



Ongoing Cancer Research: School of Public Health and Health Professions



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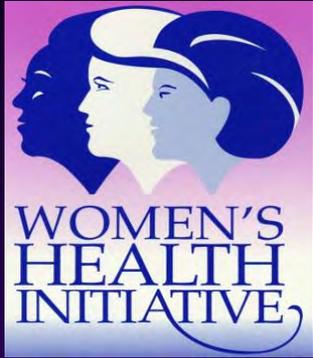
Monday, February 16, 2016
UB Council Meeting

Cancer is a national priority

- ❑ Obama “Cancer Moonshot” (Targeting treatments, screening and prevention)
- ❑ Cuomo NYS funding to Screen/Treat Cancer
- ❑ 2016 estimates:
 - 1.69 million new cancer cases in the US (110K NYS)
 - 596,000 deaths (35K NYS)
- ❑ US lifetime risk: 1 in 3 women; 1 in 2 men

Public Health

- Focus on disease occurrence in larger populations and groups
- Prevention focused
- Research on risk factors for disease; Prevention trials
- Mechanistic studies (clinical translational)
- ***At UB SPHHP, we have a tremendous amount of ongoing work in cancer***

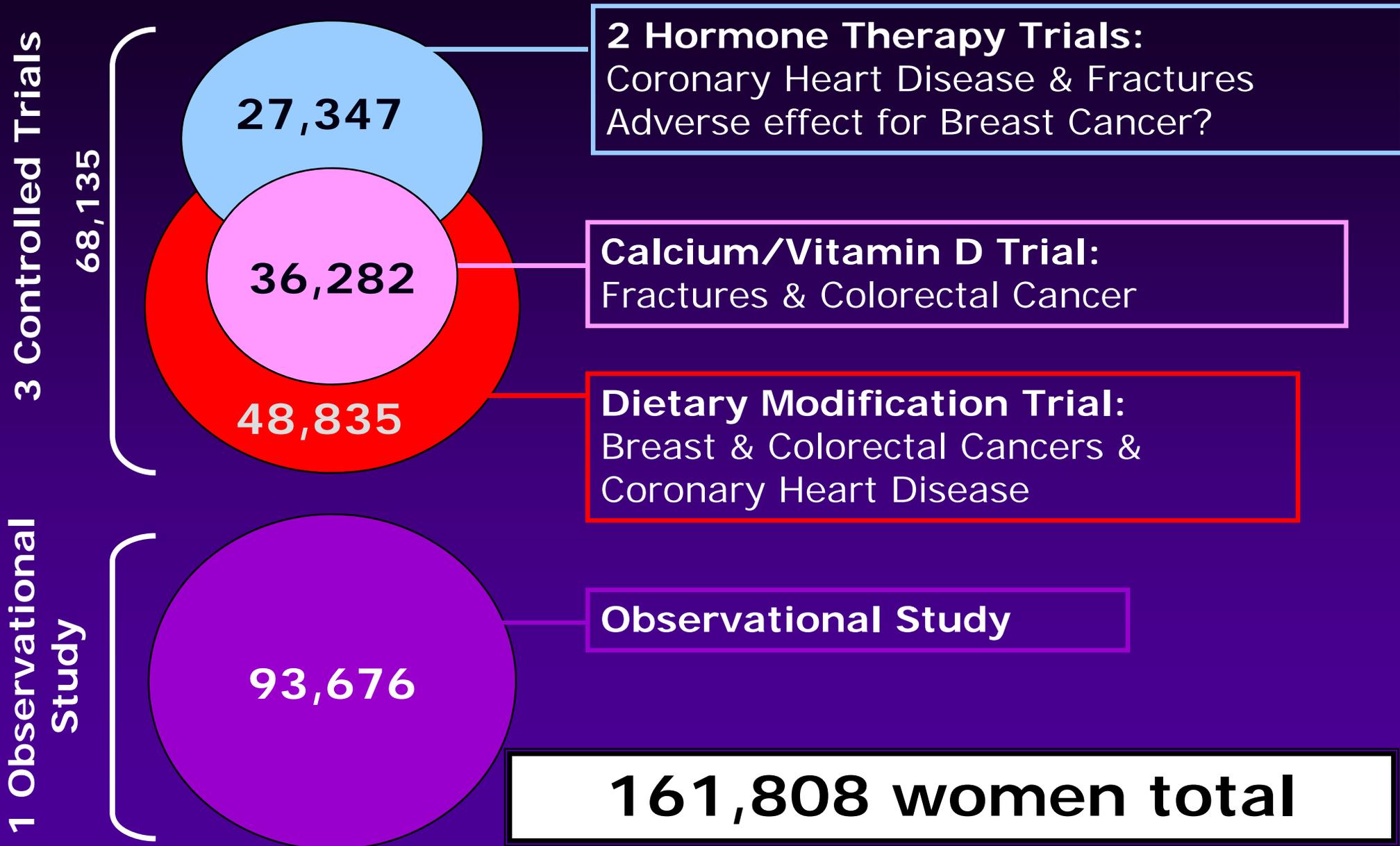


Women's Health Initiative

1993 – present (now thru 2020...)

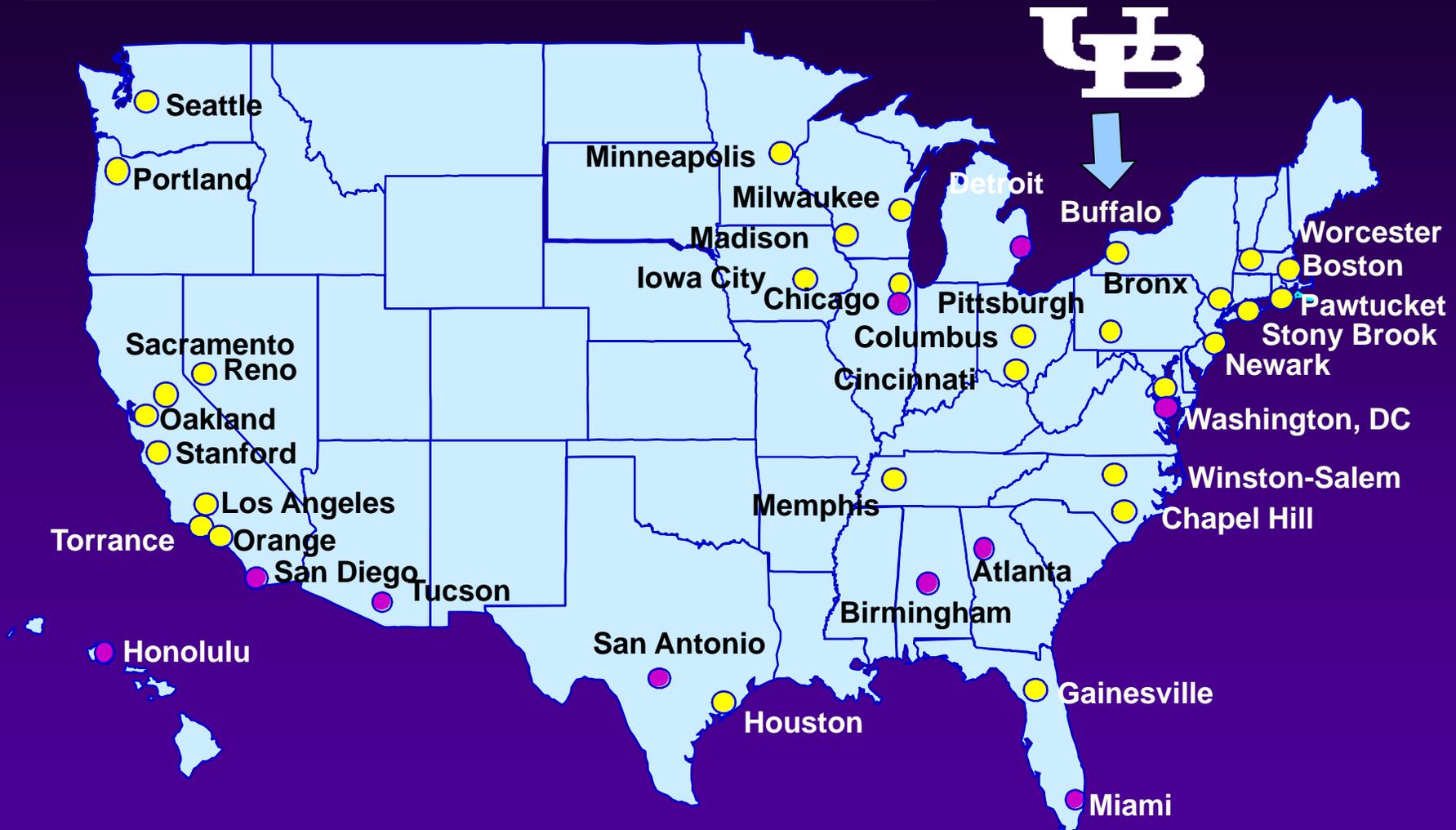
A 12 year (now 22+) study of the major causes of disease and death in postmenopausal women.

Women's Health Initiative



WHI Clinical Centers (40)

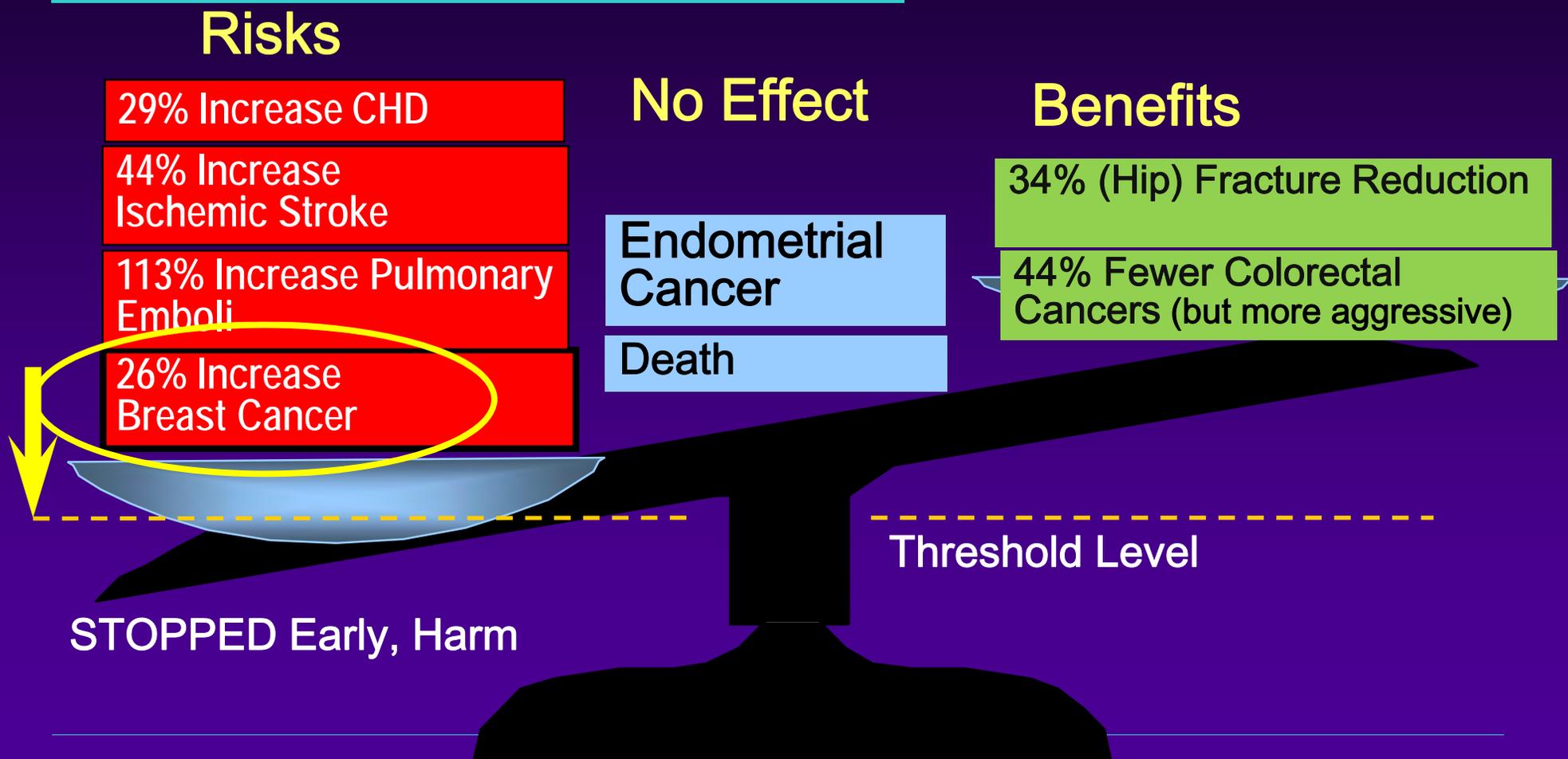
- Pool 1 Clinical Centers (30)
- Minority Clinical Centers (10)



Balance of Risks & Benefits:

The WHI E+P Trial, 2002

(Mean Follow-up = 5.6 yrs)



INSIDE HARKEN AND HALLIBURTON • THE OLDEST SKULL

Newsweek

July 22, 2002

A New Study
Raises Fears
About the Risks
For Millions
Of Women.
Here's What
You Should Do

Beyond Hormone Therapy

JULY 22, 2002

WALL STREET: LOSING SAVINGS—AND TRUST

IS THIS OUR FIRST ANCESTOR?

TIME

THE TRUTH ABOUT HORMONES

Hormone-replacement therapy
is riskier than advertised.
What's a woman to do?

Susan Pierres, 60, of Miami, has been on hormones for 10 years. She is angry and confused but not yet ready to stop taking them.

www.time.com ADL Keyword: TIME

MARTHA'S HARD TIME • KERRY'S VP HUNT

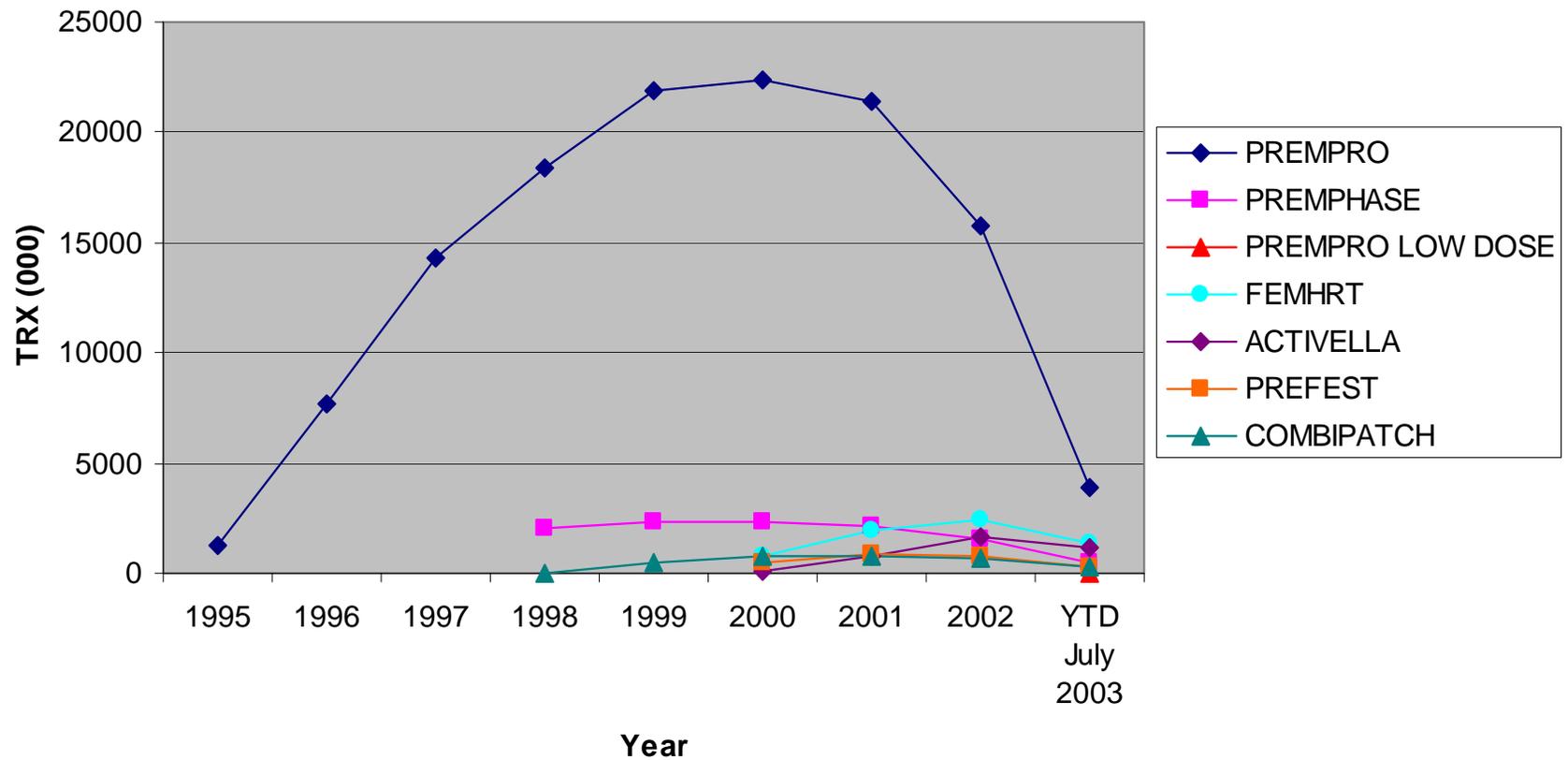
U.S. News & World Report

MARCH 15, 2004

THE MENOPAUSE MAZE

WHAT WOMEN NEED TO KNOW NOW
NEW RISKS AND REWARDS OF TREATMENT
HOW MEN ARE AFFECTED

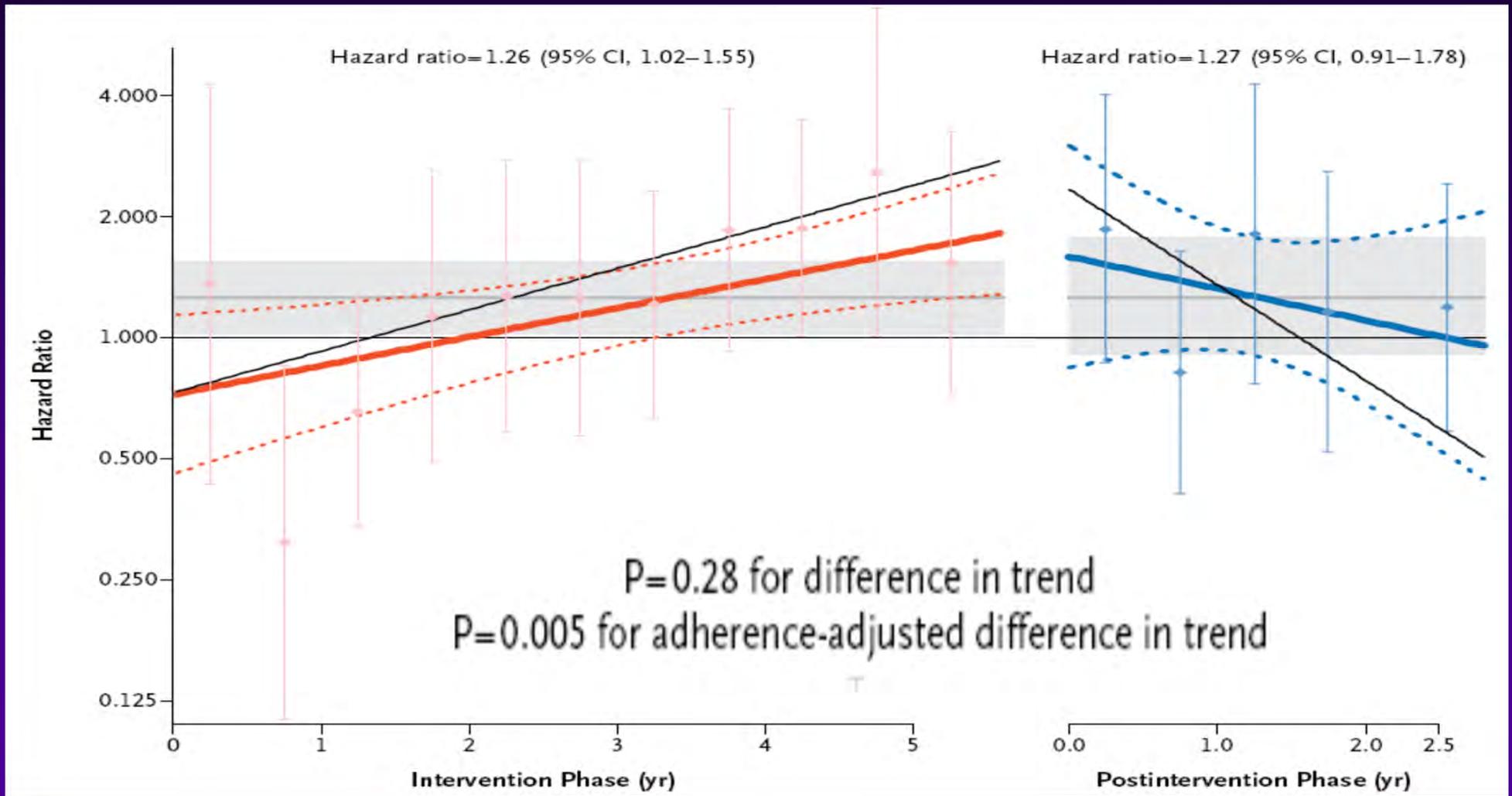
Total Prescriptions Dispensed for Combination Estrogen/Progestin Products, 1995 - July 2003



IMS Health, National Prescription Audit *Plus*TM, 1995 – July 2003, extracted August 2003.

Public Health Impact...one example

Clinical Trial: CEE+MPA vs. Placebo Breast Cancer Risk During Intervention and Postintervention



Economic and Public Health Impact...

...another example

Economic and Health Impact of the WHI Estrogen+Progestin Trial

Roth et al, Annals of Internal Medicine, May 2014

Trial cost **\$260 million** (in 2012 dollars), produced a net economic return of **\$37.1 billion**:

- a return of \$140 for every dollar invested in the trial.

Estimated health benefits (10 years following):

- \$4.3 million fewer women used HT from 2002-2012
- Prevented (estimated in the following 10 years):
 - **126,000 fewer cases of breast cancer**
 - 76,000 fewer cases of cardiovascular disease
 - 80,000 fewer cases of venous thromboembolism (VTE)

Cancer Focus in WHI : Additional research

□ Risk Factors:

- Diet, 2nd hand smoke, co-morbidities, medications, physical activity, race/ethnicity...
- Periodontal Disease – total cancer, lung, upper GI, breast

□ Blood/Tumor biomarkers:

- Telomeres, proteome, metabolome, genetics/genomics (consortium)

□ Hundreds of scientific papers, ancillary grants

□ Two national team science awards for this work

Oral Microbiome, Periodontal Disease



Oral bacteria

Gingivitis

Periodontitis

**Bone and tissue
destruction**

Tooth loss



Periodontal
pocket

Gingiva

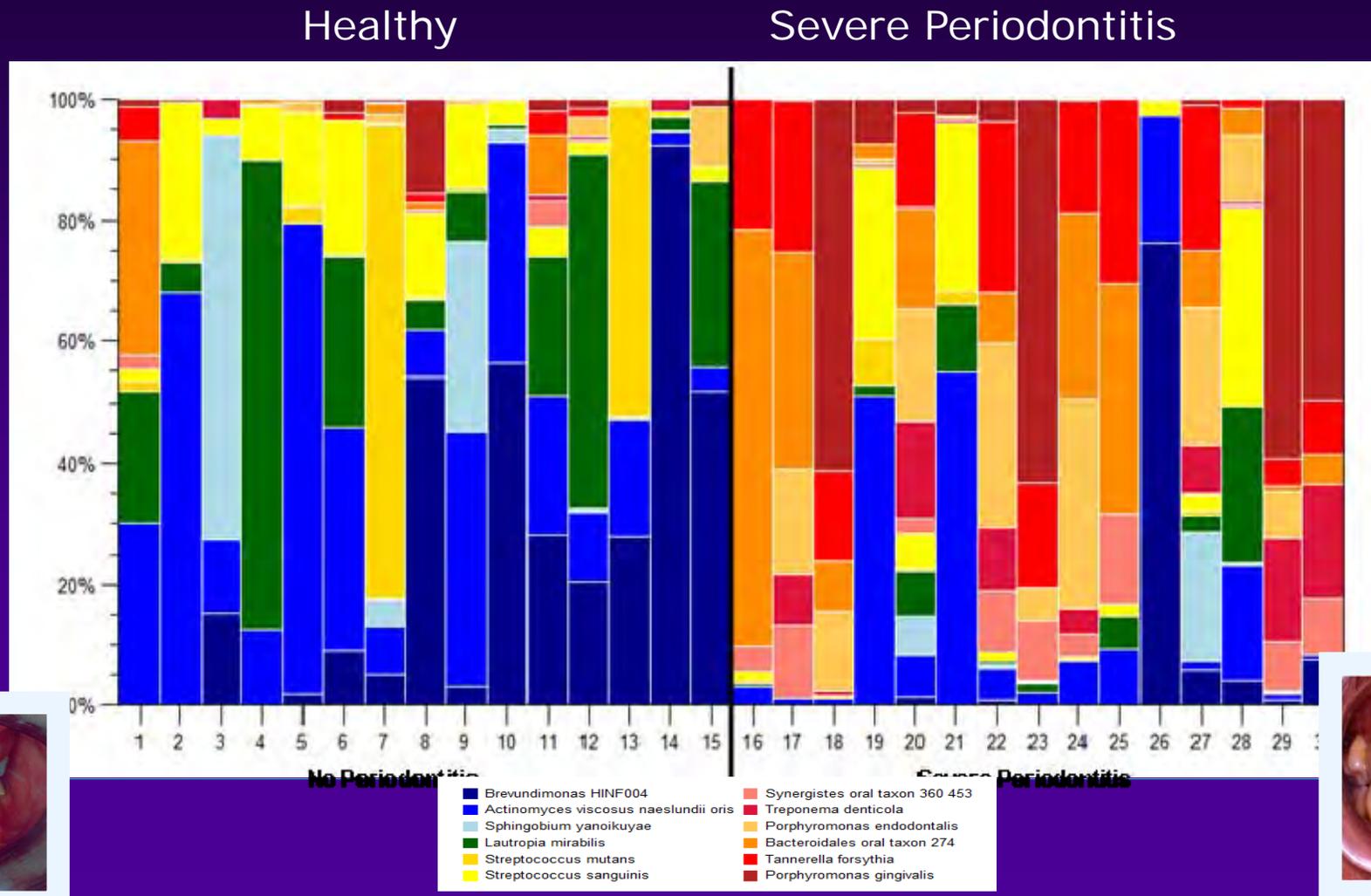
Periodontal ligament

Alveolar bone

Inflammation

OsteoPerio 15-Year Follow-up Feasibility Study:

Microbiome Composition Differs by Periodontal Health/Disease



Cancer:

Buffalo OsteoPerio Microbiome Study

OsteoPerio Microbiome:

Ongoing \$4M NIH funded study (2014-2019)

1000 women, 15 years, 3 time points

Bacterial composition in:

- Cancer Cases vs No Cancer
 - Tumor Blocks compared to Oral samples
 - Potential to develop new targeted interventions
-



SPHHP Faculty Active in Cancer Research



R25 Training grant



Thank you. Questions?

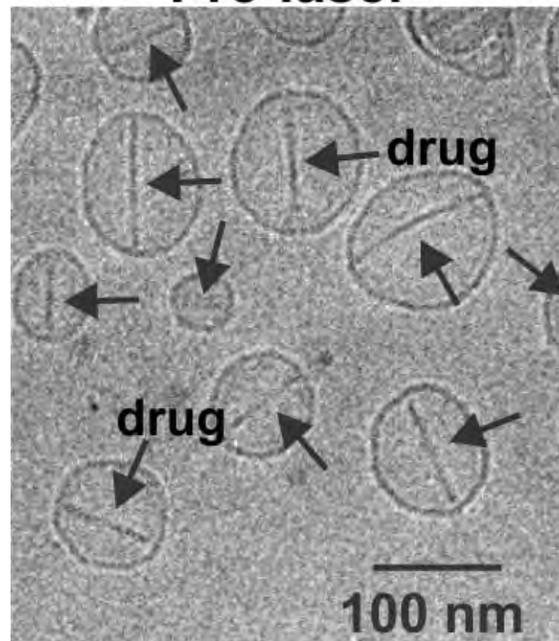


Anti-cancer Approaches with PoP Nanoparticles

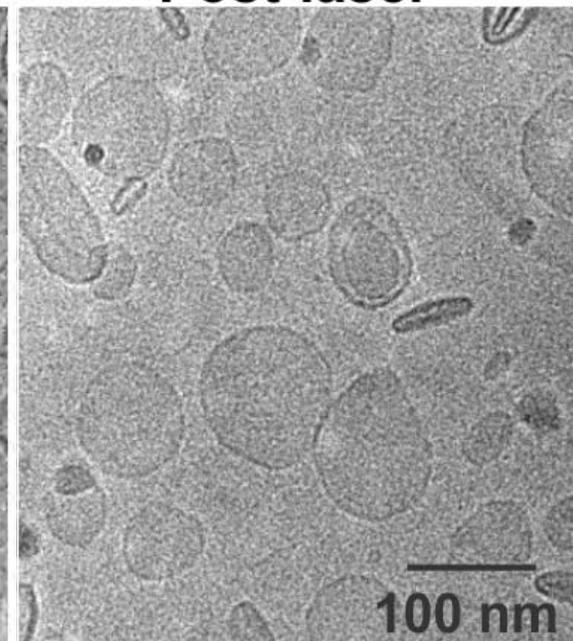
Jonathan Lovell

Department of Biomedical Engineering

Pre-laser



Post-laser

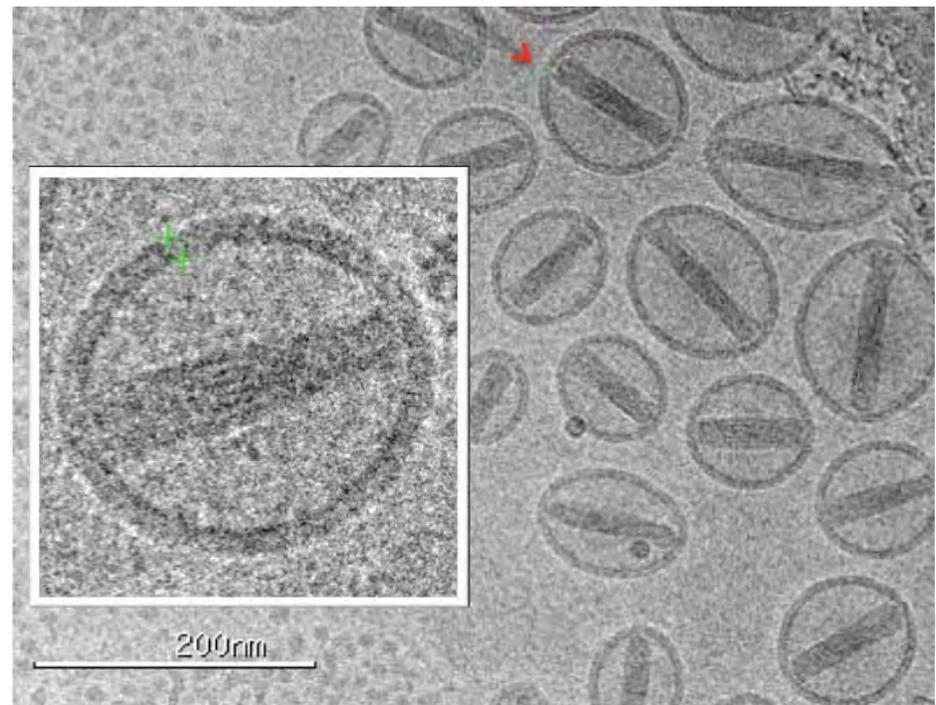


February 15, 2015

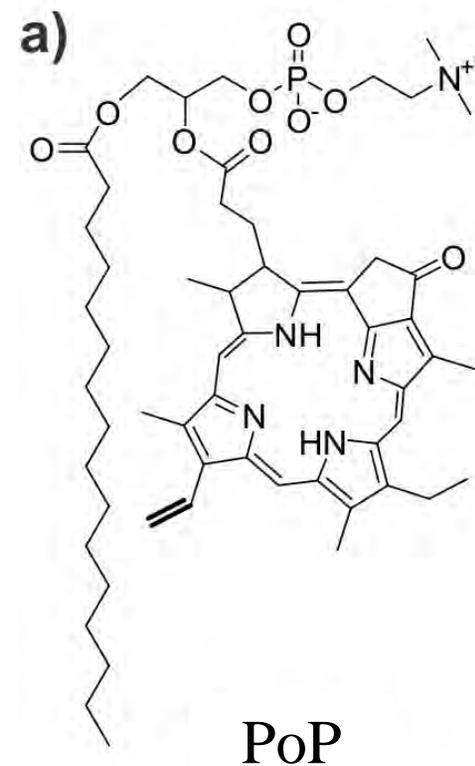
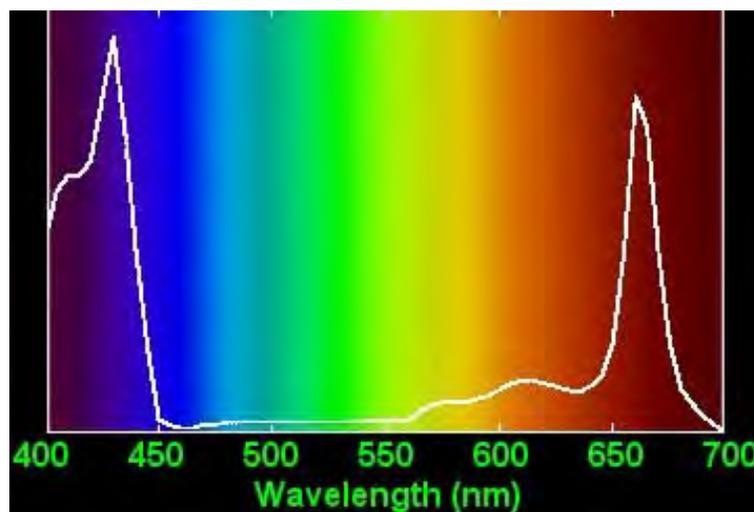
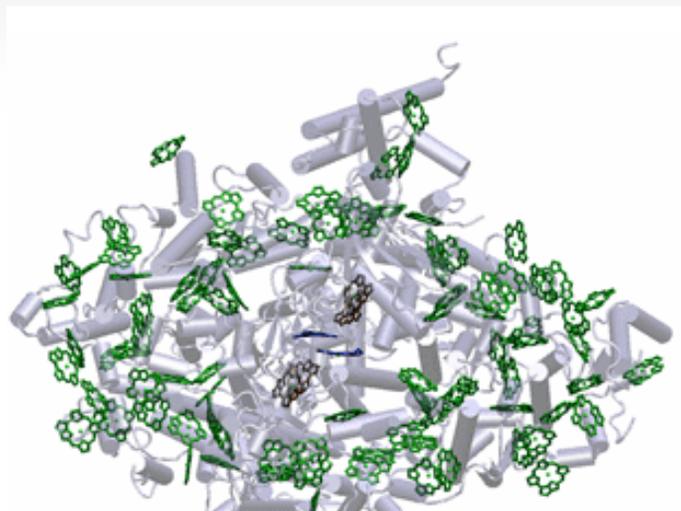
UB council presentation

DOXIL – the first “nanomedicine”

- Long circulating doxorubicin “liposome” by J&J
- Kaposi’s sarcoma, multiple myeloma, metastatic ovarian, breast (off label)
- Less cardio-toxic vs free drug
- Poor drug bioavailability

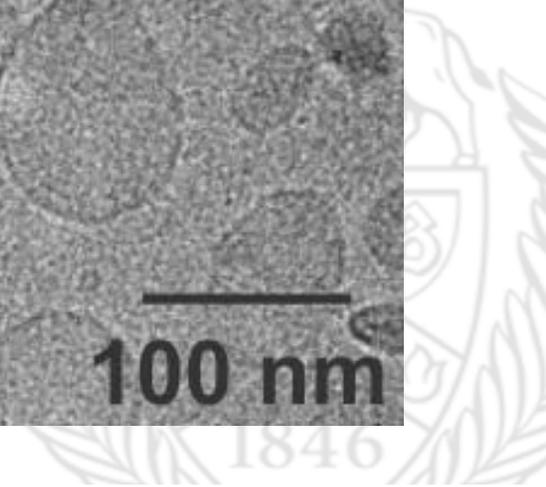
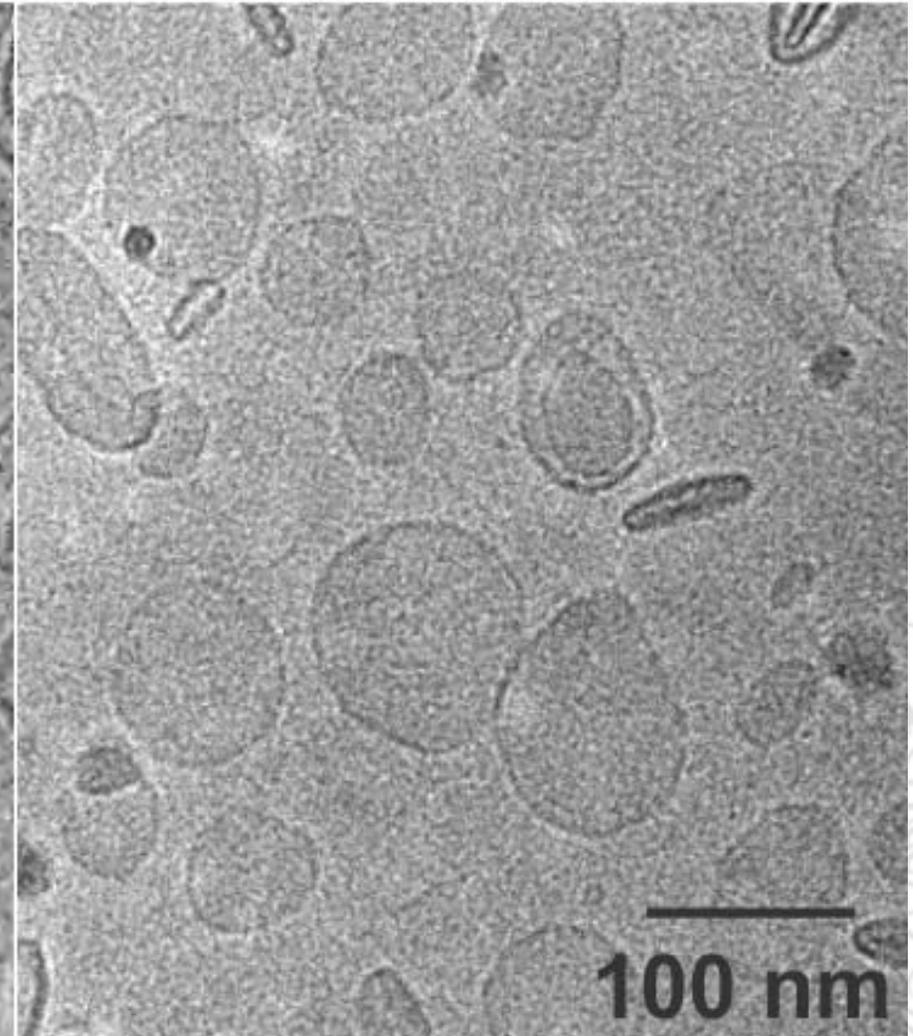
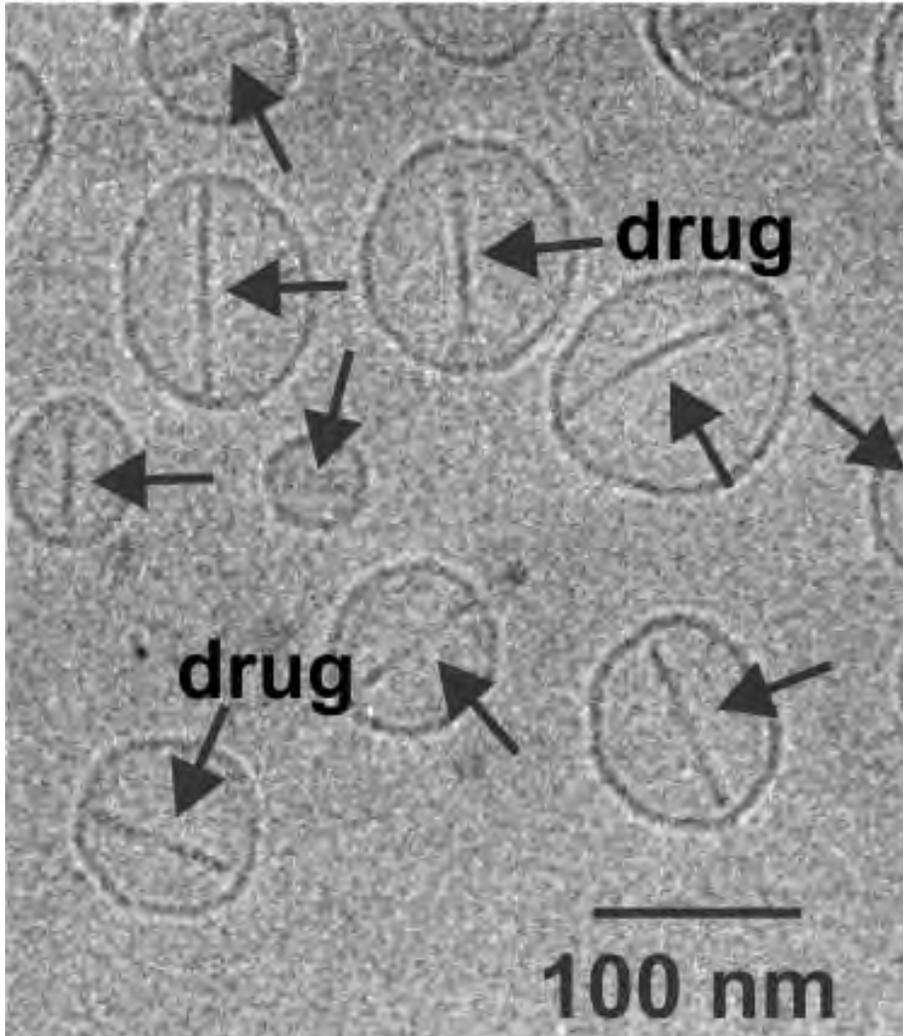


Putting chlorophyll to work

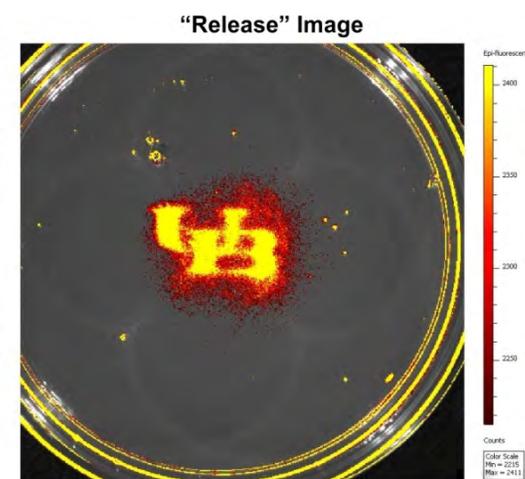
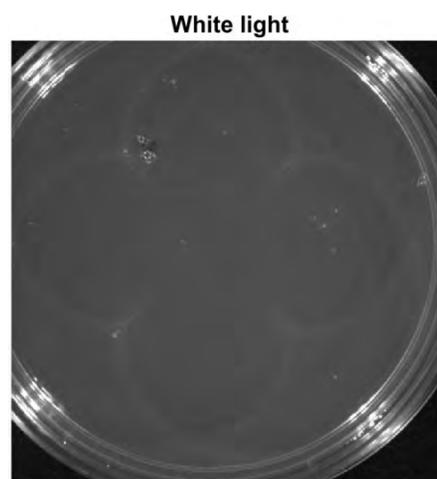
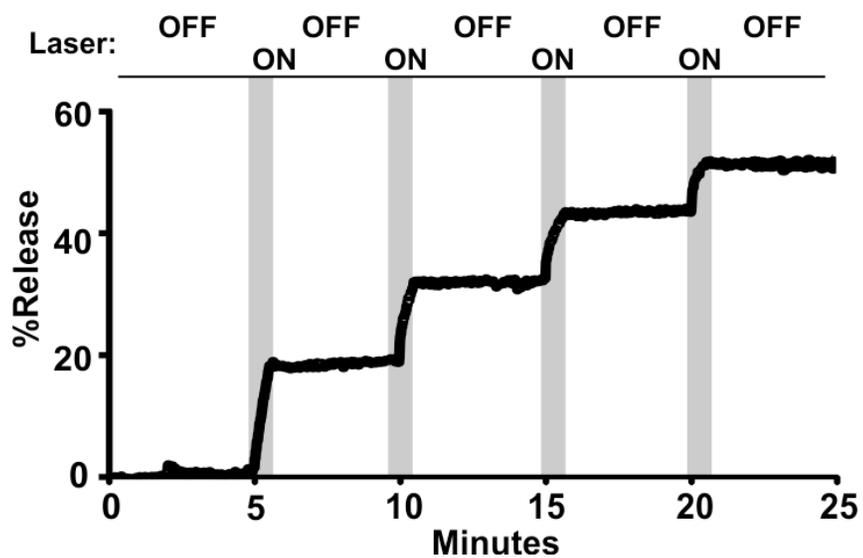


Pre-laser

Post-laser



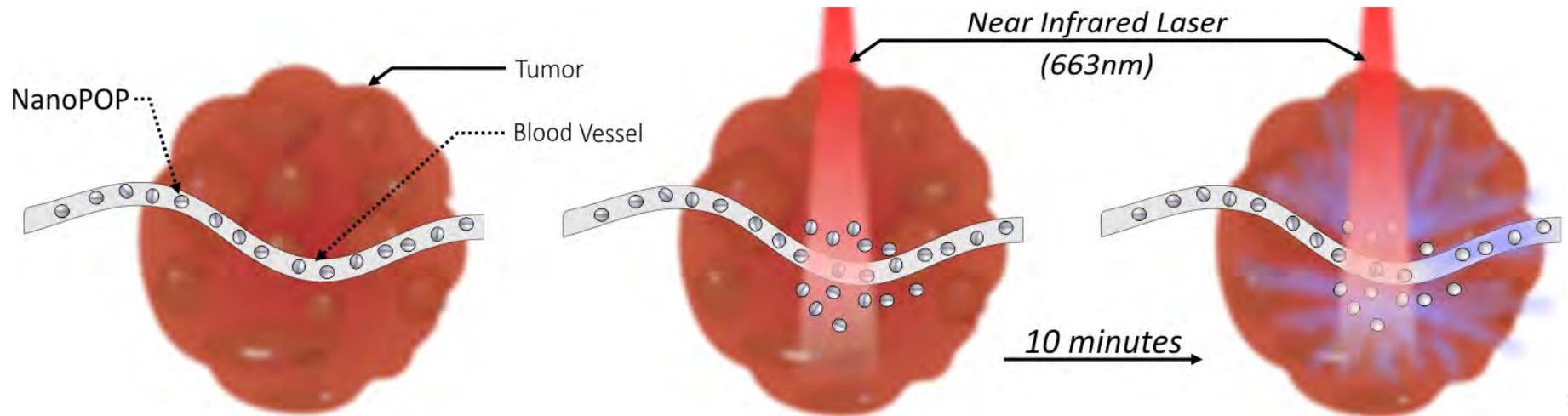
Spatial and temporal control of release



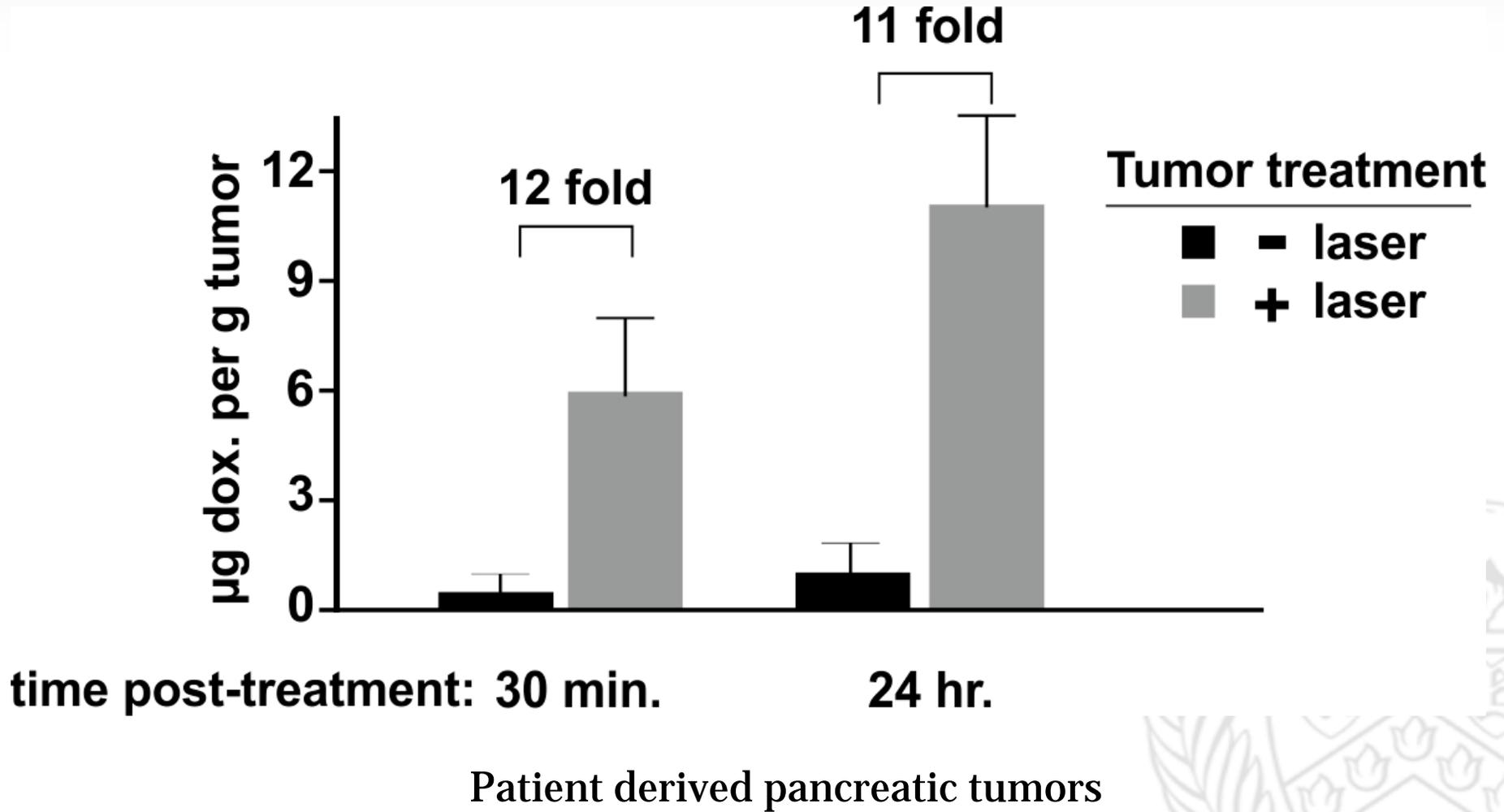
Carter al., Nature Communications, 2014



Chemophototherapy

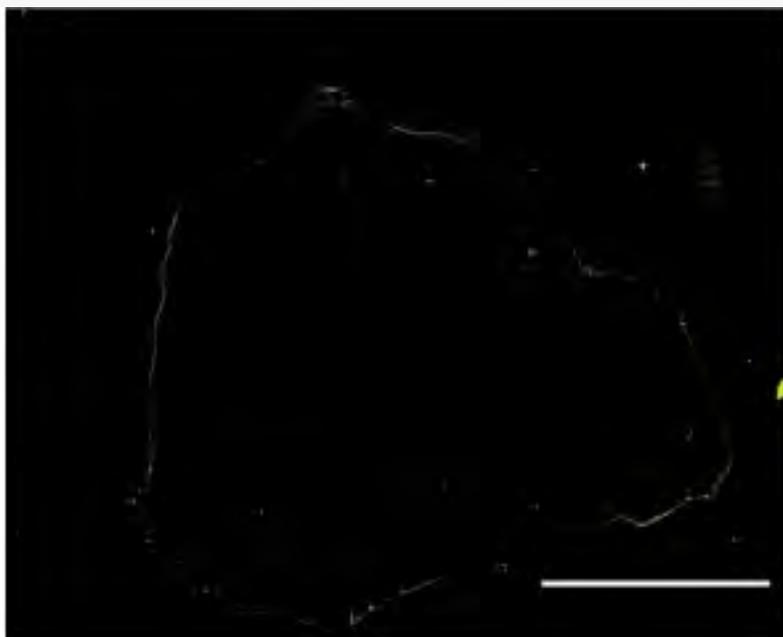


Enhanced accumulation

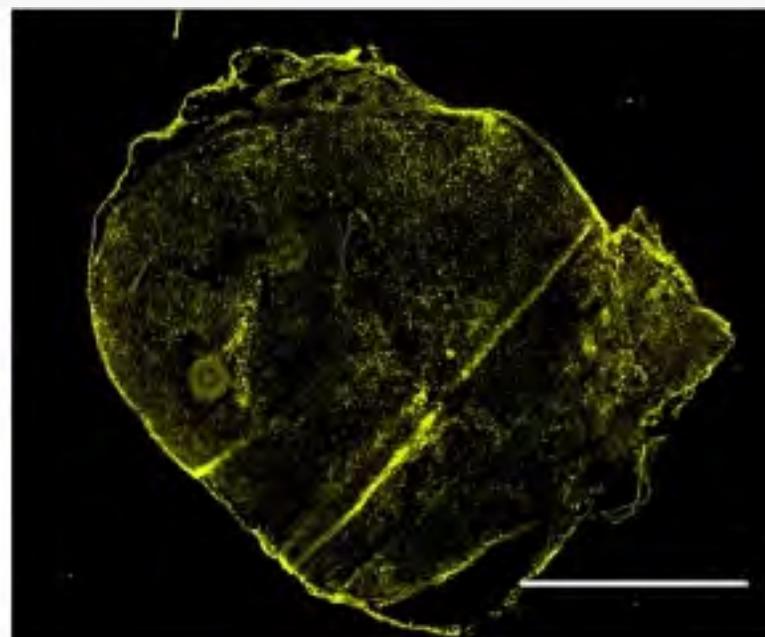


Enhanced distribution

Dox



- laser

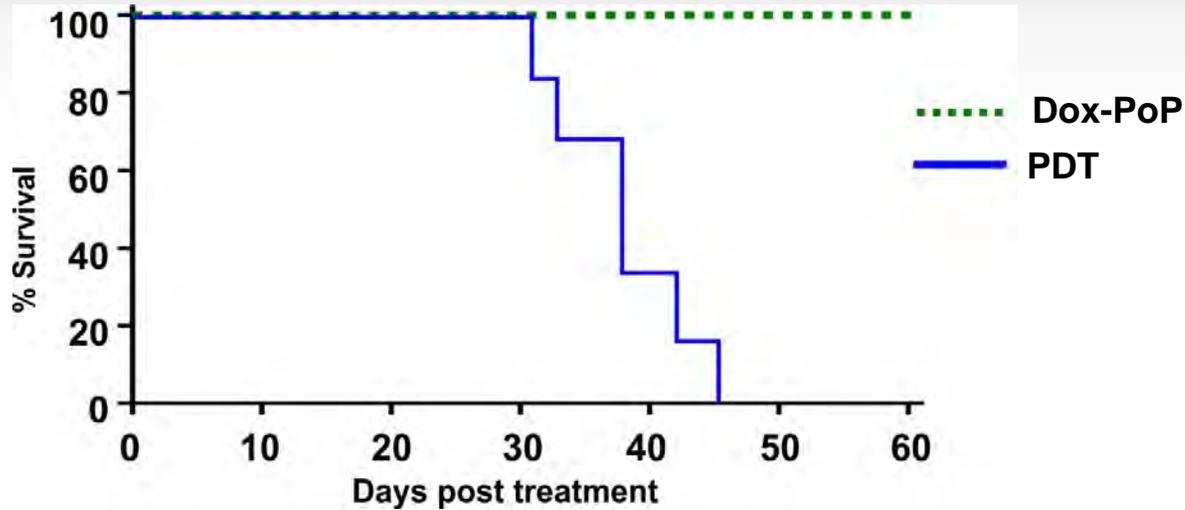


+ laser

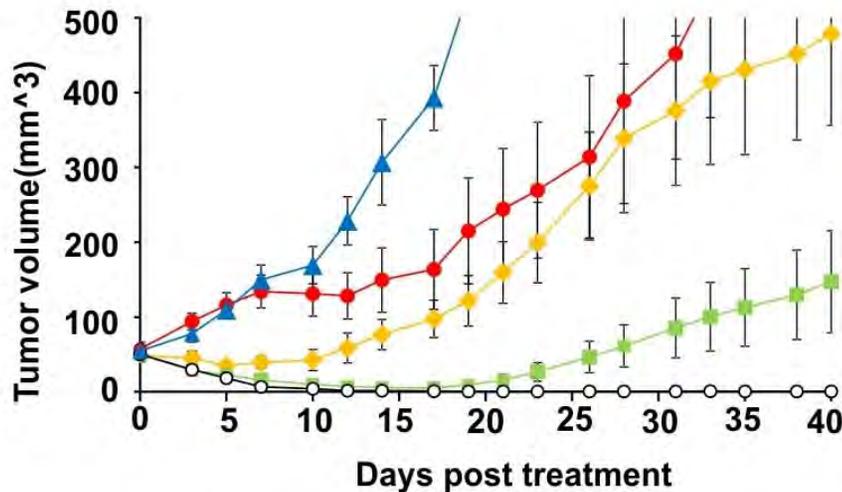
Luo et al., J Controlled Release, 2015



PoP-liposomes vs. photodynamic therapy



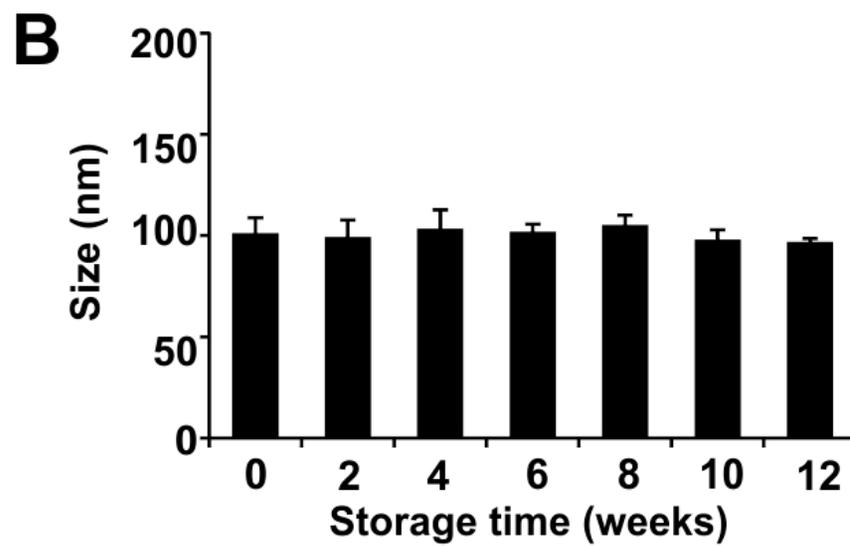
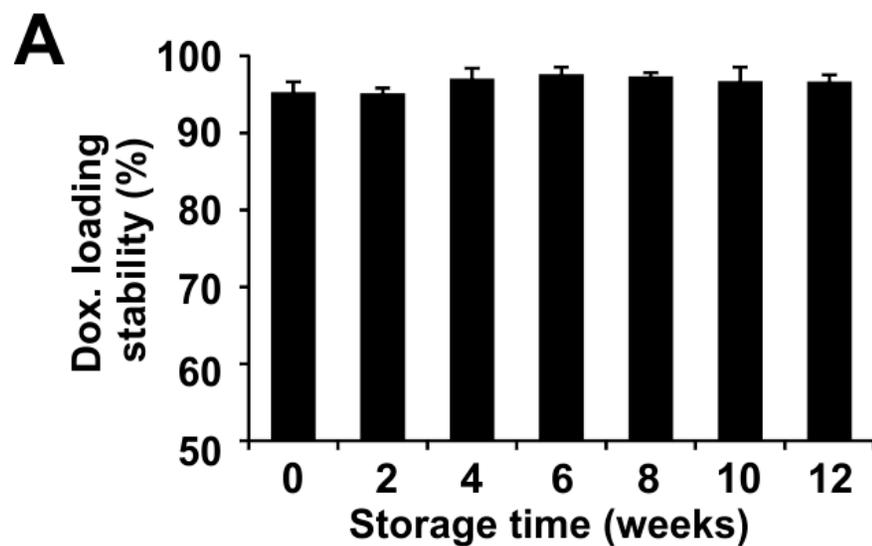
PoP-liposomes vs. conventional chemo.



	Dox. dose (mg/kg)
Free Dox	7 (~MTD)
SSL Dox	21 (~MTD)
Dox-PoP + laser	3
Dox-PoP + laser	5
Dox-PoP + laser	7



Dox-PoP-liposomes: Storage Stability

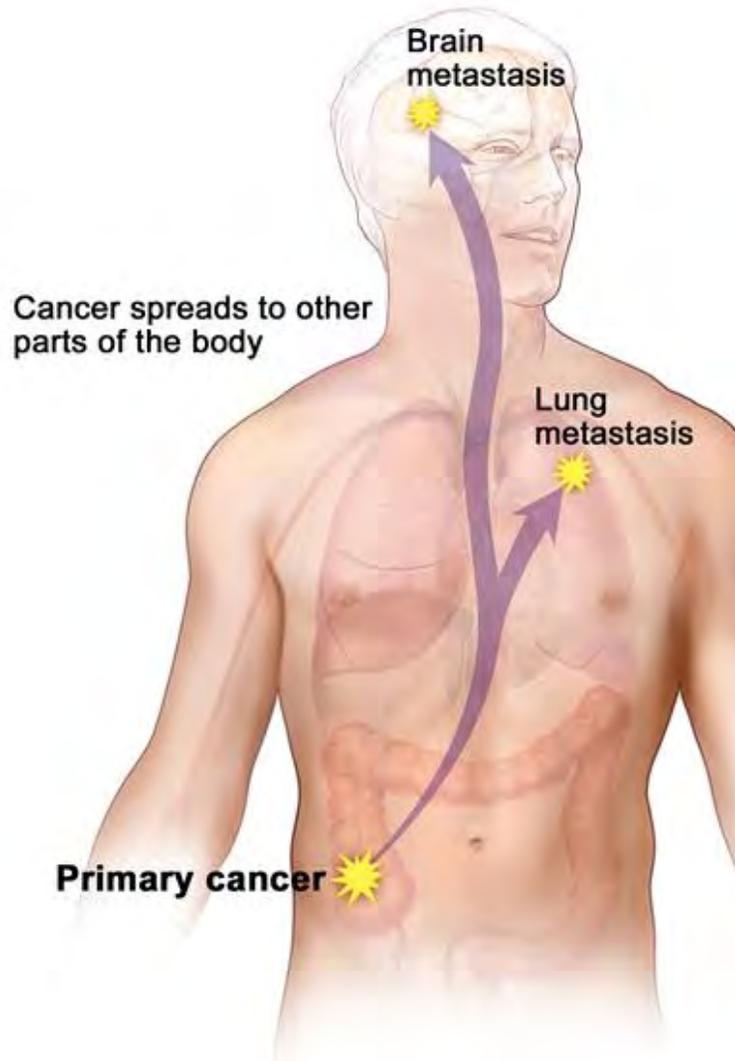


Translational strategy for chemophototherapy

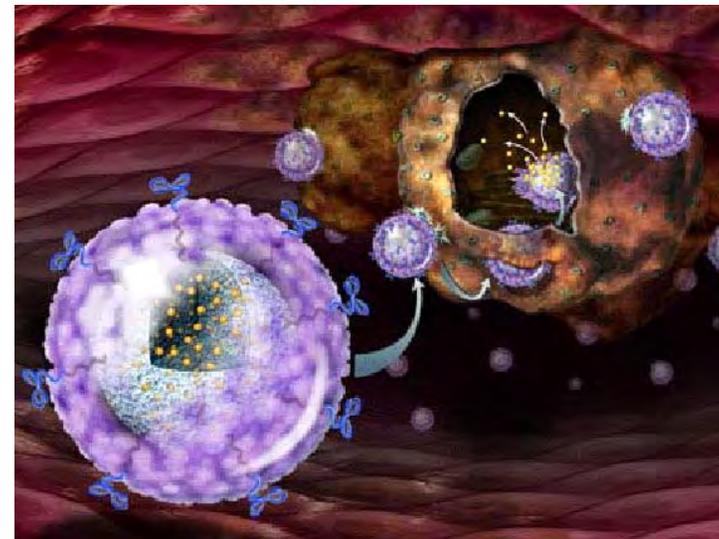
1. Manufacture
2. Stability/Sterility
3. PK/tox
4. Phase I/II trial
 - Local breast cancer recurrence
 - No anesthesia, easy irradiation
 - High prevalence
 - Dox used for breast
 - Other candidates: liver & brain via fibers.



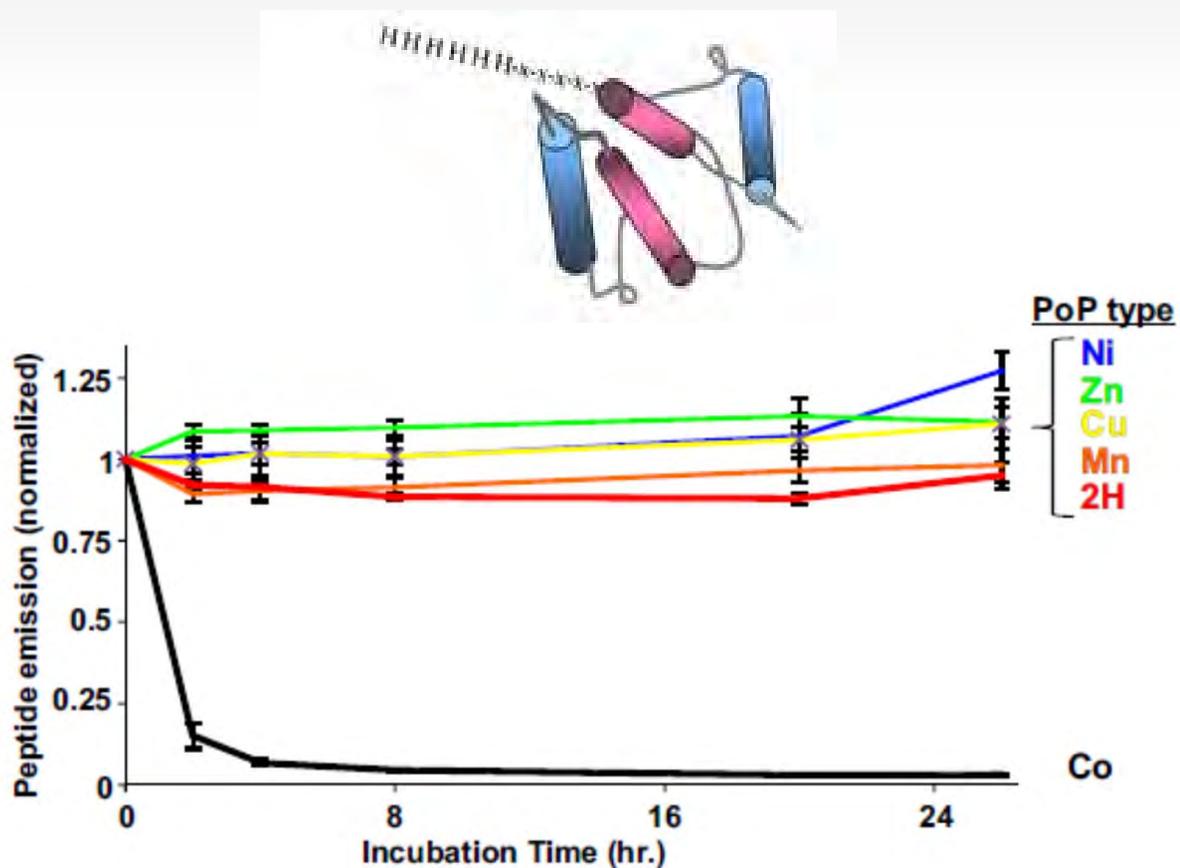
Local and metastatic cancer



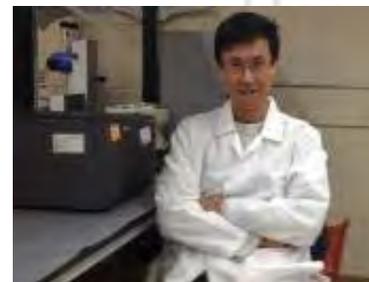
Targeted therapy

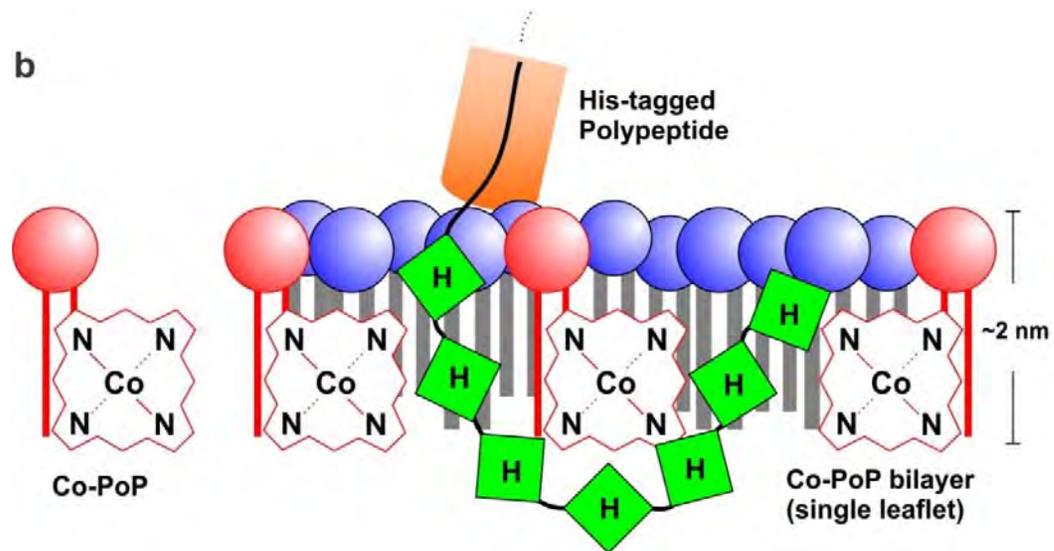
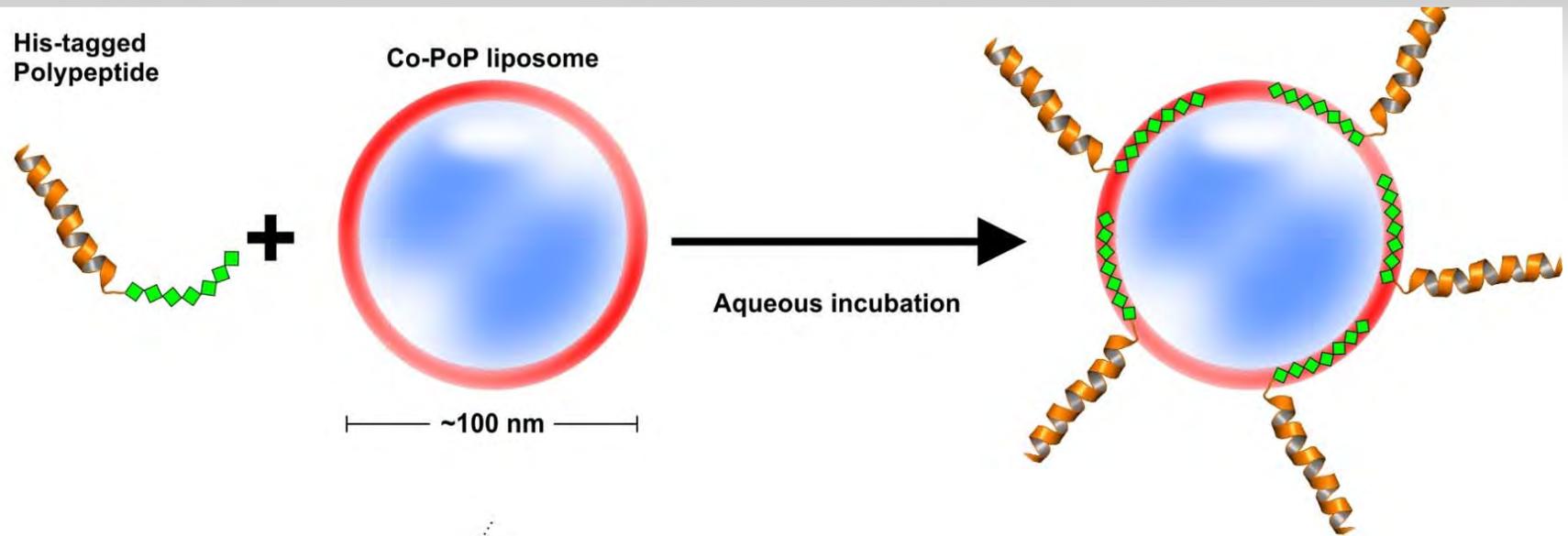


Functionalization of Co PoP with tagged proteins

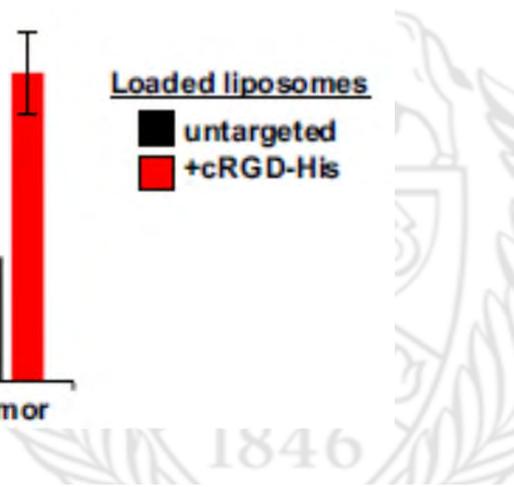
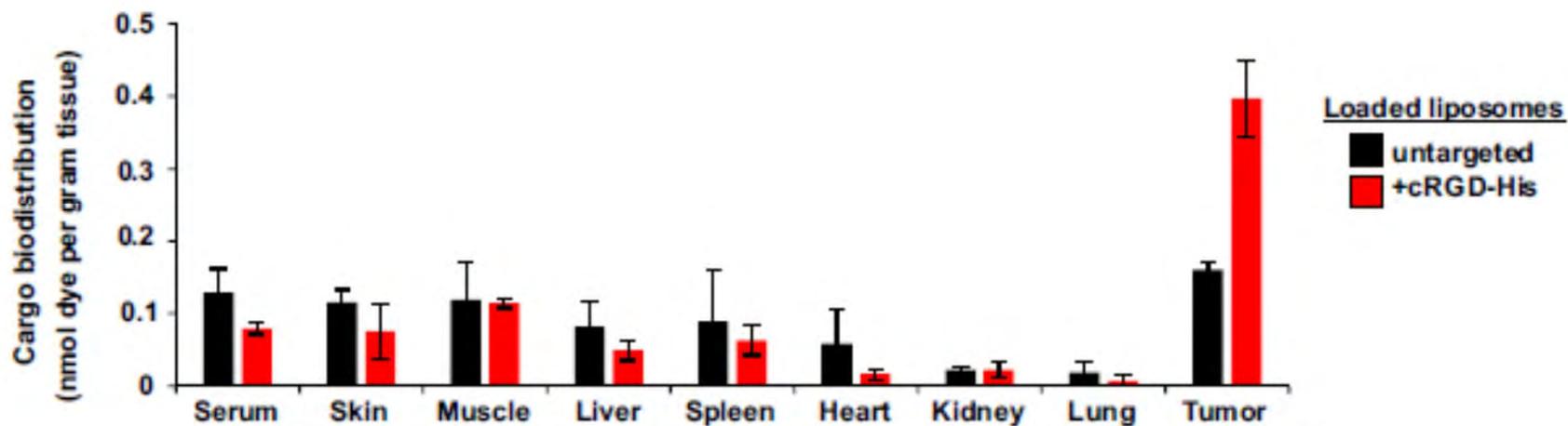
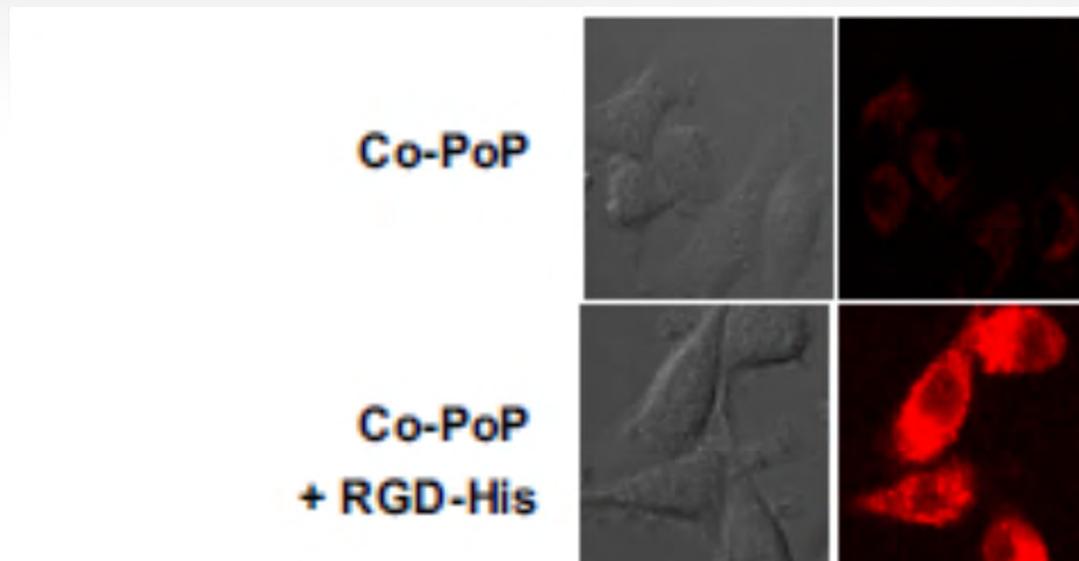


Shao et al., Nature Chemistry, 2015





Cargo-loaded liposomes with a targeting ligand



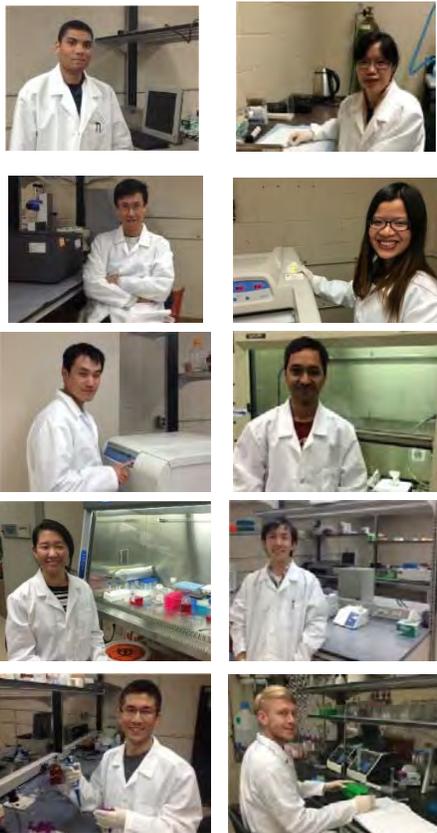
Summary

- Light-activated PoP liposomes
 - New local tumor treatment
 - Higher drug deposition
 - Uniform drug distribution
 - Formulation finalized
 - Future directions: clinical manufacturing and trials
- Targeted Cobalt PoP liposomes
 - Enabling technology for ligand attachment
 - Translatable screening platform for targeted delivery
 - Future directions: drug targeting; multivalent targeting
 - Future directions: vaccines



Acknowledgements

Lab members



Collaborators

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McMaster University

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University of Waterloo

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