

# Chemoprevention Clinical Trials at UCI: Past, Present, and Future

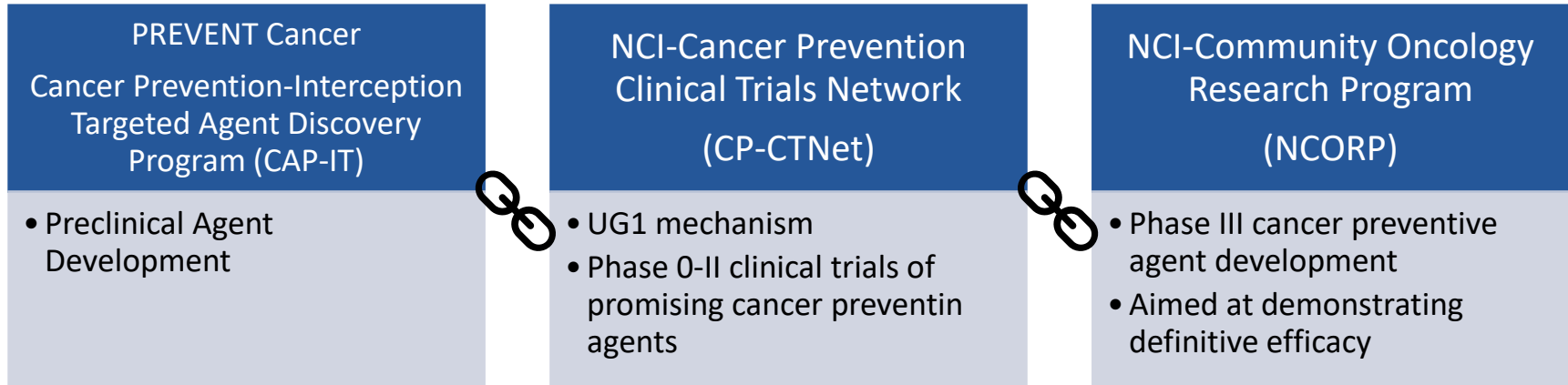
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**Jason A. Zell, DO, MPH**

Vice Chief for Academic Affairs, Division of Hem/Onc  
Director, Hematology/Oncology Fellowship Training Program

# NCI Cancer Prevention Research Programs

<https://prevention.cancer.gov/major-programs/cancer-prevention-clinical-trials-network-cp-ctnet>



# The Past: UCI Chemoprevention Program

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2008 Jun;1(1):32-8

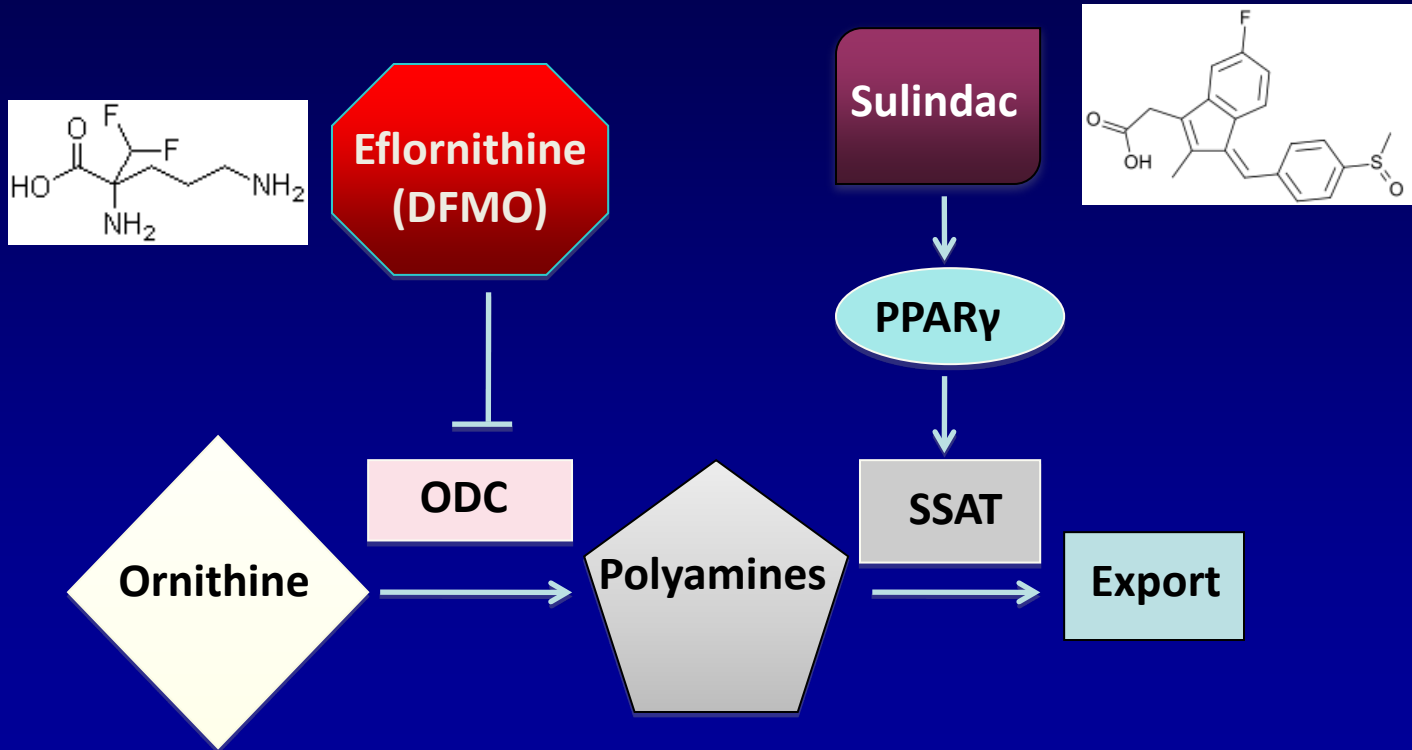
Cancer **Prevention** Research

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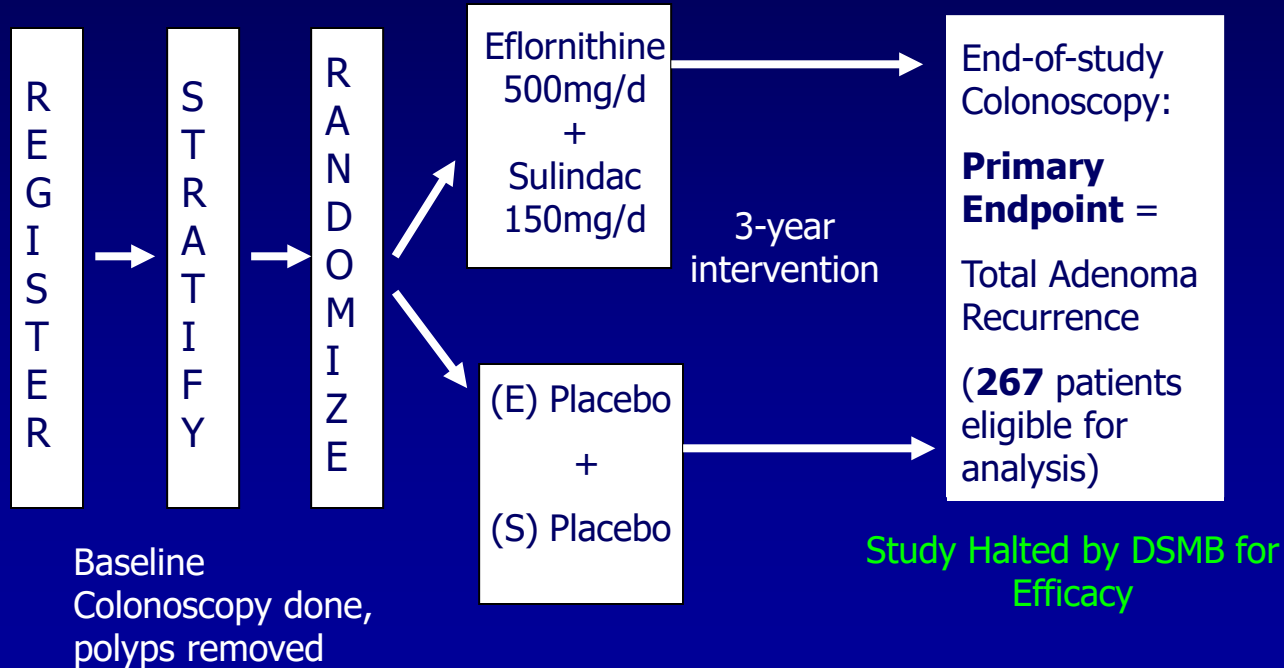
## **Difluoromethylornithine Plus Sulindac for the Prevention of Sporadic Colorectal Adenomas: A Randomized Placebo-Controlled, Double-Blind Trial**

Frank L. Meyskens, Jr.,<sup>1</sup> Christine E. McLaren,<sup>1</sup> Daniel Pelot,<sup>1</sup> Sharon Fujikawa-Brooks,<sup>1</sup> Philip M. Carpenter,<sup>1</sup> Ernest Hawk,<sup>9</sup> Gary Kelloff,<sup>9</sup> Michael J. Lawson,<sup>7</sup> Jayashri Kidao,<sup>3</sup> John McCracken,<sup>4</sup> C. Gregory Albers,<sup>1</sup> Dennis J. Ahnen,<sup>6</sup> D. Kim Turgeon,<sup>5</sup> Steven Goldschmid,<sup>2</sup> Peter Lance,<sup>2</sup> Curt H. Hagedorn,<sup>8</sup> Daniel L. Gillen<sup>1</sup> and Eugene W. Gerner<sup>2</sup>

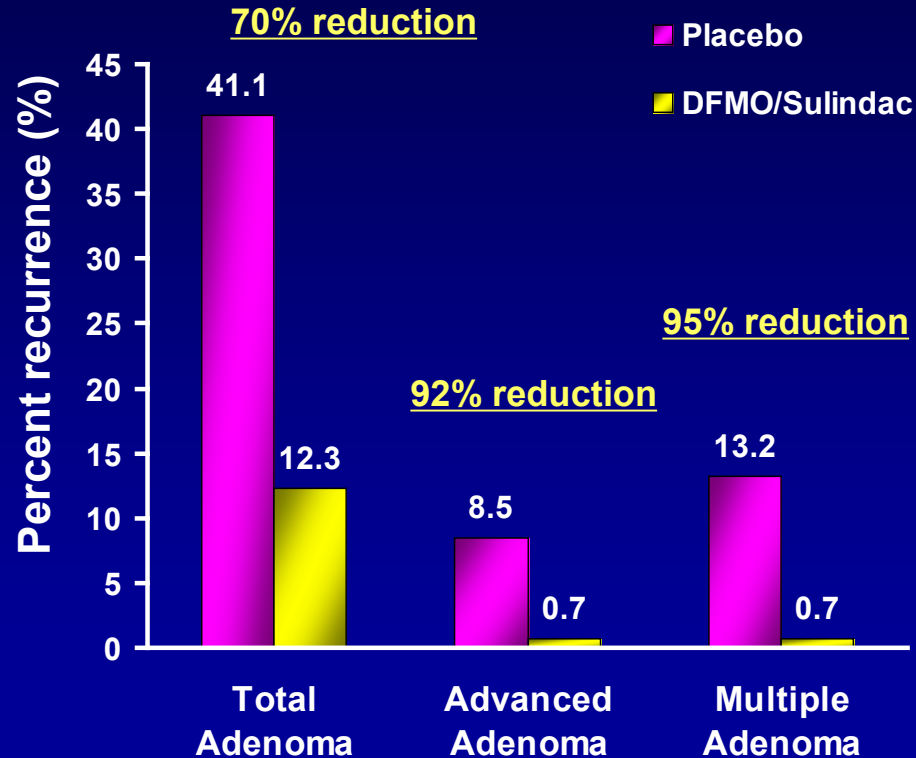
# Eflornithine and Sulindac Effects on Polyamine Metabolism



# Secondary Prevention: UCI 02-06, Eflornithine/Sulindac vs. Placebo in Patients with Colorectal Adenomas



# Marked Reduction of Adenomatous Polyps by Eflornithine + Sulindac vs. Placebo



# The Past: UCI/NCI Chemoprevention Consortium 2008-2013\*

## The Effect of Difluoromethylornithine on Decreasing Prostate Size and Polyamines in Men: Results of a Year-Long Phase IIb Randomized Placebo-Controlled Chemoprevention Trial

Anne R. Simoneau,<sup>2,4</sup> Eugene W. Gerner,<sup>5</sup> Ray Nagle,<sup>5</sup> Argyrios Ziogas,<sup>3,4</sup> Sharon Fujikawa-Brooks,<sup>4</sup> Hagit Yerushalmi,<sup>5</sup> Thomas E. Ahlering,<sup>2,4</sup> Ronald Lieberman,<sup>6</sup> Christine E. McLaren,<sup>3,4</sup> Hoda Anton-Culver,<sup>3,4</sup> and Frank L. Meyskens, Jr.<sup>1,4</sup>

\*NCI N01-CN-35160  
PI: F Meyskens

Research Article

## A Phase II Randomized, Controlled Trial of S-Adenosylmethionine in Reducing Serum α-Fetoprotein in Patients with Hepatitis C Cirrhosis and Elevated AFP

Timothy R. Morgan<sup>1,2</sup>, Kathryn Osann<sup>3</sup>, Teodoro Bottiglieni<sup>4</sup>, Neville Pimstone<sup>5</sup>, John C. Hoefs<sup>6</sup>, Ke-Qin Hu<sup>7</sup>, Tarek Hassanein<sup>7</sup>, Thomas D. Boyer<sup>8</sup>, Lorene Kong<sup>9</sup>, Wen-Pin Chen<sup>10</sup>, Ellen Richmond<sup>11</sup>, Rachel Gonzalez<sup>2</sup>, Luz M. Rodriguez<sup>11,5</sup>, and Frank L. Meyskens<sup>4</sup>

Cancer Prevention Research

Research Article

## Phase IIa Clinical Trial of Curcumin for the Prevention of Colorectal Neoplasia

Robert E. Carroll<sup>1</sup>, Richard V. Benya<sup>1</sup>, Danielle Kim Turgeon<sup>2</sup>, Shajui Vareed<sup>3</sup>, Mallorie Neuman<sup>3</sup>, Luz Rodriguez<sup>4</sup>, Madhuri Kakarala<sup>2,5</sup>, Philip M. Carpenter<sup>3</sup>, Christine McLaren<sup>6,7</sup>, Frank L. Meyskens, Jr., and Dean E. Brenner<sup>2,3,5</sup>

Cancer Prevention Research

Brief Communication

## Phase IIA Trial Testing Erlotinib as an Intervention against Intraductal Pancreatic Mucinous Neoplasms

Steven Lipkin<sup>1</sup>, John Lee<sup>1</sup>, David Imagawa<sup>1</sup>, Stephen M. Hewitt<sup>2</sup>, Chris Tucker<sup>3</sup>, Jason A. Zell<sup>1</sup>, Vanessa Wong<sup>1</sup>, Angela Garcia<sup>1</sup>, Rachel Gonzalez<sup>1</sup>, Gary Della Zanna<sup>1</sup>, Ellen Richmond<sup>4</sup>, L.M. Rodriguez<sup>4</sup>, M. Bigg<sup>5</sup>, F. Schnoll-Sussmans<sup>5</sup>, and Frank Meyskens<sup>1</sup>

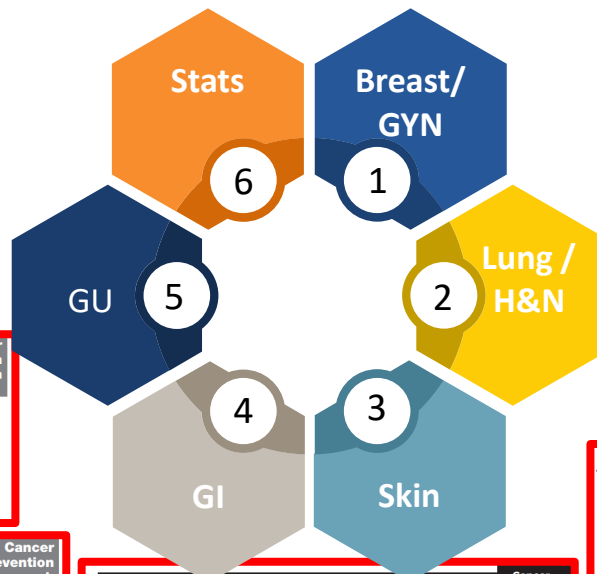
Cancer Prevention Research

Research Article

## A Phase IIa Randomized, Double-Blind Trial of Erlotinib in Inhibiting Epidermal Growth Factor Receptor Signaling in Aberrant Crypt Foci of the Colorectum

Daniel L. Gillen<sup>1,2</sup>, Frank L. Meyskens<sup>2</sup>, Timothy R. Morgan<sup>2,3</sup>, Jason A. Zell<sup>4</sup>, Robert Carroll<sup>1</sup>, Richard Benya<sup>1</sup>, Wen-Pin Chen<sup>2</sup>, Allen Mo<sup>3</sup>, Chris Tucker<sup>3</sup>, Asmita Bhattacharya<sup>8</sup>, Zhiliang Huang<sup>8</sup>, Myra Arcilla<sup>8</sup>, Vanessa Wong<sup>2</sup>, Jinah Chung<sup>2</sup>, Rachel Gonzalez<sup>2</sup>, Luz Maria Rodriguez<sup>10</sup>, Eva Szabo<sup>9</sup>, Daniel W. Rosenberg<sup>6</sup>, and Steven M. Lipkin<sup>8</sup>

Cancer Prevention Research



Research Article

See related commentaries by Mulshine and Ondrey, p. 371 and by William and Papadimitrakopoulou, p. 375

## Bowman Birk Inhibitor Concentrate and Oral Leukoplakia: A Randomized Phase IIb Trial

William B. Armstrong<sup>1,2</sup>, Thomas H. Taylor<sup>1,3,4</sup>, Ann R. Kennedy<sup>5</sup>, Raymond J. Melrose<sup>6</sup>, Diana V. Messadi<sup>7</sup>, Mai Gu<sup>8</sup>, Anh D. Le<sup>8</sup>, Marjorie Perloff<sup>10</sup>, Francisco Civantos<sup>11</sup>, William Jarrard Goodwin<sup>11</sup>, Lori J. Wirth<sup>12</sup>, Alexander Ross Kerr<sup>13</sup>, and Frank L. Meyskens Jr.<sup>1,14</sup>

Cancer Prevention Research

Research Article

## A Randomized, Double-Blind, Placebo-Controlled Phase II Clinical Trial of Lovastatin for Various Endpoints of Melanoma Pathobiology

Kenneth G. Linden<sup>1,2</sup>, Sancy A. Leachman<sup>6</sup>, Jonathan S. Zager<sup>7</sup>, James G. Jakowatz<sup>1</sup>, Jaye L. Viner<sup>8</sup>, Christine E. McLaren<sup>1,3</sup>, Ronald J. Barr<sup>4</sup>, Philip M. Carpenter<sup>4</sup>, Wen-Pin Chen<sup>1</sup>, Craig A. Elmets<sup>9</sup>, Joseph A. Tangrea<sup>10</sup>, Sung-Jig Lim<sup>11</sup>, Alistair J. Cochran<sup>6</sup>, and Frank L. Meyskens Jr.<sup>1</sup>

Cancer Prevention Research

CANCER PREVENTION RESEARCH | RESEARCH ARTICLE

## A Phase IIa Trial of Metformin for Colorectal Cancer Risk Reduction among Individuals with History of Colorectal Adenomas and Elevated Body Mass Index

Jason A. Zell<sup>1,2,3</sup>, Christine E. McLaren<sup>2,3</sup>, Timothy R. Morgan<sup>4</sup>, Michael J. Lawson<sup>5</sup>, Sherif Rezk<sup>6</sup>, C. Gregory Albers<sup>7</sup>, Wen-Pin Chen<sup>3</sup>, Joseph C. Carmichael<sup>7</sup>, Jinah Chung<sup>3</sup>, Ellen Richmond<sup>8</sup>, L.M. Rodriguez<sup>9</sup>, Eva Szabo<sup>10</sup>, Leslie G. Ford<sup>8</sup>, Michael N. Pollak<sup>10</sup>, and Frank L. Meyskens<sup>13,11</sup>



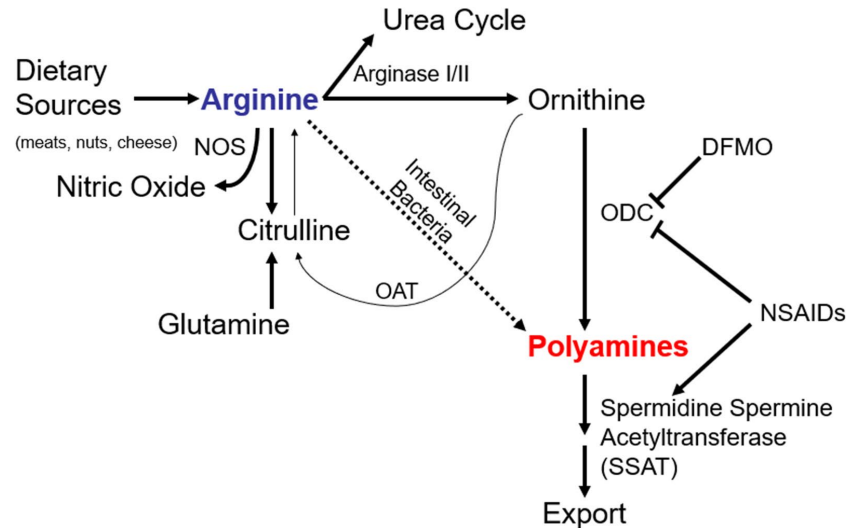
# The Past: UCI Cancer Prevention Program



Article

## Phase IIa Clinical Biomarker Trial of Dietary Arginine Restriction and Aspirin in Colorectal Cancer Patients

Jason A. Zell <sup>1,2,\*</sup>, Thomas H. Taylor <sup>3</sup>, C. Gregory Albers <sup>4</sup>, Joseph C. Carmichael <sup>5</sup>, Christine E. McLaren <sup>2,6</sup>, Lari Wenzel <sup>2,6</sup> and Michael J. Stamos <sup>5</sup>



PI: Zell NIH-K23CA133142



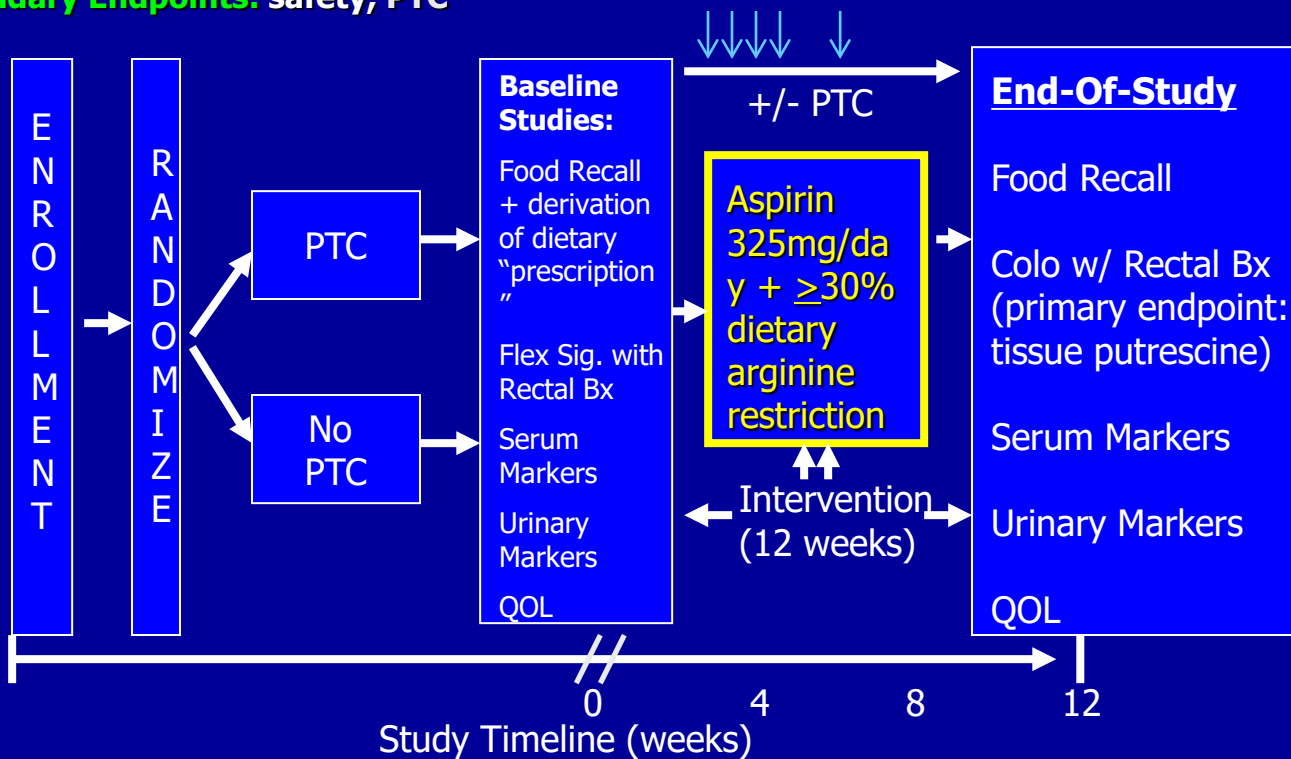
# Phase IIa clinical biomarker study, UC Irvine: Aspirin and arginine restriction in colorectal cancer patients

**Eligibility:** stage I-III colon or rectal cancer

**Primary Endpoint:** decrease tissue putrescine by >50%

**Secondary Endpoints:** safety, PTC

Accrual: 24



PI: J. Zell

Funding: NIH-NCI K23 CA133142, & ICTS via NCRR M01 RR00827

# The Present

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15 UCI faculty from the prior Chemoprevention Consortium remain active in research, along w/ new basic, translational, and clinical research faculty.

# NCI-NCORP / SWOG Trial: S0820

“A Double Blind Placebo-Controlled Trial of Eflornithine and Sulindac to Prevent Recurrence of High Risk Adenomas and Second Primary Colorectal Cancers in Patients with Stage 0-III Colon or Rectal Cancer, Phase III”



## SWOG Lead Investigator:

Jason Zell, DO, MPH  
Division of Hematology/Oncology  
Dept. of Medicine  
School of Medicine  
Chao Family Comprehensive Cancer Ctr  
University of California, Irvine

SWOG co-PI: Powel Brown, MD, PhD  
SWOG Lead Statistician: Joe Unger, PhD  
SWOG co-I: Robert Krouse, MD

## NCTN co-PI's:

Raymond Bergan, MD (ECOG-ACRIN)  
Jennifer Dorth, MD (NRG)  
Y. Nancy You, MD (ALLIANCE)

## Funding:

- 1) NCI-NCORP
- 2) NCI 1R50CA285412-01 (PI: Zell)

**S0820 Primary Objective:** to assess whether the polyamine-inhibitory combination: eflornithine 500 mg/d and sulindac 150 mg/d (vs. placebos) are effective in reducing the 3-year rate of high-risk adenomas or 2<sup>nd</sup> primary CRCs in stage 0, I, II, and III colon and rectal cancer patients.

- **Primary Endpoint:**

- **High risk adenomas (HRA)**

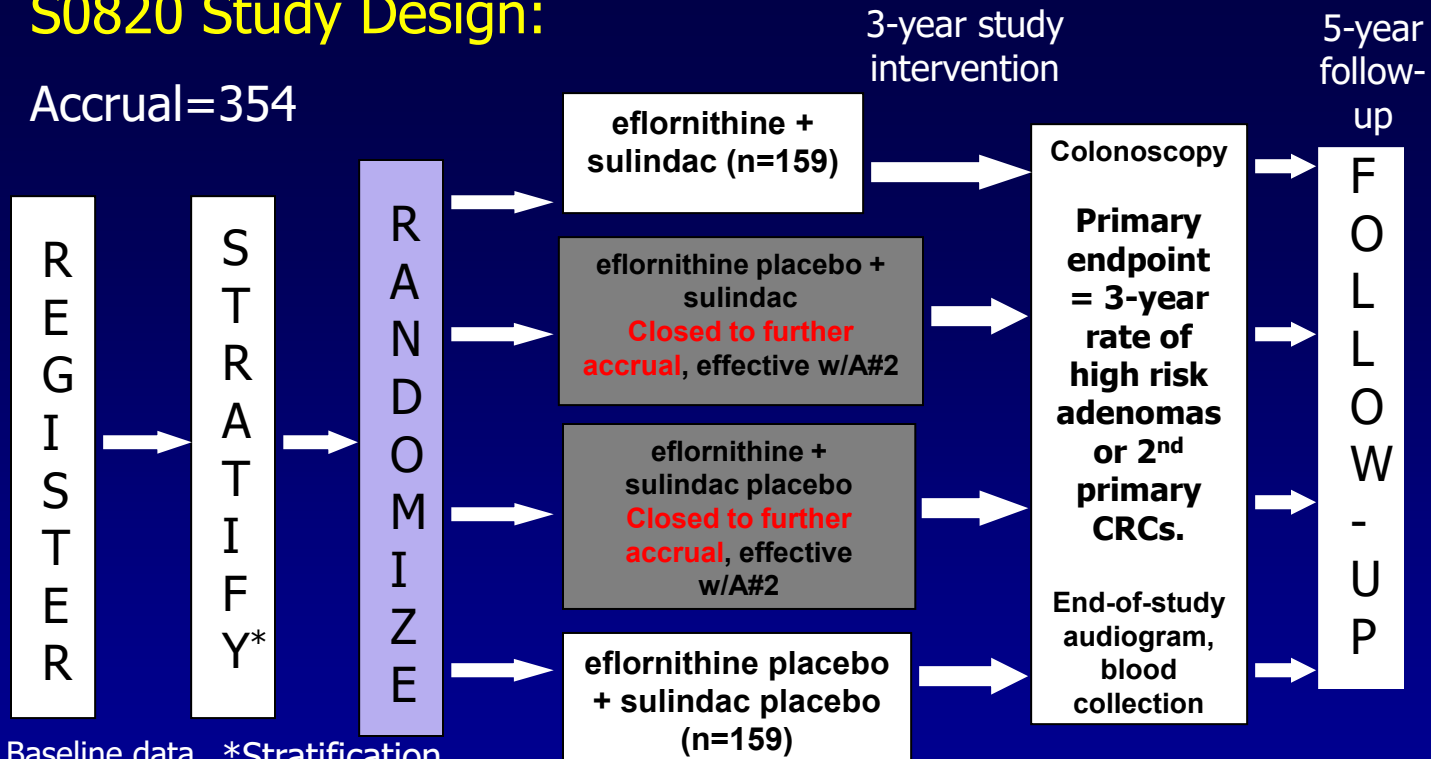
- high-grade dysplasia
    - villous features
    - size  $\geq$  1 cm
    - Multiple (3 or more) adenomas

- **Second Primary Colorectal Cancers (SPCRC)**

Goal is a 50% \*(proposed: 60%) reduction in HRAs or SPCRCs at 3 years for combination E+S vs. combination placebos

# S0820 Study Design:

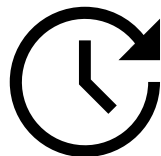
Accrual=354



Baseline data collection, audiogram, blood, CT-scans, & colonoscopy @ Year-1 post

\*Stratification by stage

Passed the Single Planned Interim Analysis (for futility): May 2023  
Accrual: March 2013 to June 2023



UC Irvine as Affiliate Organization (AO), U. Arizona-NCI  
Cancer Prevention Clinical Trials Network (UA-CP-CTNet)

UCI-AO Site PI: J. Zell (1R50CA285412-01)

# UA CP-CTNet OBJECTIVES



- ❑ To design and conduct Phase 0/I/II clinical trials to assess the cancer preventive potential of repurposed drugs, nutraceutical agents, regional/topical drug delivery, alternative dosing regimens, and immune modulators.
- ❑ To characterize the clinical activity and biological effects of putative cancer preventive agents.
- ❑ To develop further scientific insights into the mechanisms of cancer prevention by the agents studied and to develop novel potential markers as determinants of response and for selecting subpopulations who may differentially benefit from the studied agent.

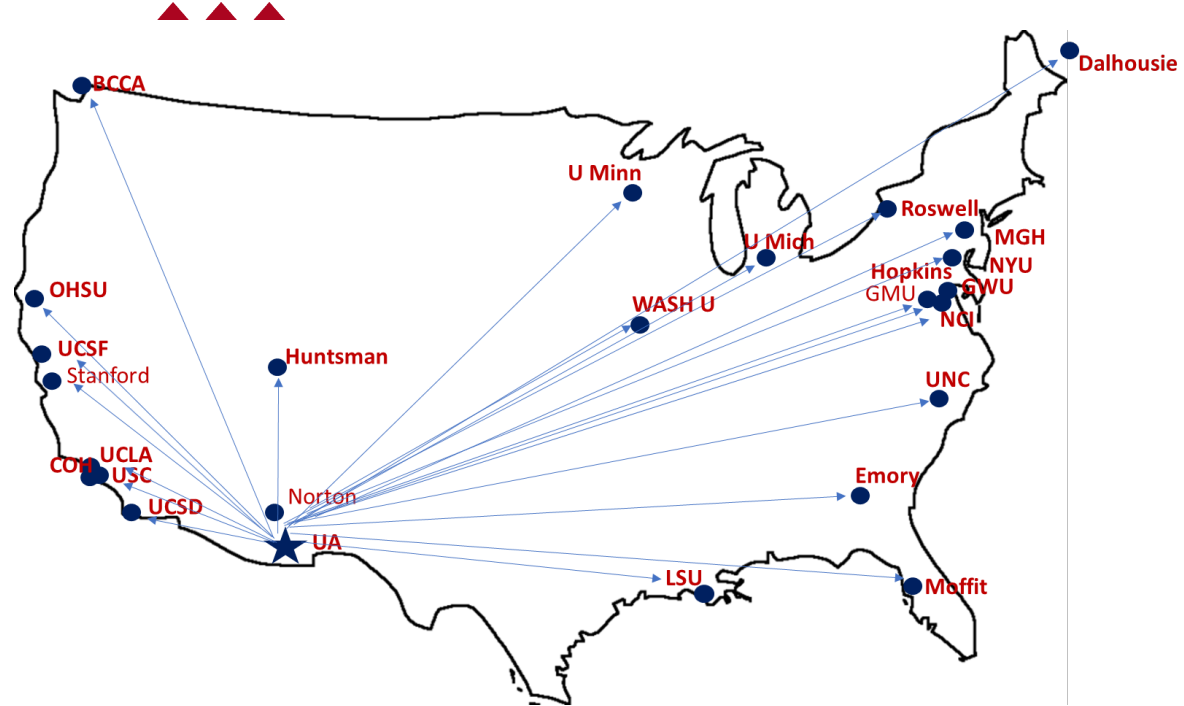


# UA CP-CTNet

**LAO: University of Arizona**

**AOs:**

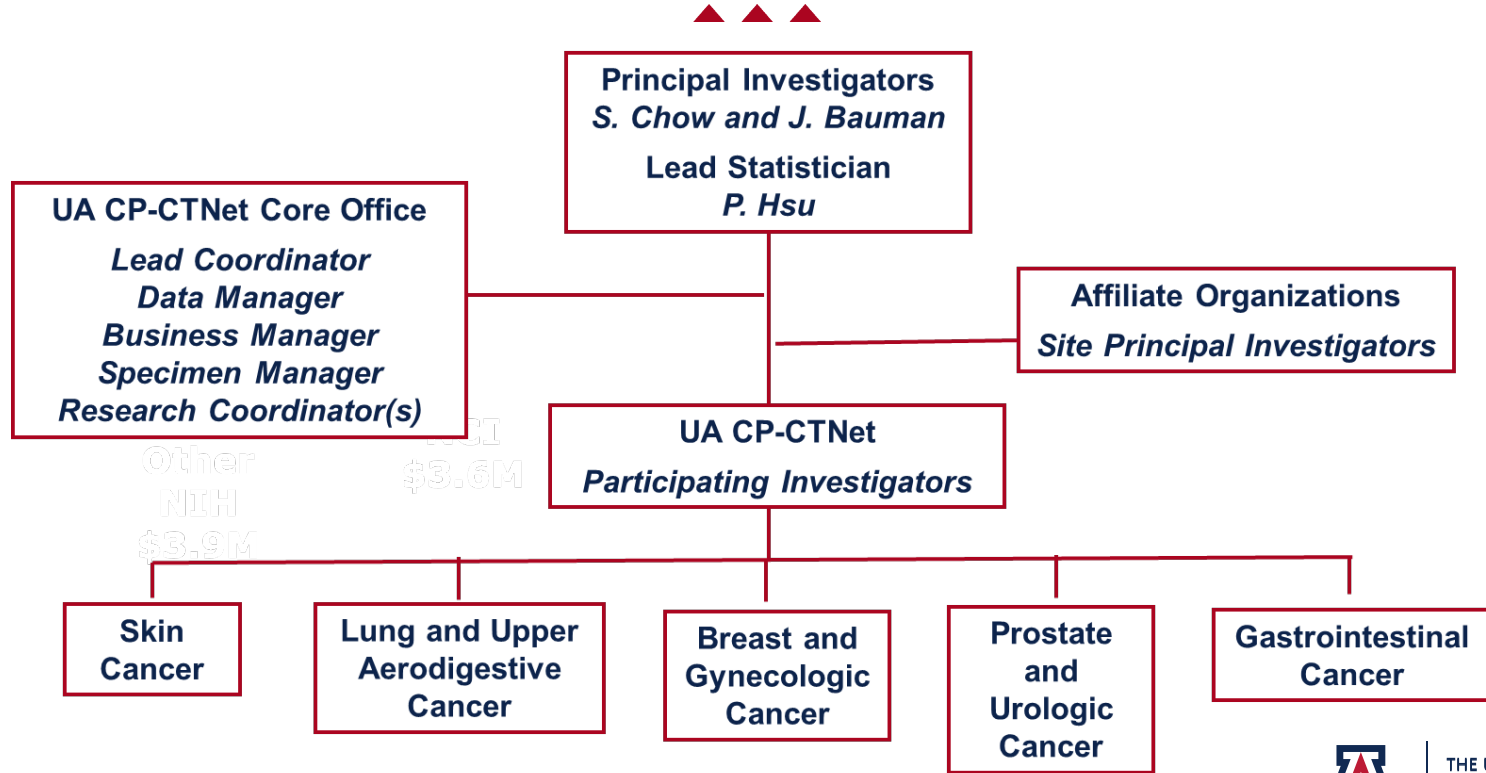
- **British Columbia Cancer Agency**
- City of Hope
- **Dalhousie University**
- **Emory University**
- Huntsman Cancer Institute
- George Mason University
- **George Washington University**
- **Johns Hopkins University**
- **Louisiana State University**
- **Massachusetts General Hospital**
- **Moffitt Cancer Center**
- **NCI Clinical Center for Cancer Research**
- **New York University**
- Norton Thoracic Institute
- **Oregon Health & Science University**
- **Roswell Park Cancer Institute**
- Stanford University
- **University of California Los Angeles**
- **University of California San Diego**
- **University of California San Francisco**
- **University of Michigan**
- **University of Minnesota**
- **University of North Carolina**
- **University of Southern California**
- **Washington University**



THE UNIVERSITY OF ARIZONA  
**Cancer Center**



# ORGANIZATIONAL STRUCTURE



Other  
NIH  
\$3.9M  
\$3.6M

## Current UA CP-CTNet Studies

Protocol	Target Organ	Study Cohort	Agent	Study Site
UAZ20-01-01	Prostate	PCa patients scheduled for prostatectomy	Apalutamide	UA USC Hopkins NCI Clinical Center GWU
UAZ20-01-02	HPV-associated cancers	Healthy teens	N/A; Follow-up on immune response after delayed Gardasil 9 booster	UA UCLA
UAZ20-BIO-01	Skin	Specimens representing melanoma progression (BN, DN, MM)	N/A; Molecular biomarker development	UA
UAZ21-06-01	Lung & upper aerodigestive tract	Current heavy smokers	Broccoli seed & sprout extract	UA Roswell GWU



## Current UA CP-CTNet Studies

<b>Protocol</b>	<b>Target Organ</b>	<b>Study Cohort</b>	<b>Agent</b>	<b>Study Site</b>
UAZ21-07-01	Oral	Patients with oral leukoplakia	Metformin	UA UCSD Dalhousie BCCA U Minnesota U Michigan NYU LSU Moffit Emory City of Hope
INT21-05-01	GI	Lynch syndrome	TriAd 5 (CEA/MUC1/Brachyury) N-803 (IL15 superagonist)	UA Huntsman NCI Clinical Center



# UA-CP-CTNet Affiliate Organization: UC Irvine

- Opportunities:
- 1) Open Phase 0/I/II cancer prevention clinical trials at UCI across all major disease sites
  - 2) Compete as PI for quarterly RFA's, leveraging the 25-site consortia for accruals
  - 3) Develop translational research aims for emerging early phase cancer prevention clinical trials

## Statistics

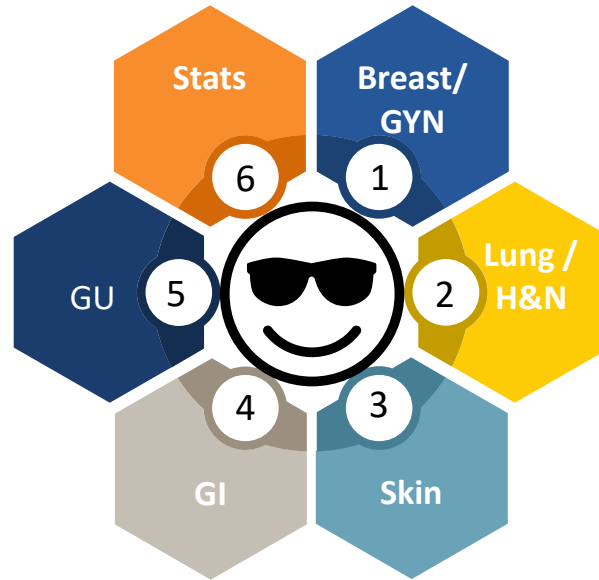
Christine McLaren, PhD  
Wen-Pin Chen, MS  
Thomas H. Taylor, PhD

## Genitourinary

Arash Rezazadeh, MD (Med Onc)  
Nataliya Mar, MD (Med Onc)  
Xiolin Zi, PhD (Basic Science)

## Gastrointestinal

William Karnes, MD (Gastroenterology)  
Joseph Carmichael, MD (Colorectal Surgery)  
Valerie Vilchez, MD (Colorectal Surgery)  
Matthew Whealon, MD (Colorectal Surgery)  
Jason Zell, DO (Medical Oncology)



## Breast/Gyn

Kiran Clair, MD (GynOnc)  
Ritesh Parajuli, MD (Med Onc)  
Sayeh Lavasani, MD (Med Onc)

## Lung/Head-Neck

Ann Arter, MD (Med Onc)  
Shirin Attarian, MD (Med Onc)

## Skin Cancer

Kristen Kelly, MD (Dermatology)  
Warren Chow, MD (Med Onc)

# Questions?

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