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INDIVIDUALIZED HEALTH
A NEW ERA IN MEDICINE
Igniting INOVAtion. Empowering Care.

THE PROBLEM
Disease burdens are at epidemic levels and costs

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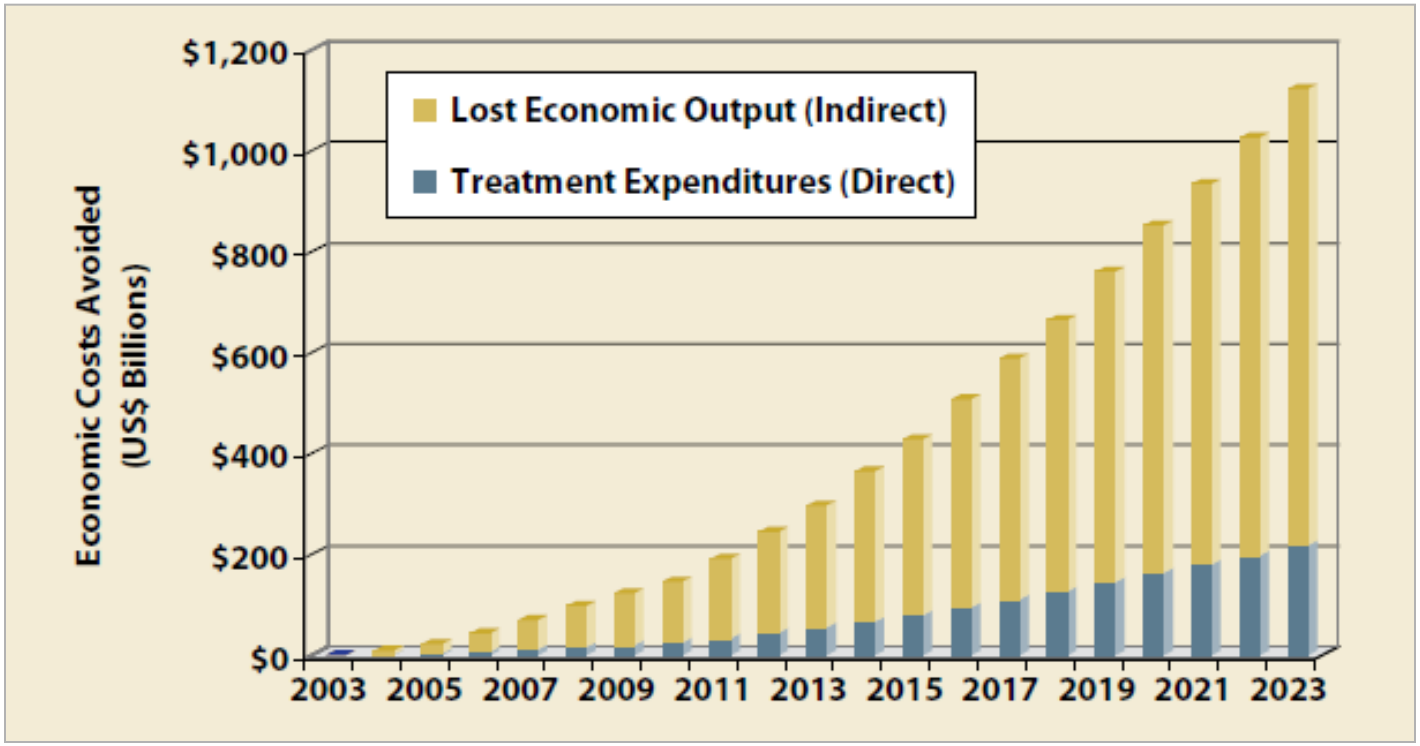
Better Prevention and Management of Chronic Disease are Critical to Improving Health Outcomes and Lowering Healthcare Costs



Source: DeVol, R, Bedroussian, A, et al. An Unhealthy America: The Economic Burden of Chronic Disease. The Milken Institute. October 2007.

Mission and Vision

A unique medical research institute:

- first fully integrated entity to make “personalized medicine” a reality
- weaving together discovery, commercialization, and application of new personalized diagnostics and therapeutics
- the model for 21st century care that applies the latest knowledge to prevent, delay onset, or cure disease

What is Personalized Medicine?

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Genomic Profile / Predisposition / Environmental Risks

Family Members' Health Care

Learning Health Care System

Personal Health / Wellness (Disease pre-emption)

Interaction with Health Care Provider (Early diagnosis if needed)

Interventions (Targeted treatment individualized to my molecular profile and that of my disease)

Post-Disease Management


SCIENCE & TECHNOLOGY
DECODING THE HUMAN BODY

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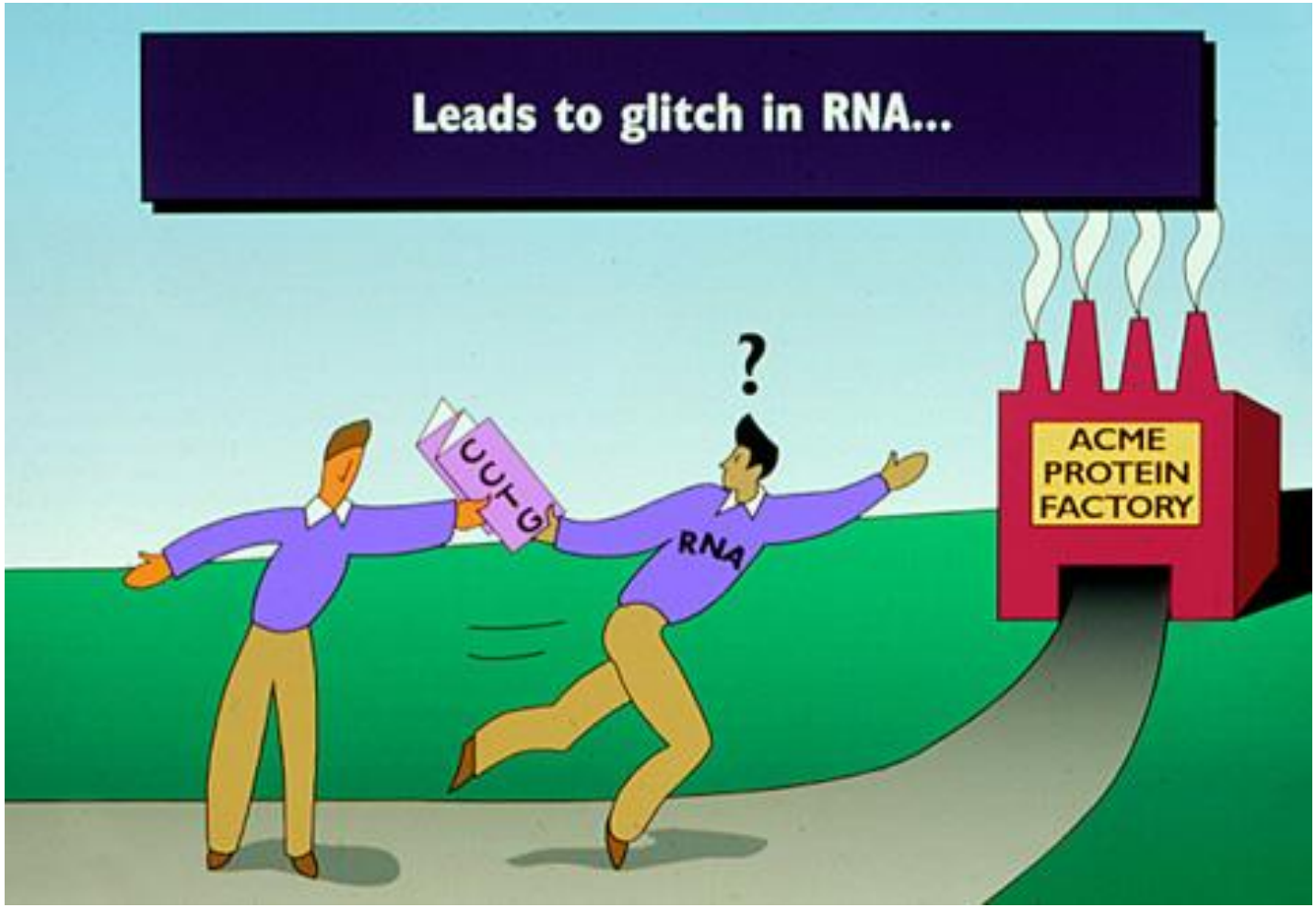

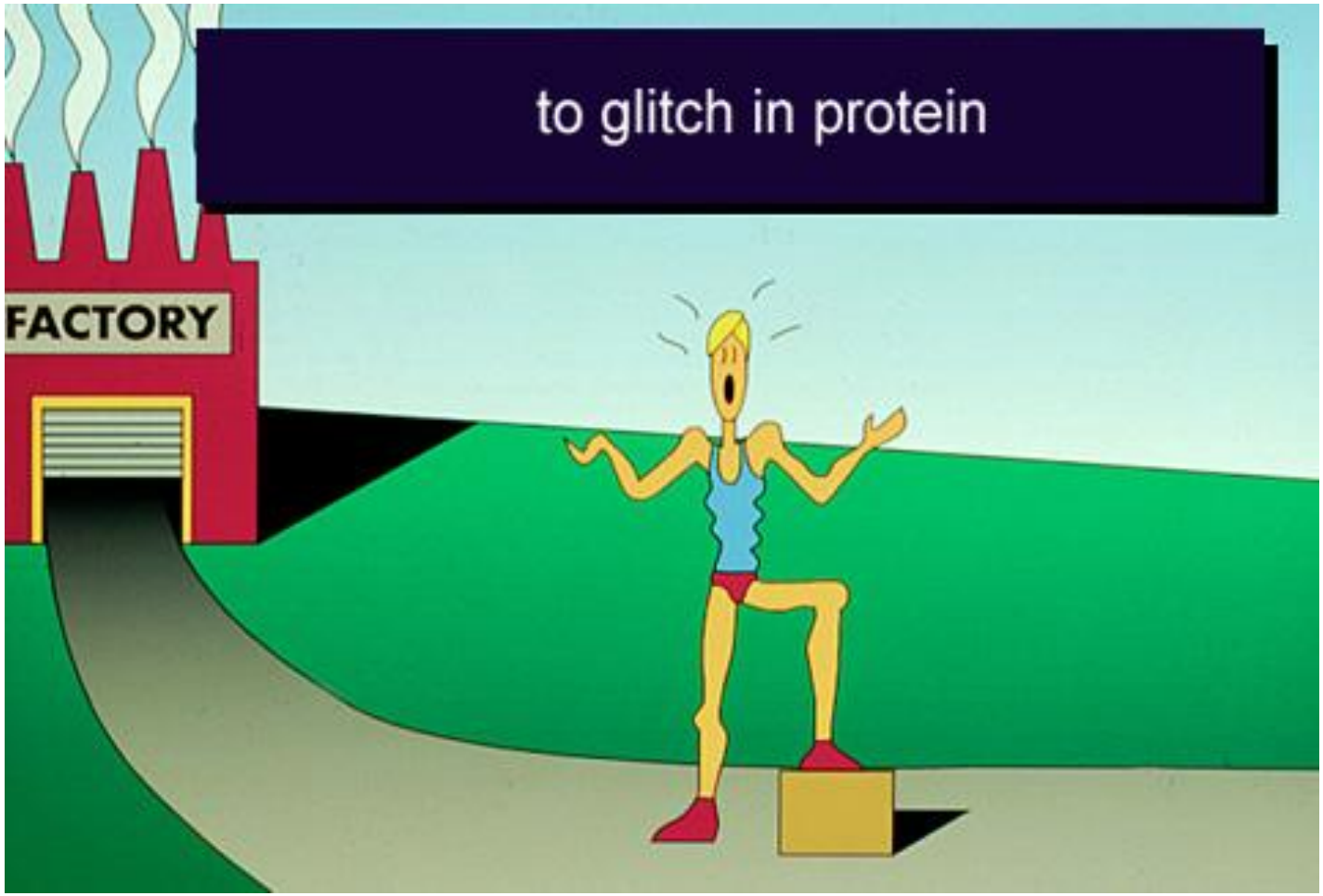
to glitch in protein
FACTORY

Large-Scale Science

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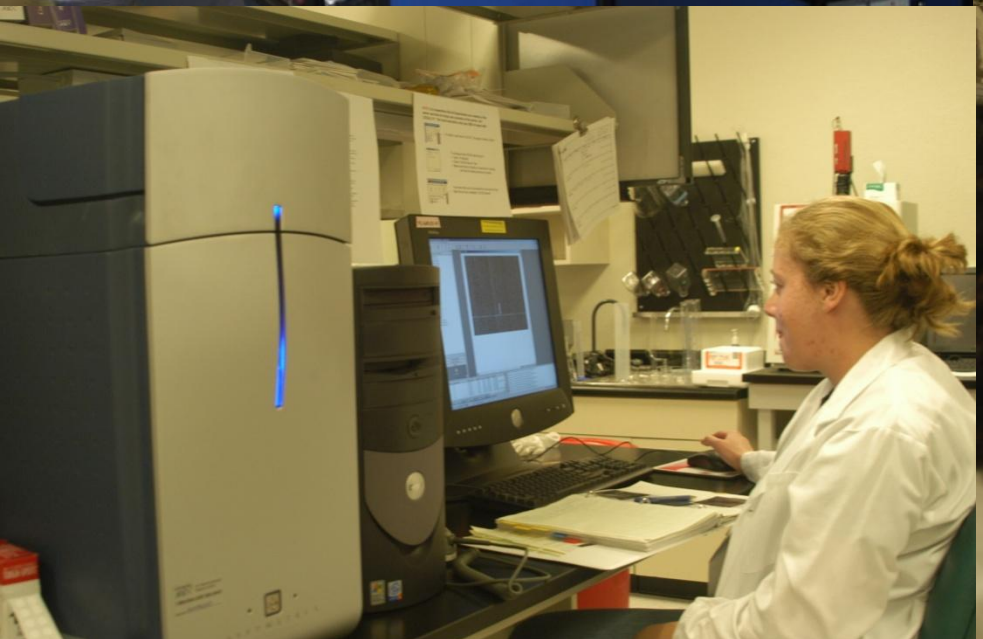
- 4 site NIH Microarray Consortium (funded by 15 NIH institutes at Duke, Yale, UCLA, Stanford, TGen)
- 10 years of experience with Affymetrix platform
- 5 years experience with Illumina
- >60,000 RNA expression profiles run
- >100,000 SNP genotyping arrays run (10k, 50k, 100k, 500k, 1M)
- Software developed with industry to call and analyze genotype data
- Public access data warehousing
- First “Genomics Collaborators” , “Center of Excellence”, and “TransMed” site of Affymetrix
- NHLBI Programs in Genomic Applications
- NEI intramural contract site
- NIH Neuroscience Array Consortium
- NCI funded leukemia catalog
- NIA funded Alzheimer’s disease catalog
- ADNI Consortium hub
- International Autism Genome Project Genotyping Site
- High throughput sequencing (Illumina/ABI)
- ENDGAME Consortium

The Shop


GENECHIP 3
DID YOU REMOVE TOUGH SPOTS?
GENECHIP 4
GENECHIP 1




2004

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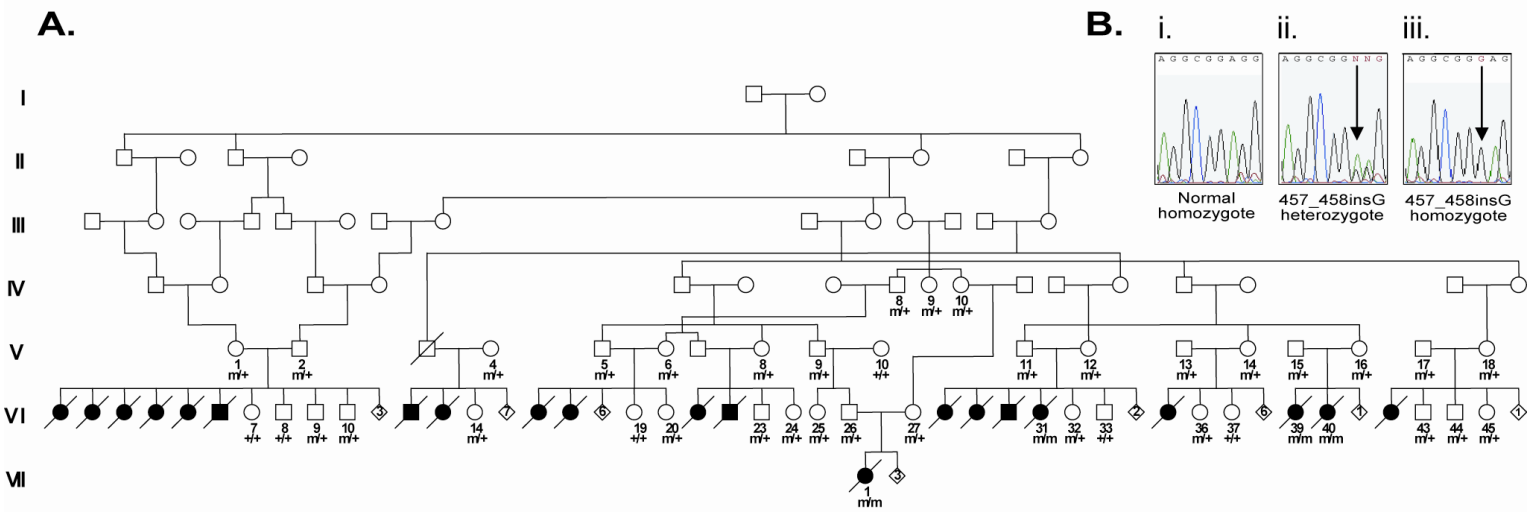
Sudden Infant Death Syndrome (SIDDT)



Puffenberger et al. *Proc Natl Acad Sci U S A*. 2004 Aug 10;101(32):11689-94

SNP-Linkage Software Development

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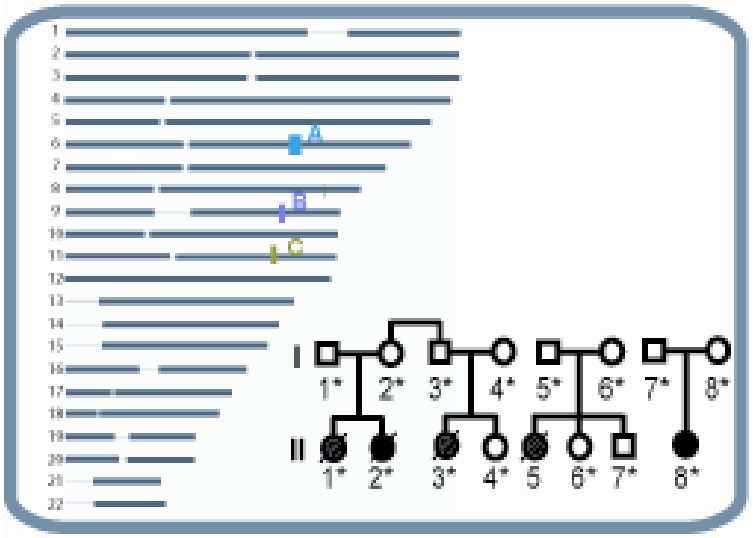

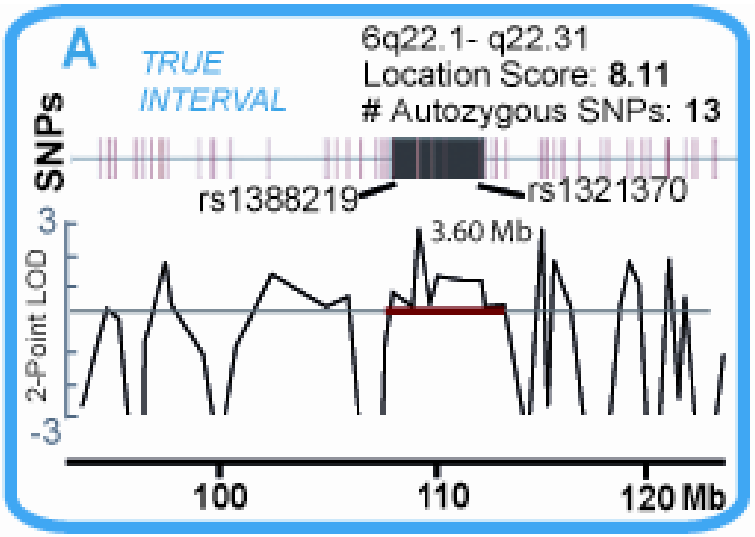

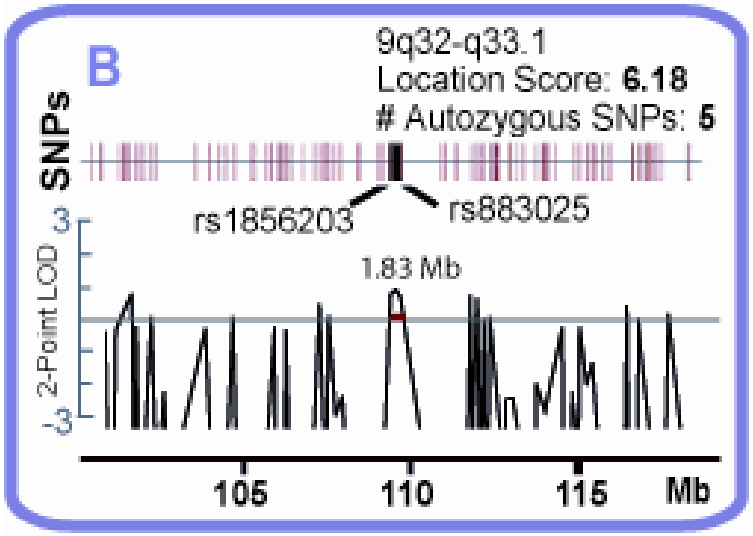

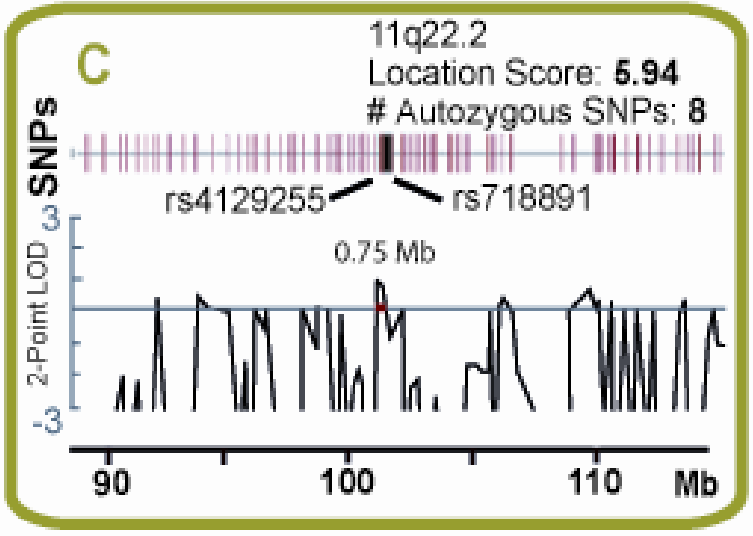

High-Throughput Mutation Identification

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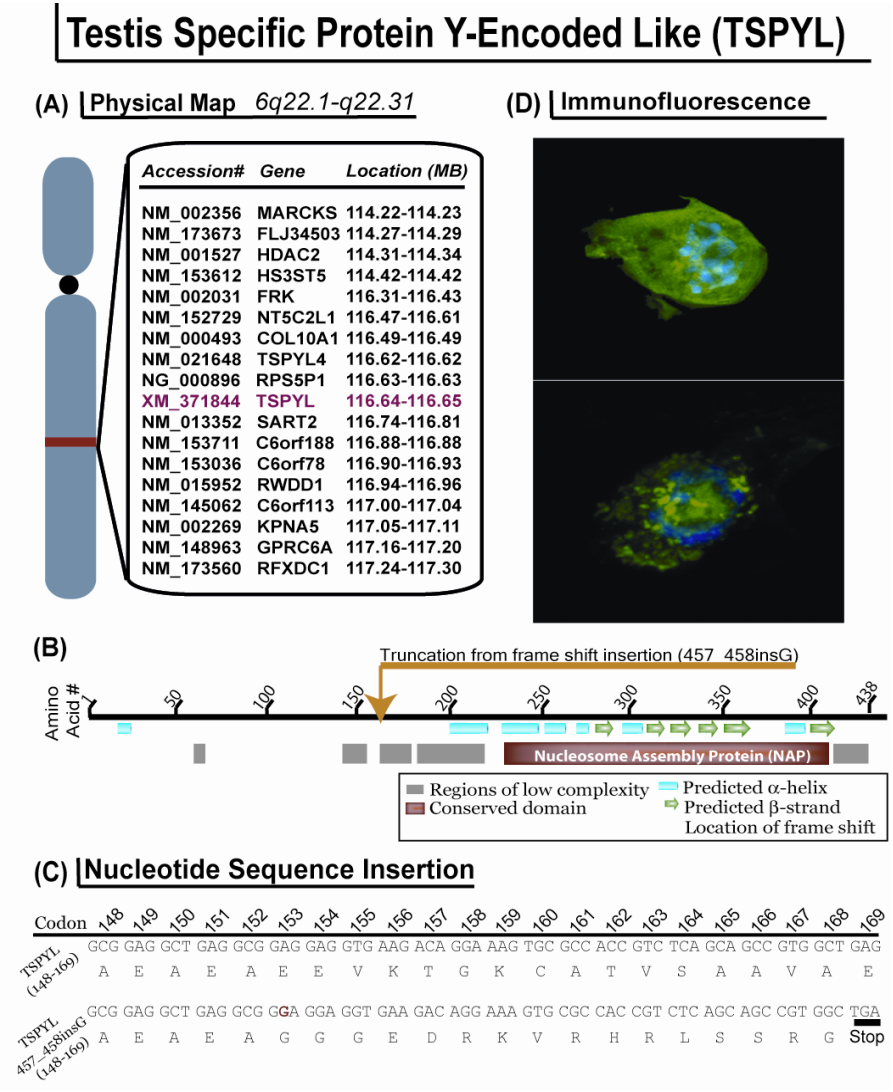
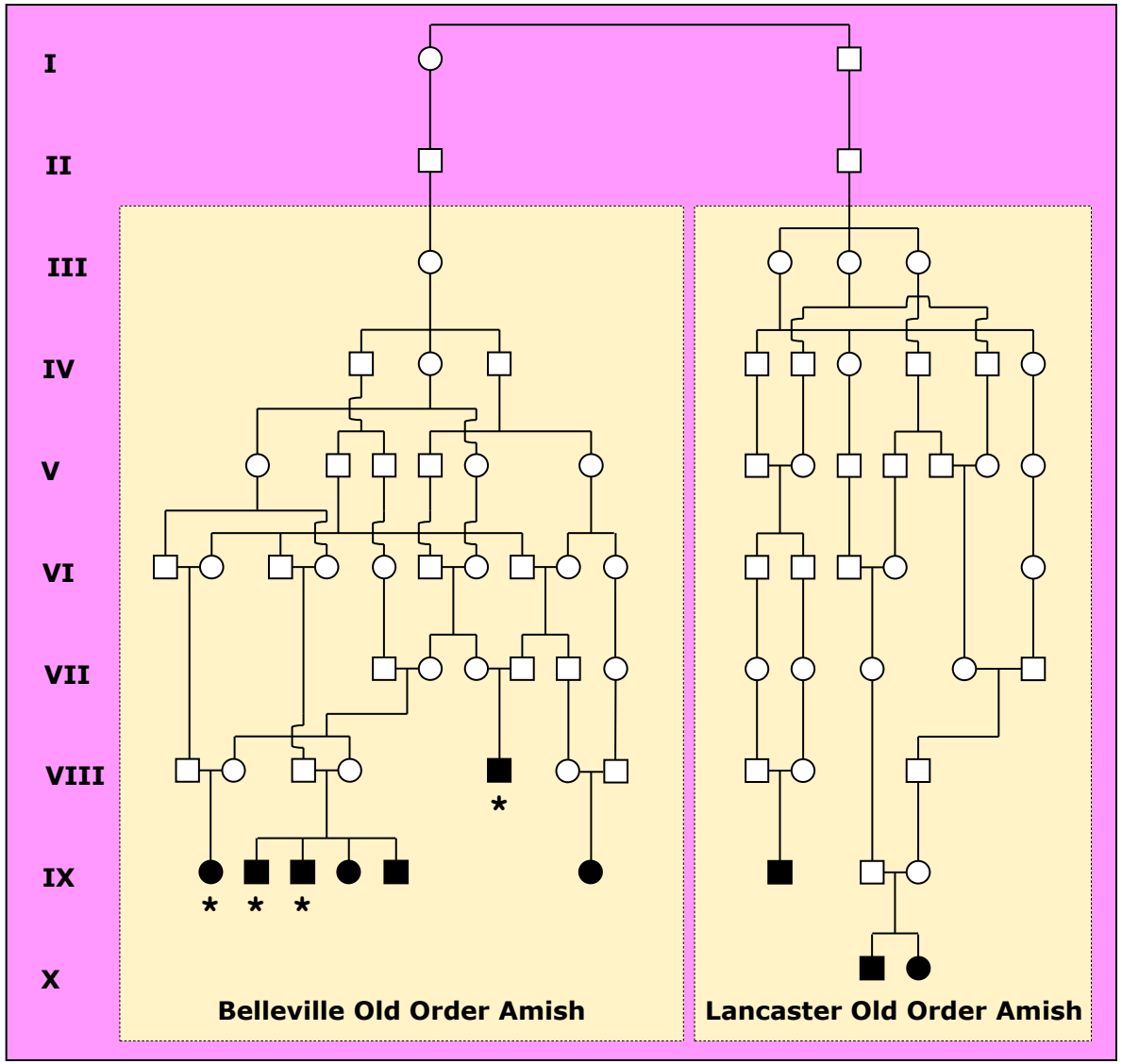


Autism Spectrum Disorder



Cortical Dysplasia with Focal Epilepsy and Autism (CDFE)

Strauss *et al*. Recessive symptomatic focal epilepsy and mutant contactin-associated protein-like 2. New England Journal of Medicine, March 30, 2006


The NEW ENGLAND JOURNAL of MEDICINE
March 30, 2006

THIS WEEK IN THE JOURNAL
Article Summaries

PERSPECTIVE
Politics and Independence — The Collapse of the *Canadian Medical Association Journal*
M. Shuchman and D. A. Redelmeier

Part "D" for "Defective" — The Medicare Drug-Benefit Chaos
J. Avorn

ORIGINAL ARTICLES
Safety and Immunogenicity of an Inactivated Subvirion Influenza A (H5N1) Vaccine
J. J. Treanor and Others

Outpatient Gatifloxacin Therapy and Dysglycemia in Older Adults
L. Y. Park-Wyllie and Others

Prevalence of Monoclonal Gammopathy of Undetermined Significance
R. A. Kyle and Others

Brief Report: Recessive Symptomatic Focal Epilepsy and Mutant Contactin-Associated Protein-like 2
K. A. Strauss and Others

IMAGES IN CLINICAL MEDICINE
Bilateral Renal-Vein Thrombosis Associated with the Nephrotic Syndrome
S. Phonsombat and M. L. Stoller

Enterobius vermicularis
M. D. Brown

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL
Case 10-2006 — A 66-Year-Old Woman with Barrett's Esophagus with High-Grade Dysplasia
N. S. Nishioka and G. Y. Lauwers

EDITORIALS
Vaccines against Avian Influenza — A Race against Time
G. A. Poland

Serious Adverse Drug Effects — Seeing the Trees through the Forest
J. H. Gurwitz

Better Behavioral Health Care Coverage for Everyone
S. Glied and A. Cuellar

COMMENTARY

Unraveling Autism

Dietrich A. Stephan[1,*]

In this issue of *AJHG*, Alarcón et al.,[1] Arking et al.,[2] and Bakkaloglu et al.[3] identify a series of functional variants in the *CNTNAP2* gene that unequivocally implicate this gene as causing Type 1 autism in the general population.

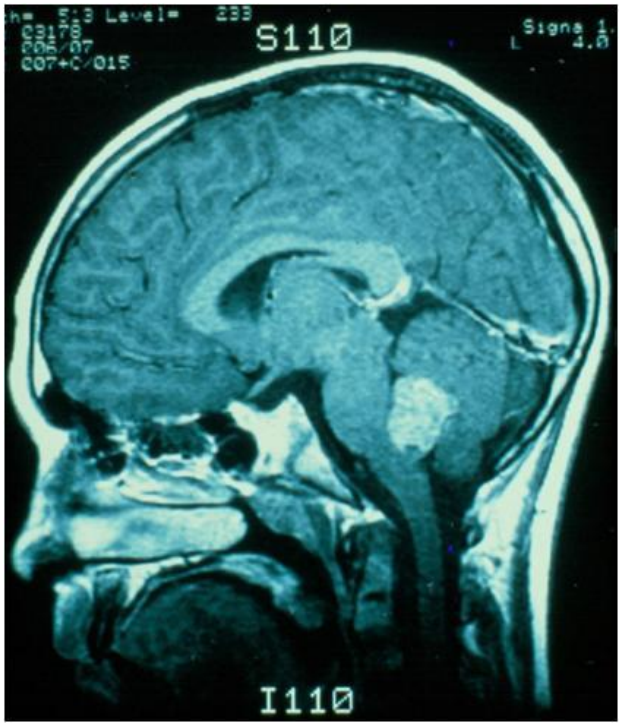
Autism Spectrum Disorder (ASD) is a catch-all diagnosis for a set of poorly understood neurodevelopmental disorders that are clinically heterogeneous, with a spectrum of severity, characterized by repetitive self-stimulatory behaviors and communication and socialization deficits. ASD is traditionally diagnosed by the age of 3 years and the severe forms can be accompanied by language regression, seizures, and low measured IQ. The more strict diagnosis of "autism" is made through behavioral testing on the ADOS and/or ADI-R rating systems. The umbrella diagnosis of ASD ject) have reproducibly identified several loci by studying ASD phenotypes segregating through rare pedigrees with multiple affecteds.[4] Because the more common forms of ASD are sporadic and ASD individuals are less likely to reproduce, we can assume that this majority of ASD predisposition is caused by either SNP variants segregating through the population or by a high new mutation rate in predisposition genes.

Until recently, there existed only three genes with limited evidence (often only in a few probands) implicating them as causative of ADOS/ was truncated through a homozygous loss-of-function mutation in a single family.[9] The mechanism of action of the mutation is likely altered attachment of the axon to the glia via the TAG-1 protein and mislocalization of ion channels at the juxtaparanodal junction leading to cortical dysplasia. This finding is now replicated in a large sampling of the autism population by three groups in this issue of *AJHG* and places the *CNTNAP2* gene as the first widely replicated autism-predisposition gene. Alarcón et al.,[1] Arking et al.,[2] and Bakkaloglu et al.[3] all describe functional variants (both

Medulloblastoma

- Undifferentiated embryonal neuroepithelial tumor of the cerebellum
- Most common malignant brain tumor in children

- *Frequently metastasizes*



Brown KM, MacDonald TJ, LaFleur B, Peterson KM, Lawlor C, Chen Y, Packer RJ, Cogen P, & Stephan DA. ***Nature Genetics***. 29:143-152, 2001

Medulloblastoma Treatment

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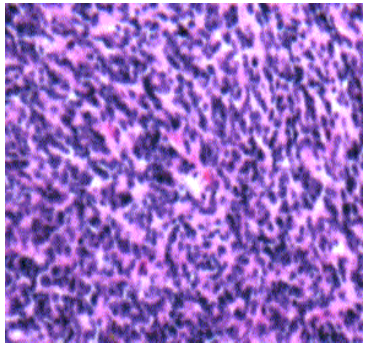
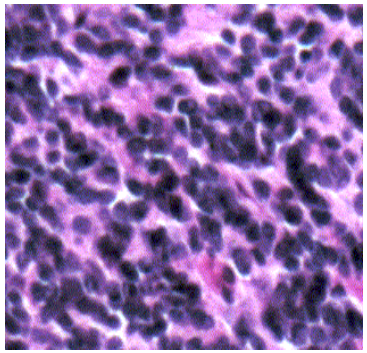
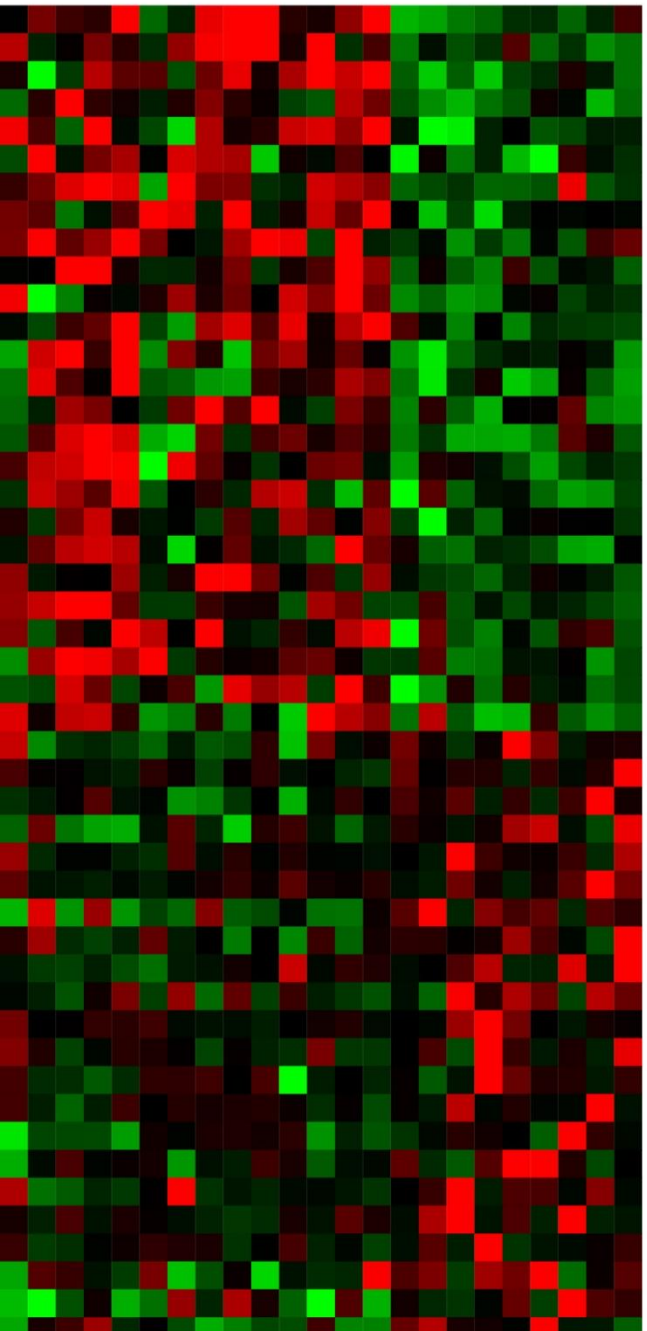
1. Surgery
2. Usually chemotherapy
3. Craniospinal radiation <u>to prevent metastasis</u>





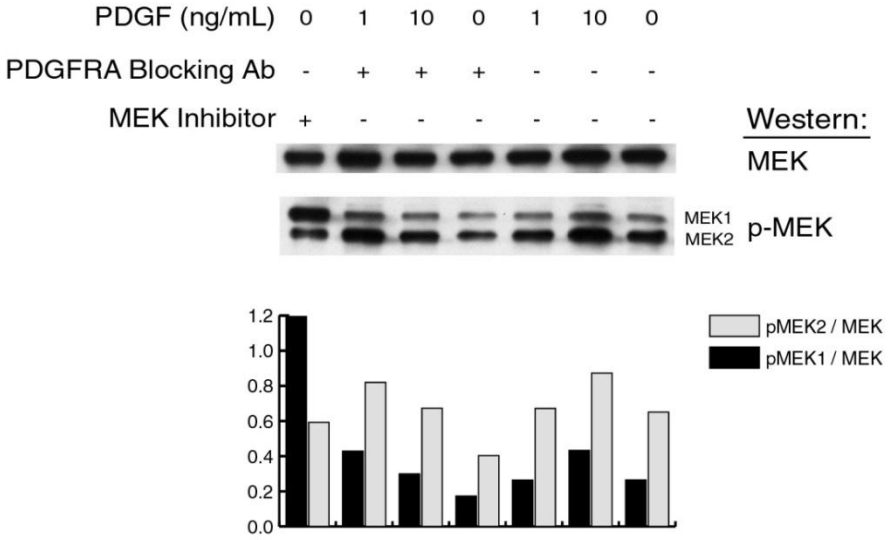
Surviving patients have poor quality of life due to side-effects of radiotherapy:

- Neurocognitive deficits
- Neuroendocrine deficits
- Hearing loss

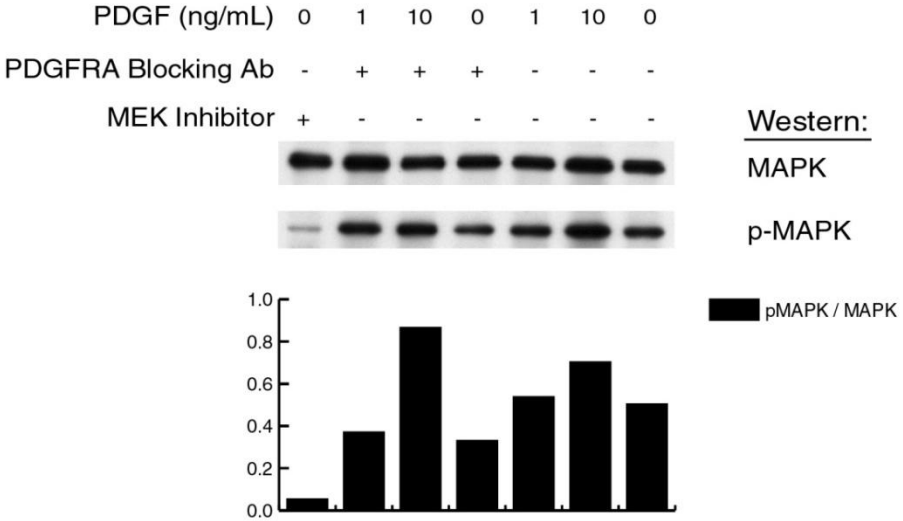


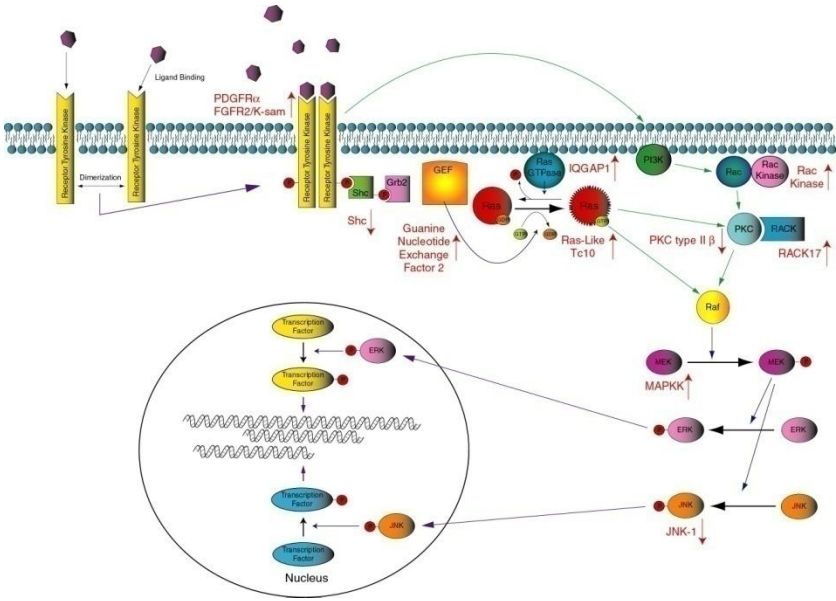
Probe Set	Gene Name	Average Intensity, Non-Metastatic	Average Intensity, Metastatic	Permutational p-value	Average Fold Difference	
1937_at	Retinoblastoma 1	3606	1998	0.004	1.80	
624_at	GTP-binding protein (RAB3B)	134	23	0.005	5.93	
1611_s_at	Interferon (IFN-gamma)	111	39	0.007	2.85	
1548_s_at	Interleukin 10 (IL10)	381	171	0.007	2.23	
2042_s_at	c-myb	117	36	0.010	3.24	
885_g_at	Integrin alpha-3 chain	507	297	0.018	1.71	
529_at	Human dual-specificity protein phosphatase	1309	440	0.018	2.98	
2070_i_at	Protein kinase (JNK1)	241	71	0.024	3.42	
785_at	Nedd-4-like ubiquitin-protein ligase WWP2	273	107	0.028	2.54	
1912_s_at	APC	1367	516	0.034	2.65	
304_at	Guanine Nucleotide Exchange Factor 2	47	10	0.035	4.69	
463_g_at	Nuclear factor I B3	3367	1654	0.036	2.04	
1380_at	Keratinocyte growth factor	239	140	0.036	1.71	
1600_at	Tyrosine kinase (TXK)	322	183	0.037	1.76	
654_at	MXI1	3264	1812	0.037	1.80	
1467_at	Epidermal growth factor receptor kinase substrate (Eps8)	960	471	0.037	2.04	
1127_at	Ribosomal protein S6 kinase 2 (RPS6KA2)	857	368	0.040	2.33	
2046_at	Erg protein (ets-related gene), 3' flank	718	365	0.044	1.97	
2022_at	Rac protein kinase beta	125	60	0.045	2.09	
528_at	Heat shock protein 27 (HSP27)	489	269	0.046	1.82	
547_s_at	TINUR= NGFI-B/nur77 beta-type transcription factor homolog	314	11	0.047	28.22	
1216_at	Protein kinase C (PKC) type beta II	162	32	0.048	5.01	
1012_at	p300/CBP-associated factor (P/CAF)	130	68	0.048	1.92	
1511_at	p52 and p64 isoforms of N-Shc	996	670	0.049	1.49	Down in M+
726_f_at	Chorionic Somatomammotropin Hormone Cs-5	757	437	0.049	1.73	
139_at	Guanylate kinase associated protein (GKAP)	52	26	0.050	2.05	
205_g_at	Homeobox 1.4	15	213	0.000	14.40	
829_s_at	Glutathione S-transferase-P1c	2882	11495	0.000	3.99	Up in M+
239_at	Cathepsin D (catD)	2889	6098	0.001	2.11	
652_g_at	Replication protein A 14kDa subunit (RPA)	790	1530	0.003	1.94	
1693_s_at	Tissue inhibitor of metalloproteinases (HUMTIMP)	158	3185	0.004	20.14	
2062_at	MAC25	3356	11374	0.004	3.39	
191_at	Mucin (MUC8)	192	370	0.004	1.92	
651_at	Replication protein A 14kDa subunit (RPA)	217	615	0.006	2.84	
671_at	SPARC/osteonectin	4165	8588	0.007	2.06	
1818_at	Ras-Like Protein Tc10	578	1318	0.007	2.28	
1741_s_at	Insulin-like growth factor binding protein-2	417	2012	0.008	4.83	
841_at	Protein kinase C-binding protein RACK17	72	447	0.009	6.19	
1321_s_at	Tumor-associated membrane protein homolog (TMP)	33	184	0.009	5.57	
1143_s_at	FGF Receptor K-Sam, Alt. Splice 3	90	343	0.009	3.80	
1173_g_at	Spermidine/Spermine N1-Acetyltransferase, Alt. Splice 2	2401	3486	0.009	1.45	
709_at	Beta-tubulin gene, clone m40	3393	5071	0.010	1.49	
1319_at	X74764cds receptor protein tyrosine kinase	80	408	0.012	5.10	
368_at	5T4 Oncofetal antigen	358	780	0.012	2.18	
1001_at	Putative receptor tyrosine kinase (tie)	281	749	0.013	2.67	
982_at	P1-Cdc46	558	847	0.013	1.52	
1052_s_at	NF-IL6-beta	864	1413	0.013	1.64	
283_at	Ubiquinol cytochrome-c reductase core I	2645	4256	0.013	1.61	

a.


PDGF (ng/mL) 0 1 10 0 1 10 0
PDGFRA Blocking Ab - + + + - - -
MEK Inhibitor + - - - - - -
Western:
MEK
MEK1
MEK2
p-MEK
1.2
1.0
0.8
0.6
0.4
0.2
0.0
pMEK2 / MEK
pMEK1 / MEK

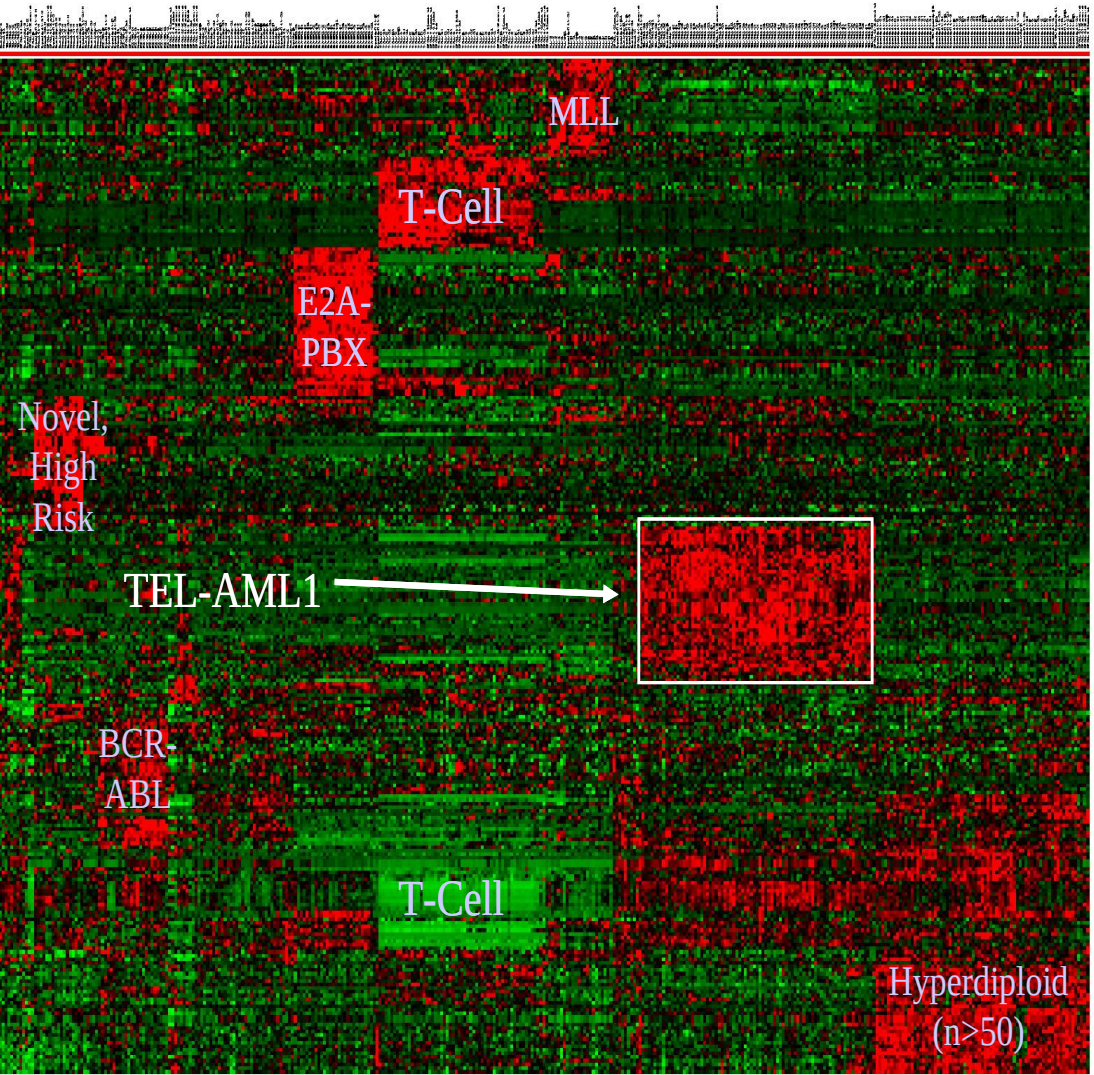
b.

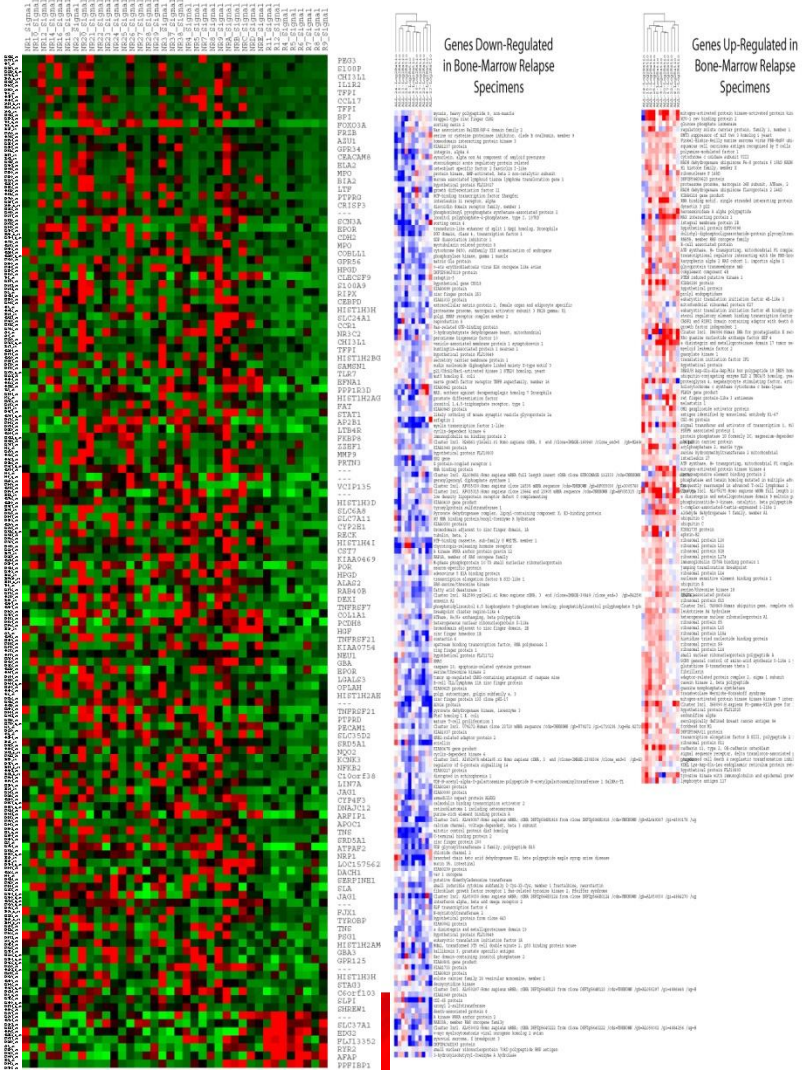

PDGF (ng/mL) 0 1 10 0 1 10 0
PDGFRA Blocking Ab - + + + - - -
MEK Inhibitor + - - - - - -
Western:
MAPK
p-MAPK
1.0
0.8
0.6
0.4
0.2
0.0
pMAPK / MAPK


Ligand Binding
PDGFRα
FGFR2/K-sam
Receptor Tyrosine Kinase
Dimerization
Shc
Grb2
GEF
Ras GTPase
IQGAP1
PI3K
Rac
Rac Kinase
PKC
RACK
RACK17
PKC type II β
Guanine Nucleotide Exchange Factor 2
Ras-Like Tc10
Raf
MEK
MAPKK
ERK
JNK
JNK-1
Transcription Factor
Nucleus

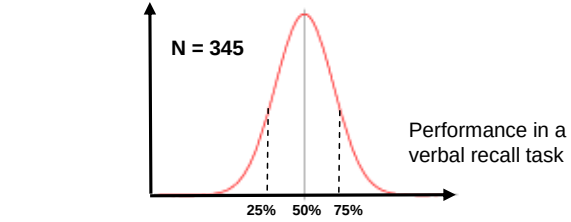
Pediatric ALL – Diagnosis and Treatment

Mitchell S *et al*, *BMC Genomics. 2004 Sep 23;5(1):71.*
Henry M *et al, Submitted*
Brown KM *et al, In Preparation*





Diagnostics and Therapeutics for Complex Genetic Disease:



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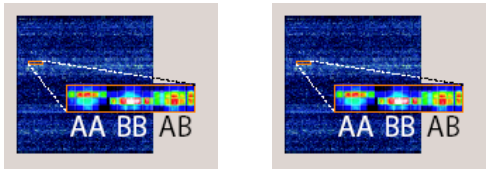
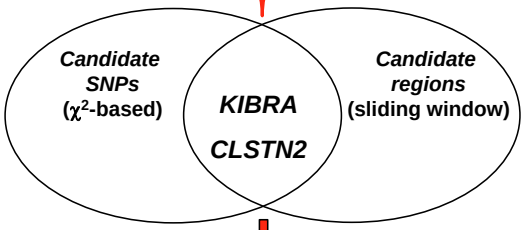
top 50% performers vs low 50% performers

top 25% performers vs low 25% performers

DNA Pooling



500K SNP Chips



Individual genotyping population 1

KIBRA

CLSTN2

Individual genotyping population 2

KIBRA

Stephan et al, Science, 2006

First to use >500,000 SNPs to scan the genome

Alzheimer's Disease

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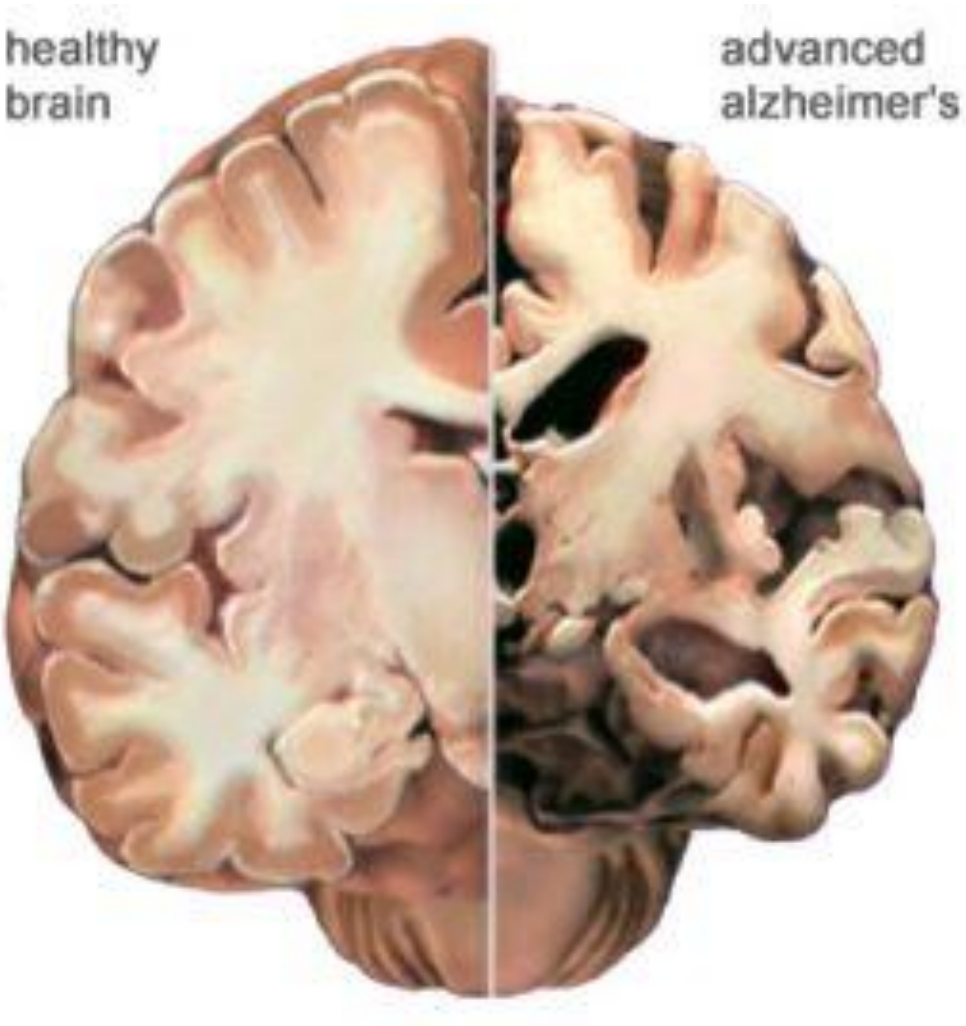
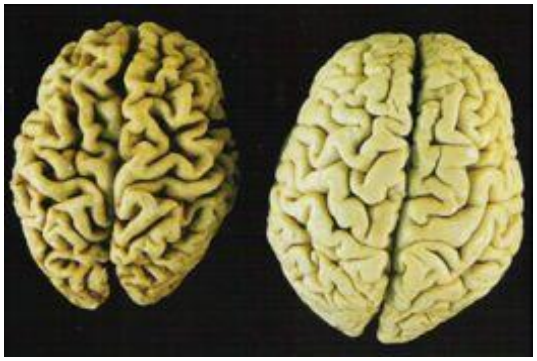
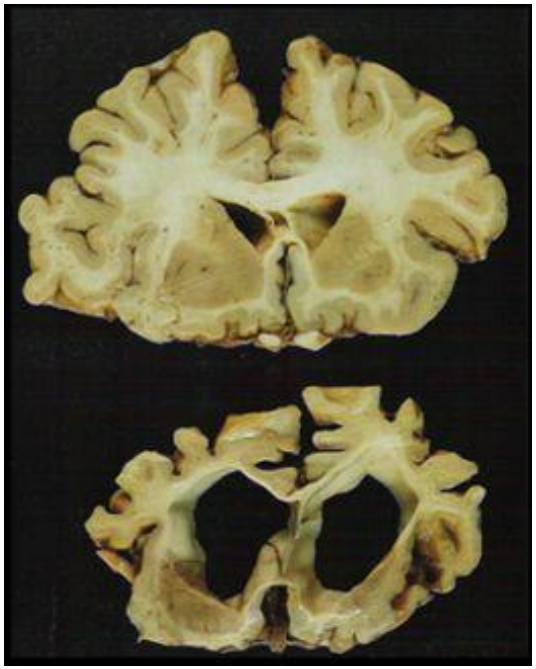






Common *Kibra* Alleles Are Associated with Human Memory Performance

Andreas Papassotiropoulos,[1,3*†] Dietrich A. Stephan,[3*†] Matthew J. Huentelman,[3] Frederic J. Hoerndli,[1] David W. Craig,[3] John V. Pearson,[3] Kim-Dung Huynh,[1] Fabienne Brunner,[1] Jason Corneveaux,[3] David Osborne,[4] M. Axel Wollmer,[1] Amanda Aerni,[1] Daniel Coluccia,[1] Jürgen Hänggi,[1] Christian R. A. Mondadori,[1] Andreas Buchmann,[1] Eric M. Reiman,[3,6] Richard J. Caselli,[5] Katharina Henke,[1] Dominique J.-F. de Quervain[1,2]

Human memory is a polygenic trait. We performed a genome-wide screen to identify memory-related gene variants. A genomic locus encoding the brain protein KIBRA was significantly associated with memory performance in three independent, cognitively normal cohorts from Switzerland and the United States. Gene expression studies showed that *KIBRA* was expressed in memory-related brain structures. Functional magnetic resonance imaging detected *KIBRA* allele–dependent differences in hippocampal activations during memory retrieval. Evidence from these experiments suggests a role for KIBRA in human memory.

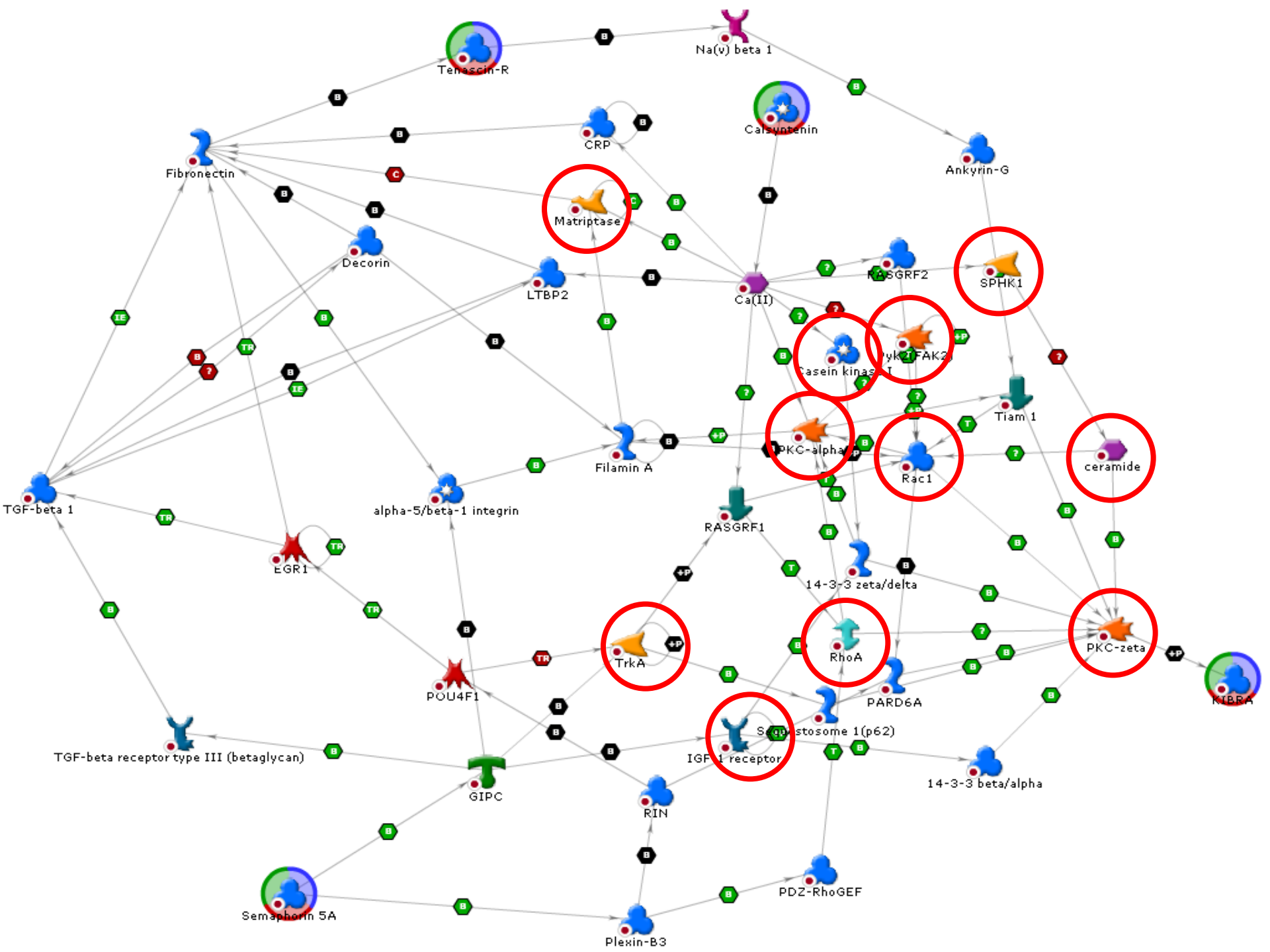
Human memory is a polygenic cognitive trait. Heritability estimates of ~50% suggest that naturally occurring genetic variability has an important impact on this fundamental brain function (*1*). Recent candidate-gene association studies have identified some genetic variations with significant impact on human memory capacity (*2*–*5*). However, the success of these studies depends upon preexisting information, which limits their potential to identify unrecognized genes and molecular pathways (*6*, *7*).

Recent advances in the development of high-density genotyping platforms now allow for high-resolution whole-genome as-

ogeneity within the study sample (population structure) can lead to spurious associations between a genetic marker and a phenotype (*11*). Therefore, we controlled for genetic background and found no evidence of significant population stratification; the participants' genetic backgrounds formed one normally distributed cluster ($P = 0.6$) (*10*, *12*). We identified 10 participants as outliers (probability of cluster allocation lower than 25%) and excluded them from the genetic association studies. The remaining population ($n = 341$) was stratified into four groups according to their performance in a verbal memory task which quantified the retrieval process 5 min

high statistical confidence (*10*). Two SNPs fulfilled these selection criteria and were prioritized for subsequent individual genotyping to exclude pooling-related false positives: rs17070145 and rs6439886. Both SNPs map within genes expressed in the human brain: rs17070145 is a common T → C substitution within the ninth intron of *KIBRA* (GenBank accession number NM_015238), encoding a neuronal protein, and rs6439886 is a common T → C substitution within the first intron of *CLSTN2* (encoding the synaptic protein calsyntenin 2) (NM_022131).

Both the *KIBRA* and *CLSTN2* SNPs were also significantly associated with differential human memory performance when we genotyped them individually in Swiss cohort 1 using an independent genotyping technology (*10*). Carriers of *KIBRA* rs17070145 T allele had 24% better free recall performance 5 min after word presentation ($P = 0.000004$) and 19% better free recall performance 24 hours after word presentation ($P = 0.0008$) than did noncarriers (Table 1, table S1, and fig. S2). TT and CT genotype groups of rs17070145 were combined because the frequency of the TT genotype was low and because both groups displayed similar memory performance (table S1). SNP rs6439886 yielded similar results; however, the mean difference of memory performance between genotype groups was lower than that of rs17070145 (Table 1 and table S1). Both the 5-min and the 24-hour delayed free recall reflected


Tenascin-R
Na(v) beta 1
Calsyntenin
CRP
Fibronectin
Ankyrin-G
Matriptase
Decorin
LTBP2
Ca(II)
RASGRF2
SPHK1
Casein kinase I
Pyk2/FAK2
Tiam 1
PKC-alpha
Rac1
ceramide
Filamin A
TGF-beta 1
alpha-5/beta-1 integrin
RASGRF1
EGR1
14-3-3 zeta/delta
TrkA
RhoA
PKC-zeta
KIBRA
POU4F1
PARD6A
Sequestosome 1(p62)
TGF-beta receptor type III (betaglycan)
IGF-1 receptor
14-3-3 beta/alpha
GIPC
RIN
Semaphorin 5A
PDZ-RhoGEF
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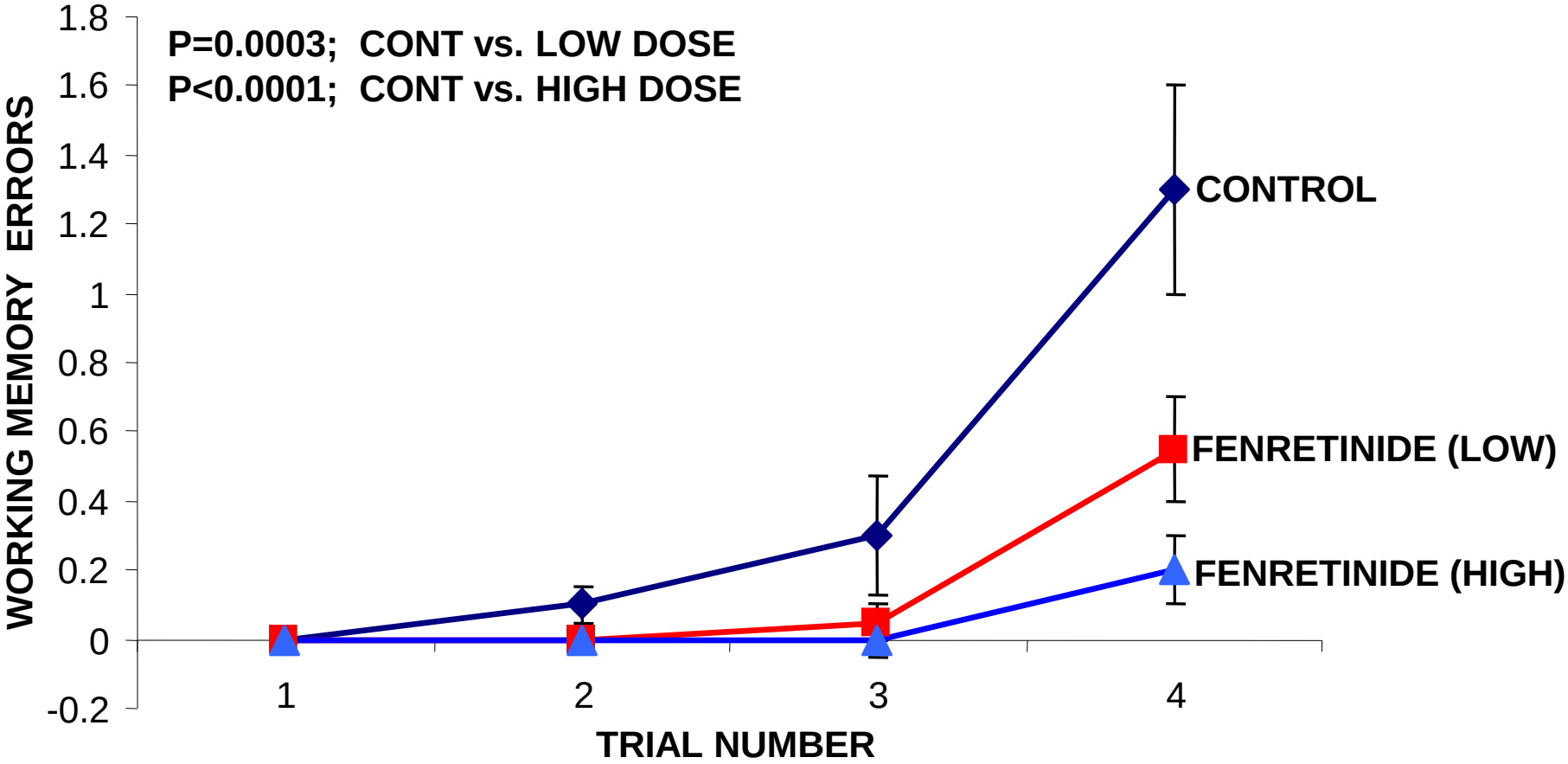

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More Genetic Risk Factors

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Neuron
Report

Cell PRESS

GAB2 Alleles Modify Alzheimer's Risk in *APOE* ε4 Carriers

Eric M. Reiman,[1,2,3,17,18,*] Jennifer A. Webster,[1,17,18] Amanda J. Myers,[4,5,18] John Hardy,[5,6] Travis Dunckley,[1,17] Victoria L. Zismann,[1,17] Keta D. Joshipura,[1,17] John V. Pearson,[1,17] Diane Hu-Lince,[1,17] Matthew J. Huentelman,[1,17] David W. Craig,[1,17] Keith D. Coon,[1,7,17] Winnie S. Liang,[1,17] RiLee H. Herbert,[1,17] Thomas Beach,[8,17] Kristen C. Rohrer,[5] Alice S. Zhao,[5] Doris Leung,[5] Leslie Bryden,[5] Lauren Marlowe,[5] Mona Kaleem,[5] Diego Mastroeni,[8] Andrew Grover,[8,17] Christopher B. Heward,[9] Rivka Ravid,[10] Joseph Rogers,[8,17] Michael L. Hutton,[11] Stacey Melquist,[11] Ron C. Petersen,[12] Gene E. Alexander,[13,17] Richard J. Caselli,[14,17] Walter Kukull,[16] Andreas Papassotiropoulos,[1,15] and Dietrich A. Stephan[1,2,17,*]

[1] Neurogenomics Division, Translational Genomics Research Institute, Phoenix, AZ, 85004, USA
[2] Banner Alzheimer's Institute, Phoenix, AZ 85006, USA
[3] Department of Psychiatry, University of Arizona, Tucson, AZ 85724, USA
[4] Department of Psychiatry and Behavioral Sciences, University of Miami, Miller School of Medicine, Miami, FL 33136, USA
[5] Laboratory of Neurogenetics, National Institute on Aging, Bethesda, MD, 20892, USA
[6] Reta Lila Weston Laboratories, Department of Molecular Neuroscience, Institute of Neurology, Queen Square, London WC1N, 3BG, England
[7] Division of Thoracic Oncology Research, St. Joseph's Hospital, Phoenix, AZ 85013, USA
[8] Sun Health Research Institute, Sun City, AZ 85351, USA
[9] Kronos Science Laboratory, Phoenix, AZ 85016, USA
[10] Netherlands Institute for Neurosciences, Dutch Royal Academy of Arts and Sciences, Meibergdreef 47 AB Amsterdam, The Netherlands
[11] Department of Neuroscience, Mayo Clinic, Jacksonville, FL 32224, USA
[12] Department of Neurology, Mayo Clinic, Rochester, MN 55905, USA
[13] Department of Psychology, Arizona State University, Tempe, AZ 85281, USA
[14] Department of Neurology, Mayo Clinic, Scottsdale, AZ 85259, USA
[15] Division of Molecular Psychology and Life Sciences Training Facility, Biozentrum, University of Basel, Switzerland
[16] National Alzheimer's Coordinating Center, Department of Epidemiology, School of Public Health and Community Medicine,

More Genetic Risk Factors

BRIEF COMMUNICATIONS

nature genetics

Common sequence variants on 20q11.22 confer melanoma susceptibility

Kevin M Brown[1,23], Stuart MacGregor[2,23], Grant W Montgomery[2], David W Craig[3], Zhen Zhen Zhao[2], Kelly Iyadurai[1], Anjali K Henders[2], Nils Homer[4], Megan J Campbell[2], Mitchell Stark[2], Shane Thomas[2], Helen Schmid[5], Elizabeth A Holland[5], Elizabeth M Gillanders[6], David L Duffy[2], Judith A Maskiell[7], Jodie Jetann[8], Megan Ferguson[8], Dietrich A Stephan[3], Anne E Cust[7], David Whiteman[2], Adele Green[2], Håkan Olsson[9,21,22], Susana Puig[10,22], Paola Ghiorzo[11,22], Johan Hansson[12,22], Florence Demenais[13,22], Alisa M Goldstein[14], Nelleke A Gruis[15,22], David E Elder[16,22], Julia Newton Bishop[17,22], Richard F Kefford[5], Graham G Giles[18], Bruce K Armstrong[19], Joanne F Aitken[8], John L Hopper[7], Nicholas G Martin[2], Jeffrey M Trent[20], Graham J Mann[5] & Nicholas K Hayward[2]

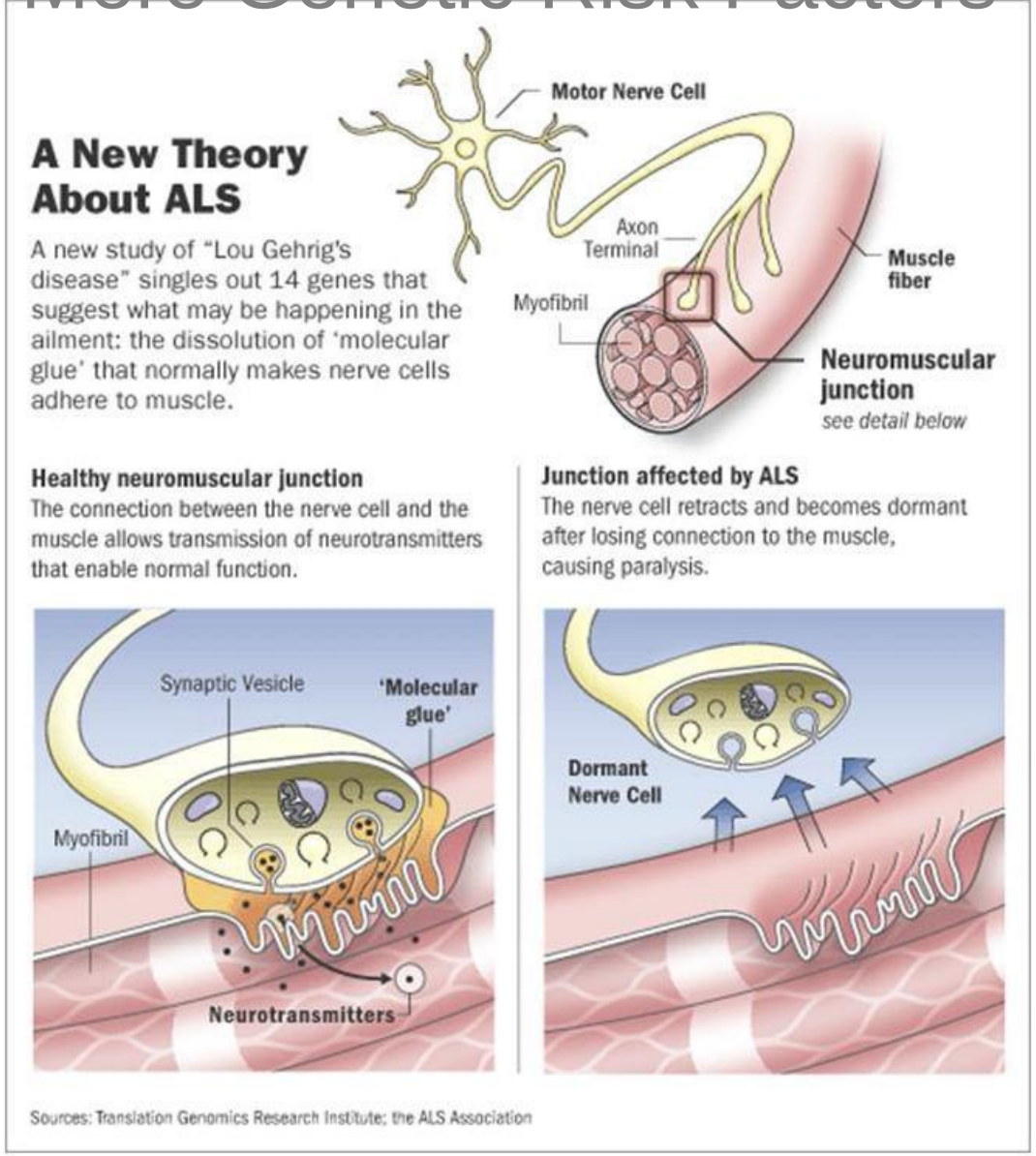
We conducted a genome-wide association pooling study for cutaneous melanoma and performed validation in samples totaling 2,019 cases and 2,105 controls. Using pooling, we

have been identified (*CDKN2A*, *ARF*, *CDK4* and a locus on 1p22)[2], and *MC1R* has been validated as a gene harboring low-penetrance risk alleles[3,4].

To identify additional low-penetrance risk alleles, we carried out a genome-wide association study (GWAS) involving the pooling of 864 cases drawn from a larger population-based sample of cases (individuals with melanoma) from Queensland, unselected for age at onset (Queensland study of Melanoma: Environment and Genetic Associations (Q-MEGA)[5]), and 864 controls (Q1). Each pool was hybridized to six Illumina HumanHap550 arrays, and SNPs were ranked after accounting for pooling error[6,7]. The proportion of SNPs with *P* values from pooling of < 0.01 was consistent with what would be expected by chance if there were no true associations. Conversely, at smaller *P*-value thresholds, there were more SNPs than expected by chance. For example, at the 0.0001 threshold, we would expect to see ~55 SNPs under the null hypothesis of no association, but we in fact observed 90 SNPs, indicating that there were a number of true associations (**Supplementary Note** online).

Here we focus on only the most significant finding from pooling. The first-ranked (rs17305657, $P = 2.56 \times 10^{-7}$) and fourth-ranked (rs4911442, $P = 2.39 \times 10^{-6}$) SNPs are 1.5 Mb apart on chromosome 20. Multiple other SNPs in this region showed evidence for association (**Supplementary Fig. 1** online). When the pooling results were validated by individual genotyping, concordance was excellent

More Genetic Risk Factors



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ALS
Multiple Sclerosis
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Bipolar
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Alzheimer's Disease
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PSP
Melanoma
Addictions
ADNI

Dunckley et al, New England Journal of Medicine, 2007

Estimated Savings in Prevalence & Costs of AD with Delayed Onset/Progression

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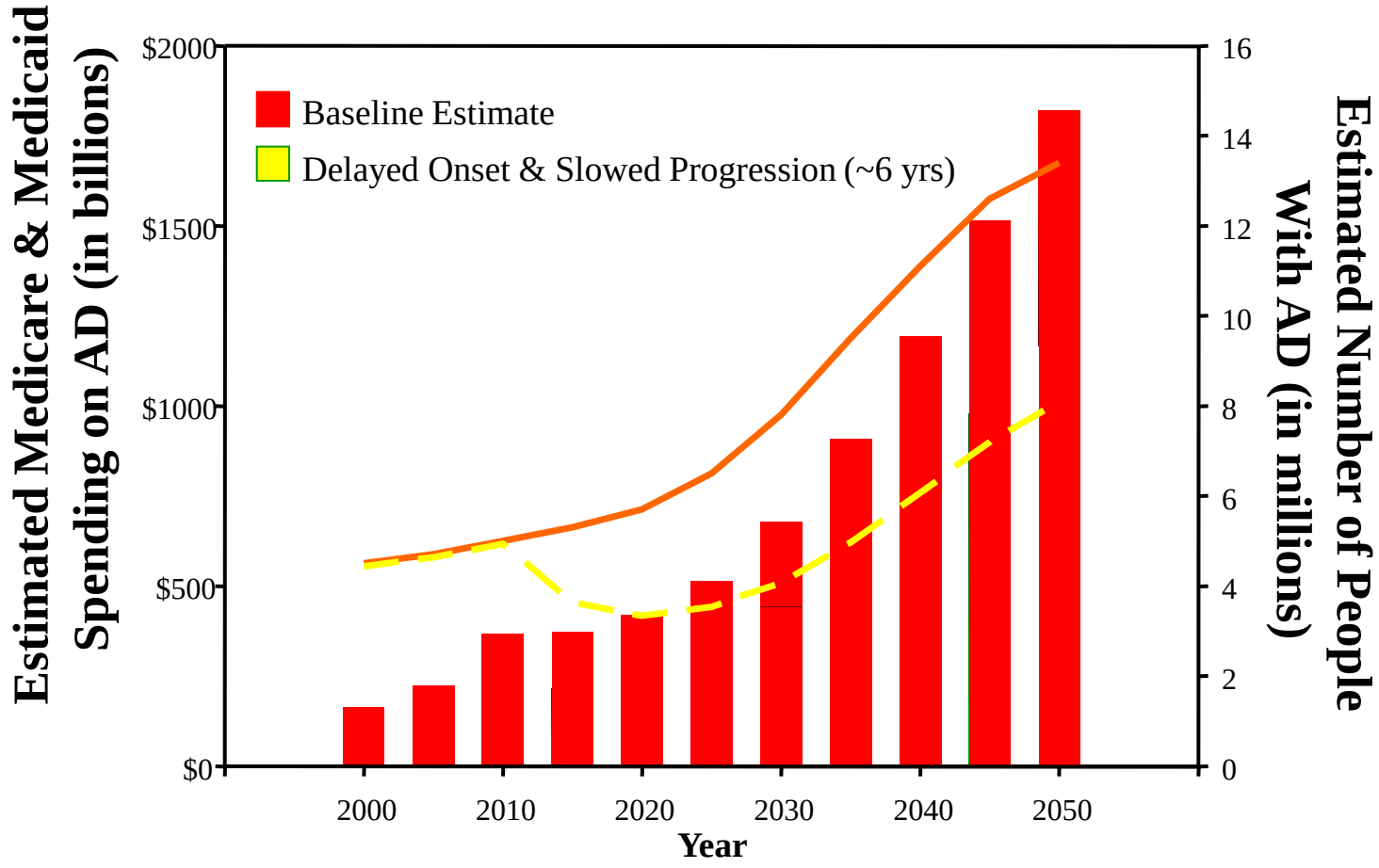

Adapted from The Lewin Group Report, June 2004, "Saving Lives. Saving Money: Dividends for Americans Investing in Alzheimer Research," The Alzheimer's Association (http://www.alz.org/Resources/FactSheets/Lewin_FullReport1.pdf)

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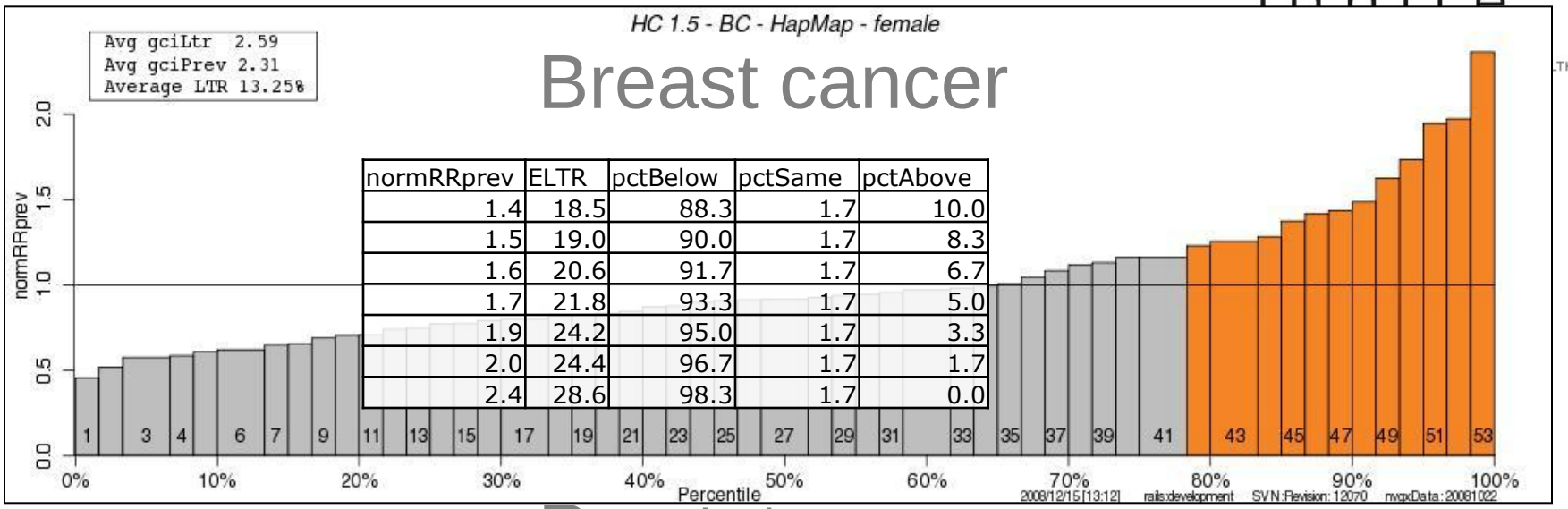
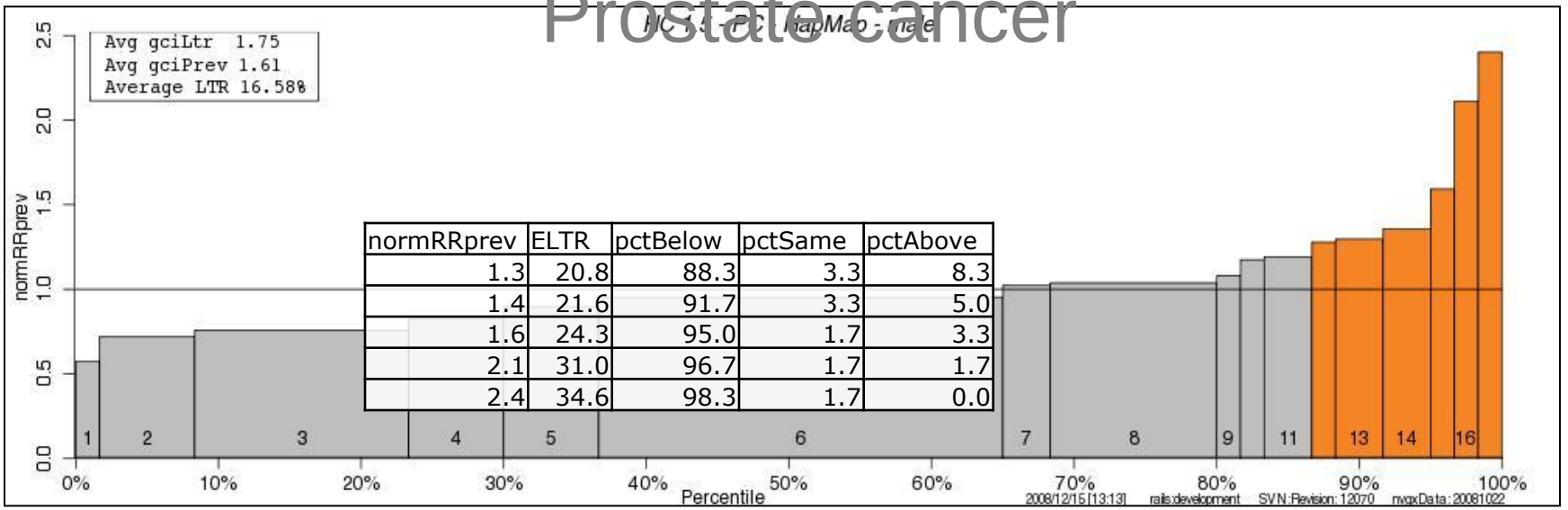
Breast/Prostate Cancer: Top 10%



Breast cancer

normRRprev	ELTR	pctBelow	pctSame	pctAbove
1.4	18.5	88.3	1.7	10.0
1.5	19.0	90.0	1.7	8.3
1.6	20.6	91.7	1.7	6.7
1.7	21.8	93.3	1.7	5.0
1.9	24.2	95.0	1.7	3.3
2.0	24.4	96.7	1.7	1.7
2.4	28.6	98.3	1.7	0.0



Prostate cancer

normRRprev	ELTR	pctBelow	pctSame	pctAbove
1.3	20.8	88.3	3.3	8.3
1.4	21.6	91.7	3.3	5.0
1.6	24.3	95.0	1.7	3.3
2.1	31.0	96.7	1.7	1.7
2.4	34.6	98.3	1.7	0.0

Physician Portal – Individual Patient Results

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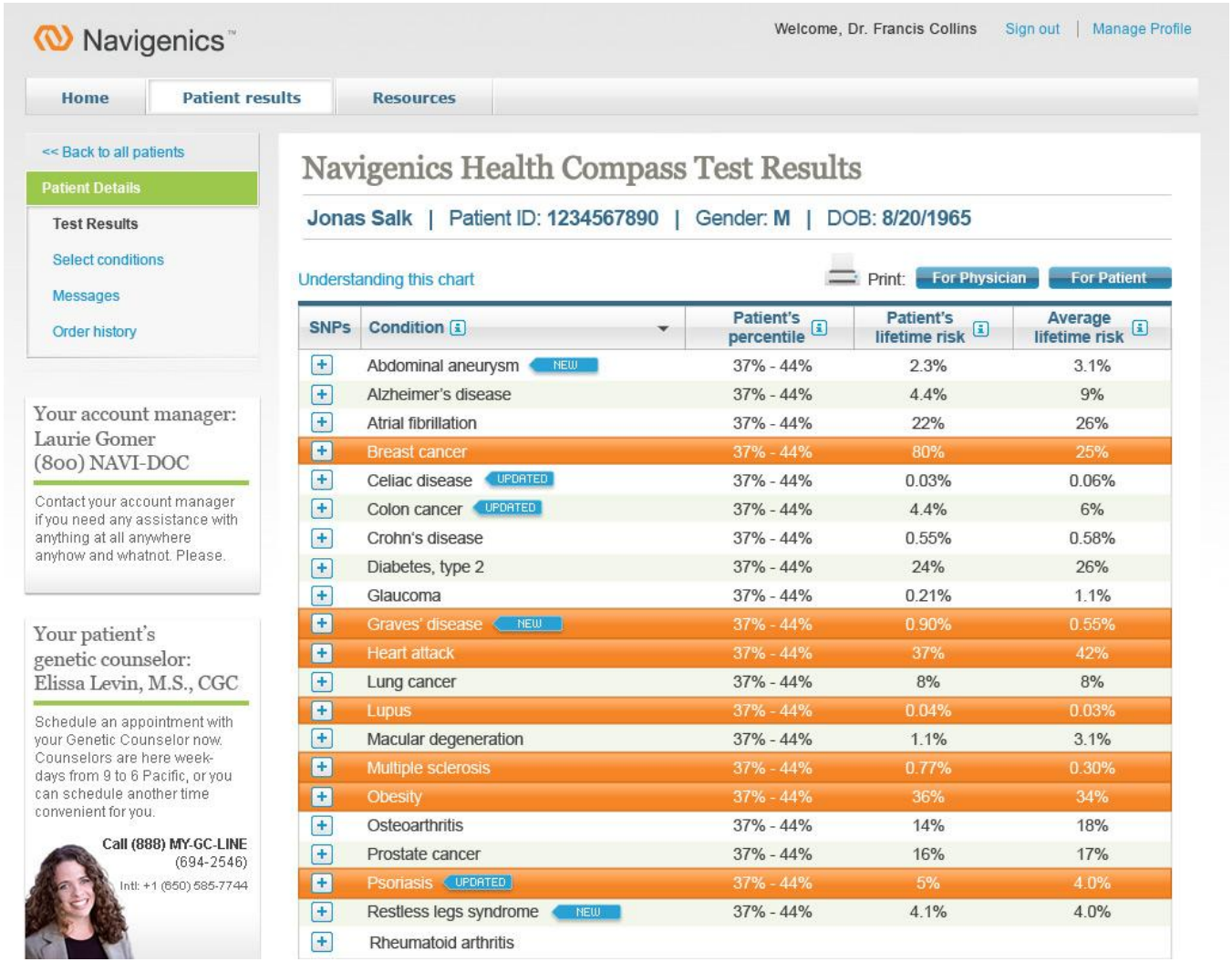

Number and Distribution of Collaborators

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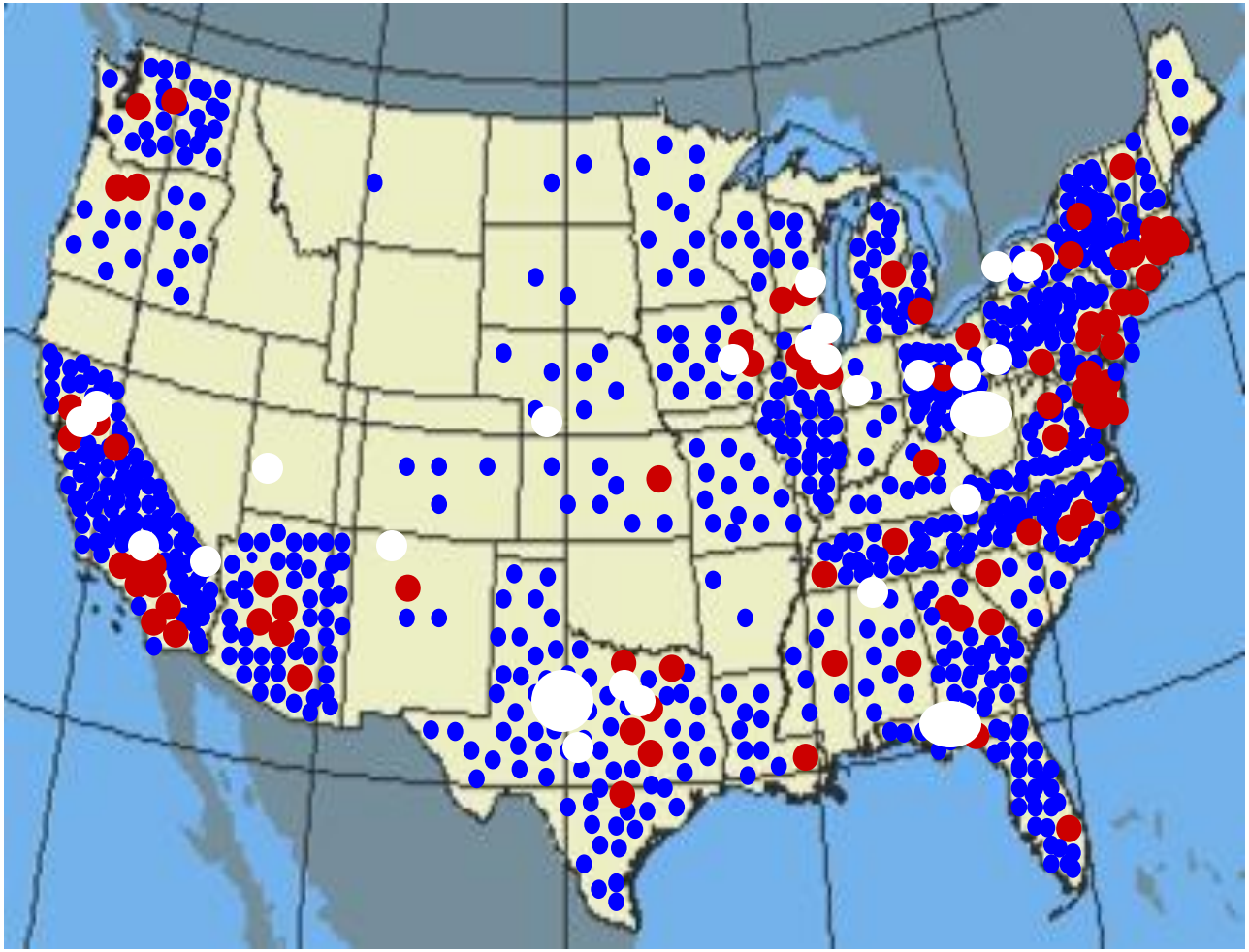

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Map Quest

New Genetic Tools May Reveal Roots Of Everyday Ills

Rapid DNA Tests Can Search Many Variations at Once; Probing Obesity, Memory

One Worry: Statistical Errors

By ANTONIO REGALADO
April 14, 2006; Page A1

In Switzerland, a group of college students and local laborers sat down for a brief memory test a couple of years ago. They were given 30 words and then asked, five minutes later, to repeat them. On average they recalled eight.

Dietrich Stephan

Last summer American scientists equipped with a powerful new gene-testing technology gave this simple test an extra twist: DNA samples of the best and worst word-recallers were flown to Phoenix, where their DNA was checked with mi chines that can scour it for 500,000 genetic variations at lightning speed.

Researchers then fed the data into a computer that compared the variations against the test scores. The goal: to identify genes that may underlie short-term memory. They hope any discoveries could be used to treat memory disorders such as Alzheimer's disease.

The project is one of dozens now using the new tools -- which include a detailed map of how DNA varies among people and sophisticated microchips that de-

THE ARIZONA REPUBLIC

RIDING TGEN MOMENTUM; INSTITUTE'S ARRIVAL TURNS VALLEY'S FOCUS TO BIOTECH

Since arriving more than two years ago, the Translational Genomics Research Institute has gotten a lot of people thinking big and thinking big.

Even before its stem research facility was ready to occupy, it spawned a bu in bio-related lab space, a push in science education and debate about a ne downtown medical school and hospital.

The goal is to turn TGen into an economic engine that could create as many as 20 biotech companies in Arizona by 2012, employing more than 12,00 workers.

"There are a lot of people out there trying to figure out bio and how it can work for them. Everyone is trying to learn together. TGen has played a hu role in that," said Stephen Chavez, a bio consultant and vice president of t Arizona Bioindustry Association.

Phoenix still flies low on the biotech radar. It has only a handful of compan in the sector and no major employers or a medical school. It has yet to cr

THE WALL STREET JOURNAL

Trail of a Killer

A Fitness Mogul, Stricken by Illness, Hunts for Genes

Study of Lou Gehrig's Disease Pinpoints DNA Variations Common to Its Sufferers

Entrepreneur's Latest Pursuit

By GAUTAM NAIK and ANTONIO REGALADO
November 30, 2006; Page A1

While water-skiing in Vietnam's Mekong Delta about two yea Augie Nieto fell several times. His muscular arms suddenly we and he couldn't haul himself up.

Augie Nieto

makers of exercise had done to deserv years old.

After an initial bout team of doctors, g Identify the genetic

In just nine months understanding of A conference in Japa deteriorating condi

U.S.News & WORLD REP

A crib-death gene?

By Elizabeth Querna
November 15, 2004

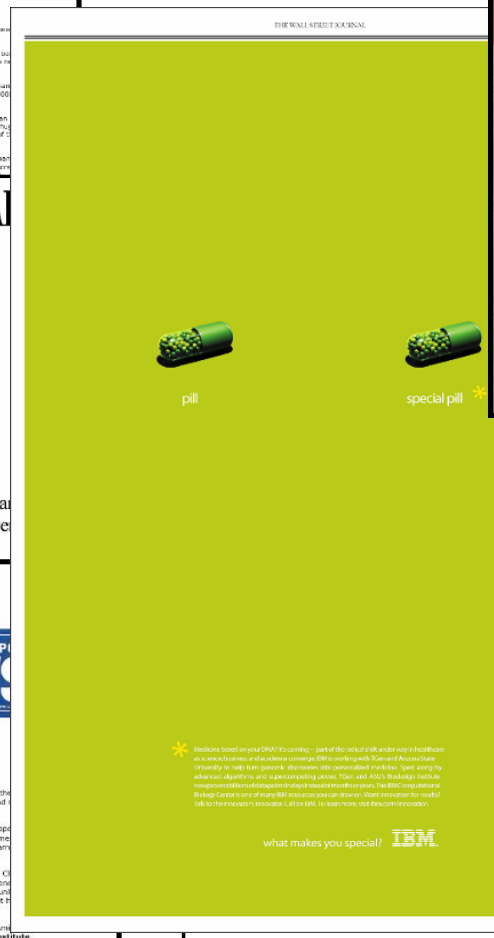
Their parents knew something was wrong. The babies cried with the staccato pitch of a goat's bleating. They had trouble breathing and easily startled.

There were other, stranger symptoms. The boys had underdevelope genitals, and some were thought to be girls, even given girls' name they were born. And then, before their first birthdays, without warn died.

This pattern was familiar to Erik Pufferberger. A geneticist at the Special Children in Strasburg, Pa., Puffenberger treats obscure gene diseases common to Pennsylvania's Amish and Mennonite communi These latest deaths are among those in an Amish community that h babies in two generations.

In a sun-drenched laboratory in Phoenix, far away from bucolic Am country, scientists at the **Translational Genomics Research Institute** analyzed tissue samples from four of the Amish babies and figured out what was happening. All of the babies who died had a mutation in a gene that regulates both genital and brain development, preventing a vital protein from developing and causing certain death.

Hereditary? Though the Amish parents knew their babies were likely to die, the deaths resembled sudden infant death syndrome, and the gene is one of a handful that scientists are now looking at to try to explain SIDS, commonly known as crib death. Babies who die from SIDS appear normal and healthy, then die suddenly, usually while they are sleeping.

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THE HEALTH ISSUE

The Fight Against Breast Cancer Expands

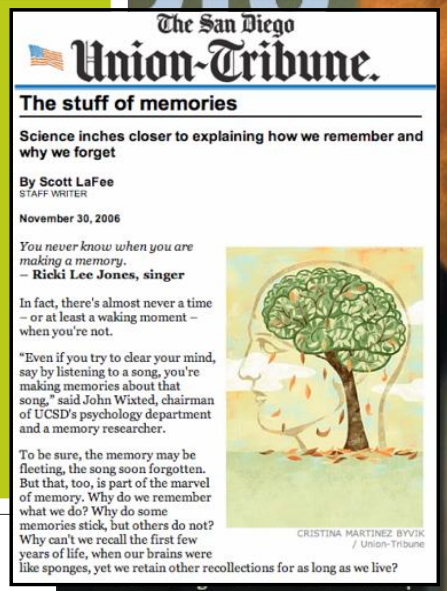
TGen's Explorers On the Verge of a Breakthrough

5 Women Who Lead Top Hospitals

Young, Smart & Addicted to Meth

SILENT SCARS: The Damage of Emotional Abuse

Raise Your Teen to Eat Right


The San Diego Union-Tribune.

The stuff of memories

Science inches closer to explaining how we remember and why we forget

By Scott LaFee
STAFF WRITER

November 30, 2006

You never know when you are making a memory.
– Ricki Lee Jones, singer

In fact, there's almost never a time – or at least a waking moment – when you're not.

"Even if you try to clear your mind, say by listening to a song, you're making memories about that song," said John Wixted, chairman of UCSD's psychology department and a memory researcher.

To be sure, the memory may be fleeting, the song soon forgotten. But that, too, is part of the marvel of memory. Why do we remember what we do? Why do some memories stick, but others do not? Why can't we recall the first few years of life, when our brains were like sponges, yet we retain other recollections for as long as we live?

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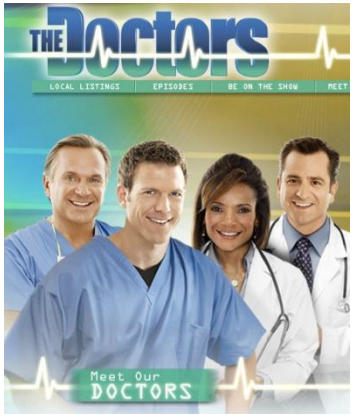

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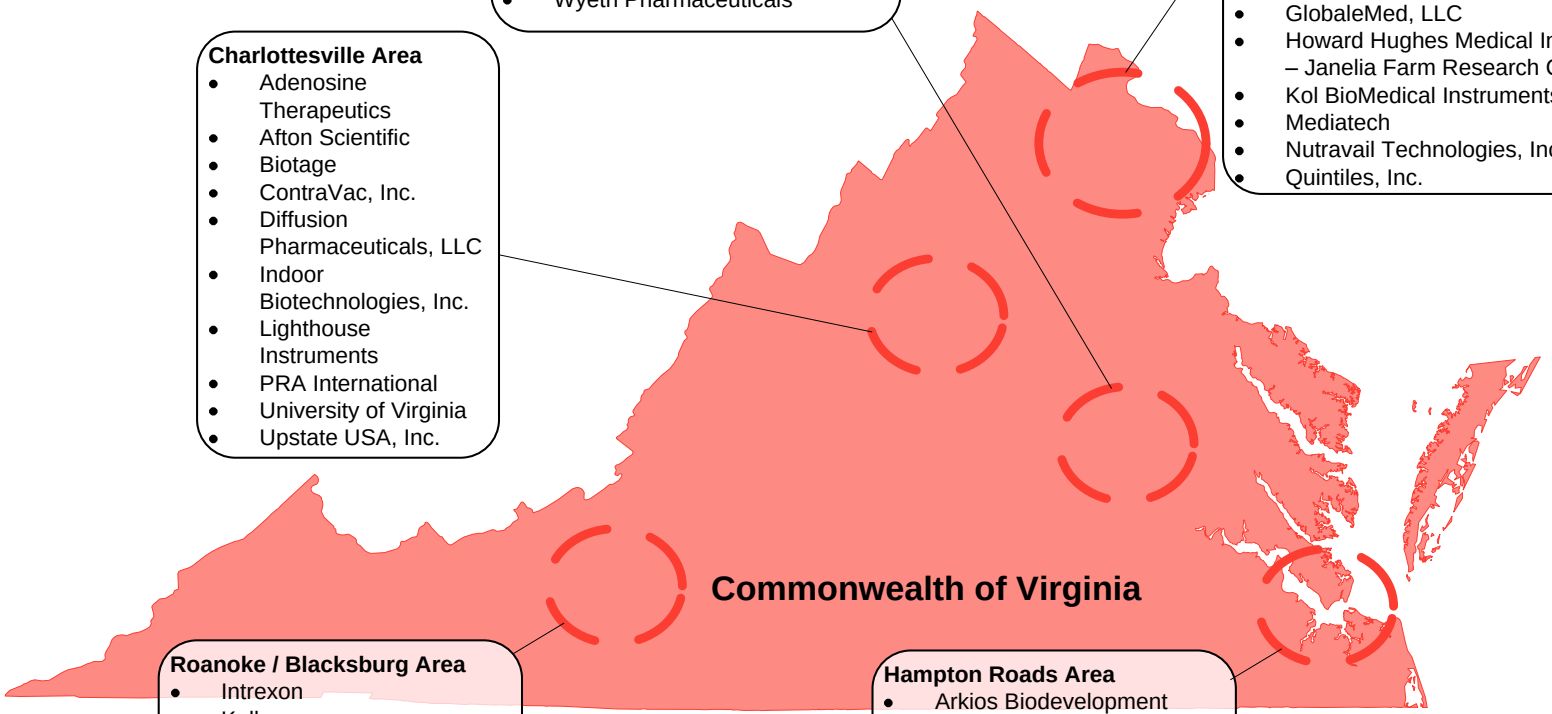

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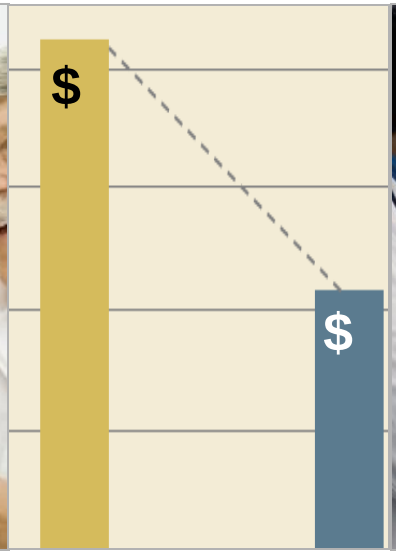
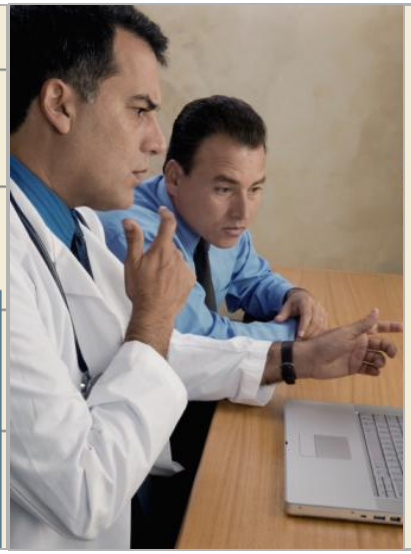
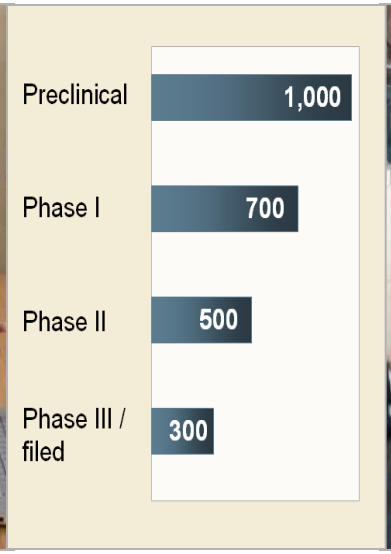
Americans living longer without disease



American health care delivering value at reduced cost



"Connected" information from bench to bedside



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