

# **Some lessons learned from Team Science**

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## Past participation in Team Science

<b>Period</b>	<b>Type of grant</b>	<b>Role in Grant</b>
1994-99;	SCORE Grant in Vascular Biology	P.I.
2000-Present	Prostate Cancer P01	P.I.
2001-Present	Prostate Cancer SPORE	Co-P.I.
2001-2008	Glue Grant	Consultant
2004-Present	Pancreatic Cancer P01	Project Leader
2005-Present	G.I. Cancer SPORE	Member
2006-Present	Hamartoma P01	Project Leader
2008-Present	Lung Cancer SPORE	Member
2009-2012	Starr Foundation Grant	P.I.
2009-Present	SU2C Dream Team	P.I.

## Some Lessons Learned:

- 1) Teams Science works best when there is a clear goal that is achievable in the funding period.
- 2) All members of the team must believe that the goal is a worthy one **AND** that it is achievable with the technology, expertise and funds available to the team.
- 3) Each member of the team must understand her/his role in achieving the goal, and must feel that she/he will get credit for making this contribution.
- 4) There must be clear, achievable **milestones with a timeline.**
- 5) Frequent teleconferences and/or face-to-face meetings are required to verify that the milestones are being met.

- 7) **The Leader is critical:** the Leader must be fully engaged in achieving the goal and must be willing to cede senior authorship on key papers to members of the team who achieve their assigned tasks (motivation). Ideally, the Leader should have a working knowledge of all aspects of technologies/disciplines utilized by the team (or be willing to learn these at a level that allows evaluation of quality).
- 8) **The Leader (or leadership team) must have the ability to redistribute resources in a timely manner to solve unanticipated problems that arise or replace team members who, for whatever reason, are not meeting their milestones. Having a significant 'Performance Fund' in reserve is critical. Carrots work better than sticks. Herding cats is easy if you have some dead fish.**
- 9) An escalating budget rather than fixed yearly budget is usually better. Some members of the team only become relevant at late stages of the project.

**10) Don't let the perfect be the enemy of the good.**

## Examples of Successful Team Science

- Making the atomic bomb
- Going to the moon
- Sequencing the human genome

### What they have in common:

Strong leadership

Clear goals

Important goals

Participants knew that the goals were important and **achievable with knowledge and tools that either already existed or could be readily acquired**

Each member knew his/her role (typically the problems were **engineering rather than discovery**)

The leaders were given power to move resources quickly to solve problems.

Sufficient funds were available to achieve the goal.

## **Reasons that Team Science can fail or underachieve.**

- 1) The goals are ambiguous, too broad, or premature with existing knowledge or tools (e.g. “Cure all lung cancer in 5 years” would probably be a poor choice of goals today).
- 2) Some members of the team are only there for the money (or fame).
- 3) A key technology needed for success is premature or oversold.
- 4) Success depends on making a highly unlikely “Discovery”.  
Most members of the team twiddle their thumbs waiting for someone to make the “Discovery” or perfect the technology needed for their role to become relevant.
- 5) The funds are divided up at the beginning with no ability of the leader to shift funds from non-performers to performers.
- 6) There are insufficient funds to achieve the goal.
- 7) Poor leadership. Members don’t like or trust each other and thus, don’t exchange ideas or even attend meetings.

Stand Up To Cancer funded Dream Team

Targeting The PI3K Pathway in Women's  
Cancers

Lewis Cantley, Gordon Mills, Charles Sawyers

Eric Winer – Clinical Trial Leader



*Beth Israel Deaconess*

**Lewis Cantley**

Gerburg Wulf

Pier Paolo Pandolfi

Andrea Myers

*Dana Farber*

**Tom Roberts**

**Eric Winer**

Ursula Matulonis

Jean Zhao

Ian Krop

Andrea Richardson

David Livingston

Joyce Liu

Dirk Iglehart

Nancy Lin

Don Watson

PI3K Dream Team

*MGH*

**Jose Baselga**

Michael Birrer

Jeff Engelman

*Sloan Kettering*

**Charles Sawyers**

Carol Aghajanian

Douglas Levine

David Solit

Neal Rosen

Robert Soslow

Chris Sander

Alex Lash

Nicholas Socci

Nikolaus Schultz

Karuna Garg

*Vanderbilt*

**Carlos Arteaga**

Ingrid Mayer

Melinda Sanders

*MD Anderson*

**Gordon Mills**

Yisheng Li

Don Berry

Rob Coleman

Russel Broaddus

Funda Meric-Bernstam

Ana Gonzalez-Angulo

Karen Lu

Pricilla McAuliffe

*Vall d'Hebron*

**Jose Baselga**

Jordi Rodon

Josep Tabernero

Yasir Ibrahim

Violeta Serra

*Columbia*

**Ramon Parsons**

Matthew Maurer

## **Advocates**

**Janet Price (HICC), Elizabeth Frank (DFCI), Don Listwin (MDACC), Jane Perlmutter (MDACC), Ruth Fax (DFCI), Judi Hirshfield-Bartec (MSN/BIDMC), Patricia Lee (VICC), Piru Cantarell (Vd'H)**

## Budget and Timeline

- \$4.5 million direct costs/year for three years (obtained additional \$1.5 million in 4<sup>th</sup> year extension).
- We provide a written report every 6 months summarizing our progress toward the proposed milestones and a summary of our expenditures.
- We are site visited every 6 months by members of the SU2C Scientific Advisory Council (headed by Phil Sharp and Arnie Levine, with representation from prominent oncologists and pharma leaders) where we report our progress.
- We have 7 clinical trials in various stages of completion, including two trials that test novel drug combinations (PI3Ki + Letrozole in neoadjuvant setting of ER positive breast cancer and PI3Ki + PARPi in late stage triple negative breast cancer and ovarian cancer).
- Most of these trials are mirrored by trials in appropriate mouse models that identify mechanisms of resistance and lead to new biomarkers for following the human trials.

## How we spend our Budget

- The baseline support to the various institutions is approximately proportional to the number of clinicians and scientists involved, with some exceptions.
- The site heads have considerable freedom as to how these funds are distributed (salary versus supplies, travel, etc.) with sign off from the Leaders (Cantley, Mills, Sawyers) when changes are made.
- **We reserved more than 1/3 of the funds for “Performance Funds”.** These funds are an increasing fraction of the budget each year. In early years they have been used to establish CLIA-compliant biomarker assays for patient enrollment or to buy and verify investigational drugs for preclinical studies, or to test drug combinations in mouse models – all directly related to the trials we are designing.
- In the third year, virtually all of the Performance Funds are directed at costs of clinical trials (reimbursement per patient enrolled, biopsies, imaging, etc.) and for retrospective analyses of mutational events in the patients on our trials.

## How we spend our budget

Year 1: 2.5 million

Year 2: 5.0 million

Year 3: ~6.5 million

Year 4: ~2.5 million carry forward for completion of trials and retrospective analyses

SU2C/PI3K Dream Team Shared Resources:  
Compounds for Pre-Clinical and Co-Clinical Trials  
(50g to 100g quantities of each - ~\$450 thousand – 80 % discount)

- |                       |  |
|-----------------------|--|
| 1. GDC0941            | Class 1 PI3K inhibitor in phase 2                      |
| 2. Rad001/Everolimus  | mTOR inhibitor - approved                              |
| 3. Lapatinib          | HER2 catalytic site inhibitor - approved               |
| 4. GSK-1120212B       | MEK inhibitor in phase 2                               |
| 5. AZD6482            | PI3K beta inhibitor                                    |
| 6. AZD2218 (Olaparib) | PARP inhibitor in phase 3                              |
| 7. BKM120             | Class 1 PI3K inhibitor in phase 2                      |
| 8. Neratinib          | Covalent HER2 and EGFR inhibitor in phase 3            |
| 9. MK2206             | Pan-AKT inhibitor in phase 2                           |
| 10. ABT737            | Bcl-2 inhibitor  |
| 11. BEZ235            | Class 1 PI3K inhibitor/mTOR inhibitor entering phase 2 |
| 12. NVP-AUY922        | HSP-90 inhibitor in phase 1/2                          |
| 13. CAL-101           | PI3K delta inhibitor in phase 2                        |

# The Clinical Trials Team

## Clinical Trial PIs are all Instructor/Assistant Prof. level

- DFCI/MGH/BI
  - Ursula Matulonis
  - Andrea Myers
  - Joyce Liu
  - Nancy Lin
  - Ian Krop
  - Gerburg Wulf
  - Steve Isakoff
  - Jose Baselga
- MDACC
  - Rob Coleman
  - Ana-Maria Gonzalez
  - Funda Meric-Berstam
  - Carol Westin
  - Don Berry
- MSKCC
  - Carol Agajanian
- Vanderbilt
  - Ingrid Mayer
  - Carlos Arteaga
- Val d’Hebron
  - Jordi Rodon
  - Cristina Saura
  - (Jose Baselga)
- Columbia
  - Matthew Myer

# The Mouse Co-Clinical Trials Team

- DFCI
  - Jean Zhao
  - Joyce Liu\*
  - Tom Roberts
- BIDMC
  - Gerburg Wulf\*
  - Andrea Myers\*
  - Pier Paolo Pandolfi
  - Lewis Cantley
- Vanderbilt
  - Carlos Arteaga\*
- Val d’Hebron
  - Yasir Ibrahim
  - Violeta Serra
  - (Jose Baselga)
- Columbia
  - Ramon Parsons

\* Involved in both mouse and human clinical trials



# The Biomarkers & Bioinformatics Team

- DFCI/MGH/BI
  - Andrea Richardson
  - Jeff Engelman
- MDACC
  - Gordon Mills
  - Russel Broaddus
- MSKCC
  - **David Solit**
  - Charles Sawyers
  - Chris Sander
  - Alex Lash
  - Nicholas Socci
  - Nikolaus Schultz
  - Douglas Levine
  - Robert Soslow

# Dream Team Meetings

## (face-to-face)

### PI3K Dream Team:

#### •Total (NOGA – Present): 11

- MDACC - Houston - (June 2009)
- BIDMC - Boston - (August 2009)
- AACR - Boston - (November 2009)
- MSKCC – New York - (January 2010)
- AACR - Washington, DC - (April 2010)
- HICCC - New York - (July 2010)
- VICC – Memphis - (December 2010)
- AACR – Orlando - (April 2011) \*\*
- DFCI – Boston - (July 2011)\*\*
- MDACC – Houston – (October 2011)
- MSKCC – NYC – (January 2012)
- BIDMC- Boston – (July 2012)

\*\* included members of the Breast Cancer Dream Team

### Inter-Dream Team Meetings:

#### •Total (NOGA – present): 8

- Team-of-Teams Teleconference - (August 2009)
- Teams Leadership Meeting – Los Angeles - (September 2009)
- AACR – Washington – (April 2010)
- SU2C Telethon – Los Angeles – (September 2010)
- SU2C Summit – Miami – (January 2011)
- AACR – Orlando – (April 2011)
- Bioinformatics Integration Meeting – Berkeley - (June 2011)
- SU2C Summit – Miami – (January 2012)

## Dream Team Teleconferences

### PI3K Dream Team:

- **Total (NOGA – Present): 67**

- Clinical Trials: 72
- Biomarkers: 29
- Leadership: 15

- Clinical Trials Work Group teleconferences are held every other Wednesday at 9:15A`M/Eastern
- Biomarkers Work Group teleconferences are scheduled quarterly
- Dream Team Leadership teleconferences are scheduled based on Team needs
- Dream Team Advocates participate in all Clinical Trials and Biomarkers teleconferences.

## **Dream Team Corporate Meetings (Total from NOGA to Present)**

- Genentech: (July 2009, June 2010, December 2010, June 2011, July 2011, November 2011) \*
  - Exelixis/Sanofi-aventis: (November 2009, December 2010)\*
  - Novartis: (July 2009, April 2010, June 2010, December 2010, April 2011, June 2011) \*
  - Astra Zeneca: (August 2009, December 2009, April 2010, June 2010, December 2010, April 2011, June 2011)\*
  - GlaxoSmithKline: (September 2010, June 2011, July 2011)\*
  - Merck: (June 2011)\*
  - Affymetrix: (July 2010, August 2010, December 2010, April 2011, July 2011, November 2011) \*
  - Myriad: December 2010, June 2011) \*
- \* Plus numerous conversations with our investigators on a one-on-one basis or on the phone