

20.109 MOD1

Genomic Instability

Fall 2023
Day 6

Bevin P. Engelward, *Sc.D.*
Professor of Biological Engineering

γ H2AX Application Example: Assessing Risk of Radiation Exposure

Analysis of Radiation-Induced DSBs

Claim that damage induced by low-dose radiation is not effectively repaired

This led some to conclude that no level of radiation is safe.

Linear no-threshold model

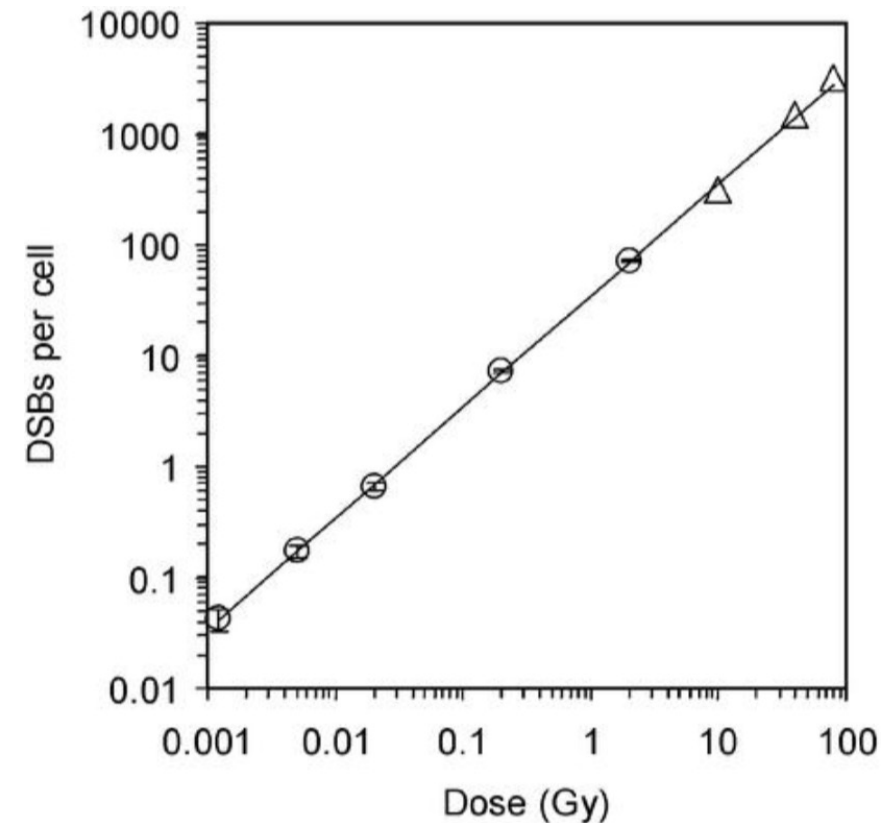
Often, the “acceptable risk” is deemed to be no more than ...

RESEARCH ARTICLE | BIOCHEMISTRY | 

Evidence for a lack of DNA double-strand break repair in human cells exposed to very low x-ray doses

Kai Rothkamm and Markus Löbrich [Authors Info & Affiliations](#)



VÖLSERHOF



Anfrage

Buchung

Specials



HOTEL

ROOMS

HIKING

GASTEIN

GASTEIN HEALING CAVES

Radon therapy health centre in the Gastein Valley



How the CometChip is made

Why and how to commercialize

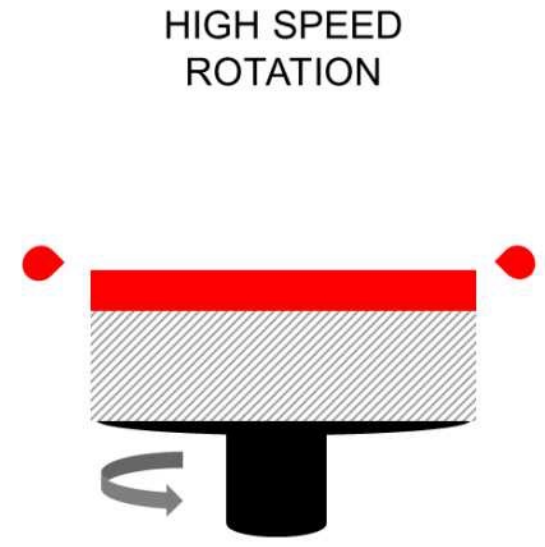
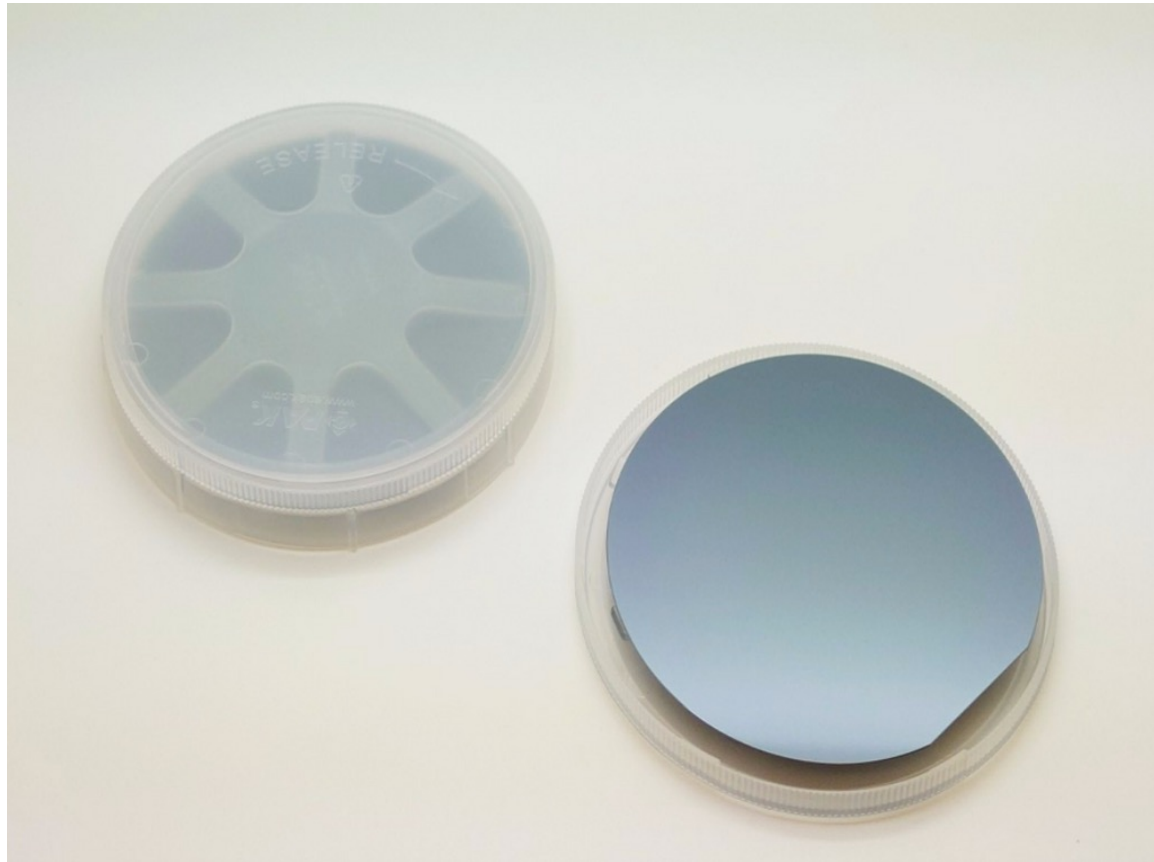
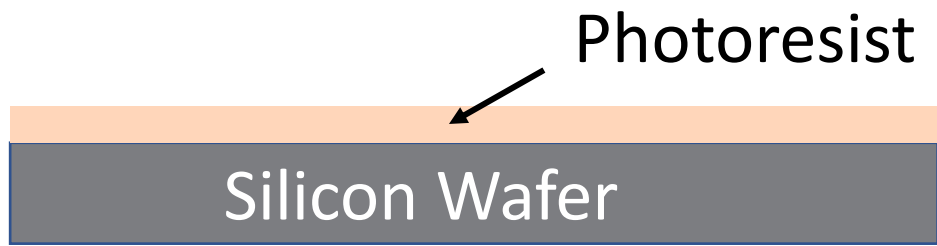
Applications of the CometChip:

- Nanoparticle assessment

- Repair capacity evaluation

- Differences in repair capacity among people

- Assessing xenobiotics for their DNA damaging potential

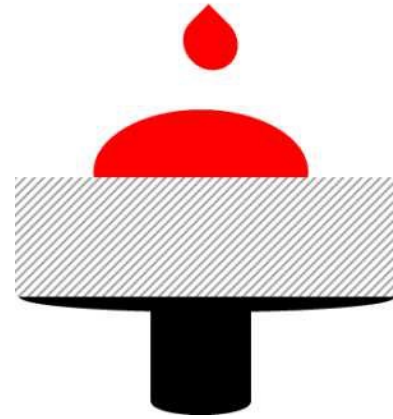




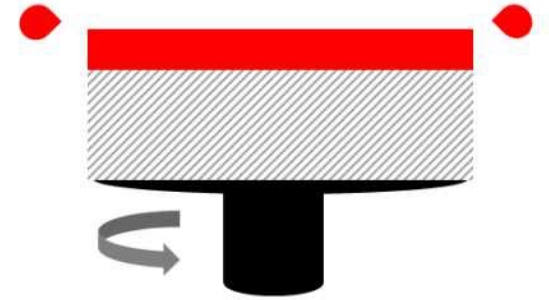


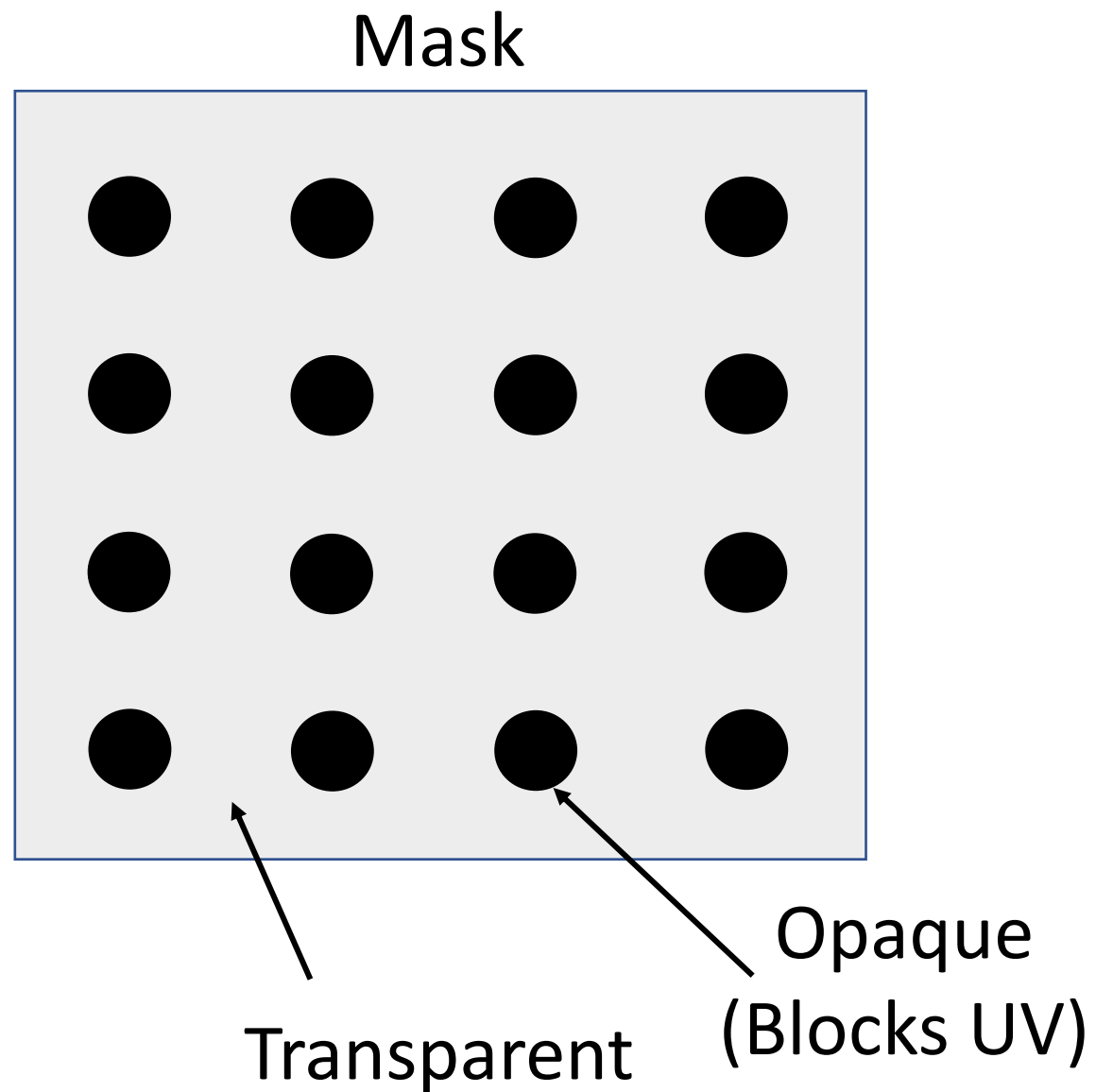
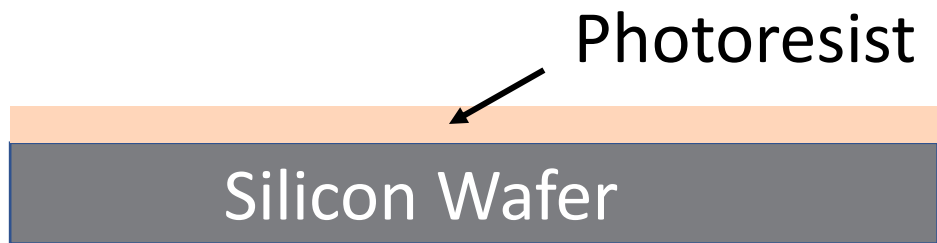


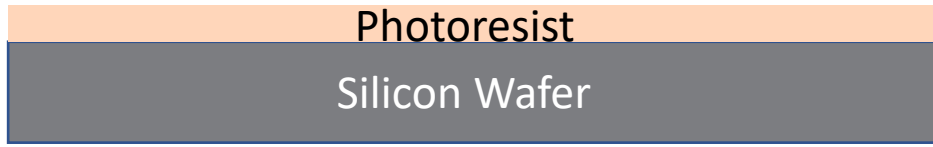
DISPENSING
OF RESIST



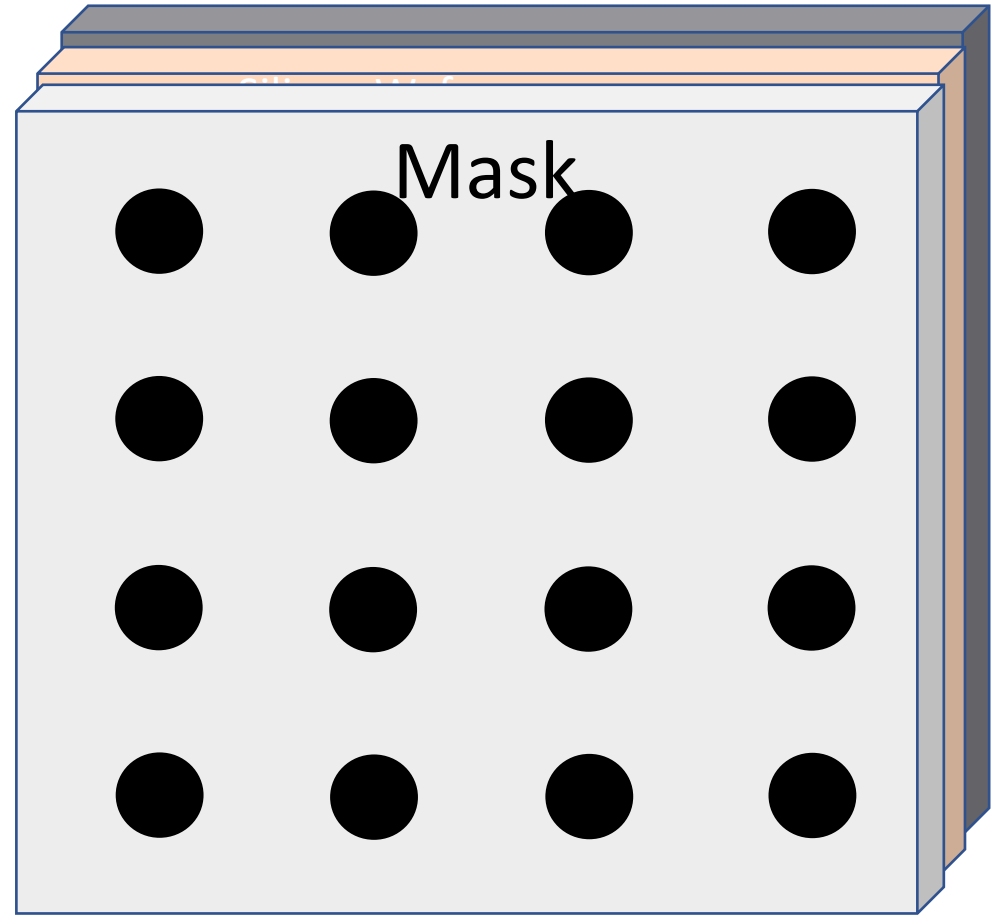
HIGH SPEED
ROTATION

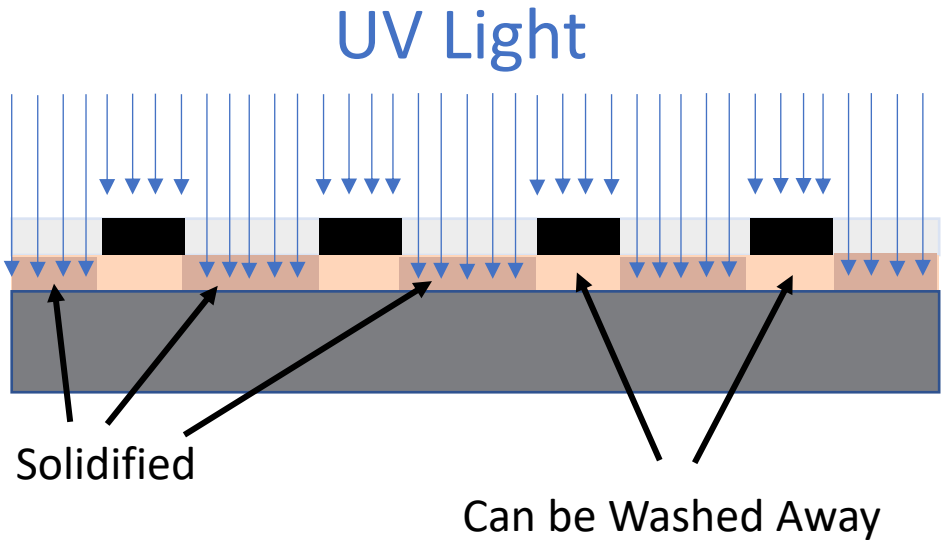


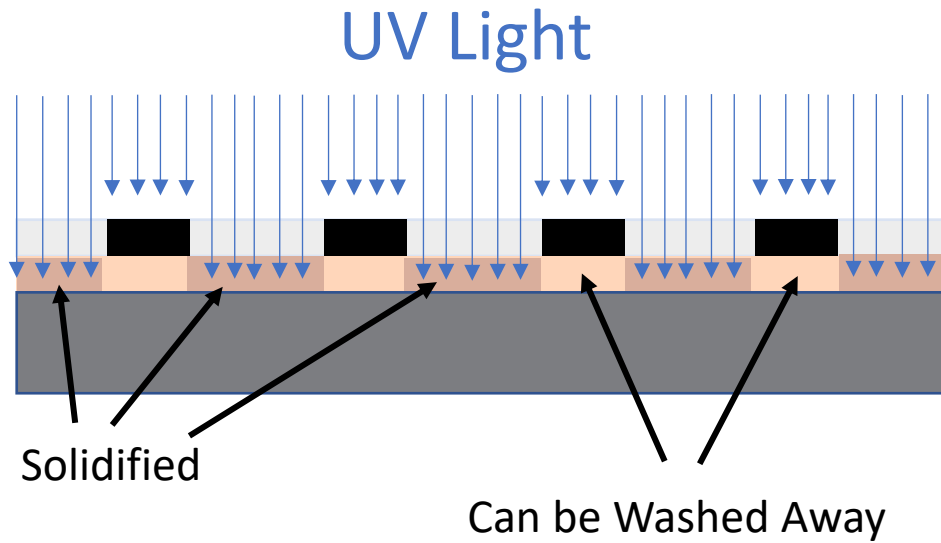
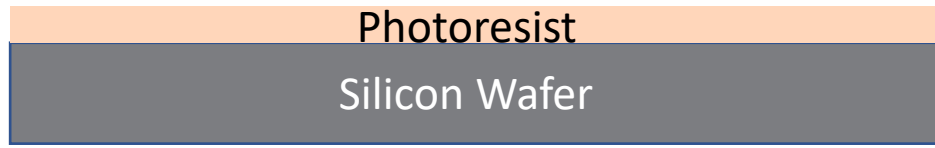


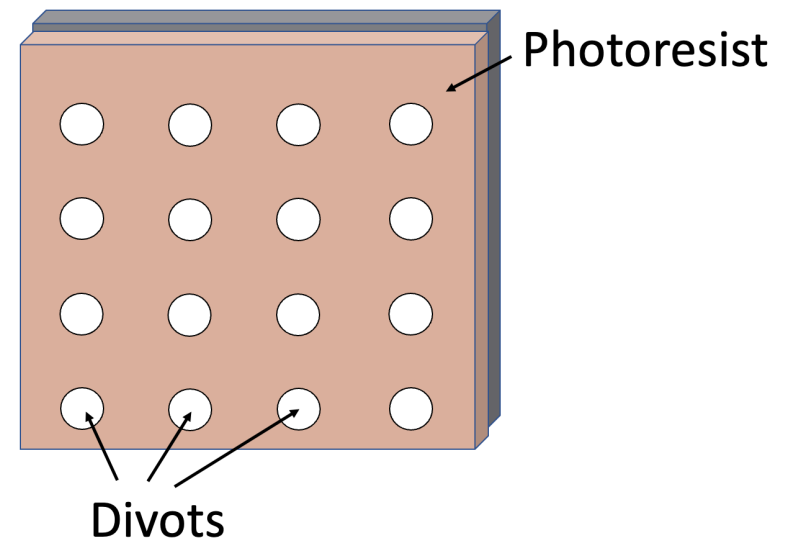
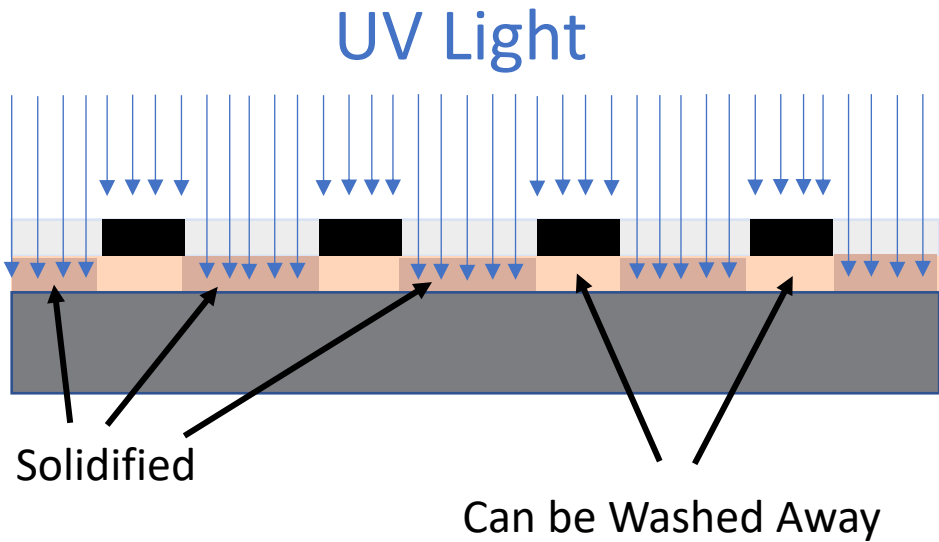
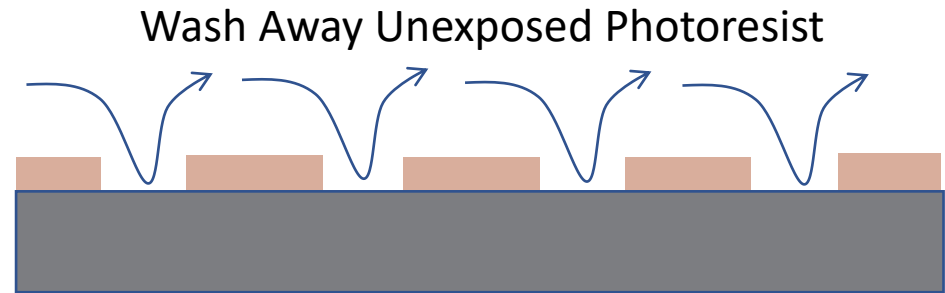
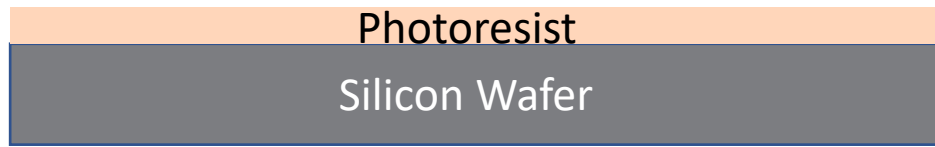


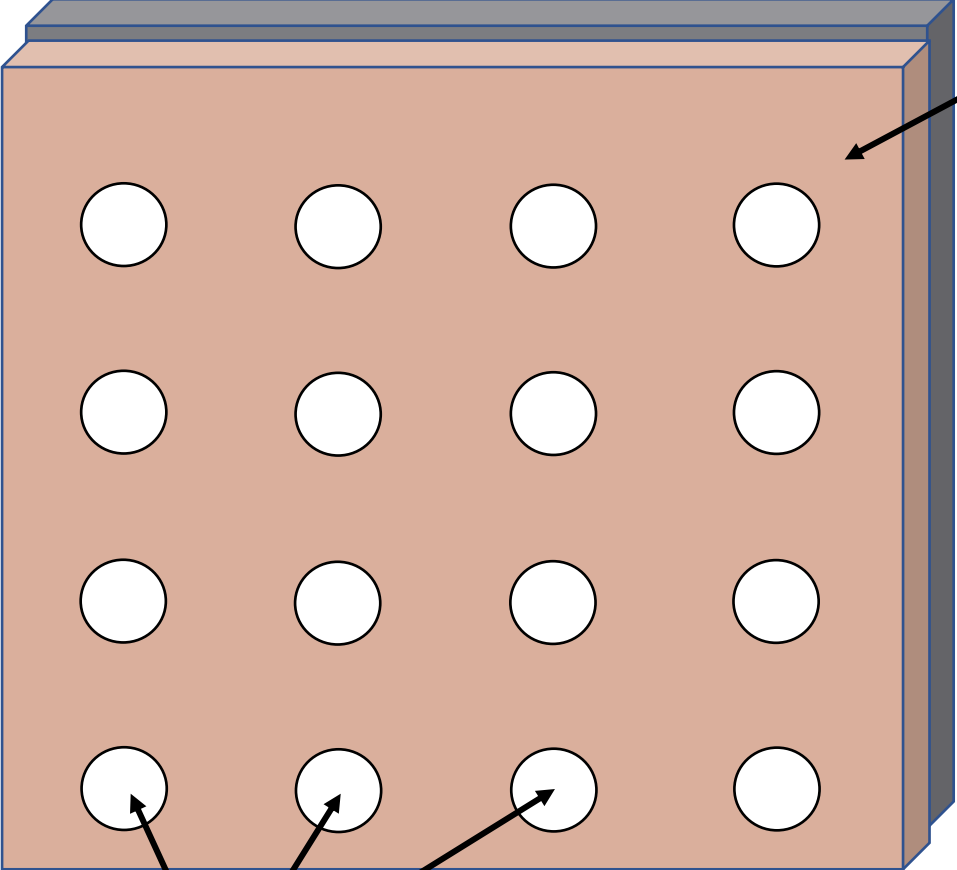
Mask





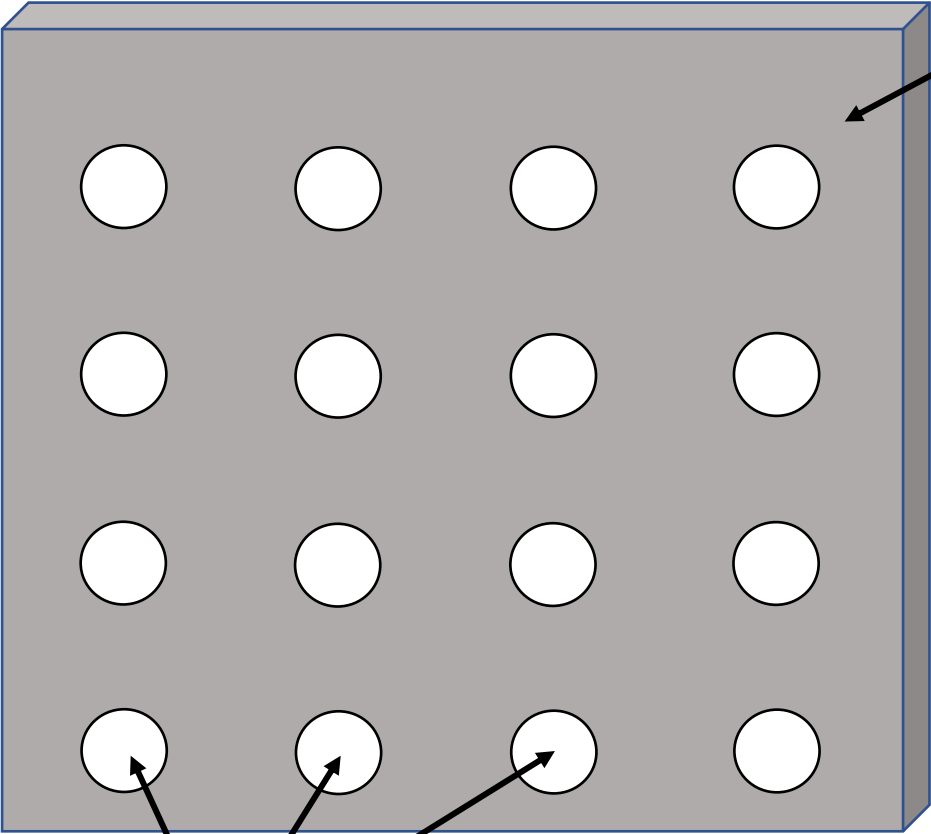






Photoresist

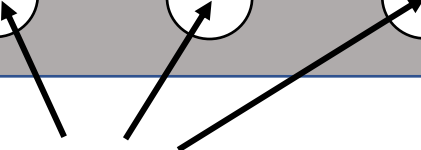
Divots

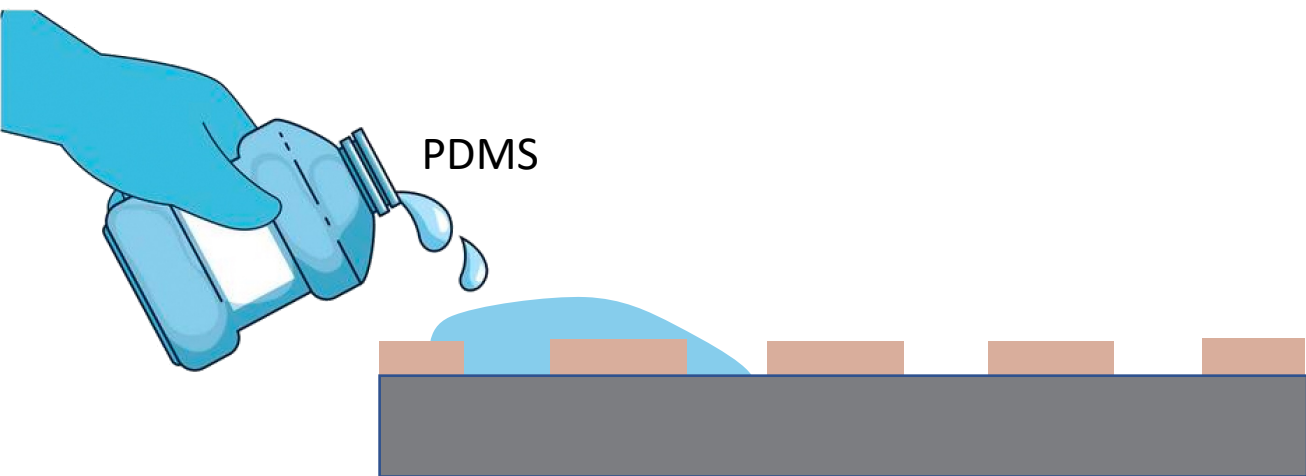


Agarose



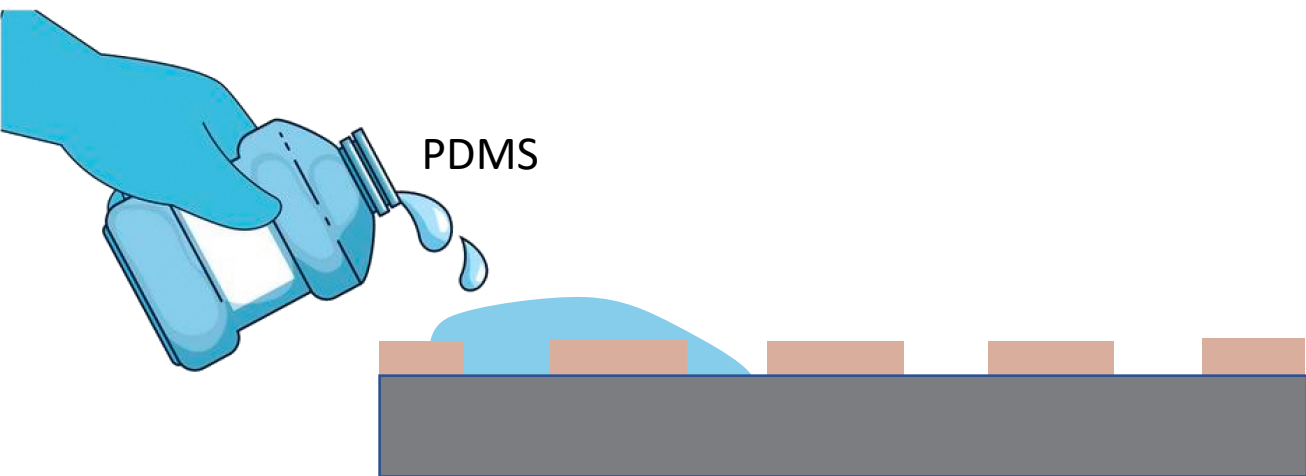
Divots =
Microwells



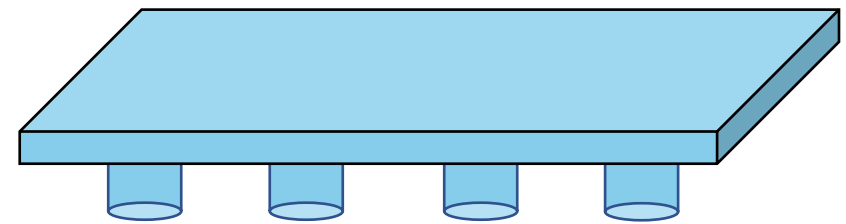


Pegs roughly
the diameter
of a single cell



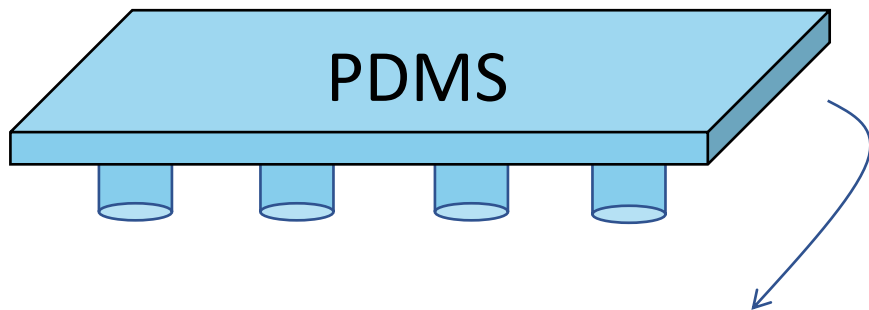


PDMS is an Array of Pegs



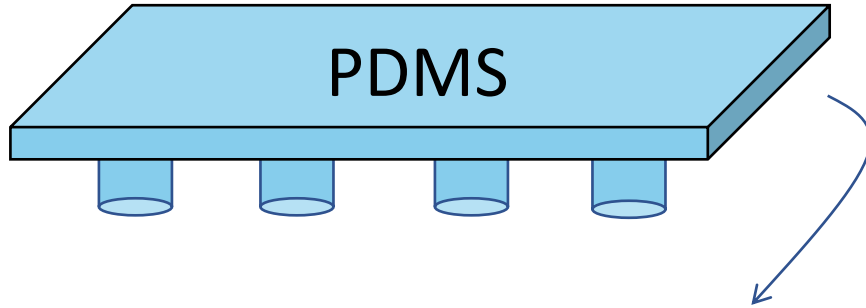
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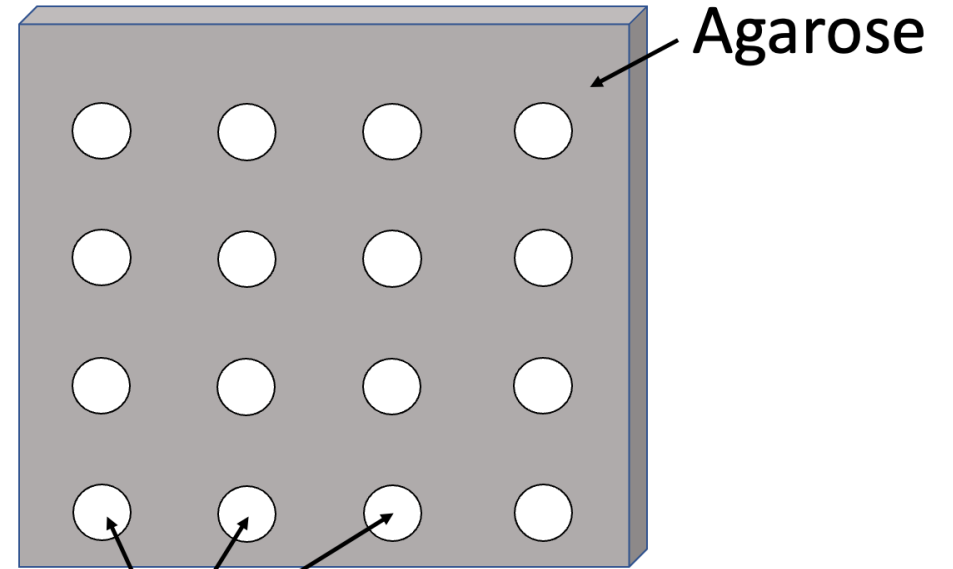
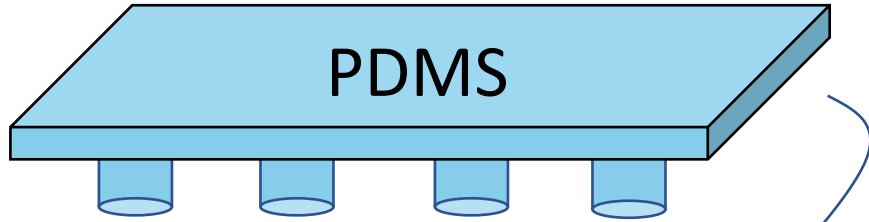


Molten Agarose

PDMS is an Array of Pegs

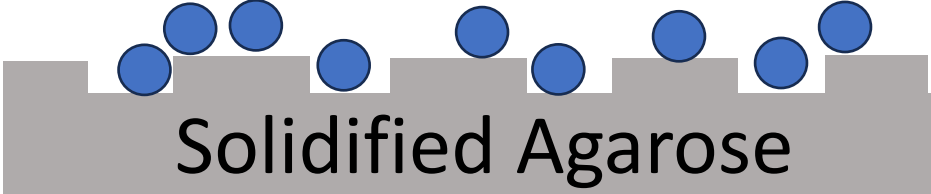


PDMS is an Array of Pegs



Divots =
Microwells





↓ Rinse



How the CometChip is made

Why and how to commercialize

Applications of the CometChip:

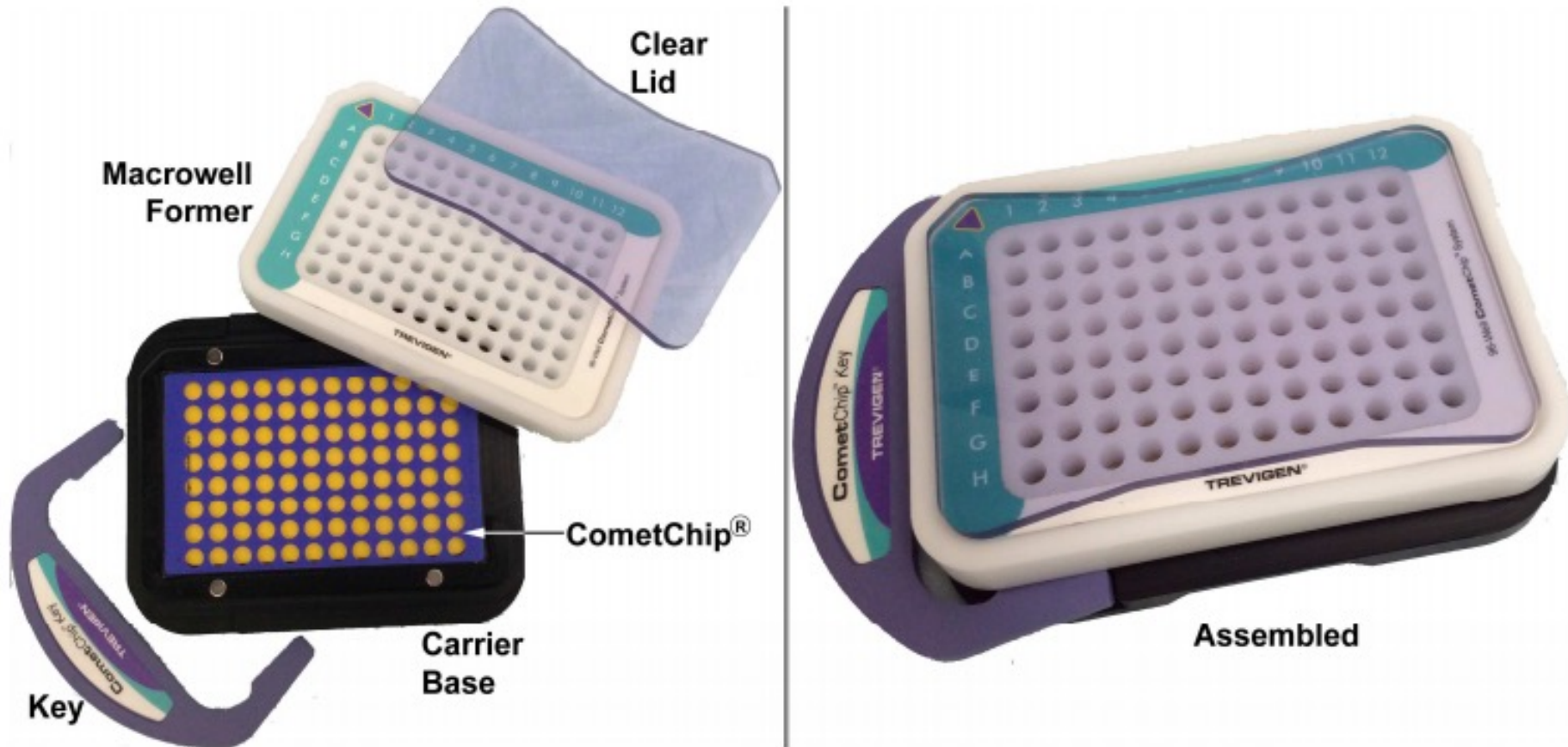
- Nanoparticle assessment

- Repair capacity evaluation

- Differences in repair capacity among people

- Assessing xenobiotics for their DNA damaging potential

How to set a Price Point for CometChip




Concept:

Price point needs to be low enough to be popular and high enough to cover costs.

96-Well CometChip System \$1250

Catalog # 4260-096-CS

	Catalog #	Availability	Size / Price	Qty
	4260-096-CS	✔ In Stock	96 Tests / \$1250.00	<input type="text" value="0"/>
		Bulk Order	Add To Cart	

Key Product Details


Features:

A reusable cassette consisting of a carrier base, a macrowell former, a lid and a key. When the CometChip is inserted into the magnetically sealable cassette, 96 separate macrowells are created on the CometChip.

CometChip Kit \$350

Catalog # 4260-096-K

[Citations \(3\)](#)

	Catalog #	Availability	Size / Price	Qty
	4260-096-K	✔ In Stock	96 Tests / \$350.00	<input type="text" value="0"/>
		Bulk Order	Add To Cart	

Key Product Details

Features:

Includes one CometChip and reagents to test 96 samples.

Key Benefits:

- CometChip for single cell capture – no overlapping comets
- Ready to use low melt agarose (LMAgarose) in convenient size
- Lysis Solution suitable for either alkaline or neutral comet assay
- Optimized electrophoresis conditions

Concept:

Time Really is Money

Cost for a Graduate Student:

Concept:

Time Really is Money

One experiment saving 2 days = \$900

10 experiments = \$9000

There is no point to a patent unless
it is cost effective.

You Need to Know Your Market

There is no point to a patent unless
someone uses it.

Have a plan:
Either a new company or a
company that wants
to license the technology

Concept:

Patents are not just about making money.

Companies need to profit from their work
and so they won't produce something
that others can take freely.

Concept:

Profits from Patents
are not what you think they are.

How the CometChip is made

Why and how to commercialize

Applications of the CometChip:

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One great application of the CometChip is as a learning experience! 😊



Why and how to commercialize

Applications of the CometChip:

Nanoparticle assessment

Repair capacity evaluation

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How the CometChip is made

Examples of CometChip Applications: Assessment of Nanoparticle Safety



Metal nanoparticles in makeup cannot be a good idea!

All You Need To Know About Nanoparticles in Cosmetics

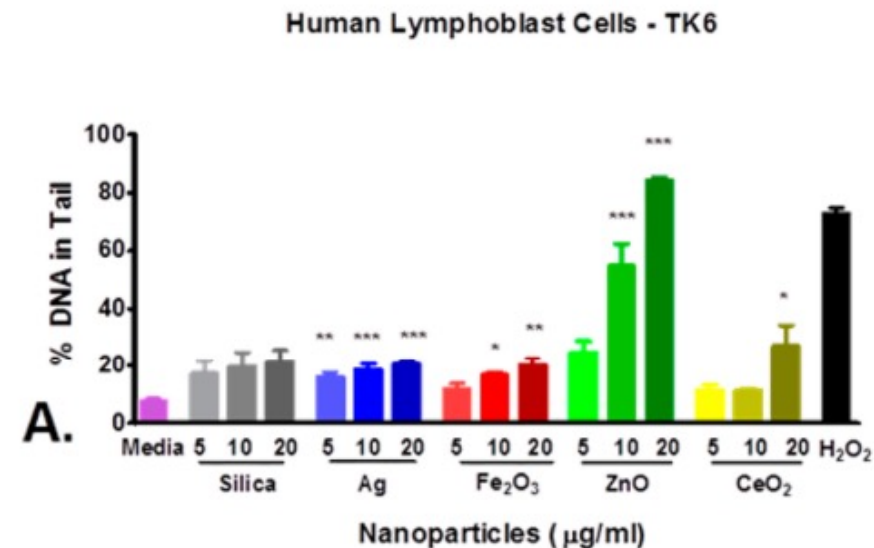
"Nanoparticles are being incorporated in other personal care products, such as: deodorants, perfumes, moisturizers, anti-aging creams, toothpastes, soaps, lip balms, and lipsticks, shampoos, etc. Nevertheless, despite claiming that nanoparticles are safe, many companies seem eager to hide the use of engineered nanoparticles in their products."

Examples of CometChip Applications: Assessment of Nanoparticle Safety



High-Throughput Screening Platform for Engineered Nanoparticle-Mediated Genotoxicity Using CometChip Technology

Christa Watson,[†] Jing Ge,[‡] Joel Cohen,[†] Georgios Pyrgiotakis,[†] Bevin P. Engelward,^{‡,§,*} and Philip Demokritou^{†,§,*}



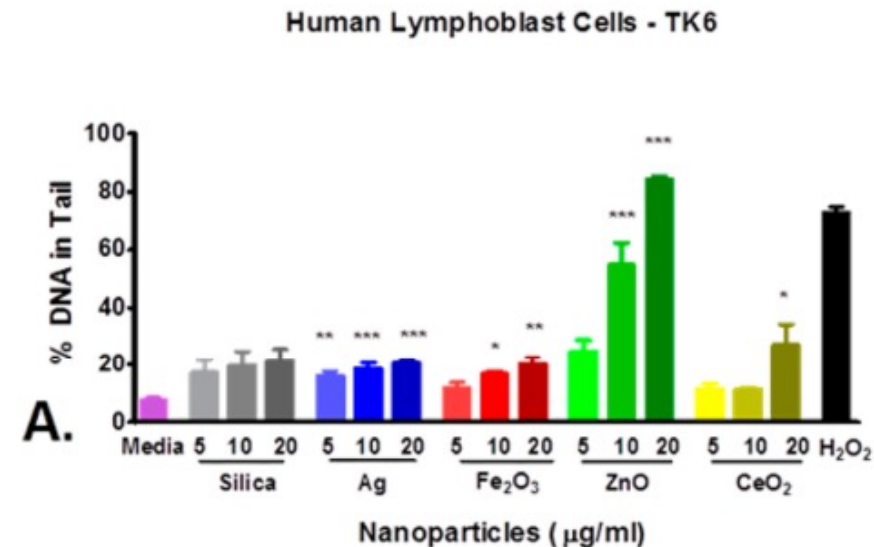
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Dr. Christa Wright
Underwriters Laboratories, Inc.

High-Throughput Screening Platform for Engineered Nanoparticle-Mediated Genotoxicity Using CometChip Technology

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Colloidal Silver (contains silver nanoparticles) can be Toxic



Paul Karason



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Applications of the CometChip:

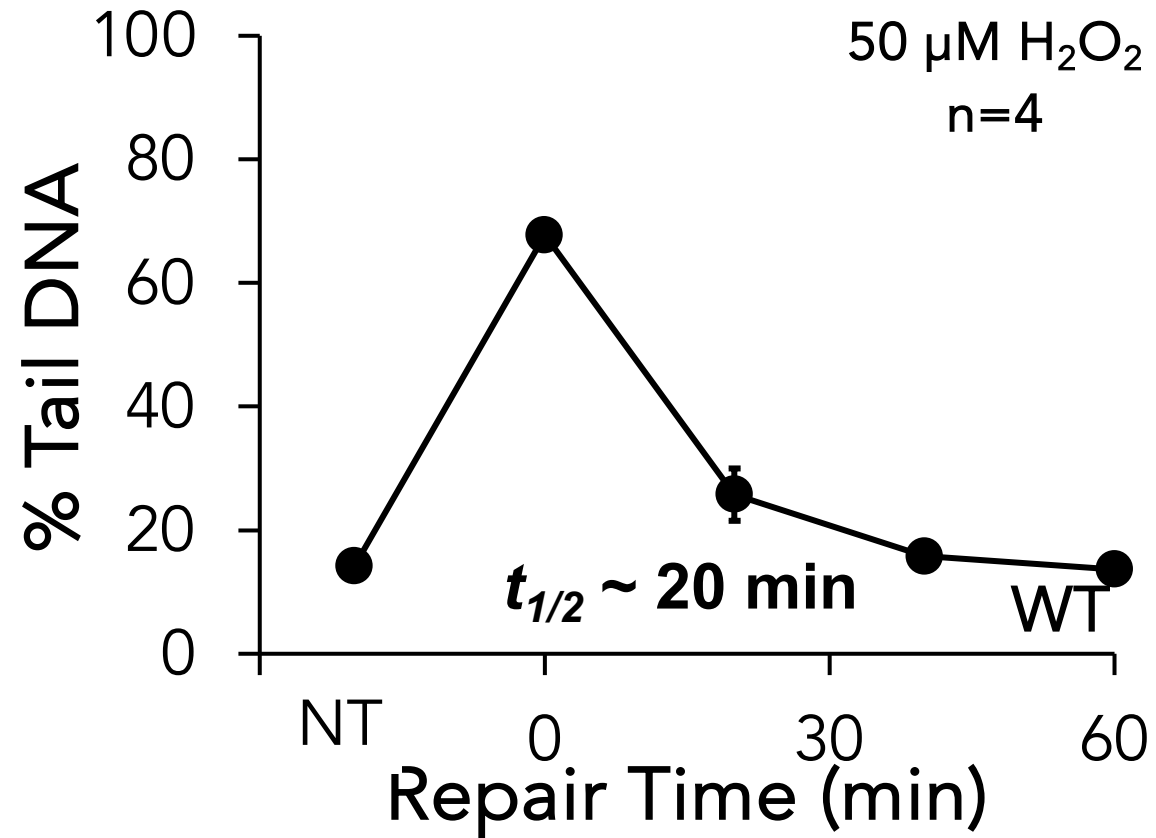
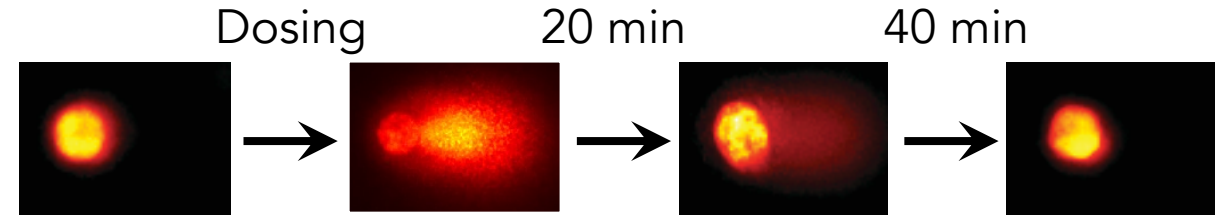
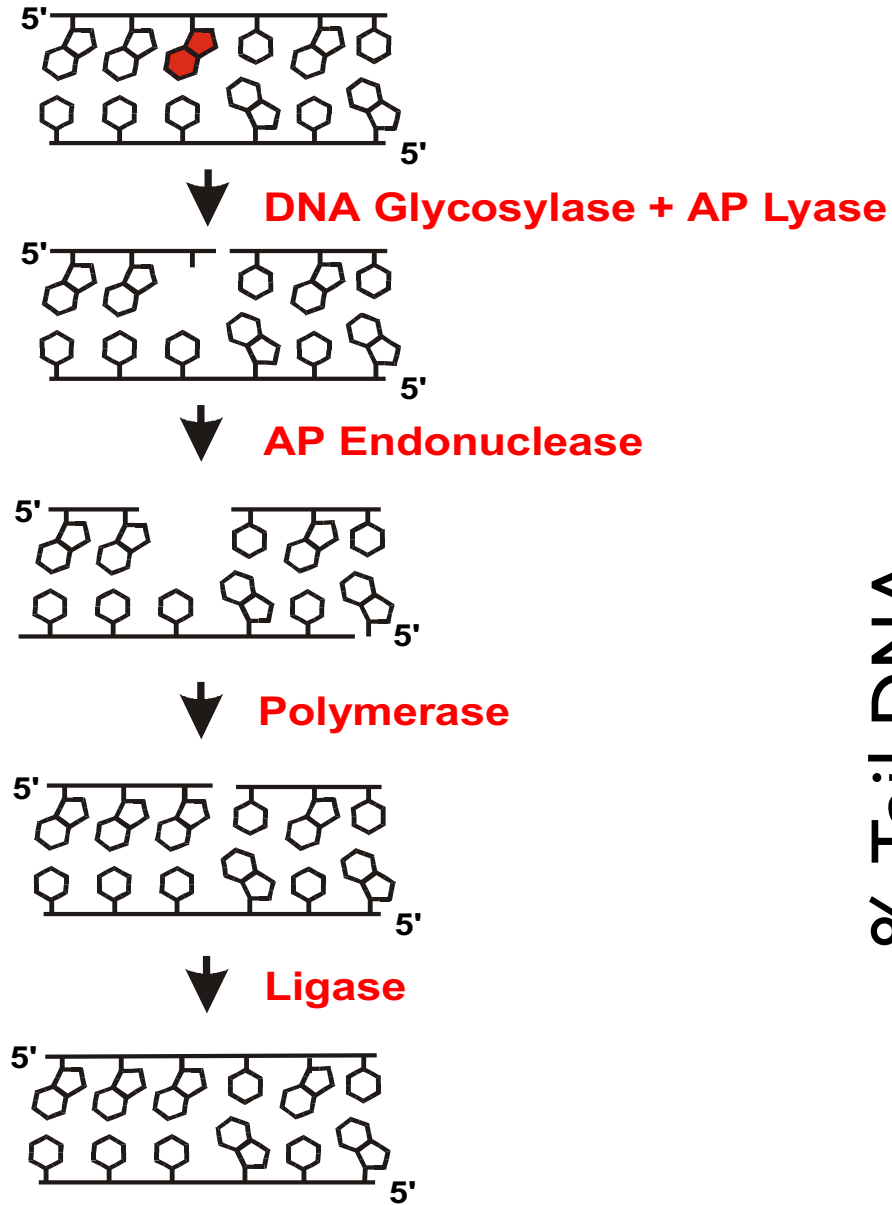
Nanoparticle assessment

Repair capacity evaluation

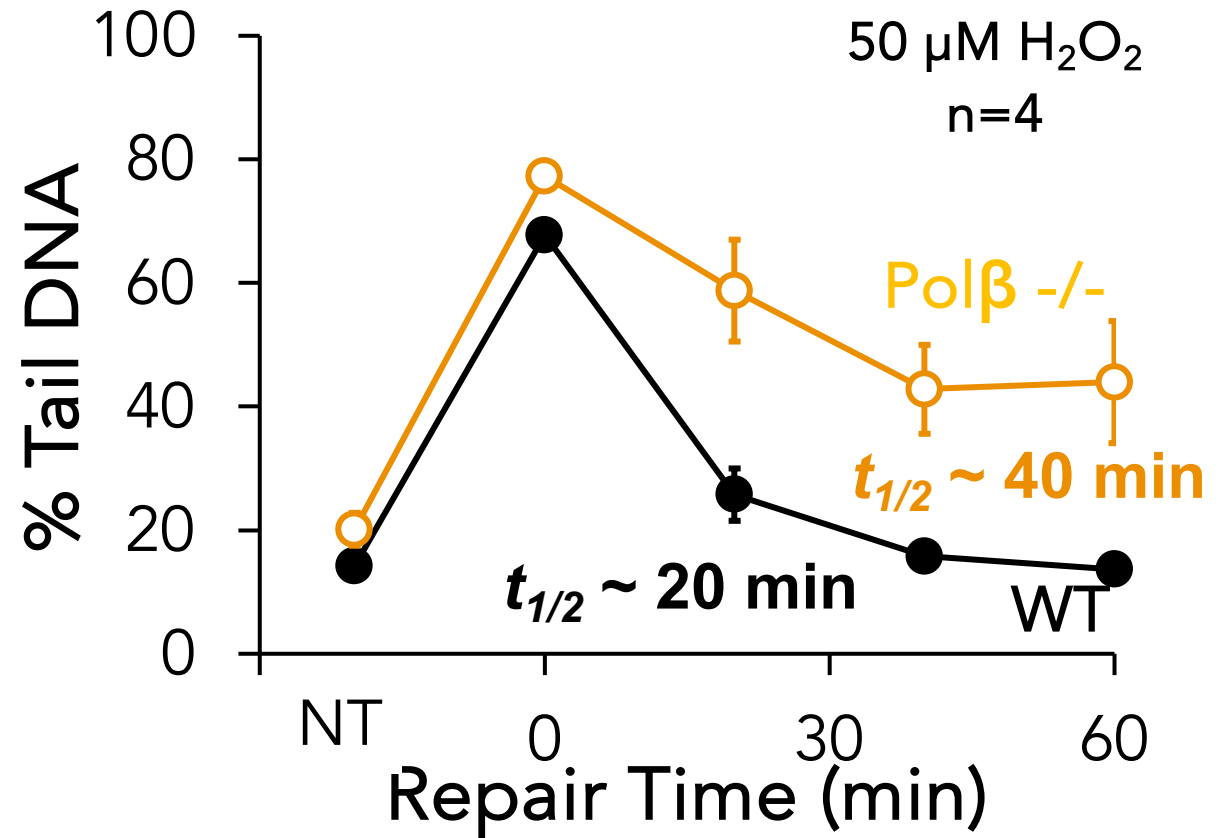
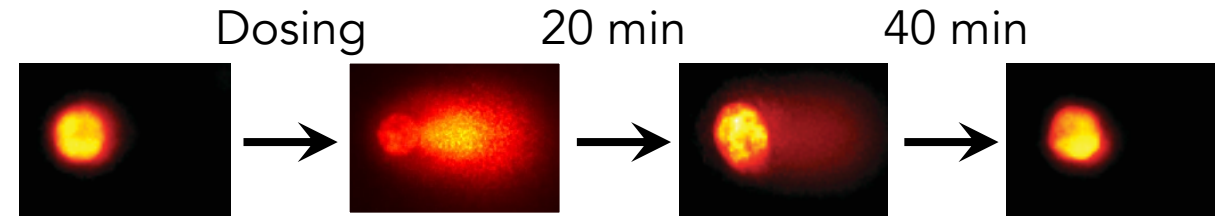
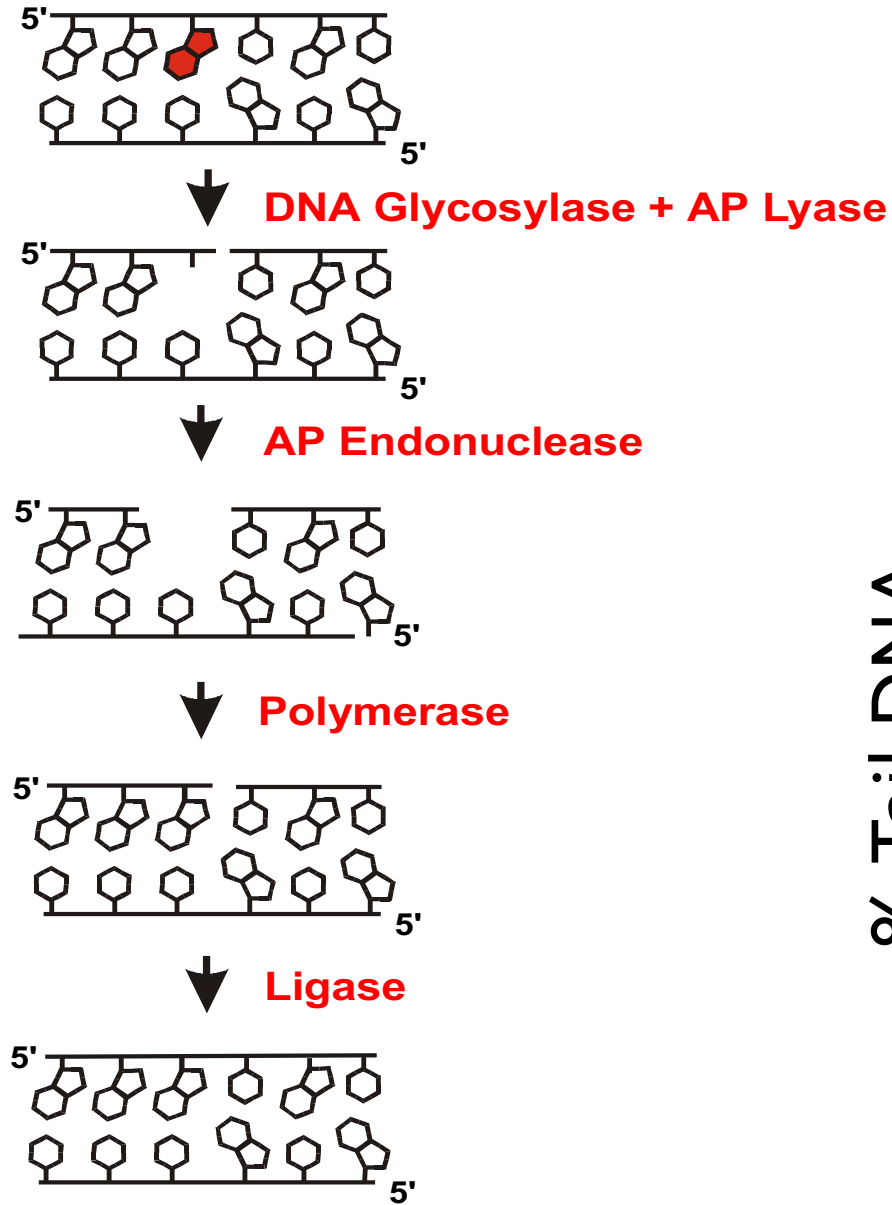
Differences in repair capacity among people

Assessing xenobiotics for their DNA damaging potential

Examples of CometChip Applications: Assessment of DNA Repair



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Applications of the CometChip:

Nanoparticle assessment

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Examples of CometChip Applications: Assessment of DNA Repair Differences among People

Everyone is different



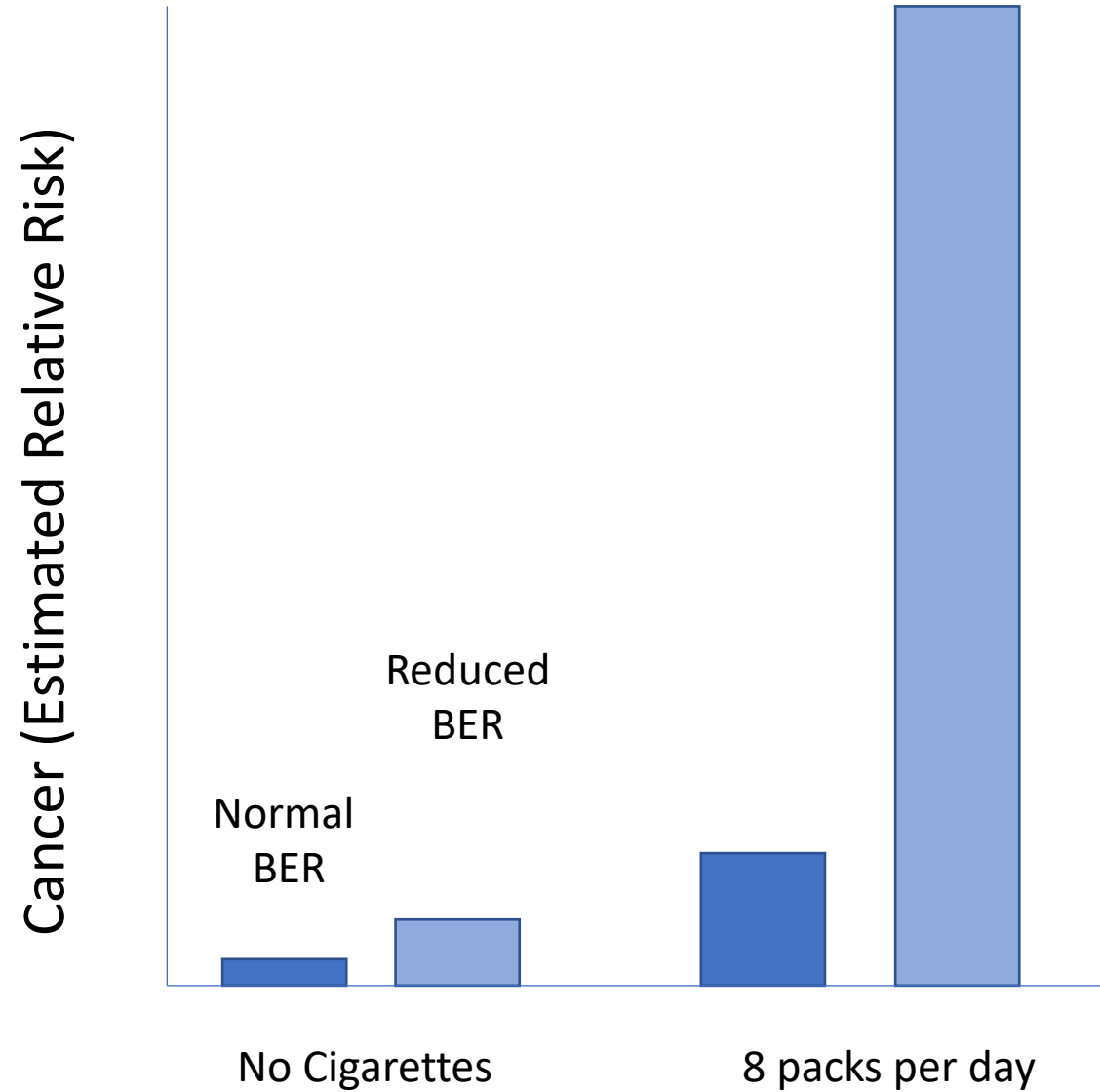
Genetics



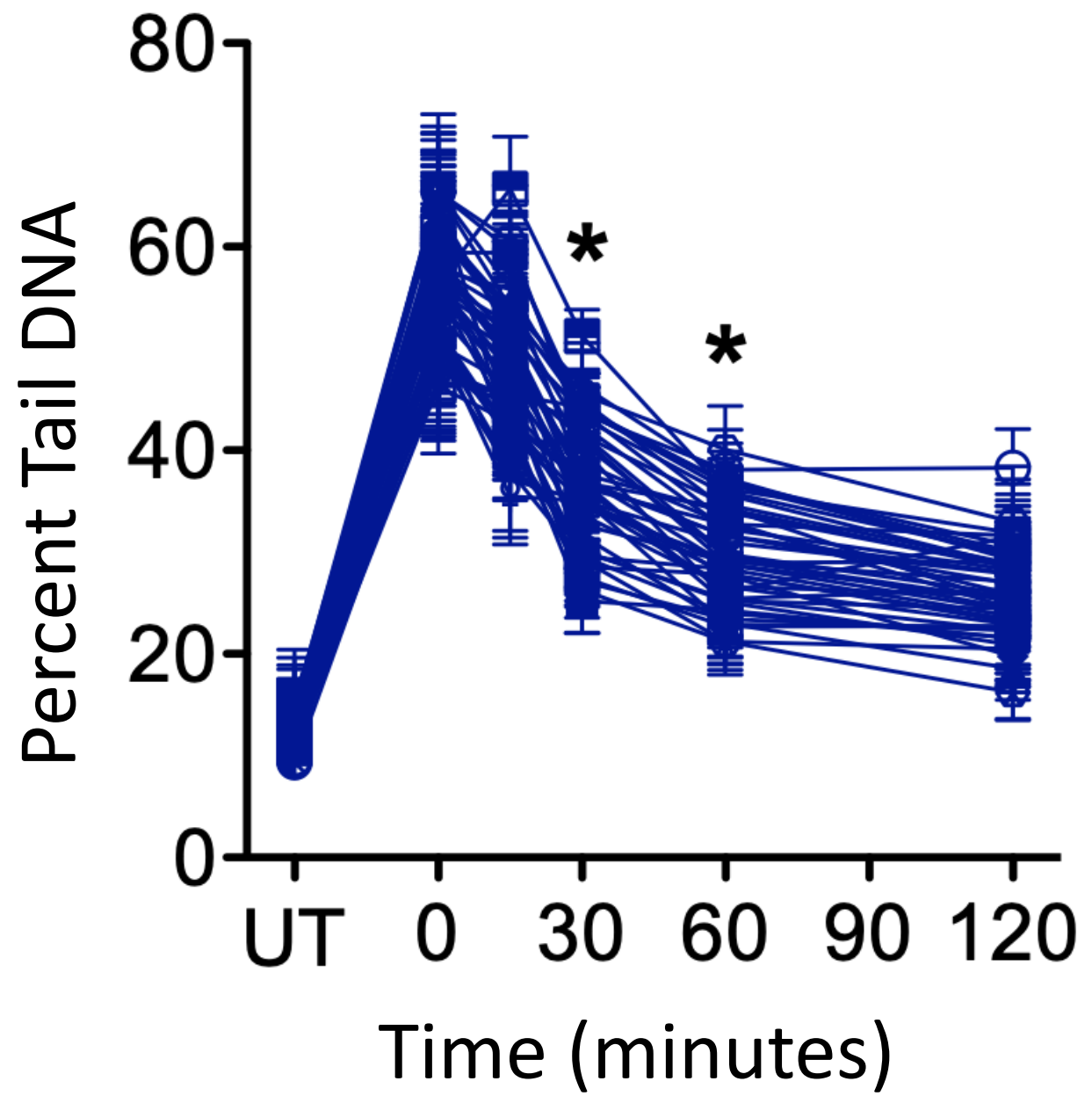
Lifestyle

Precision Prevention:
What makes some
people more
susceptible to cancer
than others?

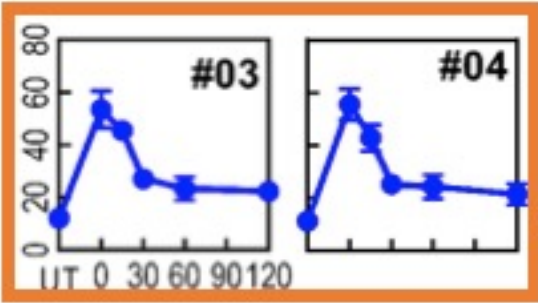
Differences in Repair Capacity Among People Affects Cancer Susceptibility



DNA Repair Kinetics are Variable Among 50 People

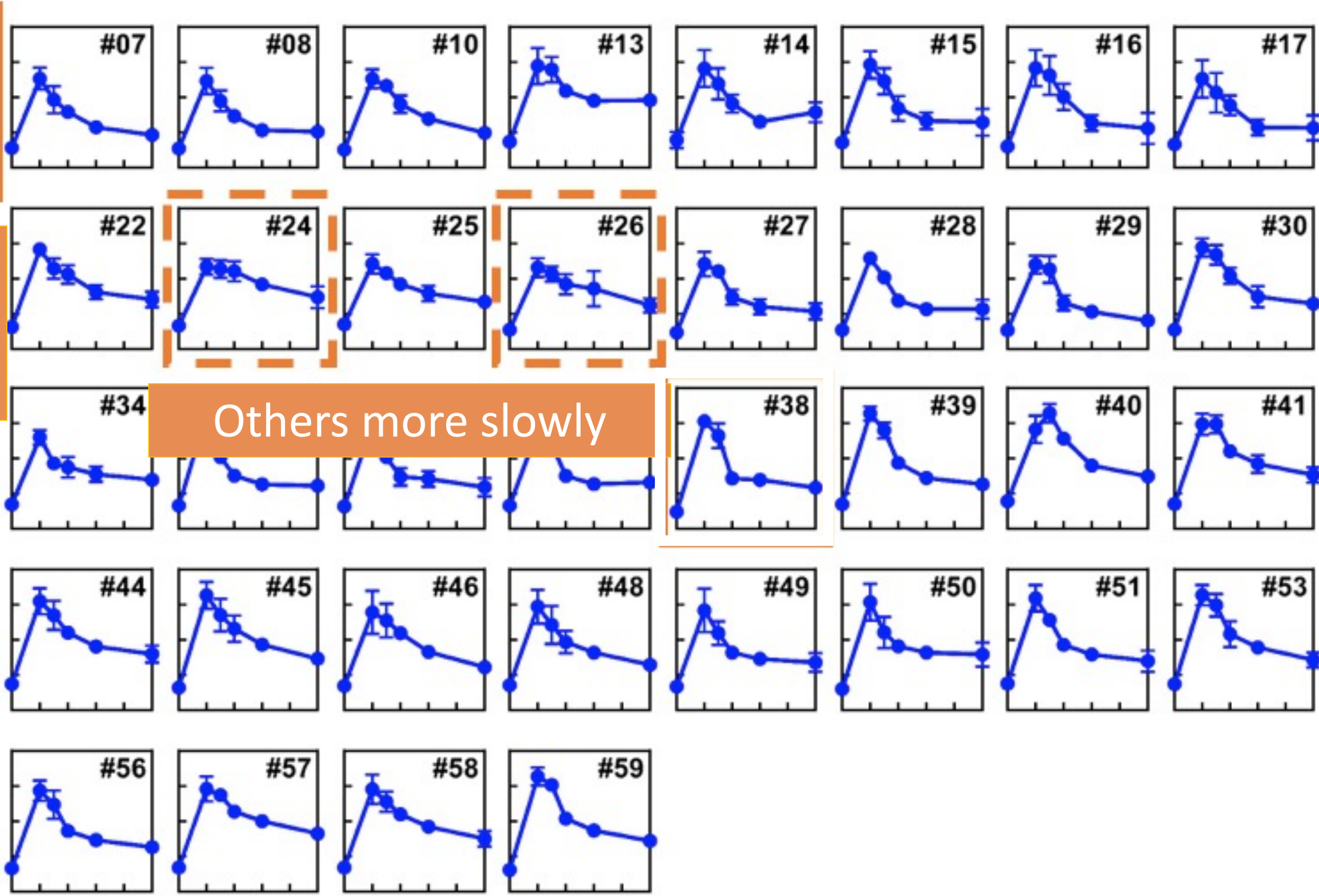


**Dr. Le P. Ngo
(Lizzie)**

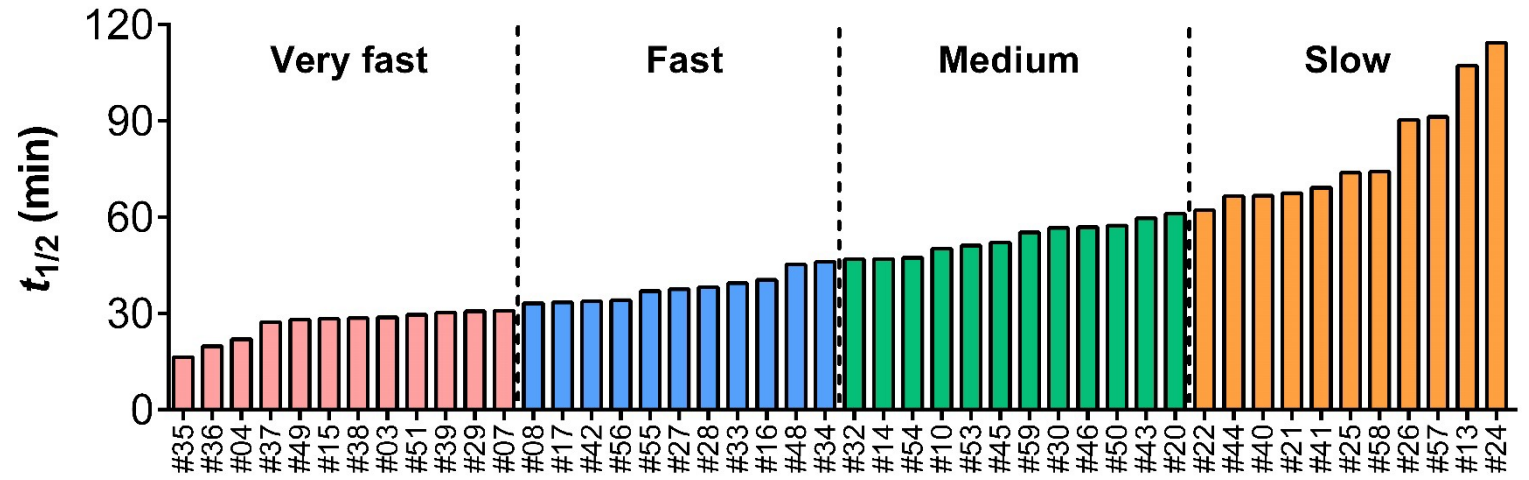
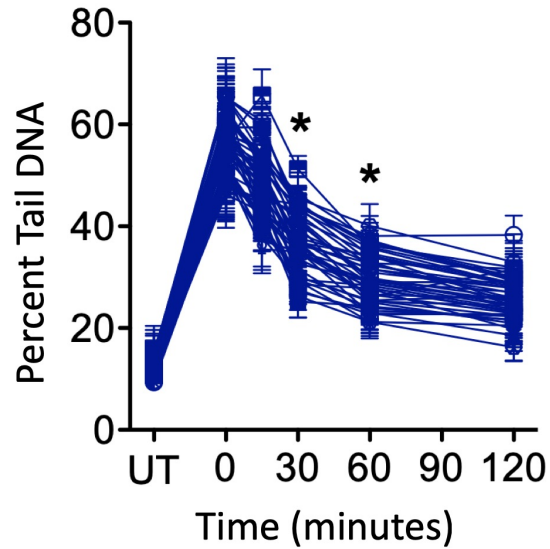


Some people repair DNA quickly

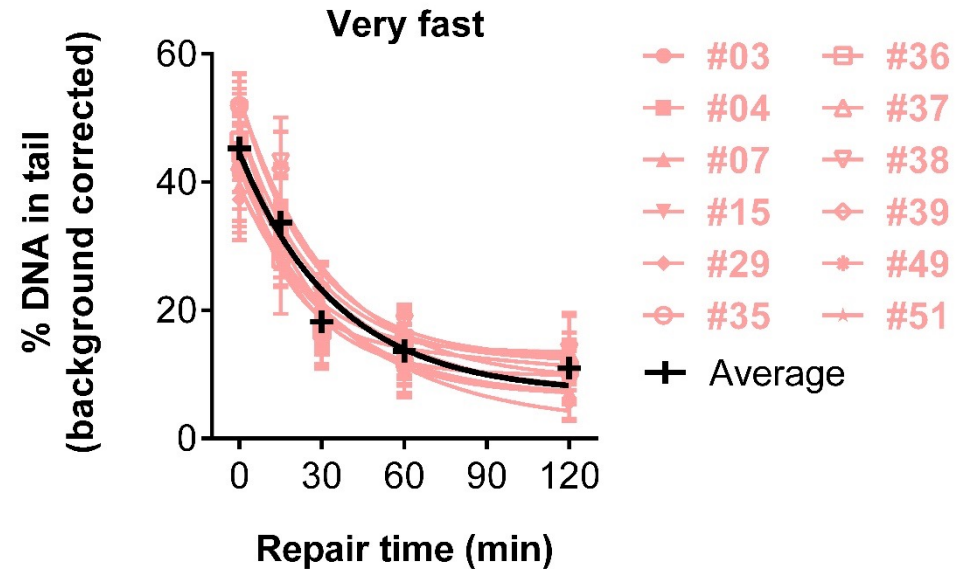
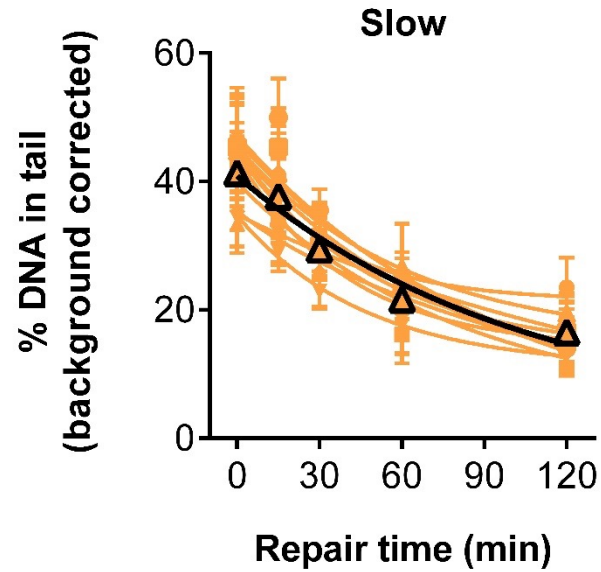
Others more slowly



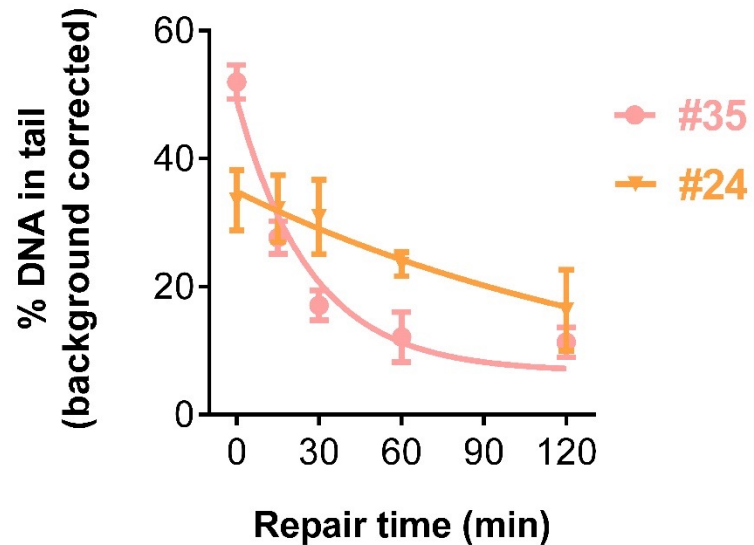
People Have Variable Rates of Repair



There are Clear Differences in Repair Kinetics Among :People



Contrast between the slowest and the fastest repair kinetics



Ongoing studies: association between repair kinetics and lung cancer risk

Strengths and weaknesses of this study

Now have a higher throughput way to look at inter-individual variation in DNA repair.

But:

- WBC's don't necessarily reflect tissues
 - WBC's are a mix of cell types
- It would be nice to know about DNA damage in the person, rather than response of cells *ex vivo*

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Examples of CometChip Applications: Assessment of Chemicals for Safety

Rapid and Sensitive Toxicity testing is Critical

>100,000 synthetic chemicals currently in use

~2,000 added every year

Occupational Exposures

Pharmaceuticals



Industrial chemicals



Household chemicals



Food



Pollutants



Cosmetics



Home Renovation Chemicals



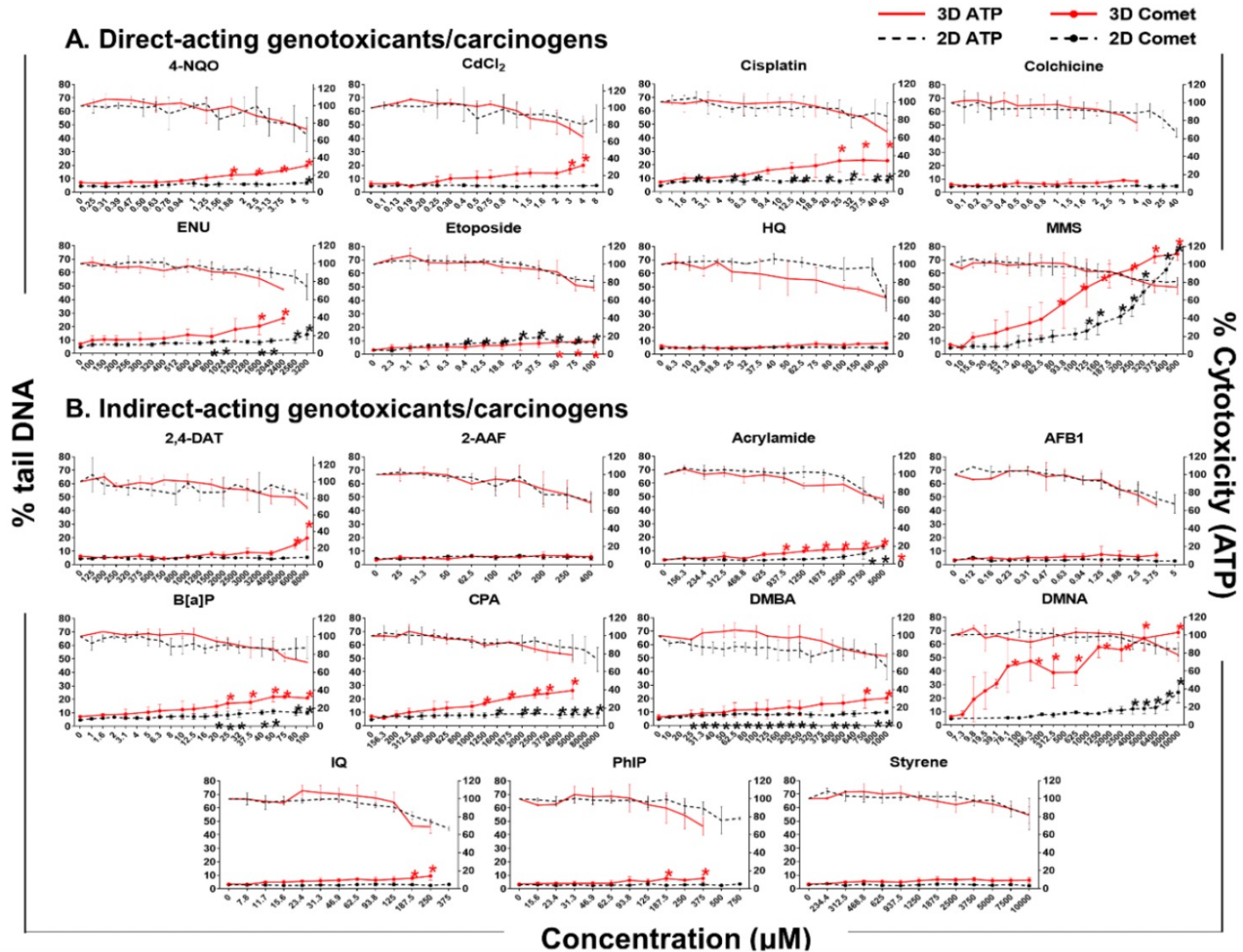
Examples of CometChip Applications: Assessment of Chemicals for Safety

19 Chemicals
20 Doses Each
2 Conditions (2D
Black
3D Red)

3 Repeats

= 2,280 Glass
Slides

= 228,000
Comets



National Center for Toxicological Research:
Work from the laboratory of Carole (Xiaoqing) Guo

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