Convergence, Cancer Research and the Koch Institute Experience at MIT

Tyler Jacks Director

NAS Workshop on Team Dynamics and Effectiveness July 1, 2013





science + engineering...conquering cancer together







President Richard Nixon signing the National Cancer Act on December 23, 1971.

"I will ask for an appropriation of an \$100 million to launch an intensive campaign to find a cure for cancer ... the time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease."



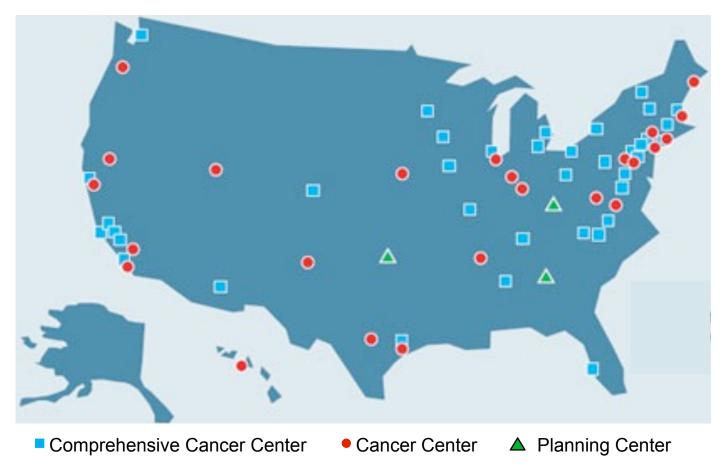
MIT Center for Cancer Research







NCI Cancer Centers





Salvador E. Luria, 1969



H. Robert Horvitz, 2002



David Baltimore, 1975



Phillip A. Sharp, 1993

Susumu Tonegawa, 1987

Of an emerging arsenal of precision cancer drugs, two of the most powerful sprang from our work at MIT.







October, 2005: MIT CCR awarded one of seven inter-disciplinary NCI grants to form a Center for Excellence in Cancer and Nanotechnology

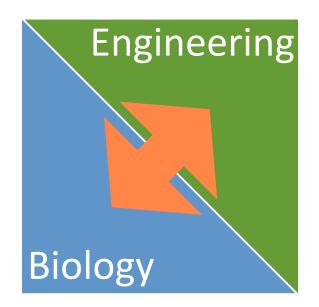
National Cancer Institute

PHYSICAL SCIENCES

October, 2004: MIT CCR awarded one of nine inter-disciplinary NCI grants to use computational and mathematical ("systems") approaches to understand complex problems in cancer biel



The Koch Institute: A New Model for Cancer Research



Integration and Collaboration Discoveries and Solutions



Intramural Koch Institute Biology Faculty



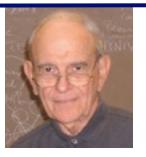
Angelika Amon



Paul Chang



Jianzhu Chen



Herman Eisen



Frank Gertler



Michael Hemann



Nancy Hopkins Da



David Housman



Richard Hynes



Tyler Jacks



Jacqueline Lees Assoc. Director



Phil Sharp



Frank Solomon



Matthew Vander Heiden



Michael Yaffe

Intramural Koch Institute Engineering Faculty



Daniel Anderson Asst. Professor Chemical Engineering, Health Sci. Tech.

Sangeeta Bhatia Professor Health Sci. Tech, Elec. Engineering & Comp. Science



Angie BelcherNProfessorPMaterial ScienceN& Engineering,&Biological Engineering8

Michael Cima Professor Material Science & Engineering



Paula Hammond Professor Chemical Engineering



Darrell Irvine Assoc. Professor Material Science & Engineering, Bio. Engineering



Robert Langer Professor Chemical Engineering, Biological Engineering



Christopher Love Asst. Professor Chemical Engineering

Scott Manalis Assoc. Professor Biological Engineering, Mechanical Engineering

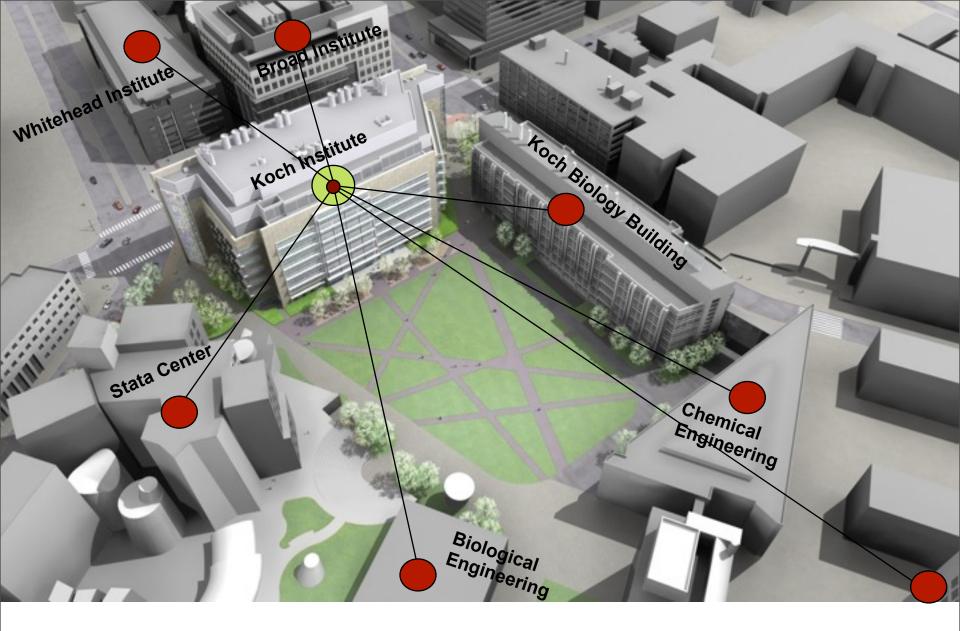
Ram Sasisekharan Professor Biological Engineering, Heath. Sci. Tech.



Forest White Assoc. Professor g, Biological Engineering



K. Dane Wittrup Professor Chemical Engineering, Biological Engineering Assoc. Director



The Hub of Cancer Research at MIT





From Renderings to Reality





BORDER COOLER



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The House voted to reput humbers tax-filing requi ment contained is the b correlion, a move that h House support. A2.

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Sunday, June 30, 13



to landn ark building ichael Levenson

subcord department store in the publicy Square, part of a broader consolidate the city's administrative gs and revitation a bong neglected



ment of POME Health, and the vacant bold-ing as part of a \$40 million plan, but Gover-nor Mitt Rossney scrapped three plans in

That year, Missino annunced plans to move the School Department to the long-domast site. Four years later, he even held a

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Dudley Sq. School D pt. would go

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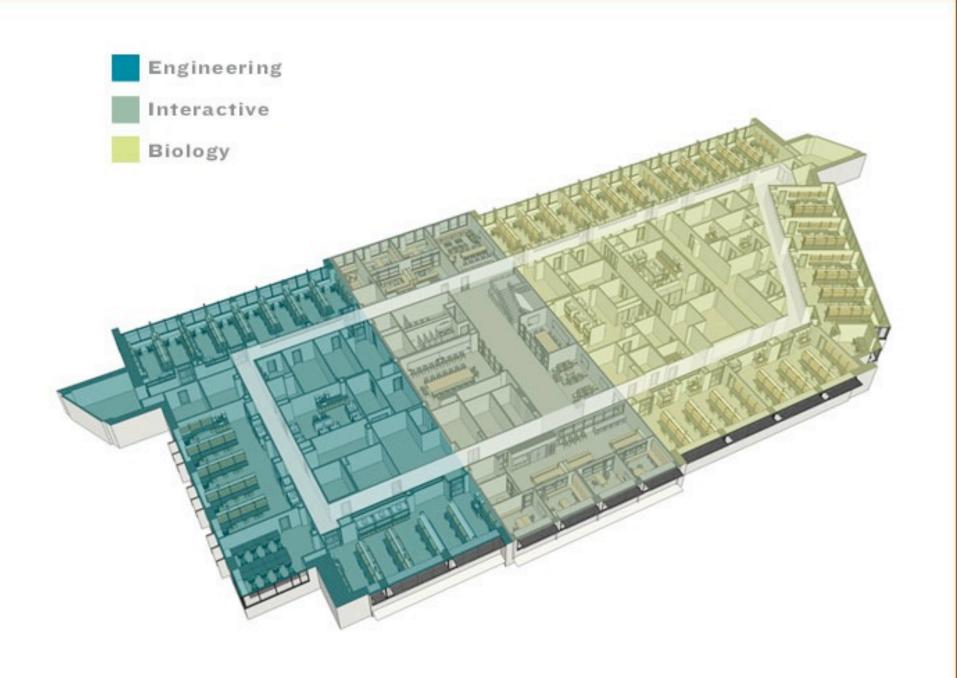


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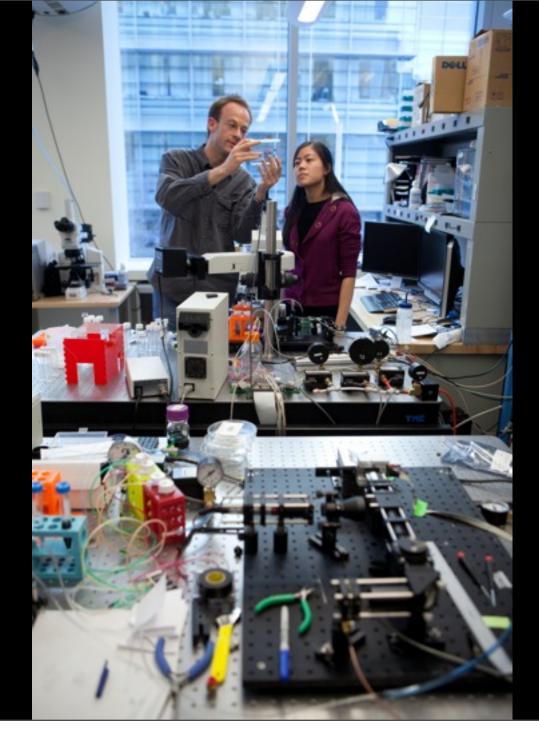
>192,000 NASF
~27 Faculty Laboratories
>22,000 NASF of core facilities











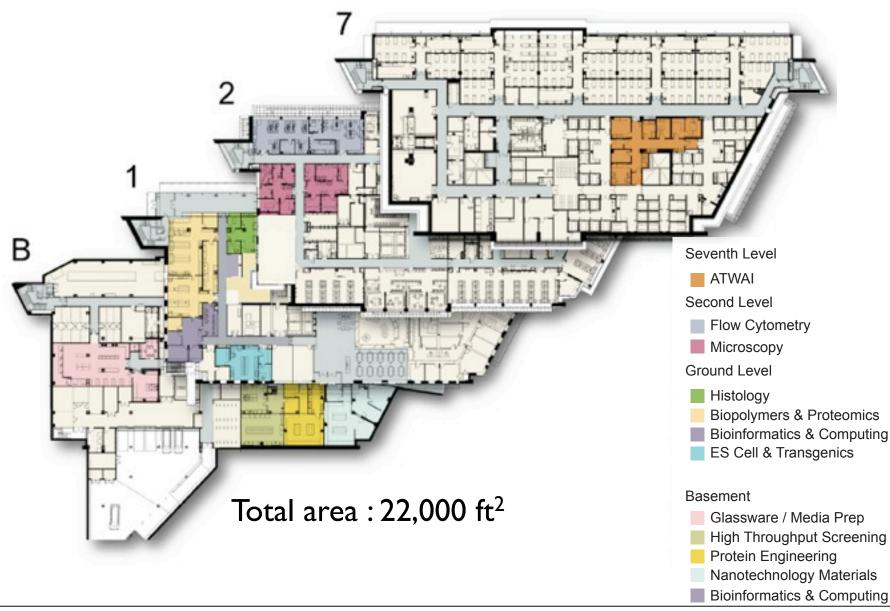








The KI Core Facilities have been organized into the Swanson Biotechnology Center



From Convergence to Confluence







A new educational series designed to bridge the Biology/Engineering divide

Modeling Cancer in the Mouse: The Basics



by David Feldser Jacks Lab

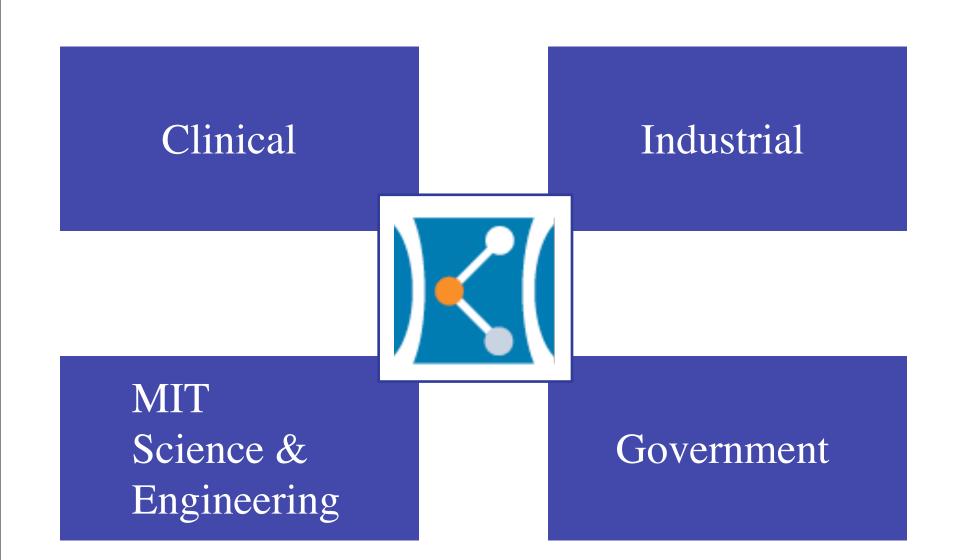
Wednesday, July 25, 3 PM 76-156 (KI auditorium)



ENGINEERING GENIUS BAR

The 2012 Koch Institute Retreat







Koch Institute Clinical Investigator: Physician Scientist

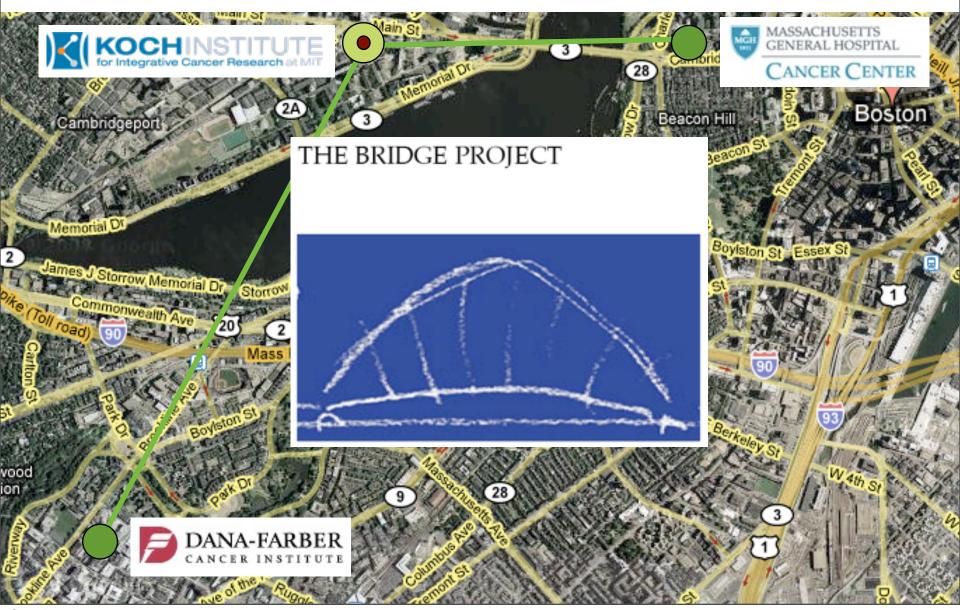
Scott Floyd, MD, PhD Koch Clinical Investigator Brain Cancer Genetics and Treatment Instructor, BI Deaconess, Radiation Oncology

ctivity in clinical, translational, and basic research is essential. The ed individuals will have dedicated lab space and research support and will work closely with faculty mentors at the new Koch Institute.



Alice Shaw, MD, PhD Koch Clinical Investigator Lung cancer genetics and treatment Assistant Professor, MGH Thoracic Oncology Center

Enhancing Clinical Partnerships





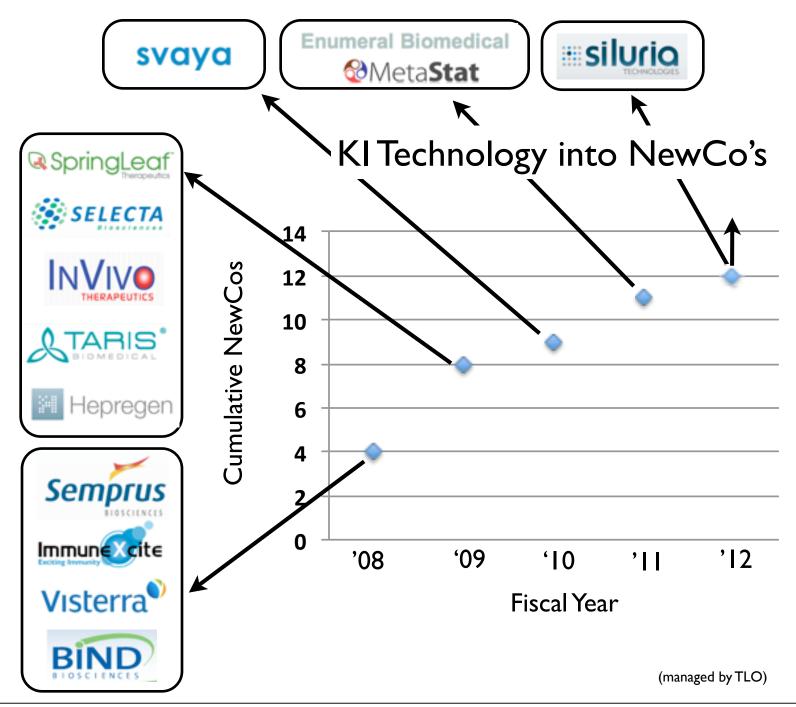
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Product And Operating Company News Ortho-McNeil-Janssen Pharmaceuticals, Inc. Announces Oncology Research Collaboration Agreement with the Koch Institute for Integrative Cancer Research at MIT

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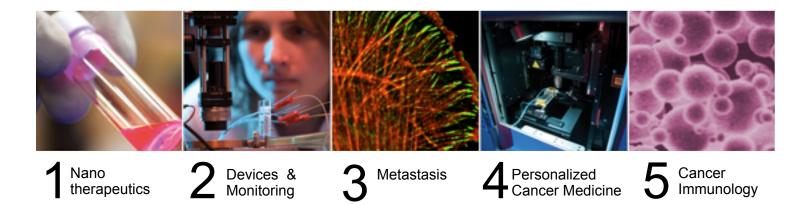


Sunday, June 30, 13

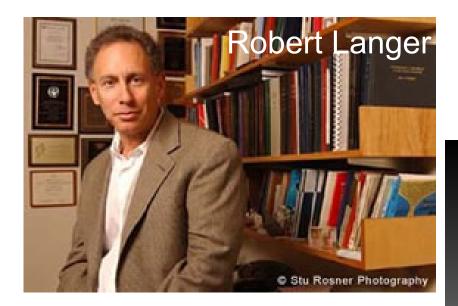




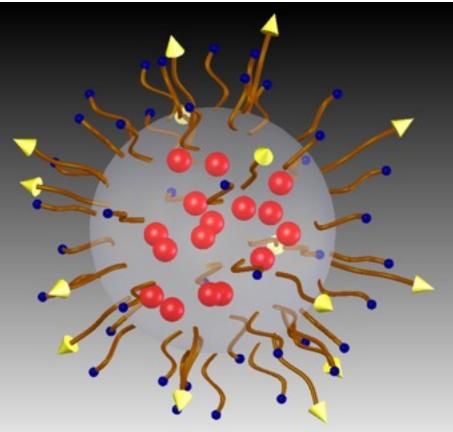
Priority Research Areas



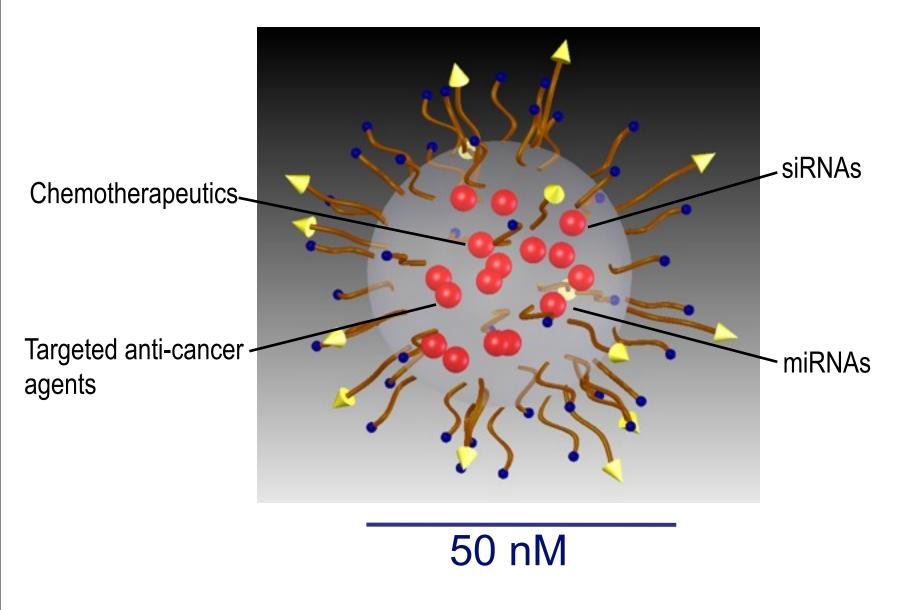




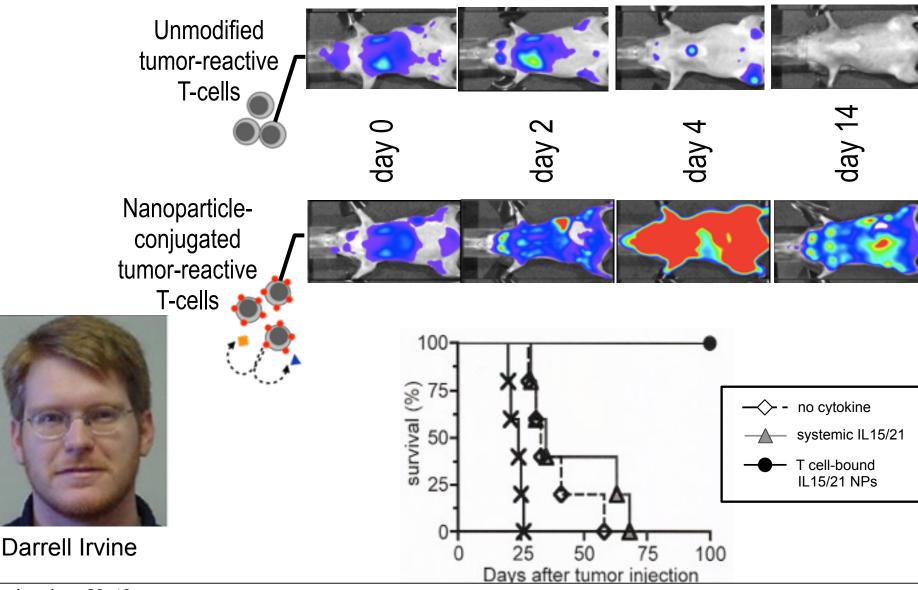




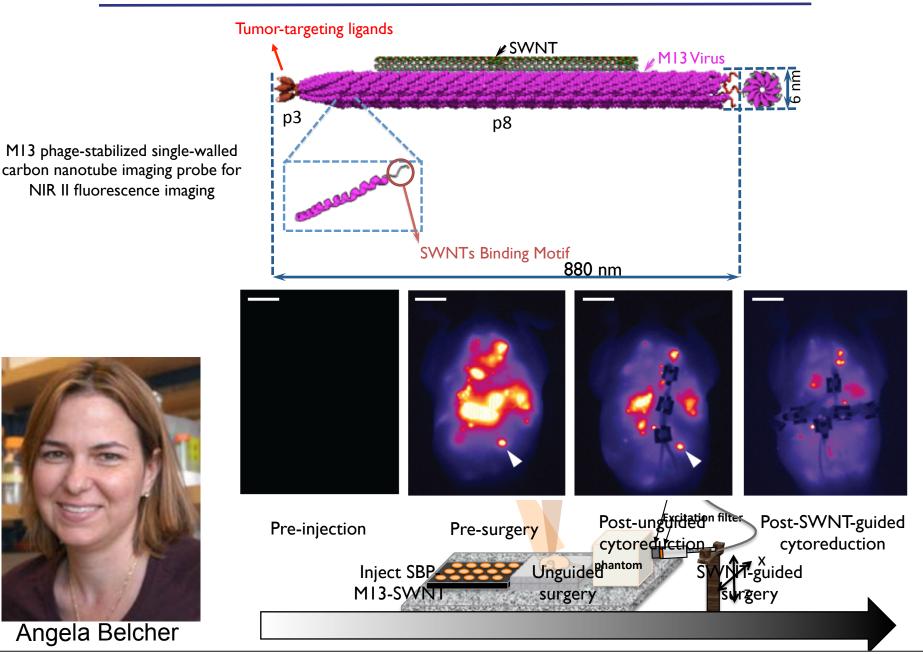
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Engineering the Immune System to Fight Cancer



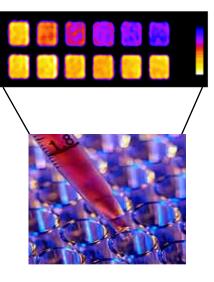
Novel cancer imaging strategies



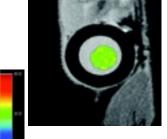
Engineer implantable devices to monitor and treat cancer

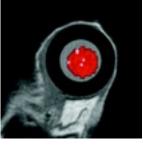






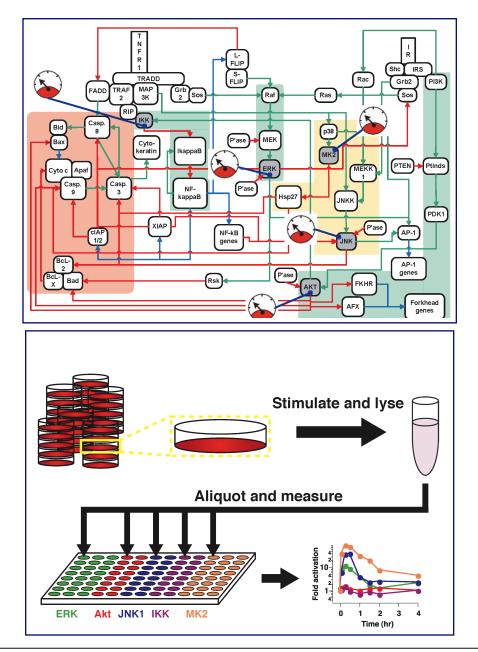






K Receptor	Receptor		Ē	R							T Antigen	
Receptor	Receptor		NFR-: NFR-: CD95	Fβ R-I ctivin cepto hibin cepto	EZF-1	PrP-Z	РтР-Ү	PrP-X	PPP-2A	EIA	Large T Antigen	6
Neurotensin	Vib		2		Bcr	PrP-2C	p55	p60	prac	denovirus	SV40 virus	G
Receptor	Receptor		TRA TRA FAI	TAK	Pitslre	PrP-2B	Calmodulin	Inh2	- p107	Middle Antigen	= p53 =	Small T Antigen
Receptor IL8	Receptor		F2	TAB1	Pictaire-3		Ca ²⁰		ap105 Rb	olyoma virus Large Antigen	IK	ß Integrin
Grocz Receptor	Sub. K Receptor	PTP 1B			Pictaire-2		, I L				Cell adhe- sion K.	CD11 α Integrin
fMLFP Receptor	Secretin Receptor	НРТРС	Tx	A1	Pictaire-1	Glyc: bigd-	Cyclin D3 Cyclin E G	CUK4 = 0 Cyclin F	Cip	CDK5	a ps	CD28
Endothelin Receptor	Prostacyclin Receptor	ΗΡΤΡγ	UPP32	Pag-1	Pitalre				7			CD4
CCK Receptor	PAF Receptor	НРТРЕ	ICH-1S	Bad	Kkialre		Cuclin Do	÷				δ chain
Cannabinoid Receptor	Oxytocin Receptor	SH-PTP1	ICH-1L	Bcl-XL	Picclra			Curlin A	CDK2 0	Csk1	Wee1	r chain ε chain
Calcitonin Receptor	Octopamine Receptor	HLRP	ICE-III	Bcl-XS	RNA-dep.		Cyclin B1 Cyclin B2 Mat1 Skp1 Skp2	Cyclin B2	Cyclin B	CDK1 8	Myt1	v chain
C5A Receptor		ΗРТРα	ICE-II	Bcl-2	β-sub.	Casein Kinase-20	Cyclin H RNA poly Casein β-sub.		CDK7 =	Cdc25		TCR ^Q
Receptor	ž	нртр	ICE	Bax	eIF-4E	Casein eIF-4E Kinase-1			Fra-2	Cip2	Ĭ	NO Rec. II
Bombesin		Нара							L		syk	NO Rec. I
Rhodopsin Receptor	Arrestin	Acetyl-CoA carboxylase Arr				, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	N-Myc		Fra-1	MKP-2	ZAPK	ANF-Rec.
Taste Receptor	cGMP PDE					÷		2 Un	C-F05		SH2 SH2	Tie-1
Olfaction	cGMP PDE	AMP-dep.	Hrp75	Hsp70 Hsc70		F	ATF2	•	1	PAC-1	Btk	Tek
TSH Y Recentor	CGMP PDE		-	Hsp10 Hsp32	-		ZIXM	SAPKa	sk2		Itk	D A+
Receptor	ing PDE	5		Glycogen Synthase	-			SAPKβ	Rsk1		Tec St	Flg-2
LH/hCG Receptor	cGMP Stim. PDE	-		Phos. Kin. B sub.	Erk5		Hogo	SAPKy	Erk2	۴K	3	Bek
Histamine Receptor	inh. PDE	╡┙	MLC	α sub.	Mek5	Mkk3	Mkk6	Sek1		Mek2	Fer	Flg-1
Receptor GHRF Receptor	"stim: PDE =stim: PDE		MLCK		Tpl2	2 Mos	Mek	:k3 Mekk1	kk2 Mekk3	? Mekk2	SH2	
GnRH	Ca ²⁺ /CaM	Ht 31	ļ		ł		•					TrkC
Glucose	n' PDE			GSK3R	S6K	FKBP12			RafB	RafA	Pvk2	TrkB
Glucagon	"stim. PDE 	AKAP 95	Type II APR inh.	GSK3α	FRAP	Ř	Paki	ŝ	Raf1	, Ksr1	Eak	TrkA
Receptor		CAPK	-LAMK-V	Synapsin I	PKB	RhoA	Cdc42 e	Rac	Ras	14-3-3	14	Stk1
Dopamine D1 Receptor	AMP	RIIa. sub.			Camk-III	Ē	Rho-GAP	p62 F	NF1			Fms
Receptor	Aden: Cyclase - II						ŀ			ß	Fgr	Kit
ACTH Receptor	Aden. clase - I	4	CaMK-IIV		PKC2 :	GG	PI 3-K	D85 SHI SHI SHI SHI		SHZ	S.	Flt
Adenosine Receptor	2	PA	-Самк-щр			3 BP-1	Arg		Щ	11	BIK	FIk1
Somatostatin Receptor		← <mark>ਲ</mark>	CaMK-IIO	= PKCA		SH3 SH3 SH3 SH3 SH3 SH2	AD SH2 Pro	₽	×	Brk SHE	H _{ck}	ß Pee.
PGE2 Receptor		PL D .	CaMK-I			ŝ	Ş	Ĭ			Yrk	α rec.
Receptor Neuropeptide Y Recentor		Ceramide	CaMKK		в РКСВ =	SH3	SH2 SH3 SH3	Pro PTB SH2	4	7	Yes	Met
FRMF	8	- <mark>N</mark>	^{E2} Calmodulin		H PKCY =	Š	Grb2	Ť	F	Ntk	Ŀck	ErbB4
Dopamine D2 Receptor Enkaphalin	<u>9</u>	Sphingo- myelinase	CAK -	$P_2 \rightarrow DAG + P_3$	FA + UPC PP	PTB	SH3 SH2 SH3	SHZ SH2		Čč 2	Src	ErbB3
Bradykinin Receptor	2	Y	GB GY	β1 Ριζβ2	PC PLCB1	PLCY	Dynamin	Grb10		H3 H2	SH3 SH2	Neu
Angiotensin II Receptor	8				PL A2	PH SH2 SH2 SH3	Pro	Grb7	ĥ			ErbB EGF rec.
Receptor GABA Receptor	6		β Stat2	Ω.	ISGF 3Y	Stat3	Stat6	Stat5		4PS/IRS-2	4 P \$/)	IGF-II Rec.
Thrombin Receptor	2		13	H3 H2 H3 H2	JAK1	Tyk2	JAK3			IRS-1	12	Rec. β Sub
Receptor Serotonin Receptor	8		(b Kinase	130 GRK6	gp130	╞┥╴		βc-sub.	G	IL-2Ry	PH	IGF-1 Rec. α Sub
α-adrenergic Receptor	÷65	fch.		- CN - L	- II	F IF	IFN	GM	E	1 - 1	, IL	Rec. α Sub Insulin Rec. β Sub
Muscarinic Receptor	Ca+2 annel	Annel Ca+2		IFR IFR GRK4	-10R 6R -11R	Ν-γRα Ν-γRβ	-12R Ν-α/βR Ν-αR	-5Rα -csfrα	L-7R PO-R 3Rα	-2Rβ L-4R	-1Rα 2Rα	Insulin

Systematic analysis of cancer networks



 $\frac{1}{k_{off}}\frac{d\overline{R}}{dt} = -\overline{R}\frac{G_{1}\overline{P}_{a} + Da\overline{C}}{1 + Da\overline{R}} + \gamma(1 - \overline{R}) + \overline{C}$ $\frac{1}{k_{off}}\frac{d\overline{C}}{dt} = \overline{R}\frac{G_{1}\overline{P}_{a} + Da\overline{C}}{1 + Da\overline{R}} - \frac{\overline{C}}{1 - \delta}$ $\frac{de_{1p}}{dt} = \frac{I_0 + G_2 R_T \overline{C}}{1 + G_4 e_{3p}} \frac{1 - e_{1p}}{K_{m,1} + (1 - e_{1p})} - \frac{V_{\max,3} e_{1p}}{K_{m,3} + e_{1p}}$ $de_{2p} = k_2 e_{1p} (1 - e_{2p}) = V_{\max,4} e_{2p}$ $dt = K_{m,2} + (1 - e_{2p}) = K_{m,4} + e_{2p}$ $de_{3p} - k_3 e_{2p}(1 - e_{3p}) - V_{\max,6} e_{3p}$ $dt = K_{m,3} + (1 - e_{3n}) = K_{m,6} + e_{3n}$ $\frac{1}{k^{P}}\frac{d\overline{P}}{dt} = \mu(1-\overline{P}) - (v_{0} + G_{3}e_{3p})\overline{P}$ $\left|\frac{1}{k^{P}}\frac{d\overline{P}_{a}}{dt} = (v_{0} + G_{3}e_{3p})\overline{P} - \overline{P}_{a}\right|$

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MIT study shows that staggered delivery

of cancer drugs is far more effective

Of Note: Yesterday Happened: Remembering H.M., by Catalyst Collaborative@MIT (tonight)

Adel F. Sarofim Memorial Symposium (today)

Launching SpaceX: How to Build a Rocket Company (today)

GIVE TO MIT O

D-Lab Decennial Gala (tomorrow)

Today's image

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