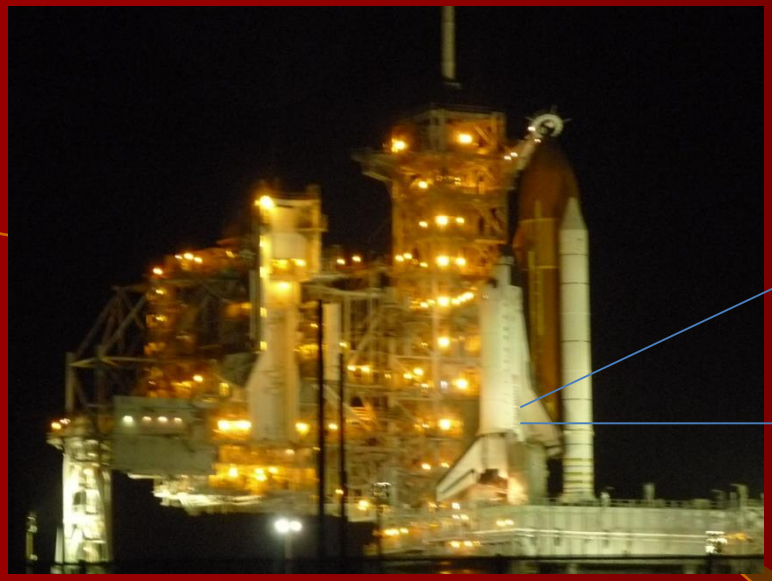
•**What is: Nanoneuroscience, Nanoneurosurgery and Nanobioelectronics?**

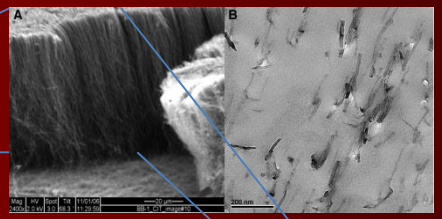
Application of nanotechnology in neuroscience is called nanoneuroscience

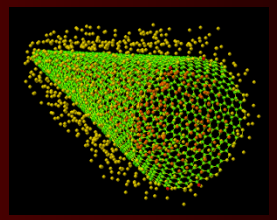
The therapeutics application of nanotechnology, which could enhance neurosurgical treatments is called nanoneurosurgery

Integration of nanotechnology, device, cellular therapy and imaging called nanobioelectronics.

Using NASA Carbon Nanotube for Drug Delivery to Brain Cancers: A NanoBioElectronic Approach







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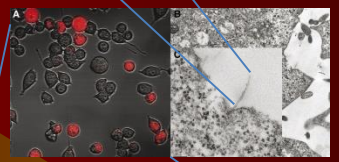

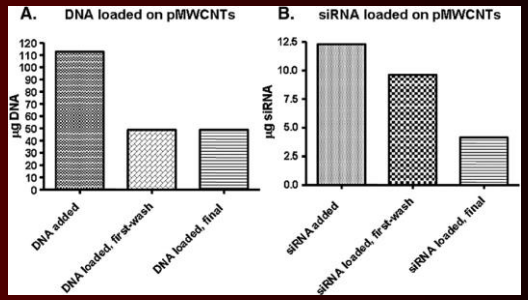

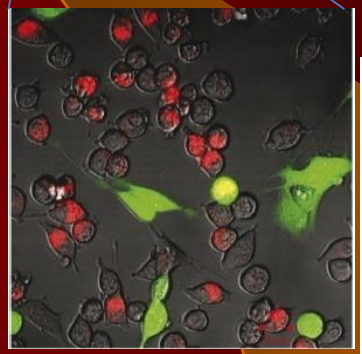

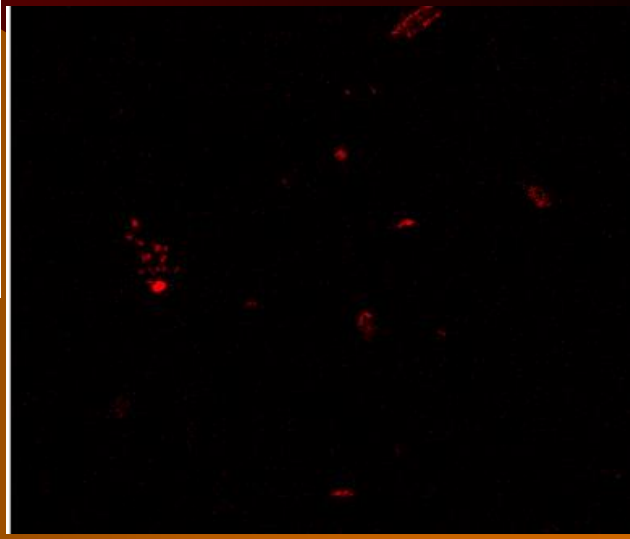

ELSEVIER

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage xx (2007) xxx–xxx

Internalization of MWCNTs by microglia: Possible application in immunotherapy of brain tumors

Babak Kateb,[a,*] Michelle Van Handel,[a] Leying Zhang,[a] Michael J. Bronikowski,[b] Harish Manohara,[b] and Behnam Badie[a,*]

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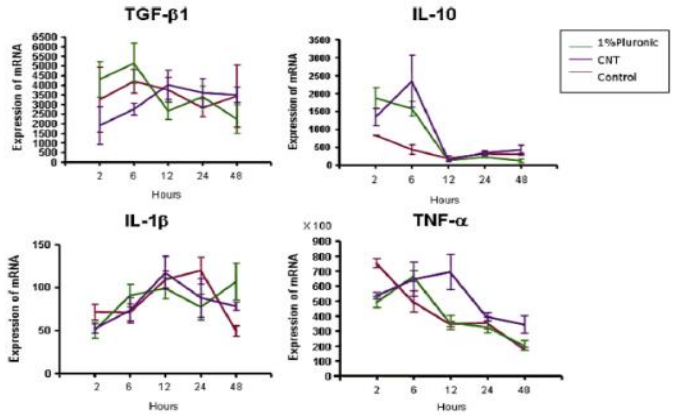

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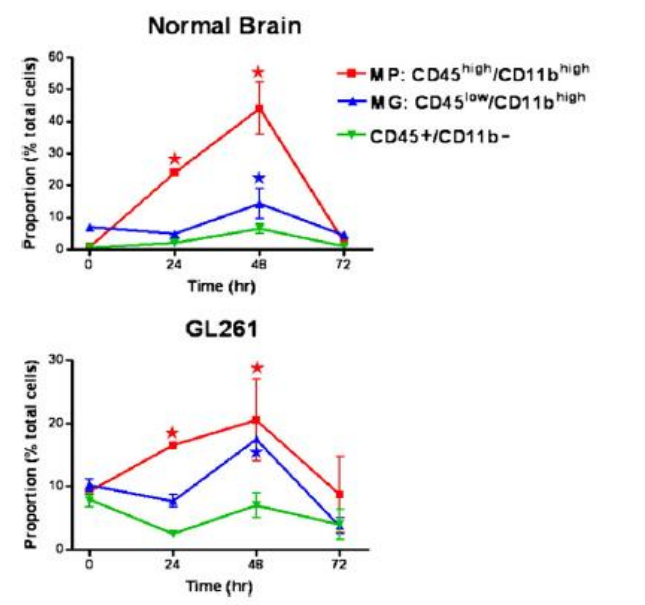
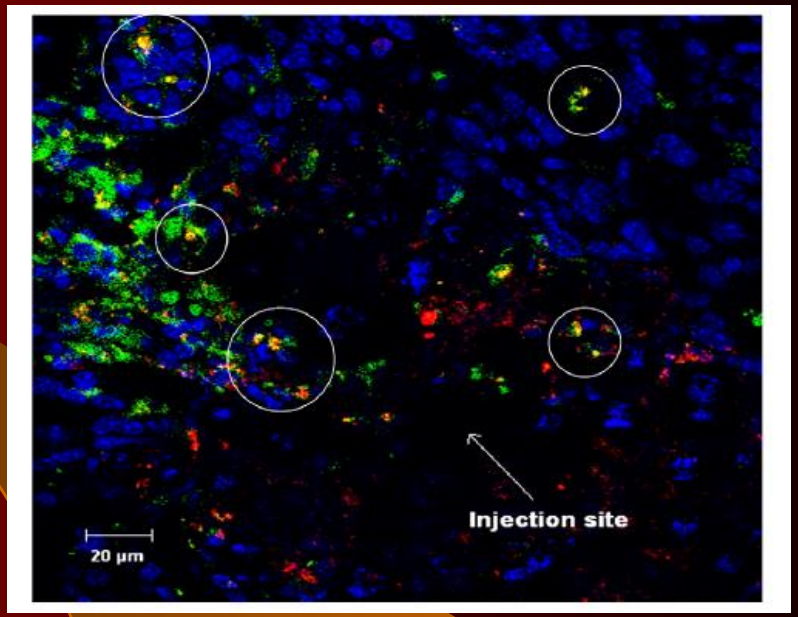
journal homepage: www.elsevier.com/locate/jneuroim

Selective uptake of multi-walled carbon nanotubes by tumor macrophages in a murine glioma model

Michelle VanHandel [a], Darya Alizadeh [a], Leying Zhang [a], Babak Kateb [a,c], Michael Bronikowski [b], Harish Manohara [b], Behnam Badie [a,*]

[a] Division of Neurosurgery, City of Hope Medical Center and Beckman Research Institute, 1500 East Duarte, Duarte, CA 91010, USA
[b] Jet Propulsion Laboratory, 4800 Oak Grove Drive Pasadena, CA 91109 and California Institute of Technology, 1200 East California Boulevard, Pasadena, CA 91125, USA
[c] Brain Mapping Foundation, 8159 Santa Monica Blvd Suite number 200, Hollywood, CA 90046, USA





Effect of MWCNT on inflammatory cell infiltration

*PKH26: a non-toxic hydrophobic red fluorescent dye

-2 days post Injection of 5pg of MWCT-PKH* intratumorally in mice
-MWCNTs are depicted in red (PKH),
-CD68+ cells (macrophage and microglia) in green (FITC), and
-tumor nuclei in blue (DAPI).
-MWCNT-PKH-positive CD68+ cells were noted throughout the tumor and tumor periphery (circles)
-MWCNTs can be detected in vivo

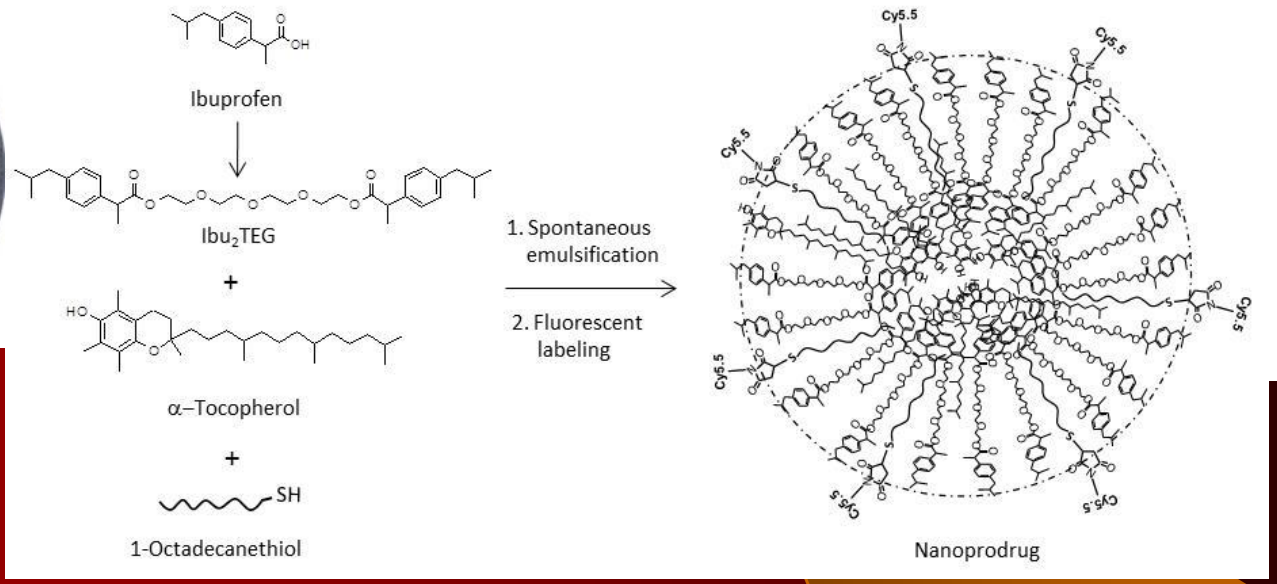
OPEN ACCESS Freely available online

PLOS ONE

Reactive Oxygen Species-Activated Nanoprodrug of Ibuprofen for Targeting Traumatic Brain Injury in Mice

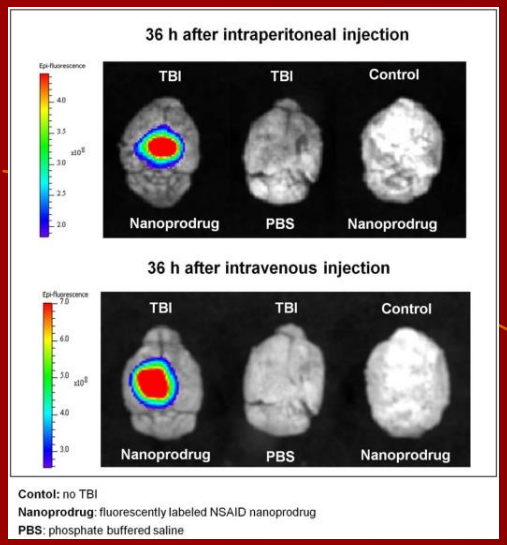
Morgan A. Clond[1], Bong-Seop Lee[2], Jeffrey J. Yu[2], Matthew B. Singer[1], Takayuki Amano[2], Alexander W. Lamb[1], Doniel Drazin[2], Babak Kateb[2], Eric J. Ley[1], John S. Yu[2]*

1 Department of Surgery, Division of Trauma and Critical Care, Cedars-Sinai Medical Center, Los Angeles, California, United States of America, 2 Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, California, United States of America



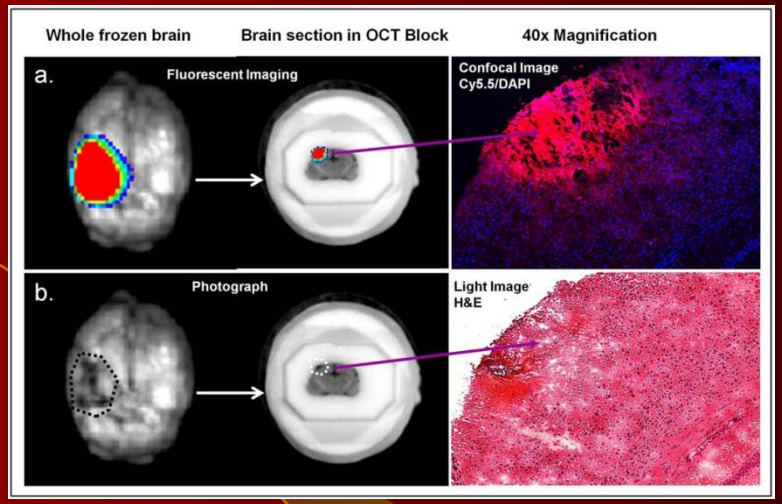
Nanoprodrug preparation and characterization. This chemical schematic shows the molecular structures of the individual ibuprofen molecule, the Ibu2TEG complex consisting of two ibuprofen molecules jointed by a **tetraethylene glycol (TEG**) spacer, the anti oxidant **a-tocopherol,** and the **hydrophobic 1-octadecanethiol** which is joined to **Cy5.5 (maleimide fluorescent tracer)** after emulsification. The final product is represented on the right hand side of the schematic.

Reactive Oxygen Species Activated Nanoprodrug of ibuprofen for Targeting Traumatic Brain Injury in Mice



Contol: no TBI
Nanoprodrug: fluorescently labeled NSAID nanoprodrug
PBS: phosphate buffered saline

Comparing accumulation for IV and IP administration. The injection of nanoprodrug either IV or IP results in similar accumulation in animals with TBI, while normal animals given nanoprodrug and TBI animals ***do not show any background flourescence***. Brains are oriented with the rostral portion toward the top of the image.

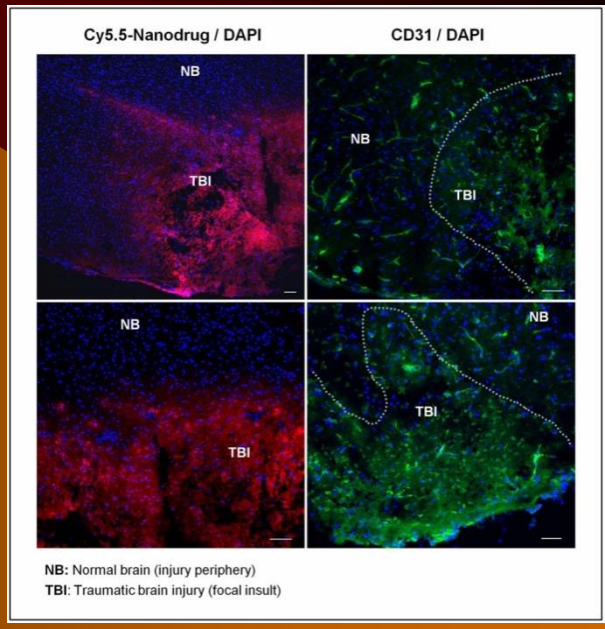


Drug accumulation in the area of injury. Accumulation of the drug in the left parietal area is visualized (a) using fluorescent imaging
in the top panels and (b by traditional photography and hemotoxylin and eosin staining in the lower pannels.

Disorganized vascular structures at the region of nanoprodrug uptake.

Representative images from two brains showing nanoprodrug uptake on the left column and CD31 staining of vascular endothelial cells on the right.

Outside of the TBI region, vascular structures exist in normal tubular arrangements, but these are disorganized within the region of injury. The nuclei are stained with DAPI are displayed in blue. Scale bar, 50 mm



NB: Normal brain (injury periphery)
TBI: Traumatic brain injury (focal insult)

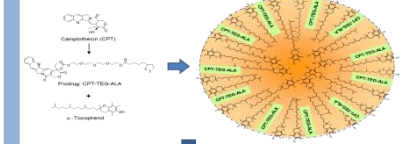
NanoProdrug

Bong Seop Lee[a], Lei Zhang[a], Takayuki Amano[a], Nam-Ho Kim[a], Hong Qiang Wang[a], Minzhi M. Liu[a], Paul Lapchak[a], Maya Koronyo-Hamaoui[a], Yosef Koronyo[a], Eric J. Ley[b], Morgan A. Clond[b], Jeffrey J Yu[a], Matthew B. Singer[b], Alexander W. Lamb[b], Doniel Drazin[b], Babak Kateb[a], Keith L. Black[a] and John S. Yu[a]

[a] Department of Neurology & Neurosurgery, Cedars-Sinai Medical Center, [b] Department of Surgery, Cedars-Sinai Medical Center

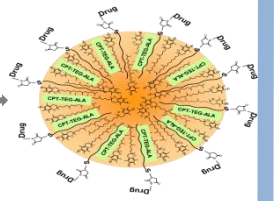
Targeted Chemotherapy

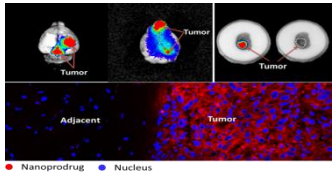
Chemotherapeutic nanoprodrug



Multi-targeting nanoprodrug

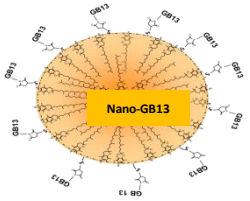
Therapeutic agents (chemos, peptide, antisense, DNA, RNA, protein), imaging or diagnostic agents





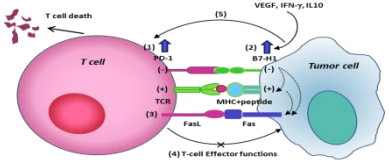
The in vivo study in mice demonstrated that the CPT nanoprodrug passed through the BBB and specifically accumulated in brain tumor tissue, but not in healthy brain tissue and other organs.

Nanoprodrug of cytotoxic fusion protein GB13



GB13 comprises a mutated IL13 as a targeting igand and Pseudomonas exotoxin as an anticancer cytotoxic agent. The vast majority of gliomas express a receptor for IL13. IL13 receptor on gliomas can be used as an active target for IL13. Mutated hIL13 is less toxic on normal cells.

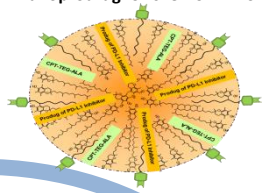
Chemo-Immunotherapy



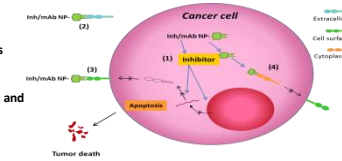
B7-H1 induced immune suppression

(1) Tumor microenvironment leads to up-regulation of the programmed death 1 receptor (PD-1) in tumor-reactive T cells. (2) B7-H1 is an immune suppressive molecule that is overexpressed in cancer cells . (3) B7-H1 positive cancer cells become resistant to Fas-mediated apoptosis despite of high expression of surface Fas. (4) Binding of B7-H1 on cancer cells to PD-1 on T cells induces resistance of cancer cells against T cell-mediated killing. (5) The activation of B7-H1/PD-1 pathway induces T cell anergy or promotes T-cell apoptosis.

Nanoprodrug for chemo-immonotherapy



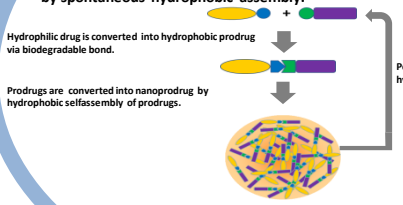
- ❑ The nanoprodrug can reverse cancer-induced immunosuppression, and thus enhance the efficacy of immunotherapy.
- ❑ The nanoprodrug can reverse chemotherapy-induced immuno-suppression, and thus enhance the efficacy of chemotherapy.
- ❑ The nanoprodrug strategy can be used to combine chemotherapy and immunotherapy.



- PD-1/PD-L1 pathway plays a pivotal role in the ability of tumor cells to evade the host's immune system.
- Blockade of PD-1/PD-L1 pathway can reverse cancer-induced immunosuppression.

NanoProdrug

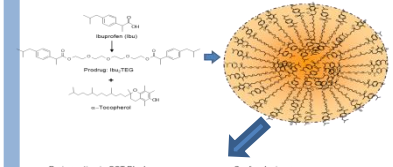
While most of the efforts to improve bioavailability and therapeutic efficacy of drugs have strived to develop a more water-soluble prodrug, we aimed to design a more hydrophobic prodrug that can be transformed into a nanoprodrug by spontaneous hydrophobic assembly.



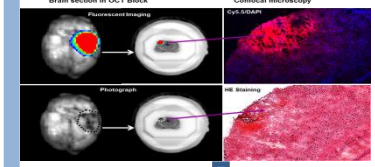
The formation into nanoprodrugs generates a large reactive surface area on which the interaction between hydrolytic enzymes and prodrugs can take place.

Traumatic Brain Injury (TBI)

In industrialized countries, traumatic brain injury (TBI) is the leading cause of death in those under the age of 45 and traumatic injuries account for a greater number of potential years of life lost than all other causes of death .

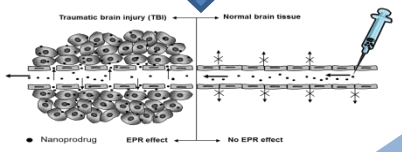


Non-steroidal anti-inflammatory drugs (NSAIDs) are a promising candidate for controlling the effects of inflammation after TBI. In order to circumvent the adverse side effects associated with NSAIDs and improve bioavailability, various NSAID prodrugs have been developed through the formation of bioreversible ester bonds. The hydrophobic NSAID prodrugs can be converted into nanoprodrug.



Blood brain barrier in TBI

In TBI, the integrity of the BBB is known to be severely compromised at the site of injury . The destruction of the BBB interface can be a direct result of the traumatic injury itself, as well as due to secondary consequences of inflammation-related mechanisms, metabolic disturbances, and astrocyte dysfunction. This permeability may represent a serendipitous opportunity to deliver drugs to the site of injury .

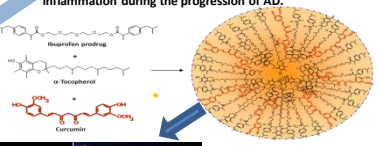


EPR effect in TBI

The phenomenon of failing vascular barrier activity has been described in oncology literature as the enhanced permeability and retention (EPR) effect . Although the etiology for the EPR effect is different in TBI than it is in tumor, the effect is the same .

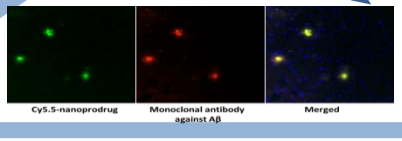
Alzheimer

Alzheimer's disease (AD) is a progressive and invariably fatal degenerative dementia characterized by a progressive deterioration of cognitive and behavioral functions. The progressive accumulation of Aβ aggregates *via* a fibrillation process is widely believed fundamental to initialize the neurodegenerative pathology and trigger a cascade of events, which include neurotoxicity, oxidative stress and inflammation during the progression of AD.



Studies have indicated that curcumin can interact with high affinity to oligomeric Aβ1-42, and inhibiting its aggregation and deposition, even disrupting the existing plaques, and partially restoring the distorted neuritis. As most neurodegenerative diseases, AD is characterized by excessive inflammation and production of reactive oxygen species (ROS).

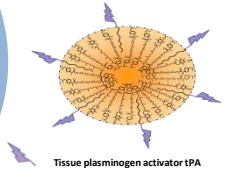
- The nanoprodrug is a ROS scavenger.
- The nanoprodrug is anti-inflammatory.
- The nanoprodrug has an anti-amyloid function.



Neurodegenerative disorders such as Alzheimer's disease and amyotrophic lateral sclerosis (ALS) are characterized by neurovascular dysfunctions and defective BBB function. We hypothesize that the defective BBB may facilitate the transport of the nanoprodrug through BBB into the brain and thus the targeting Aβ aggregates and pathological conditions in the Aβ environment such as excessive inflammation and ROS.

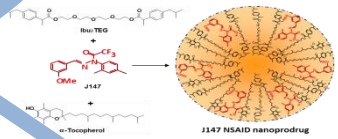
Stroke

tPA-NSAID nanoprodrug for the treatment of AIS



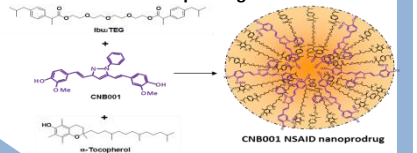
Acute ischemic stroke (AIS) is the third leading cause of death and the leading cause of adult disability in the USA. Tissue plasminogen activator tPA (Alteplase) is currently the only FDA-approved treatment of acute ischemic stroke. tPA promotes thrombolysis by activating the endogenous fibrinolytic system: tPA catalyzes the conversion of plasminogen to plasmin, which in turn degrades fibrin and leads to clot lysis and cerebral reperfusion. Blood brain barrier in the ischemic brain is significantly leaky and permeable.

J147 NSAID nanoprodrug



J147 has the ability to enhance memory in normal animals as well as to prevent memory deficits in AD transgenic mice. The neurotrophic and memory-enhancing activities of J147 are associated with an increase in brain derived neurotrophic factor (BDNF) levels and the expression of BDNF responsive proteins, the enhancement of LTP, synaptic protein preservation, the reduction of markers for oxidative stress and inflammation, the reduction of amyloid plaques, and lower levels of soluble Aβ1–42 and Aβ1–40.

CNB001 NSAID nanoprodrug



CNB-001 is neuroprotective in a variety of nerve cell toxicity assays, including excitotoxicity, oxidative stress, amyloid toxicity, and glucose starvation. It activates CaMKII by a cAMP-independent mechanism, facilitates the induction of hippocampal LTP, and is orally active in a rat object recognition test for memory.

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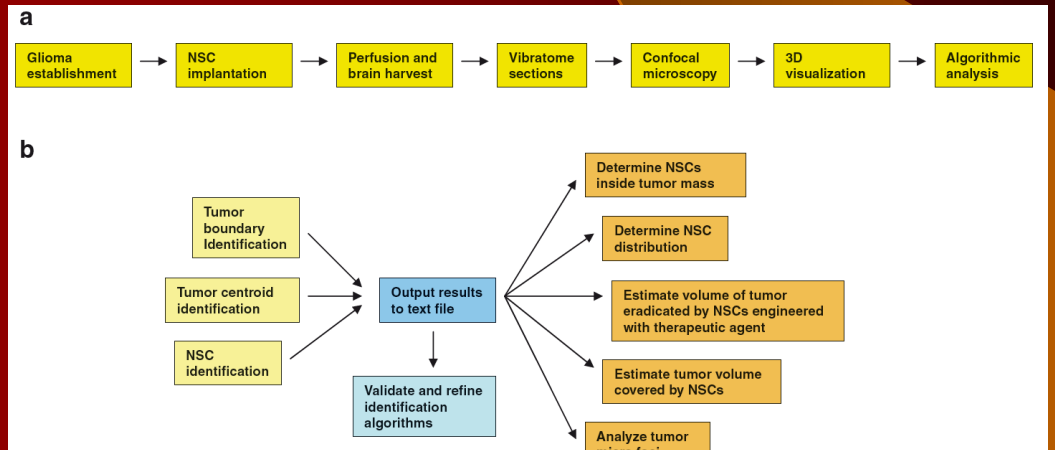
NeuroImage 37 (2007) S18–S26

Novel method for visualizing and modeling the spatial distribution of neural stem cells within intracranial glioma

David Lin,[a,b,c,1] Joseph Najbauer,[a] Paul M. Salvaterra,[b] Adam N. Mamelak,[d,2] Michael E. Barish,[b] Elizabeth Garcia,[a] Marianne Z. Metz,[a] Stephen E. Kendall,[e] Marisa Bowers,[a,b] Babak Kateb,[d] Seung U. Kim,[f,g] Margaret Johnson,[c] and Karen S. Aboody[a,b,*]

Neural Stem Cell have tumor-tropic properties
Analysis of visualization & quantification of the spatial distribution of Tumor-tropic NSC in mouse glioma model
We used mathematical modeling in order to predict therapeutic efficacy of representation NSC based glioma therap



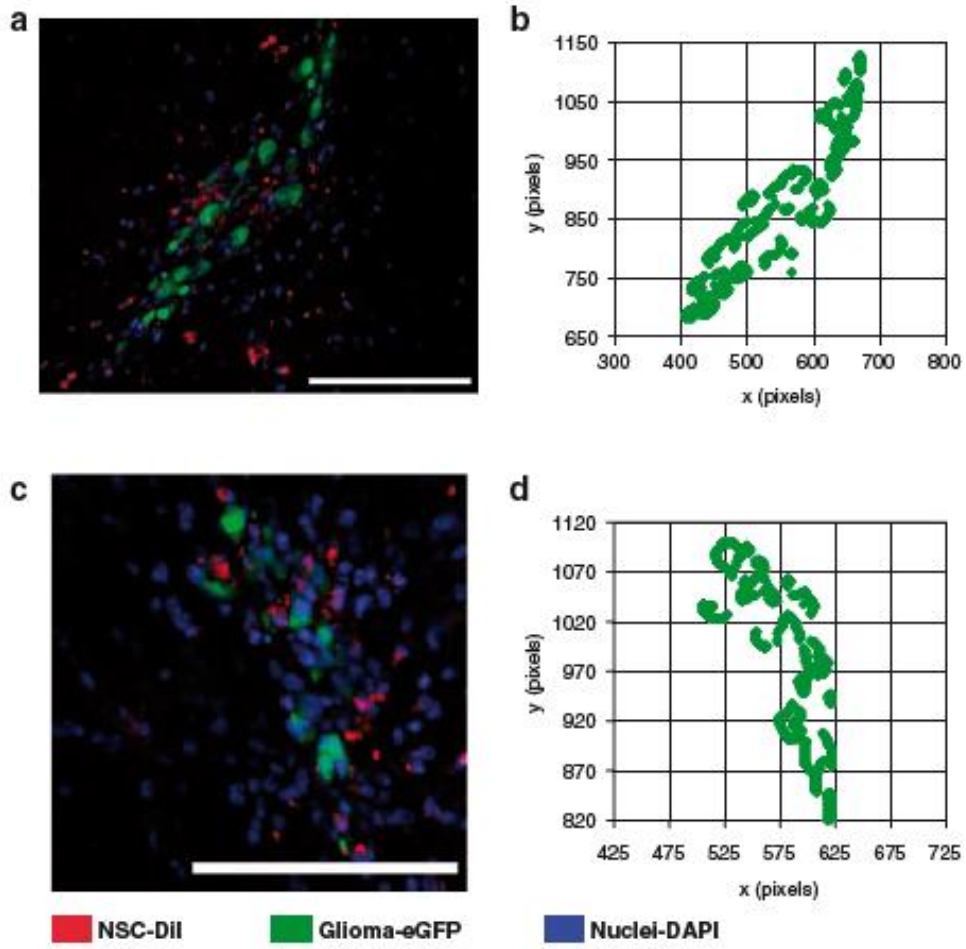
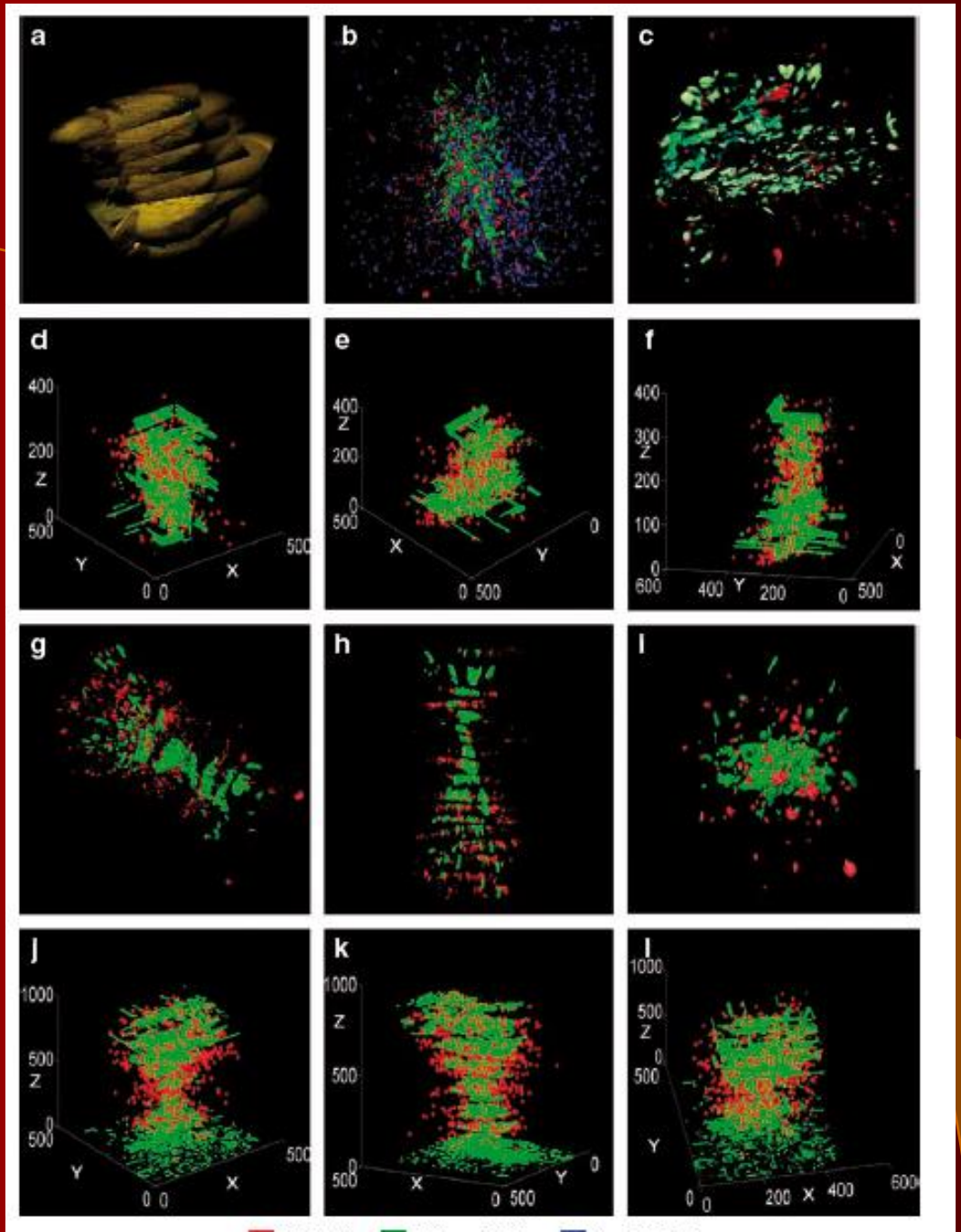


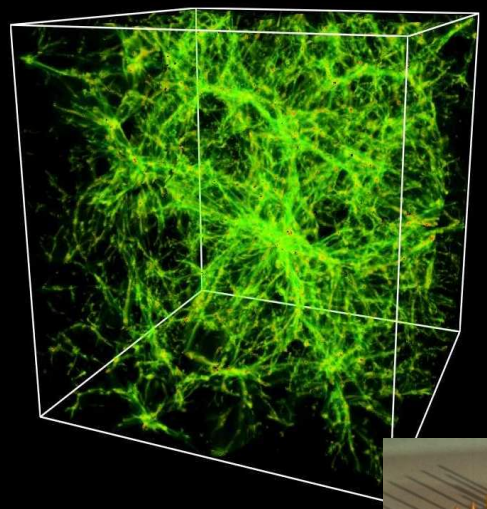
Fig. 3. Validation of tumor boundary estimation algorithm. (a, c) Single optical sections obtained from confocal microscope at 20× showing CM-DiI-labeled NSCs (red), nuclei (blue), and eGFP-expressing tumor cells (green). Scale bar= 100 μm. (b, d) Scatterplots of points marking the estimated tumor boundary outputted by the tumor boundary estimation algorithm in panels a and c, respectively. The shapes of these scatterplots matched the eGFP labeled tumor boundary in panels a and c.

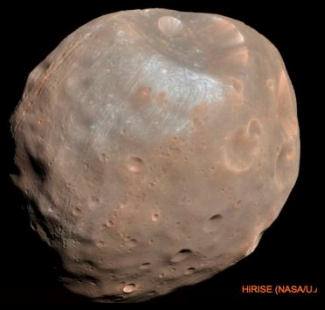
Method:
AMIRA Software
Mathematical Modeling
(MATHLAB)

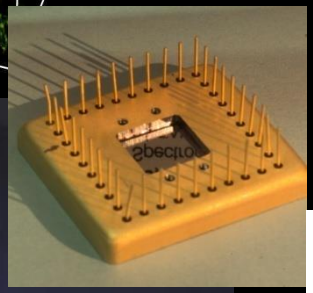


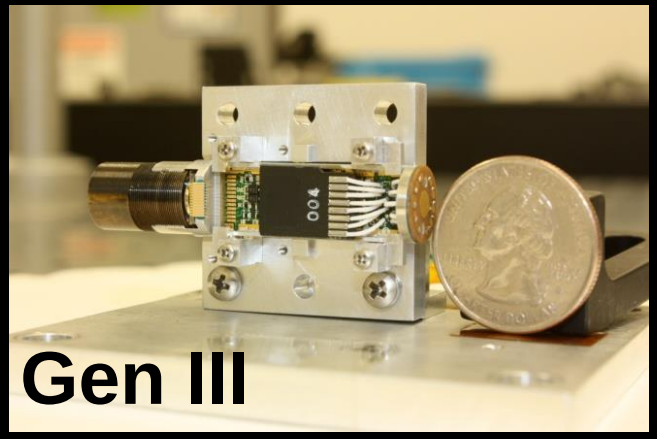
Visualization and quantification modeling of NSC distribution for brain mapping and therapeutics.

High Performance UV Imaging Technology: NASA-JPL's Delta doping Technology





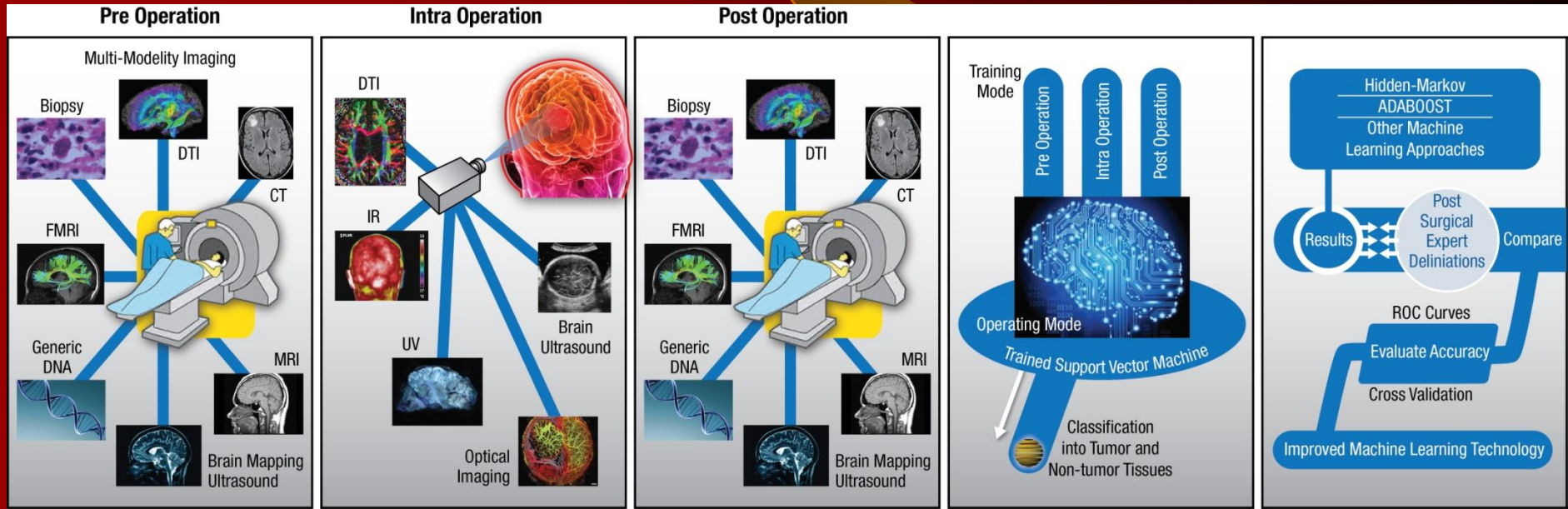




Smart Microscope & Supercomputing Project:

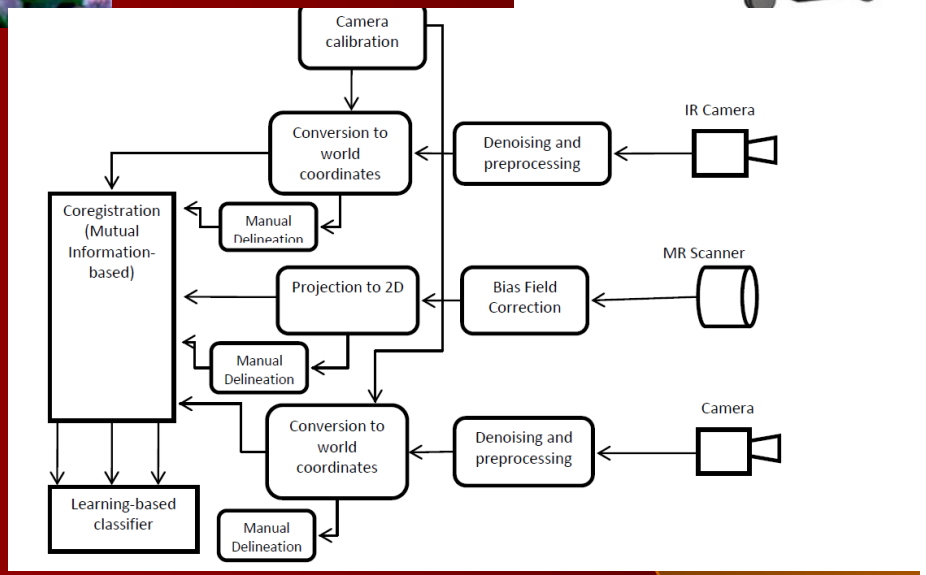
Babak Kateb, Ray Chu, Lakshman Prasad, Frank Alexander, Shouleh Nikzad and Keith Black

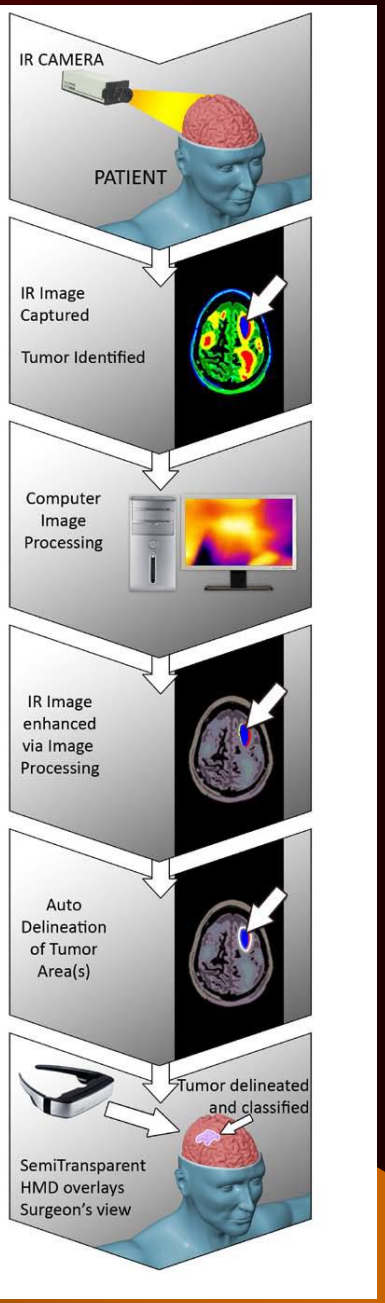
How surgical cases, artificial intelligence , Pattern Recognition and Meta Data, could help predict diseases behavior and response to a treatment

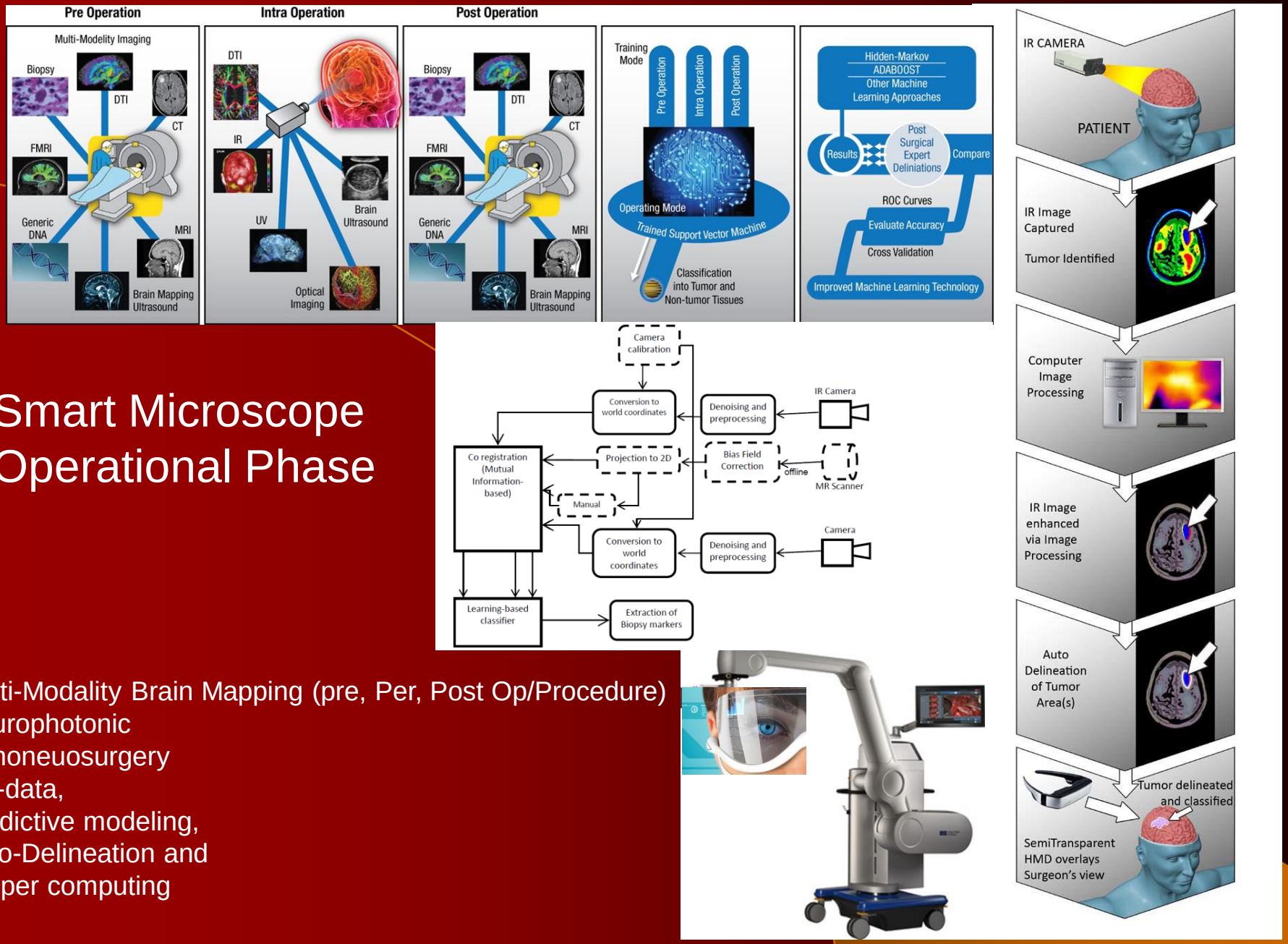


Auto-deliniation Machine Learning

AUGMENTED REALITY







Smart Microscope Operational Phase

ulti-Modality Brain Mapping (pre, Per, Post Op/Procedure)
europhotonic
anoneuosurgery
ig-data,
redictive modeling,
uto-Delineation and
upper computing

Conclusion:

1.Application of computer science in brain mapping and therapeutics, Nanoneuroscience, nanoneurosurgery and nanobioelectronic will be revolutionizing the field of clinical neuroscience in next decade though none/less invasive targeted therapies for the neurological disorder;

2.Advance therapeutics could ONLY be provided to the patients if government, academia, industry and private partnership take place.

3. Scientists must be involved in shaping brain policy and help standardize the neurotechnologies.

4. Development of advance therapeutics and intelligent microscopy only possible through partnership and collaborations.

5. We are advocating for funding and creation of Global Alliance for NanoBioElectronics between EU-USA (Horizon 2020 nanomedicine)

Thank you