Chemicals and Health: Preventing Cancer through TUR Dick Clapp Lowell Center for Sustainable Production November 13, 2012

Outline of presentation

- > Background on rates and causes of cancer
- Cancer as a "multi-factorial" disease
 Opportunities for prevention
 Camp Lejeune water contamination and
 - cancer studies
- > President's Cancer Panel report

Current Mechanistic Understanding

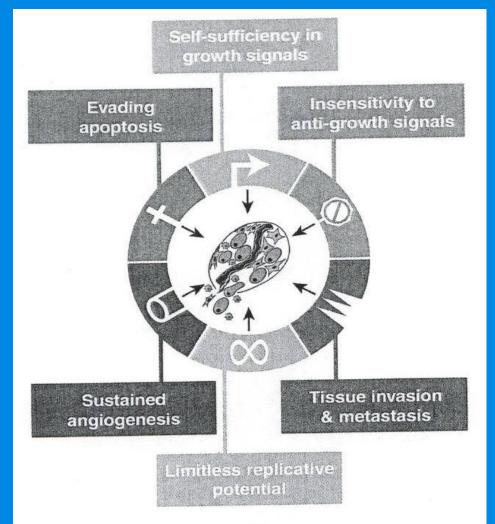


Figure 1. Acquired Capabilities of Cancer

We suggest that most if not all cancers have acquired the same set of functional capabilities during their development, albeit through various mechanistic strategies.

Source: Hanahan D and Weinberg R. The Hallmarks of Cancer. Cell 2000;100:57-70

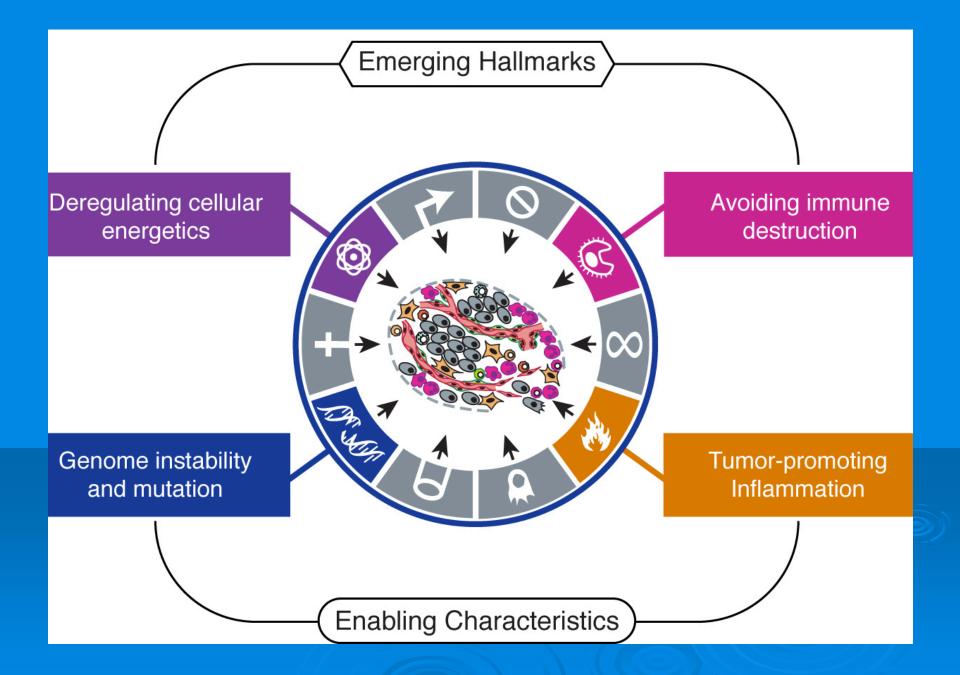
Current Mechanistic Understanding

| A Component | Acquired Capability | Example of Mechanism |
|----------------|--------------------------------------|--------------------------------|
| | Self-sufficiency in growth signals | Activate H-Ras oncogene |
| | Insensitivity to anti-growth signals | Lose retinoblastoma suppressor |
| f | Evading apoptosis | Produce IGF survival factors |
| ∞ | Limitless replicative potential | Turn on telomerase |
| n | Sustained angiogenesis | Produce VEGF inducer |
| | Tissue invasion & metastasis | Inactivate E-cadherin |
| B | W 9 7 ∞ | |
| | | |
| | P ∞ + W | Cancer |
| | P M ∞ | |
| | | |

Figure 4. Parallel Pathways of Tumorigenesis

While we believe that virtually all cancers must acquire the same six hallmark capabilities (A), their means of doing so will vary significantly, both mechanistically (see text) and chronologically (B). Thus, the order in which these capabilities are acquired seems likely be quite variable across the spectrum of cancer types and subtypes. Moreover, in some tumors, a particular genetic lesion may confer several capabilities simultaneously, decreasing the number of distinct mutational steps required to complete tumorigenesis. Thus, loss of function of the p53 tumor suppressor can facilitate both angiogenesis and resistance to apoptosis (e.g., in the five-step pathway shown), as well as enabling the characteristic of genomic instability. In other tumors, a capability may only be acquired through the collaboration of two or more distinct genetic changes, thereby increasing the total number necessary for completion of tumor progression. Thus, in the eight-step pathway shown, invasion/metastasis and resistance to apoptosis are each acquired in two steps.

Source: Hanahan D and Weinberg R. The Hallmarks of Cancer. Cell 2000;100:57-70



International Agency for Research on Cancer (IARC)

Evaluations of agents, mixtures, and exposures (as of Sept. 2012)

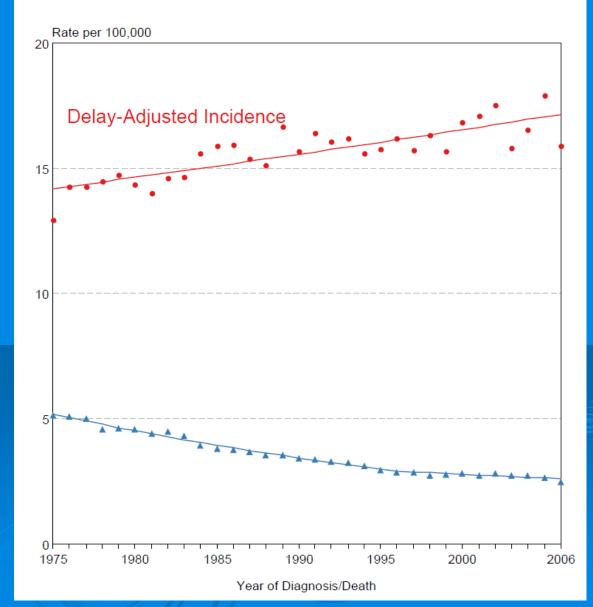
| | Total agents evaluated | 953 |
|---|---------------------------------|-----|
| • | Carcinogenic to humans | 108 |
| • | Probably carcinogenic to humans | 64 |
| • | Possibly carcinogenic to humans | 272 |
| • | Not classifiable | |
| | 508 | |

Probably not carcinogenic to humans

Source: International Agency for Research on Cancer. http://www-cie.iarc.fr/.

Childhood cancers: diet, exercise & smoking?

SEER Delay-Adjusted Incidence and US Mortality All Childhood Cancers, Under 20 Years of Age Both Sexes, All Races, 1975-2006



Childhood Leukemias: Documented Links

Ionizing radiation [Strong] > Chlorinated solvents [Good] Metal dusts [Good] > Specific Pesticides [Good] Secondhand smoke [Good] > Trichloroethylene (TCE) [Good] > Pesticides [Good]

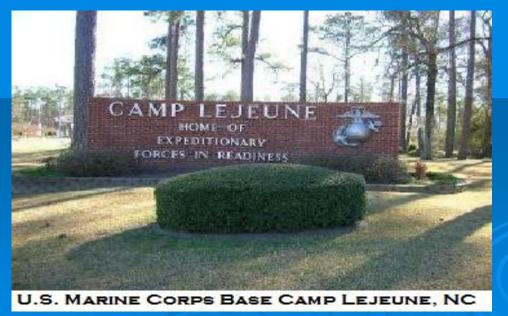
Source: Solomon G, Schettler T, Janssen S. "CHE Toxicant and Disease Database." Accessed 9-17-12: http://database.healthandenvironment.org/.

Childhood Brain Cancer: Documented Links

- > Ionizing radiation [Strong]
- > Dichlorvos [Good]
- > Lindane [Good]
- Second-hand smoke [Good]
- > Solvents [Good]
- > Pesticides [Good]

Source: Solomon G, Schettler T, Janssen S. "CHE Toxicant and Disease Database." Accessed 9-17-12: http://database.healthandenvironment.org/.

Camp Lejeune, NC Drinking Water Contamination



Camp Lejeune, NC water contamination studies

TCE, Perc, benzene and other exposures in 1950s through 1985 at Marine training base; drinking water system modeled Hundreds of thousands of veterans and dependents exposed to contaminated drinking water (low ppb to 1,600 ppb of TCE) **ATSDR studies began in 1997; Community**

Assistance Panel formed in 2006

Camp Lejeune studies, cont.

- Marines and families (see website called "The Few, The Proud, The Forgotten") driving the process
- Community Assistance Panel work with ATSDR has been extraordinary



Congress passed legislation in 2012 to compensate veterans and family members

Camp Lejeune studies, cont.

- Cohort follow-up study comparing Camp Lejeune to Camp Pendleton veterans near completion
- Health survey requested by CAP
 - Marines publicized ATSDR (contractor) survey in order to recruit participants
- Male breast cancer case-control study begun
 - Over 80 cases of male breast cancer identified
 - VA cancer registry involved in case identification

A New Approach to Cancer Prevention in the US: the President's Cancer Panel

With input from Molly Jacobs, Richard Clapp, David Kriebel, Jeanne Rizzo, Michael Lerner, Ted Schettler, Charlotte Brody



U.S. President's Cancer Panel What is it?

> Function statement:

- "To monitor the development and execution of the activities of the National Cancer Program, and report directly to the President."
- > 3 member panel appointed by the President
 - Previous Chair: Dr. LeSalle Lefall, Professor of Surgery, Howard University College of Medicine
 - Previous Member: Dr. Margaret Kripke, University of Texas MD Anderson Cancer Center

Management and support services provided by NIH



Environmental Factors in Cancer

Industrial and Manufacturing Exposures

Chair

LaSalle D. Leffall, Jr., M.D., F.A.C.S. Charles R. Drew Professor of Surgery Howard University College of Medicine

Member

Margaret L. Kripke, Ph.D. Special Assistant to the Provost The University of Texas M.D. Anderson Cancer Center

Executive Secretary Abby B. Sandler, Ph.D. National Cancer Institute

PRESIDENT'S CANCER PANEL

Tuesday, September 16, 2008 East Brunswick, New Jersey Hilton East Brunswick 8:00am-4:15pm

The focus of this meeting will be:

- · Effects of industrial pollutants
- The status of U.S. regulation of occupational and environmental exposures
- Research barriers in environmental health
- Occupational exposures
- Other industrial and manufacturing health concerns

For more information, please visit <u>http://pcp.cancer.gov</u> or contact Karen Parker at <u>klparker@mail.nih.gov</u>, or (301) 451-9462.

No registration required

This meeting is free and open to the public. Proceedings will be recorded.

Industrial and Manufacturing Exposures

Presenting Experts:

- > Richard Clapp
- > Devra Davis
- > Adam Finkel
- Elizabeth Fontham
- David Kriebel
- > Philip Landrigan
- > Christopher Portier
- Paul Schulte
- Jeanne Stellman
- > Daniel Wartenberg
- Frank Mirer
- > Jeanne Rizzo

"The true burden of environmentally induced cancers has been grossly underestimated."

Pres. Obama: "Use the power of your office to remove the carcinogens and other toxins from our food, water, and air that needlessly increase healthcare costs, cripple our nation's productivity and devastate American lives."

2008–2009 Annual Report 🚽 President's Cancer Panel

REDUCING ENVIRONMENTAL CANCER RISK

What We Can Do Now

Solutions going forward

2008–2009 Annual Report 🛑 Pre

President's Cancer Panel

"A precautionary prevention-oriented approach should replace current reactionary approaches to environmental contaminants in which human harm must be proven before action is taken to reduce or 77 eliminate exposure

REDUCING ENVIRONMENTAL CANCER RISK

What We Can Do Now

Solutions going forward

2008–2009 Annual Report 🐗 President's Cancer Panel

" 'Green chemistry initiatives and research, including process redesign, should be pursued and supported more aggressively ... "

REDUCING ENVIRONMENTAL CANCER RISK

What We Can Do Now

Lowell Center Materials





Environmental and Occupational Causes of Cancer

A Review of Recent Scientific Literature

Richard W. Clapp, D.Sc. Genevieve K. Howe, MPH Molly M. Jacobs, MPH

Prepared by

Boston University School of Public Health and Environmental Health Initiative, University of Massachusetts Lowell

For the

Cancer Working Group of the Collaborative on Health and the Environment

September 2005

A Publication of the Lowell Center for Sustainable Production

> University of Massachusetts Lowell

Richard W. Clapp, D.Sc. Genevieve K. Howe, MPH Molly M. Jacobs, MPH Ed Loechler, Ph.D.

September 2005 And Update October 2007

www.sustainableproduction.org

Other recent research

- > Neurological disease and toxic exposures
 - Lou Gehrig's Disease among semiconductor workers
 - Potential link to solvent exposure
 - Parkinson's Disease and farm work
 - Potential link to pesticide exposure
 - Neurobehavioral effects in Gulf War veterans
 - Khamisiyah nerve gas exposure altered psychomotor and visuospatial abilities

SEMPER FI



WIDER FILM PROJECTS ARESENTS A TIED TO THE TRACKS FILMS PRODUCTION IN ASSOCIATION WITH CHICKEN & EGG PICTURES "SEMPER FLAUWAYS FAITHFUL"

SAMERAL SCONE IVOR BUEST & ROBERT LOGAN DISECTORS OF ENOTOGRAPHY TONY HARDMON EXEMP PURCELL CARSON DOCUMENT PRODUCTS JULY APARTER BENELLO, WENDY ETTINGER, JUDITH HELFAND PRODUCTO BY JEDD WIDER & TODO WIDER IN DISECTOR AND PRODUCTO SY ACHEL LIBERT & TONY HARDMON



EDESTATES COMMENTS COST



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MCB Camp Lejeune et al.

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