Is the Tripartite Mission Still Valid? (Analyzing theTripartite Terroir)

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Association of Professors of Dermatology
Chicago IL

Terroir

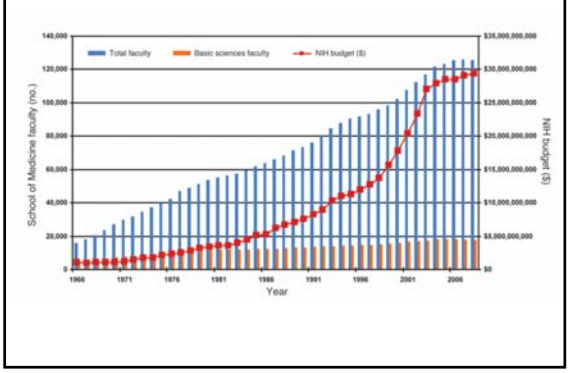
Terroir comes from the French word for earth or soil but in the wine world has taken on a quasi-mystical meaning to include not only the soil in a region, but also the climate, the weather, the location of the vineyards and anything else that can possibly differentiate one piece of land from another

Terroir at Chateau Cheval Blanc St Emilion Bordeaux Summer 2015

Terroir and the Tripartite Mission

The Changing Terroir of Academic Dermatology in the United States

Increases in the NIH Budget and the Total Number of Medical School Basic Science and Clinical Faculty Members (1966-2006)



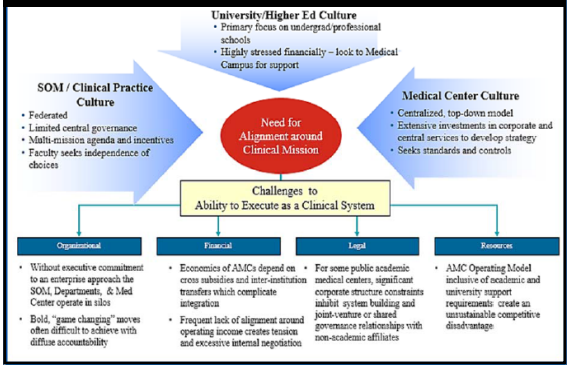
Changes in Medical School Graduates, Residents, Faculties, Federal Research Funding, Clinical Revenues, and State Support, 1975–2000*

	1975	2000	% Increase	Adjusted for Inflation: % Increase
No. U.S. graduates	15,351	15,901	3.6	
No. U.S. residents	37,140	98,806	161	
No. basic science faculty	10,728	17,651	65	
No. clinical faculty	26,602	85,902	223	
No. total faculty	39,330	103,353	163	
State support—all medical schools	$723 M	$3,430 M	374	$1,017 M/41%
State support—public medical schools	$643 M	$2,347 M	405	$963 M/50%
Federal grant support	$659 M	$8,209 M	1,146	$2,434 M/269%
Clinical revenues	$410 M	$14,758 M	3,500	$4,376 M/967%

*Sources: JAMA annual medical education issues, and the annual AAMC Data Book.

*Grigsby RK: Acad Med 2003:78:660.

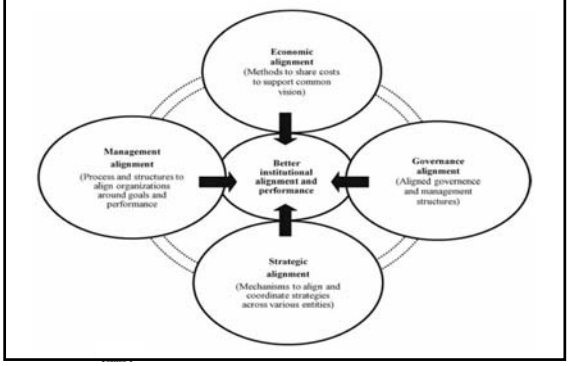
Barriers to Systemic Change in Academic Medical Centers



Options for AMCs in Health System Formation

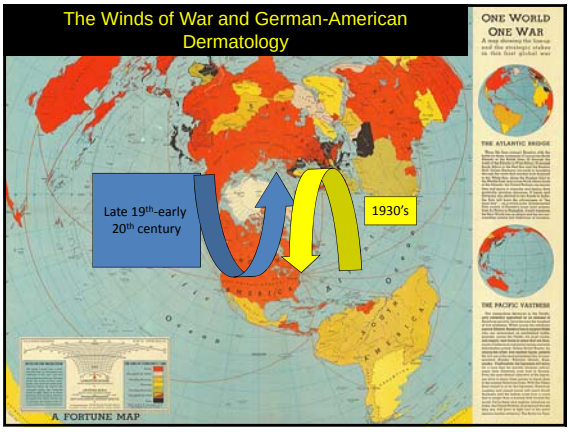
Merge / Affiliate with Mega-System	Specialized Complex Care Leader	High Performance Regional System	Public Entity Statewide Hub	Population Health Manager
➢Merge or establish primary preferred affiliation with large health system and become the "academic brand" for the system	➢Renown regional, national, international for a selected comprehensive specialty service (e.g. Cancer) ➢ Contractor to large systems ➢ Expert at Complex Care management ➢ Very strong Brand promise	➢ Independent AMC with tightly controlled system of care in attractive geography ➢ Market share leader in an attractive "sub-regional" geography with "must-have" status ➢ Strong brand promise	➢Sole/primary AMC in state ➢ Safety net provider for state; major Medicaid provider ➢ Tertiary/quartenary care provider for specialized services ➢Referral based services combined with local primary care	➢Regionally / nationally distributed health care system ➢Risk bearing "population manager" ➢ Health Plan or payer partnership to support ➢Clinically integrated network of faculty and community based physicians
Loyola (Trinity) U. Minnesota Medical Center (Fairview)	M.D. Anderson CHOP	Penn Medicine Yale New Haven Health Emory Healthcare	U. Of Iowa Healthcare UNM Health Sciences UAB Health System	UPMC VCU Health System

The New Terroir of Academic Medicine



Advancing the Academic Health System for the Future	
1. *The AMC of the future will be system-based*, with a broad regional presence and clinical services aligned across the continuum of care.	2. *Academic health systems require strong and aligned governance, organization, and management systems* committed to a unified direction, transparency, and internal and external accountability for performance.
3. *University relationships will be challenged to evolve as academic health systems grow and develop*, requiring leadership and structure to support clinical expansion, community engagement, alignment on financial requirements, and implementation of productive industry relationships.	4. *Growth and complexity of academic health systems requires an enhanced profile and responsibilities for department chairs, new roles for physician leaders, and evolution of practice structures* to focus on organizational leadership designed to lead clinicians into a new era.
5. *Transparency in quality outcomes and financial performance across the academic health system is central to high achievement* that is demonstrable to patients and purchasers.	6. *Competitive viability and long-term mission sustainability will require radically restructuring the operating model for cost and quality performance.*
7. *Academic health systems must begin the movement to population health now*, as purchasers look to reward organizations that can demonstrate improved outcomes for attributed populations of patients, and as community leaders address the social determinants of health.	8. *Academic health systems must conduct candid assessments of strengths and weaknesses essential to achieve change; and must revamp organizational culture if necessary.*

The Winds of War and German-American Dermatology



NYU Dermatrology with Irwin Freedberg and Rudolf Baer in Front of a Portrait of Marion Sulzberger

Leonard C. Harber, M.D. (1927-2012

With My Mentor Len Harber and His Son Steven

With My Chairman/Mentor Rudolf Baer and Gunter Burg and Hans Merk at SID Meeting 1993

BAER Meeting Washington DC, 1993

The Legacy of the Yellow Berets:
The Vietnam War, the Doctor Draft, and the NIH Associate Training Program

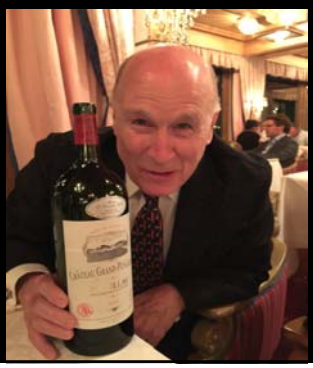
First of all, I had world class scientists as mentors. My first mentor won the Nobel Prize . . . Secondly, the colleagues coming though at the same time were all superb. . . . Thirdly, there was such a critical mass that whenever you had a question, there was always somebody down the hall or in the next building that you could go to. Fourthly, there were seminars and courses to take that rivaled anything at any university. . . . Finally, the people you were working with went out and pursued their careers so you had this whole cadre of people who you interacted with from the beginning.

Dr. Alan Schechter

With Jay Barnett and Ed Weisberg at UTAPAO USAF SAC Base Circa 1969

Yellow Berets and Other Physician-Scientists- SID Meeting 2004

Dining at Moissionnier ** in Cologne While Enjoying a 1996 Chateau Grand Puy-Lacoste



Jean Tang, M.D., Ph.D. Training Trajectory and Protected Research Time

- East LA: customer service (mom and pop store)
- BA: UC Berkeley: Biochemistry, lipoprotein lab (Trudy Forte), 3 yr (part time)
- MD/PhD: Stanford MSTP (Biophysics, NER repair, Gilbert Chu, Paul Berg, 4+4 yr)
- Internship: Guatemala, Xeroderma Pigmentosum (James Cleaver UCSF)
- FAAD: Stanford, Dermatology Residency, 2+1 (short track)
- MS Clinical Research: UCSF, KL2 CTSI; Post Doc (Ervin Epstein), GEMM and and Clinical Trials 3 yrs, K23 award
- Assistant Professor, Stanford: 2009, Damon Runyon (Philip Beachy), Bill Kaelin
- AMA (advanced maternal age): Kai age 7, Cory age 4
- Associate Professor, 2014: 90% research, 1 half-day/wk

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Goal: To Change the Standard of Care for Hereditary Skin Cancer

- Cancer Prevention in High-Risk patients (XP, BCNS)
- Seeking Novel Drug to Enhance DNA repair (Unsuccessful)
- Low hanging fruit:
  - BCCs are driven by Hedgehog pathway
  - Genentech/Curis had a Hedgehog inhibitor
  - Test this for BCC prevention

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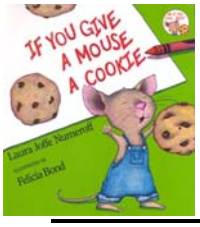
Lesson #1: Brick Walls

"The brick walls are there for a reason. The brick walls are not there to keep us out. The brick walls are there to give us a chance to show how badly we want something."

- Randy Pausch

- No T32 funding
- UCSF had a New Clinical/Translational Training Program KL2
- Funding for 3-5 yrs
- Ervin Epstein Lab
- BCC Mouse Model and BCNS Patients
- Downside: Required to Take 1 yr of Epidemiology and Biostatistics (Felt Like Homework)

Safe or Risky?



Safe but Predictable

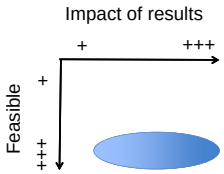
Risky but Very UnPredictable

Lesson #2: Select a Feasible Research Question

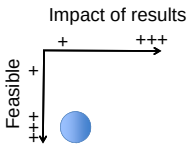
"FINER Criteria For a Good Research Question":

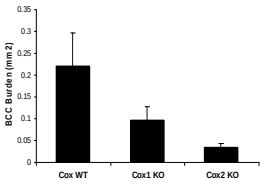
- Feasible
- Interesting (to you, follow your nose)
- Novel
- Ethical
- Relevant

-Steve Hulley, UCSF



Already Completed RCT in BCNS: Celecoxib for BCC Prevention





Clinical trial in 60 subjects: 2001-2004 (terminated early due to reports of potential cardiovascular events associated with celecoxib)

Data was sitting there: I entered the lab in 2006

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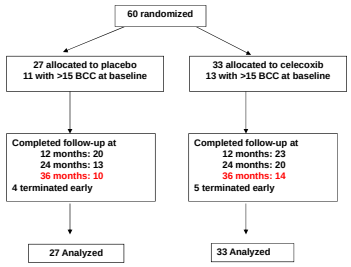
Lesson #3: Biostatistics Can Be Your Friend



Lesson #4: Learn To Do Better Clinical Trials: Measuring the Target (Subgroup Analysis)

Table 2. Percent change in BCCs per year in subjects treated with placebo or celecoxib

	No. subjects	Placebo (95% CI)	Celecoxib (95% CI)	$P_{difference}$
All subjects (BCC number)	60	37% (25-50)	26% (17-36)	0.18
≥15 BCCs at baseline	24	28% (16-43)	32% (19-48)	0.74
<15 BCCs at baseline	36	48% (27-71)	22% (10-36)	0.043
All subjects (BCC burden)	60	37% (24-50)	25% (15-36)	0.069
≥15 BCCs at baseline	24	33% (19-48)	33% (18-50)	0.97
<15 BCCs at baseline	36	50% (28-76)	20% (6.8-35)	0.024

Abbreviation: 95% CI, 95% confidence interval.

32 Cancer Prev Res; 3(1) January 2010 **Cancer Prevention Research**

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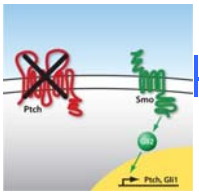
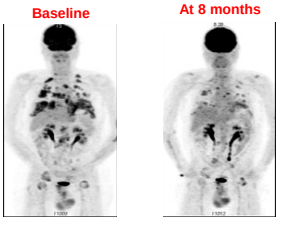
Vismodegib (GDC-0449) Was the First Hedgehog Pathway Inhibitor to Enter Clinical Trials



OFF

Vismodegib (OR:50%, PFS: 12 mon)



Von Hoff et al., NEJM 2009; 361: 1164-1172

Sekulic A et al. NEJM June 2012

Randomized, Double-blinded Trial for 18 Months

Vismodegib 150mg pill vs Placebo (2:1)

41 patients with Basal Cell Nevus Syndrome (BCNS)

- 3 clinical centers: Sept 2009 to Dec 2010 (Vismodegib was FDA-approved in 2012)

Primary Endpoint: Prevention of New BCCs

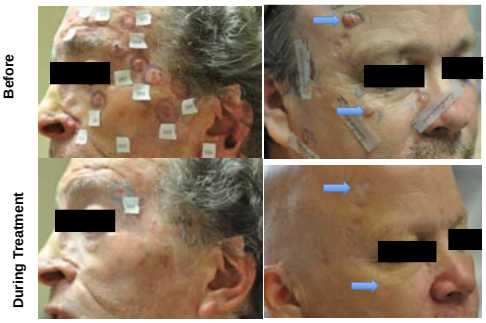
Secondary endpoint:

- Reduction in Size of Existing BCCs
- Safety/Tolerability

Lesson #5 Build Relationships with Patient Advocate Groups

BCCNS Life Support Network

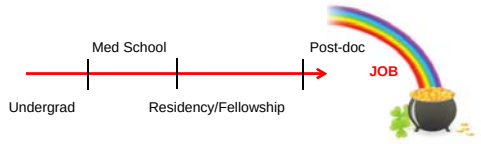
Vismodegib Shrinks BCC Tumors



Conclusions

1. Vismodegib has changed the standard of care for BCNS patients – no resistance seen even with intermittent dosage
2. In contrast, patients with advanced or metastatic BCCs develop resistance
3. Mutations in SMO (drug target) account for majority of drug resistant tumors

You Can Get From Here to There



Training

Life long career

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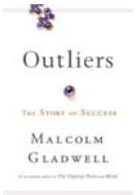
Give Yourself Enough Time



"10,000 hour rule: the key to success is practicing and putting in the time" (approximately 3yrs)

"80 percent of life/success is showing up"
- Woody Allen

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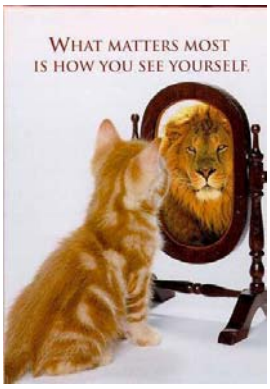
Genius is Made, Not Born

Sarasate, the great Spanish violinist of the nineteenth century, was once called a genius by a famous critic. Sarasate sharply replied, “Genius! For thirty-seven years I’ve practiced fourteen hours a day, and now they call me a genius.

from *The Power of Habit*



What is Your Mindset

Fixed Mindset
Intelligence and talent are fixed at birth.

- Success is Due to Innate Ability
- Fear of Failure and Avoiding Difficult Tasks

Growth Mindset
Intelligence and talent can go up or down.

- Talents and Abilities can be Developed Through Effort, Training, and Persistence
- Failure is Less Personal, and Performance Improves by Learning from Failure

Carol Dweck, Stanford University *Mindset: The New Psychology of Success.*

Role of PH.D. Scientists for Sustaining the Culture of Discovery in Academic Dermatology

PhD scientists are a major untapped resource in building and leading research divisions – look at the great PhDs behind many of the top programs who are leading the charge:

Dennis Roop at U of Colorado
Robert Lavker at Northwestern
Sarah Millar at Penn
Mohammad Athar at UAB
Hasan Mukhtar at U of Wisconsin
Molly Kulesz Martin at Oregon Health Sciences
Nicole Ward at Case Western

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Angela Christiano, Ph.D.
Columbia University
President,Society for Investigative Dermatology
2016-2017

NIAMS Columbia University Skin Disease Resource-based Center

epiCURE

Clinical Trials Unit with Focus on Translational Medicine

1. **Design and conduct translational research in linked closely with the Basic Science Research Group (BSRG)**

Currently Funded Grants:

- U01AR067173-01. Christiano NIH/NIAMS - Developing an **Alopecia Areata** Disease Activity Index (ALADIN)
  - Goal is to develop a new outcome instrument, the Alopecia Areata Disease Activity Index (**ALADIN**), which has the potential for use in the determination of clinically relevant endpoints for Alopecia Areata (AA)
- 1P30AR069632-01 Bickers (PI) NIH - Columbia University Skin Disease Resource-Based Center (**epiCURE**)
  - This application supports the creation of a Skin Disease Resource-Based Core center at Columbia University (**epiCURE**). The epiCURE is designed to address critical roadblocks on the Continuum of Translational research as defined by the National Academy of Medicine
- 1P50AR070588-01 Christiano (PI) NIH/NIAMS - Alopecia Areata Center for Translational Research (AACORT)
  - The mission of the **AACORT** is unravel the genetic basis of AA and exploit our discovery showing the role both innate and acquired immunity, and to synergize these findings into translational studies finding novel therapies for this disease, including the repurposing of existing drugs

Open-label Clinical Trial of the Jak-Stat Inhibitor Tofacitinib in Patients with Alopecia Areata

Columbia University Department of Dermatology, Clinical Trials Unit,
Julian Mackay-Wiggan, MD, MPH, Director

Global Skin Diseases Research Consortium (GSDRC)

The long-term goal of this established collaborative agreement is to provide **joint opportunities** to foster the creation of **novel approaches** and insights into cutaneous biology, disease pathogenesis and clinical dermatology by **coordinating multidisciplinary research** aimed at finding **innovative translational strategies** to improve the care of patients with skin disease and to **train tomorrow's scientific leaders.**

Global Skin Diseases Research Consortium (GSDRC)

- Bi-annual symposium supported by one of the six Centers at their location
- Bi-annual GSDRC summer school for PhD and MD/PhD students and postdocs
- Exchange of PhD and MD/PhD students and postdocs to learn new techniques and approaches, and to promote collaborative projects between laboratories of the Centers
- Exchange of faculty for mini-sabatticals
- Establish a web-based inventory to promote exchange of mouse models, other animal models, reagents and protocols

Herbert and Florence Irving

Herbert and Florence Irving

Alternative Sources of Funding in the New Terroir of Academic Dermatology

- Building consortia with industry sponsors, and health care insurers to achieve economies of scale
- Creating closer working relationships with community leaders as systems are created to promote population health
- Coordinating more effectively across government agencies
- Philanthropy $$$$$$$$$$$$$$$$$

Summary

Despite dire forecasts, dermatology departments at research-focused universities will continue to attract the shrinking pool of those seeking a career in academic dermatology. These departments may sustain the tripartite mission in the aggregate but at the level of individual faculty, there will be a growing bifurcation into clinician-educators on the one hand and physician scientists on the other.

Gary Wood, MD U of Wisconsin

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Gary Wood, M.D.