Photothermal Gold Nano-Rods, Detects and Gets Rid of Cancer SAFELY in Different Animals and Stops Cancer Cell Migration Which Kills 90% of Cancer Patients...

EL-SAYED RESEARCH GROUP IN COLLABORATION WITH: DR SHIN GROUP AT EMORY CANCER CENTER in Atlanta, THE RESEARCH GROUP OF DR SALAH SELIM AT CAIRO UNIVERSITY AND THAT OF DR ABDOON OF THE EGYPTION NATIONAL RESEARCH CENTER IN CAIRO.

OUTLINE

 1. Plasmonic properties of gold metals on the Nanoscale: Strong Scattering or Strong Absorption depends on their size.

2.Using plasmonic enhancement of light scattering in cancer cell detection and strong absorption(which is converted into heat) in cancer photo thermal therapy AND APPLICATIONS IN TREATING DIFFERENT ANIMALS.

- 3. Results of the Long time testing of the effect of the treatment on the body chemistry in mice, cats and dogs.
- 4. Experiments show that the GOLD NANORODS photo-thermal treatment, IN ADDITION TO KILLING

BULK GOLD IS PRECIOUS <u>BECAUSE IT DOES</u> <u>NOTHING</u> (it does not tarnish i.e. it does not react) is more precious on the nanoscale







Death Mask of Tutankhamun ~1325 B.C.

Tutankhamun's coffin

THE GREAT POTENTIAL OF NANO-TECHNOLOGY.

- AS THE SIZE OF ANY MATERIAL DECREASES TO 1-100nm length scale, ITS PROPERTY CHANGES AS ITS SIZE OR SHAPE CHANGES((the origion of Nanotechnology)..
- THUS EVERY MATERIAL CAN GIVE US MANY NEW MATERIALS EACH WITH DIFFERENT NEW PROPERTIES AS ITS SIZE OR SHAPE IS CHANGED IN THE 1-100 NANOMETERS, MANY WILL HAVE USEFUL PROPERTIES TO START NEW MEDICAL TREATMENT FOR PATIENTS, NEW INDUSTRIES,.....

WHY NANOMETER AND NOT MICRO- OR PICO-METER???

THE PROPERTIES OF ANY MATERIAL ARE DETERMINED BY THE SPACE AVAILABLE* FOR THEIR ELECTRONS TO EXECUTE THEIR ALLOWED MOTION. THIS DEFINES A CHARACTERISTIC LENGTH SCALE FOR THE PROPRTY OF EACH MATERIAL: **"USUALLY BETWEEN 1-100 NANOMETER** IN LENGTH AND DIFFERENT



1.The Electromagnetic field of the captured Photon is Enhanced by Thousands of Times on the surface of the nanoparticle as a Result of the <u>Coherent Oscillation Of the Collective Excitation of the Free Conduction</u> <u>Band Electrons in the Metal Cluster.</u>

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3.The Strongly Absorbed Energy is Rapidly Converted Into Heat That Can Have Useful Photo-Thermal Applications in Different Fields.

Some known Facts about Cancer

- In 2009 in the U.S., cancer newly diagnosed in 2.5 million people and killed 560,000
- #1 or #2 cause of death. With lung cancer most dominant followed by prostate for men or breast for women.
- Cancer cells divide rapidly as directed by its unhealthy nucleus.
- Caused either by genes and/or by environmental factors (smoking, drinking TOO MUCH alcohol, eating fatty food)
- Cancer Kills 75 Americans EVERY MINUTE.
- One fourth of dead people in the World died of cancer !!!
- <u>Most can be cured IF DISCOVERED EARLY (Get examined</u> <u>continuously) or if it is treated photothermally with gold</u>
- Nanoparticles as we will show Cancer Facts and Figures, American Cancer Society, 2009.

THE MANY USEFUL PROPERTIES OF GOLD ON THE NANOSCALE IN MEDICINE

THE LOCALIZED SURFACE PLASMON RESONANCE OF THE GOLD NANOPARTICLE (LSPR):

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- Options: surgery, radiation therapy, chemotherapy, hormone replacement, biologics
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- Surgery is used in 50% of all cancer treatments, rad/chem is tried in 5%^{*.}
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ERIK DREDEN





HaCaT *noncancerous cells*



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DETECTION OF ONE CANCER CELL USING Enhanced GOLD NANOPARTICLES LIGHT SCATTERING AND & A SIMPLE LAB

<u>MICROSCOPE</u>

HaCaT *noncancerous cells*











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DIFFRACTION UNLIMITTED IMAGING

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DIFFERENT TYPES OF CANCER TREATMENTS

Before treatment



BELOW: Tumor ON LEFT has been treated by Surgery. The ONE on righr by Surgery followed by Photothermal Treatment.





1 month later, the left half treated by surgery only is ruptured. Retreated Photothermally.

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Past attempts to develop anti-metastasis drugs have not been successful in clinical trials

- Resistance
- Side effects

Weber, G. F. Why Does Cancer Therapy Lack Effective Anti-Metastasis Drugs? *Cancer Lett.* 2013, 328, 207-11.
Morgillo, F.; Lee, H. Y. Resistance to Epidermal Growth Factor Receptor-Targeted Therapy. *Drug Resist. Updat.* 2005, *8*, 298-310.
Effects of Chemotherapy and Hormonal Therapy for Early Breast Cancer on Recurrence and 15-Year Survival: an Overview of the Randomised Trials. *Lancet (London, England)* 2005, *365*, 1687-717.

Nanoparticles can inhibit cancer cell migration or metastasis (Recently, observed by different

researchers)

Not very biocompatible

- Chor Yong Tay *et al* used nano-ceramics, such as titania, silica, and hydroxyapatite
- Arvizo *et al.* used non-specific targeted gold nanospheres (AuNSs)
- Murphy et al used gold nanoparticles (AuNPs)
- Zhou et al used gold nanorods (AuNRs) coated with bovine serum albumin (BSA)

Yang, J. A.; Phan, H. T.; Vaidya, S.; Murphy, C. J. Nanovacuums: Nanoparticle Uptake and Differential Cellular Migration on A Carpet of Nanoparticles. *Nano Lett.* **2013**, *13*, 2295-2302.

Arvizo, R. R.; Saha, S.; Wang, E.; Robertson, J. D.; Bhattacharya, R.; Mukherjee, P. Inhibition of Tumor Growth and Metastasis by a Self-Therapeutic Nanoparticle. *Proc. Natl. Acad. Sci. U.S.A.* **2013**, *110*, 6700-6705.

Tay, C. Y.; Cai, P.; Setyawati, M. I.; Fang, W.; Tan, L. P.; Hong, C. H.; Chen, X.; Leong, D. T. Nanoparticles Strengthen Intracellular Tension and Retard Cellular Migration. *Nano Lett.* **2014**, *14*, 83-8.

Nuclear targeting AuNPs:

- increase nuclear stiffness
- Increase lamin A/C proteins

Thus inhibit migration



Moustafa R. K. Ali⁺; Yue Wu⁺; Deepraj Ghosh; Brian H. Do; Kuangcai Chen; Michelle R. Dawson; Ning Fang⁺; Todd A. Sulchek⁺; Mostafa A. El-Sayed⁺ 2017, ACS N DOI: 10.1021/acsnano.6b08345

3 dimensional microscope shows the AuNPs are concentrated at the nuclear membrane The video shows the z-stack scanning of





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AuNPs stuck at the nuclear membrane cause increase in lamin A/C protein expression



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Nuclear stiffness increased by AuNPs detected by atomic force microscope (AFM)

Cells (with AuNPs)



Cell nuclear stiffness increase with AuNPs



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Migration speed as a function of AuNPs concentration



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The cells without Gold Nanoparticles moved faster and filled the empty space in 12 hours. The gold Nanoparticles Slowed Down the cells So they can only fill out part of the empty space.

Gold nanoparticles affect cytoskeleton protein formation Cytoskeleton proteins are responsible for cell movement



Ning Fang *; Ronghu Wu *; Mostafa A. El-Sayed *, 2017, PNAS accepted

CELLS and STUDIES ON DEVELOPPING DETECTION AND TREATMENT METHODS OF CANCER USING GOLD NANOPARTICLES (Georgia Tech)





Dr Xiaohua Huang



MAGAN MAC KEY



Mena Aioub



Dr Ivan El-Sayed.

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BIN KANG



MOUSTAFA ALI

ANIMAL AND LONG TIME TOXICITY



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Thank You



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One tumor has been treated by Surgery(Left). The other by Surgery followed byPPTT(Right)





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111.Metastasis(the migration of the cancer cellsfrom its origional location to more serious location) isthe cause of 90% of CancerMetastasisPatient's Death.

Weigelt, B., Peterse, J. L. & van 't Vee L. J. Breast cancer metastasis: marker and models. Nature Rev. Cancer 5, 591–602 (2005) https://www.cancer.gov/types/meta atic-cancer



Past attempts to develop anti-metastasis drugs have not been successful in clinical trials

- Resistance
- Side effects

Weber, G. F. Why Does Cancer Therapy Lack Effective Anti-Metastasis Drugs? *Cancer Lett.* 2013, 328, 207-11.
Morgillo, F.; Lee, H. Y. Resistance to Epidermal Growth Factor Receptor-Targeted Therapy. *Drug Resist. Updat.* 2005, *8*, 298-310.
Effects of Chemotherapy and Hormonal Therapy for Early Breast Cancer on Recurrence and 15-Year Survival: an Overview of the Randomised Trials. *Lancet (London, England)* 2005, *365*, 1687-717.

Nanoparticles can inhibit cancer cell migration or metastasis (Recently, observed by different

researchers)

Not very biocompatible

- Chor Yong Tay *et al* used nano-ceramics, such as titania, silica, and hydroxyapatite
- Arvizo *et al.* used non-specific targeted gold nanospheres (AuNSs)
- Murphy et al used gold nanoparticles (AuNPs)
- Zhou et al used gold nanorods (AuNRs) coated with bovine serum albumin (BSA)

Yang, J. A.; Phan, H. T.; Vaidya, S.; Murphy, C. J. Nanovacuums: Nanoparticle Uptake and Differential Cellular Migration on A Carpet of Nanoparticles. *Nano Lett.* **2013**, *13*, 2295-2302.

Arvizo, R. R.; Saha, S.; Wang, E.; Robertson, J. D.; Bhattacharya, R.; Mukherjee, P. Inhibition of Tumor Growth and Metastasis by a Self-Therapeutic Nanoparticle. *Proc. Natl. Acad. Sci. U.S.A.* **2013**, *110*, 6700-6705.

Tay, C. Y.; Cai, P.; Setyawati, M. I.; Fang, W.; Tan, L. P.; Hong, C. H.; Chen, X.; Leong, D. T. Nanoparticles Strengthen Intracellular Tension and Retard Cellular Migration. *Nano Lett.* **2014**, *14*, 83-8.

Nuclear targeting AuNPs:

- increase nuclear stiffness
- Increase lamin A/C proteins

Thus inhibit migration



Moustafa R. K. Ali⁺; Yue Wu⁺; Deepraj Ghosh; Brian H. Do; Kuangcai Chen; Michelle R. Dawson; Ning Fang*; Todd A. Sulchek*; Mostafa A. El-Sayed* 2017, ACS N

3 dimensional microscope shows the AuNPs are concentrated at the nuclear membrane The video shows the z-stack scanning of





Moustafa R. K. Ali⁺; Yue Wu⁺; Deepraj Ghosh; Brian H. Do; Kuangcai Chen; Michelle R. Dawson; Ning Fang^{*}; Todd A. Sulchek^{*}; Mostafa A. El-Sayed^{*} 2017, ACS N

AuNPs stuck at nuclear membrane cause increase in lamin A/C protein expression



Moustafa R. K. Ali [‡]; Yue Wu[‡]; Deepraj Ghosh; Brian H. Do; Kuangcai Chen; Michelle R. Dawson; Ning Fang^{*}; Todd A. Sulchek^{*}; Mostafa A. El-Sayed^{*} 2017, ACS Nano, DOI: 10.1021/acsnano.6b08345

Nuclear stiffness increased by AuNPs detected by atomic force microscope (AFM)

Cells (with AuNPs)



Cell nuclear stiffness increase with AuNPs



Moustafa R. K. Ali[‡]; Yue Wu[‡]; Deepraj Ghosh; Brian H. Do; Kuangcai Che Michelle R. Dawson; Ning Fang^{*}; Todd A. Sulchek^{*}; Mostafa A. El-Sayed^{*} 2017, ACS Nano, DOI: 10.1021/ACSnano.6b08345

Migration speed as a function of AuNPs concentration



Moustafa R. K. Ali[‡]; Yue Wu[‡]; Deepraj Ghosh; Brian H. Do; Kuangcai Chen; Michelle R. Dawson; Ning Fang^{*}; Todd A. Sulchek^{*}; Mostafa A. El-Sayed^{*} 2017, ACS Nano, DOI: 10.1021/acsnano.6b08345



The cells without Gold Nanoparticles moved faster and filled the empty space in 12 hours. The gold Nanoparticles Slowed Down the the cells So they can only fill out part of the empty space.
Gold Nanoparticles Inhibit Cancer Cell Migration

Gold nanoparticles affect cytoskeleton protein formation Cytoskeleton proteins are responsible for cell movement



Ning Fang *; Ronghu Wu *; Mostafa A. El-Sayed *, PNAS, accepted

CELLS and STUDIES ON DEVELOPPING DETECTION AND TREATMENT METHODS OF CANCER USING GOLD NANOPARTICLES (Georgia Tech)



Dr Ivan El-Sayed. M.D , UCSF



Dr Xiaohua Huang



Dr MAGAN MAC KEY



Mena Aioub



Dr Erik C. Dreaden



Dr Lauren A. Austin



Dr BIN KANG



MOUSTAFA ALI



JANE, GT Georgia Tech





Rahman Aminur **EMORY**





group

DR Salah HeadiBicAIRO U groupCairo u



Haithem **Farghaliy** Cairo u











Thank You



CLOSE

AFTER HIS PhD

MORE THAN ONE WAY TO BEAT CANCER (or any sick) Cell to death with Gold Nanoparticles

- All based on the Size and Shape Dependent Properties of GoldNano-particle:
- 1.Too Small compared to the size of the photon it captures giving rise to focusing electro-magnetic fields thus having strong scattering (USED IN CELL DETECTION) o absorption followed by heating: used in photo-thermal therapy.
- 2. Too large compared to molecular size thus it can deliver Thousands of drug molecules to sick cells Rapidly and Simultaneously: USED IN DRUG DELIVERY
- 3. Comparable to the size of the cell components that can bind to them and change cell functions, like cell