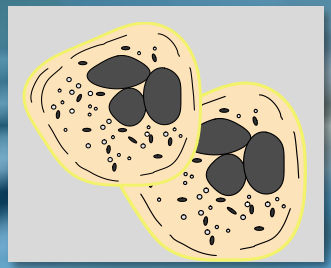
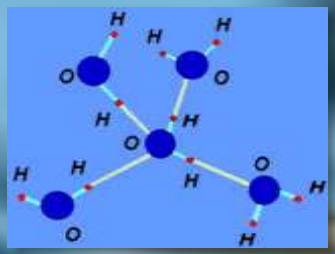
Vienna 14 june 2014
Basic research in Homeopathy
(Proposed by Verona Research Group)

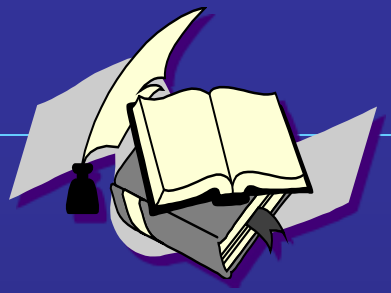
Pre-clinical research (efficacy)



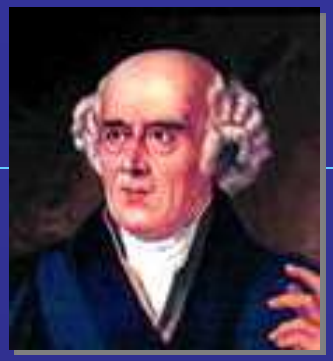
Action mechanism(s)



Physico-chemical nature



Saggio su un nuovo principio



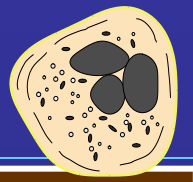
C.F.S. Hahnemann
Versuch über ein neues Princip zur Auffindung der Heilkrafte der Arzneisubstanzen -*Hufeland's Journal* 2, 381, 1796

"The true physician, whose sole aim is to perfect his art, can avail himself of no other information respecting medicines; than:

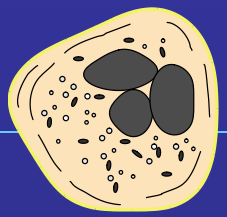
First - What is the pure action of each by itself on the human body ?

Second - What do observations of its action in this or that simple or complex disease teach us ?"

EXAMPLES OF INVERSE EFFECTS WITH HOMEOPATHIC DILUTIONS IN LABORATORY SYSTEMS



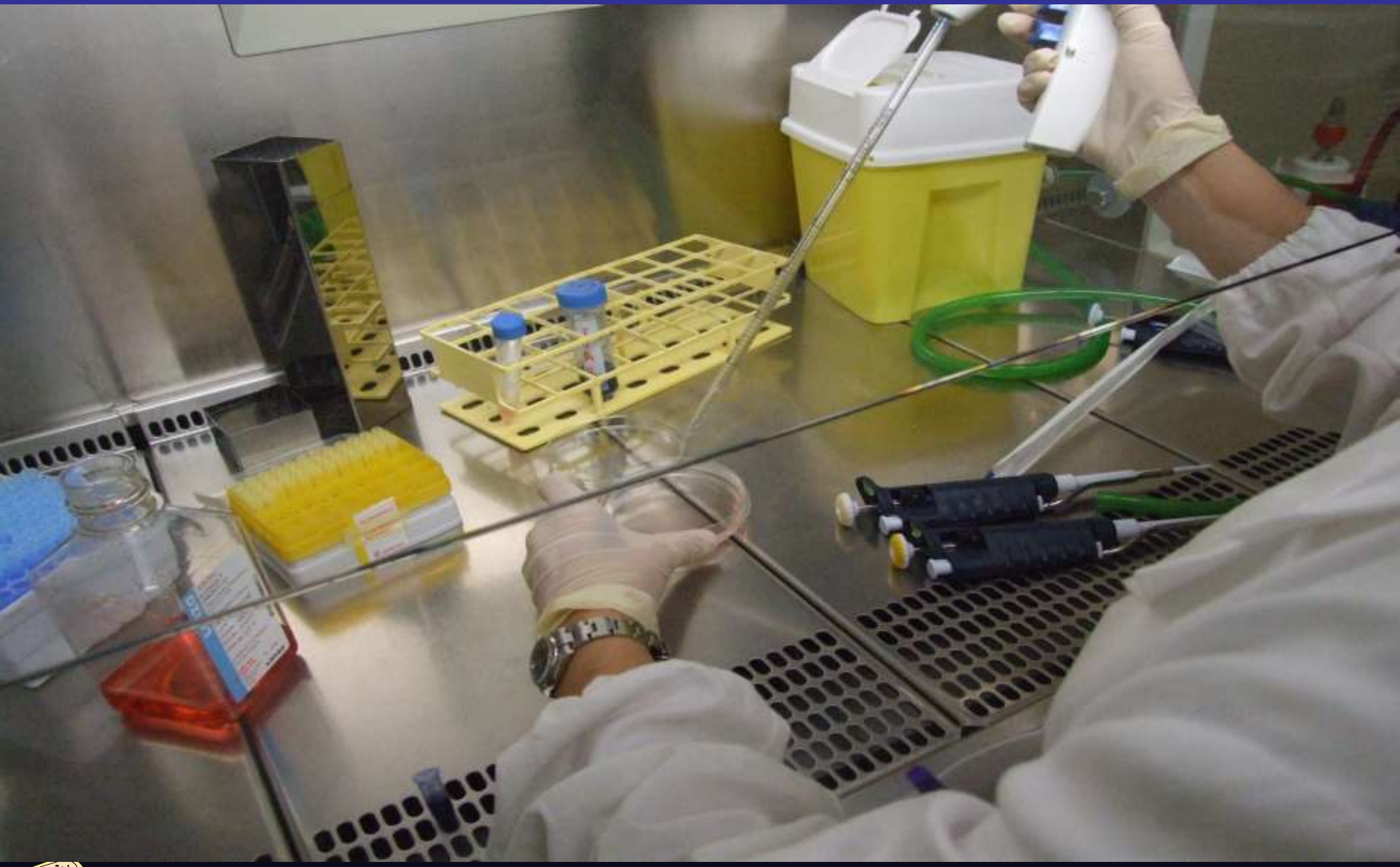
System	Agent	"High dose" effect	"Homeopathic" effect	Ref.
Basophils	Histamine Apis mellifica	Pro-inflammatory agents	Histamine (up to 60x) and Apis mellifica (10c)	Poitevin 1988, S.Laudy 1991, Belon 1996-2004
Rat, Guinea pig	Histamine Lung Histamine Apis mellifica	Pro-inflammatory agent	Histamine (30x), Lung histamine (18c) and Apis mellifica (7c/10c) reduce inflammation symptoms	Bastide 1975,Poitevin 1988, Bildet 1990 Conforti 1993
Rat, Mouse	Arsenic trioxide Arsenicum album	Whole body and liver toxicity	Arsenic trioxide (7c and 17c) and Arsenicum album (30c) protect from intoxication	Lapp 1955; Wurmser 1955; Cazin1987; Cazin 1991; Khuda-Bukhsh 1998-2000
Wheat, hepatoma cells	Arsenic trioxide (As_2O_3)	Cell toxicity	As_2O_3 40x, 42x and 45x, stimulate germination and cell vitality	Betti 1997-2000, Wiegant-van Wijk 1998-2011
Rat liver	Phosphorus	Hepatotoxicity	Phosphorus (30x) protects from toxic hepatitis	Bildet 1984, Guillemain 1987 Palmerini 1993 Gomez 1999
Tadpoles	Thyroxine	Increases the rate of metamorposis	High dilutions (up to 30x) inhibit the metamorphosis	Endler 1990-2010, Graunke 2007, Welles 2007, Lingg 2008, Weber 2008, Guedes 2011, Harrer 2013
Mouse, rat	Gelsemium sempervirens	Toxic and convulsivant	Anxiolytic effect (2C-9C)	Marrari 2010, Gahlot 2012, Meyer 2013.
Human and rat neurons	Gelsemium sempervirens	Toxic and convulsivant	No toxicity, gene down-regulation	Venard 2011, Olioso 2014, Marzotto 2014

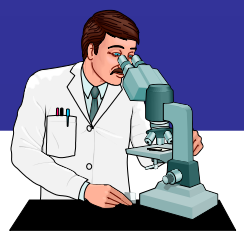


Independent repeated studies in Homeopathy – review 2010
P.C. Endler et al., Homeopathy (2010) 99, 25–36

- Five models have been reproduced by at least one independent research team with comparable results:
  1. Growth of wheat seedlings after treatment with potencies of silver nitrate,
  2. Human basophil degranulation after treatment with potencies of histamine,
  3. Amphibian metamorphosis after treatment with potencies of thyroxin or thyroidinum,
  4. Experimental hepatitis of the rat due to poisoning with carbon tetrachloride after treatment with phosphorus,
  5. Contraction of rat intestine in vitro after treatment with potencies of Atropa belladonna or atropine sulfate.

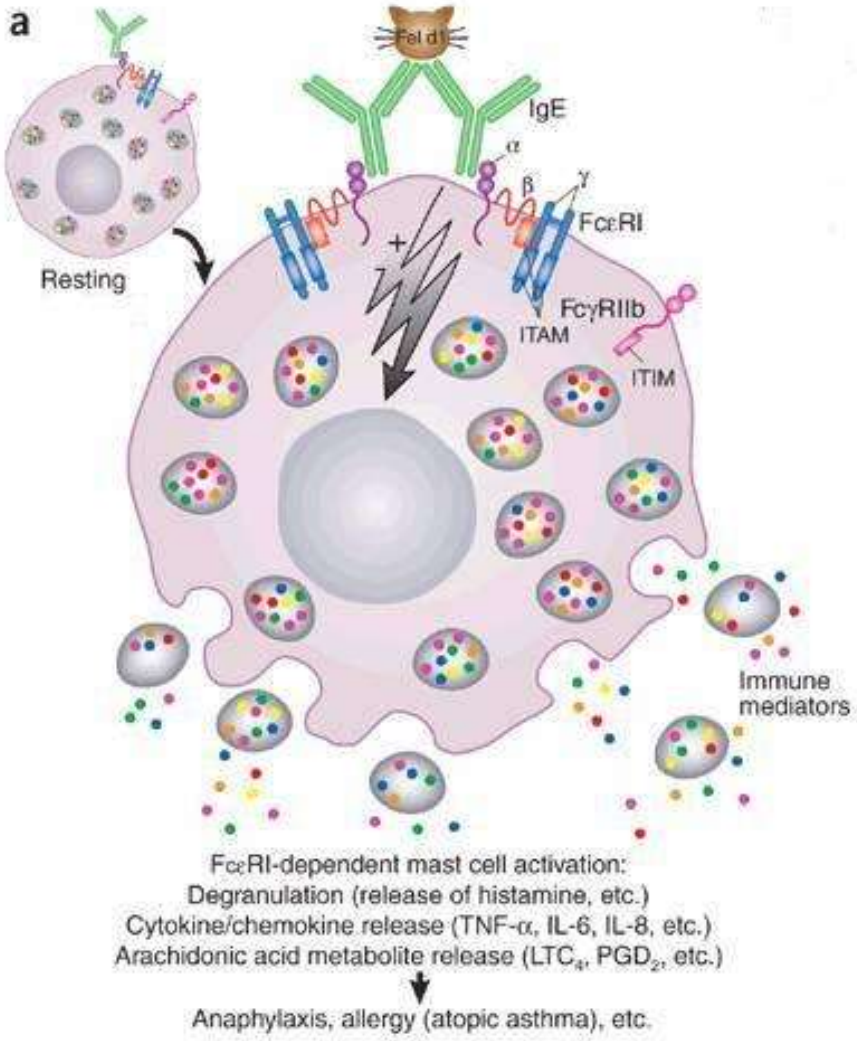
Laboratory studies





THE MODEL OF BASOPHIL ACTIVATION

(St.Laudy, Belon, Poitevin, Benveniste, Hirst, Ennis, Chirumbolo e Bellavite)



THE MODEL OF BASOPHIL ACTIVATION

Anti-IgE or allergenic compounds (conventional doses)

Membrane IgE

Histamine granules

Stimulation

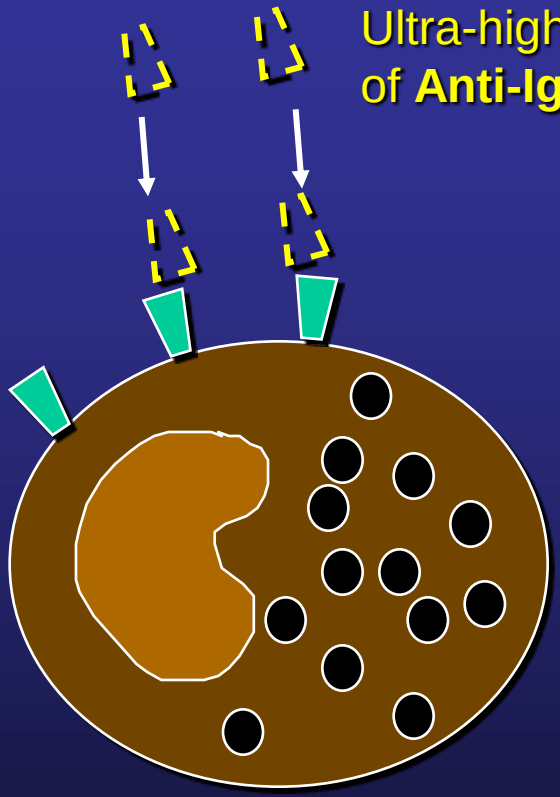
CD63
CD203c

Resting cell

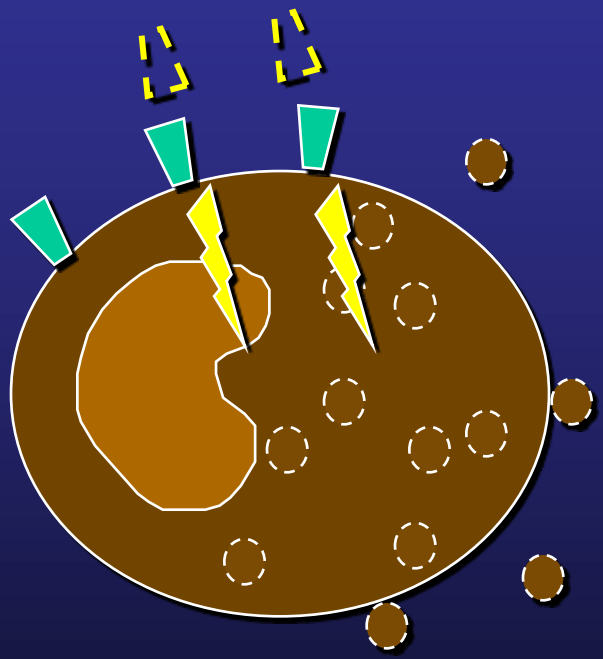
Activated cell
“Degranulation”

THE FAMOUS EXPERIMENT OF BENVENISTE (DAVENAS ET AL., NATURE1988)

Ultra-high dilution (up to 10^{-120} Moles/L) of **Anti-IgE**

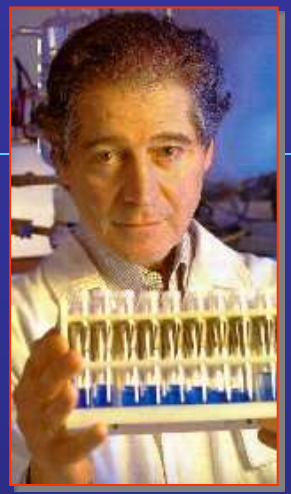


Stimulation



Resting cell

Cell activation by high dilutions

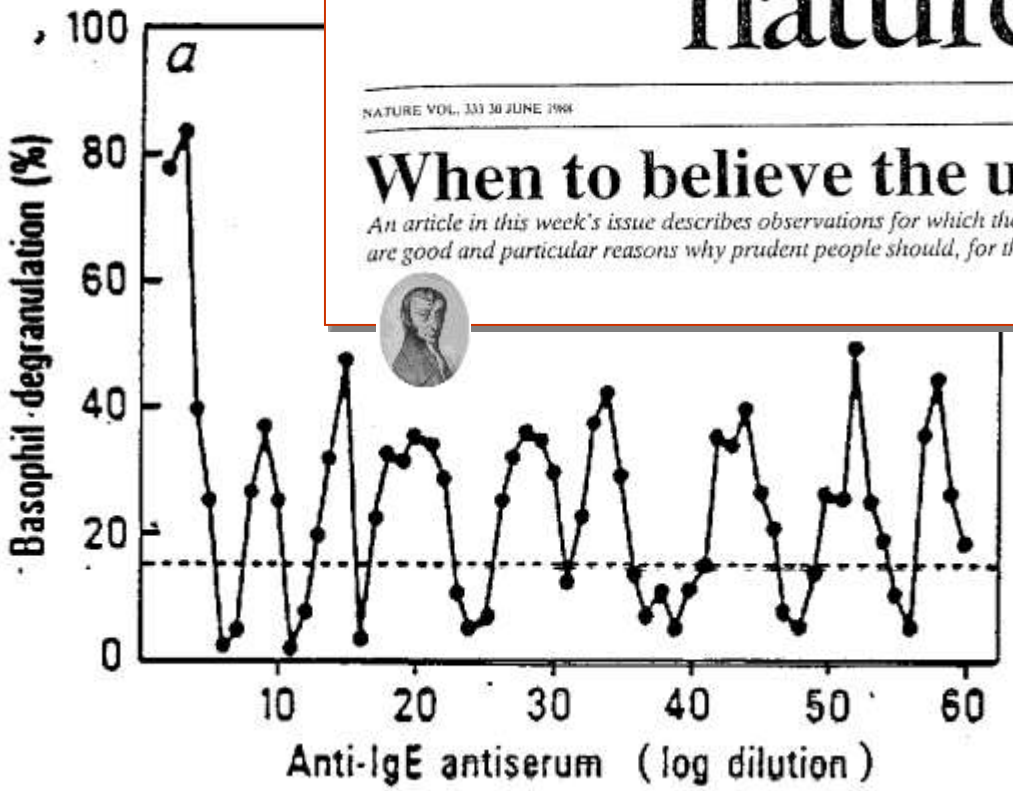


Davenas, E., Benveniste, J., et al. *Nature* 333: 816-818, 1988.

SCIENTIFIC PAPER

Human basophil degranulation triggered by very dilute antiserum against IgE

E. Davenas, F. Beauvais, J. Amara*, ...
P. Fortner§, P. Belon, J. Sainte-Laudy, ...



nature

NATURE VOL. 333 30 JUNE 1988

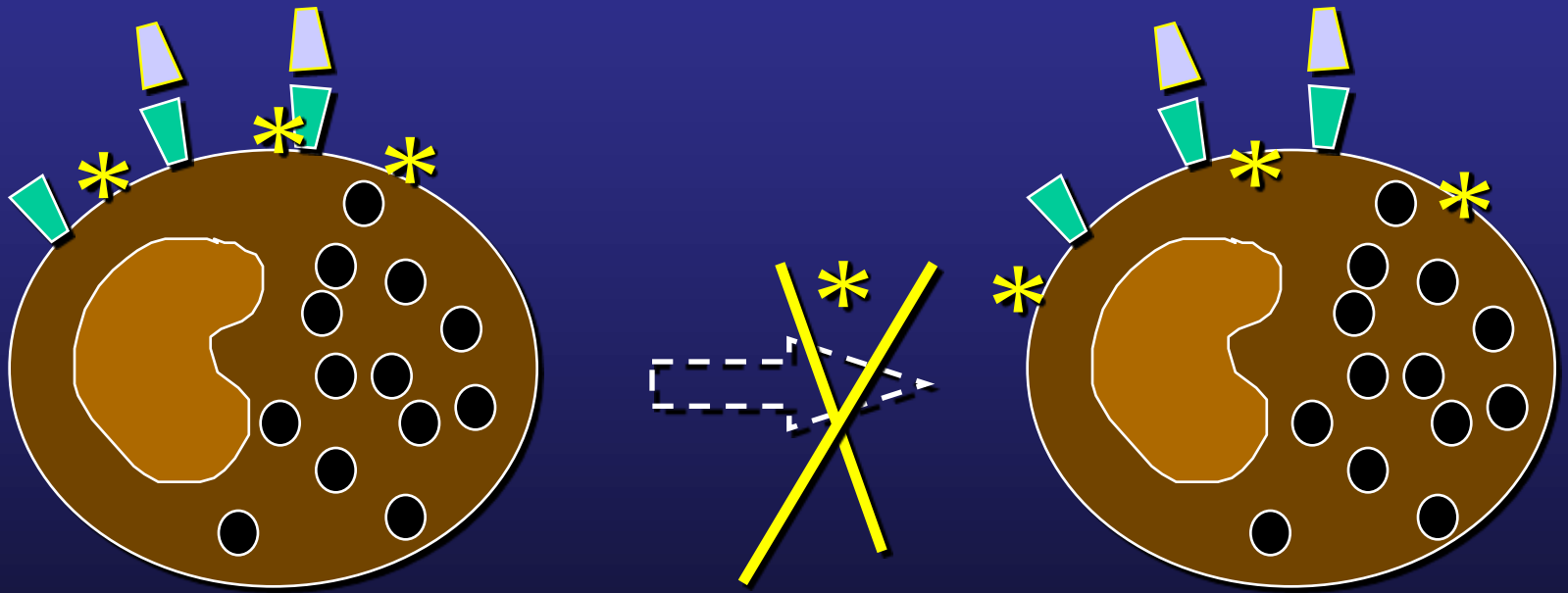
When to believe the unbelievable

An article in this week's issue describes observations for which there is no present physical basis. There are good and particular reasons why prudent people should, for the time being, suspend judgement.

EXPERIMENTS OF POITEVIN ET AL. (BR. J. CLIN. PHARM. 1988)

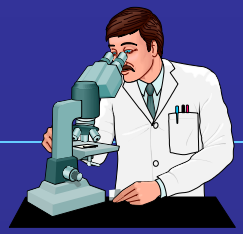
Anti-IgE
(Medium doses)

* + Homeopathic drugs
LUNG HISTAMINE (5CH, 15 CH)
APIS MELLIFICA (9CH)



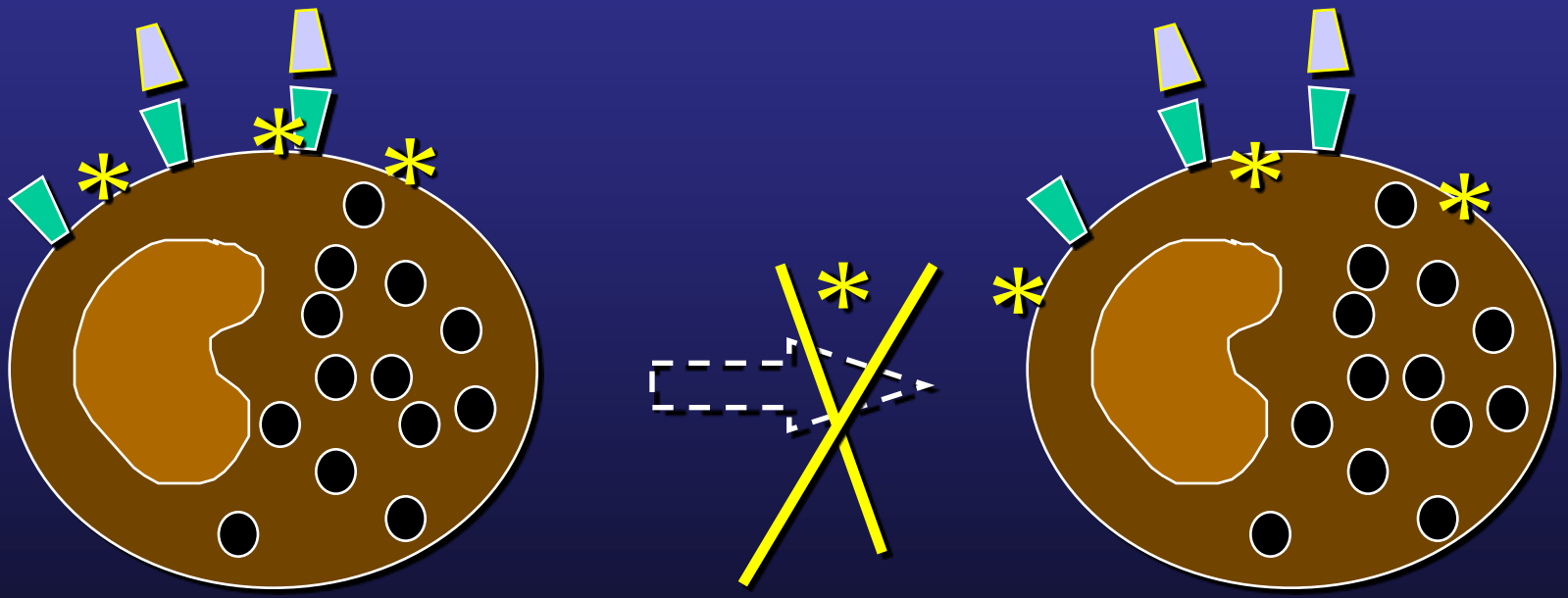
Resting cell

Inhibition of response
to Anti-IgE



* Ultra-high dilution (10^{-36} M) of **Histamine**

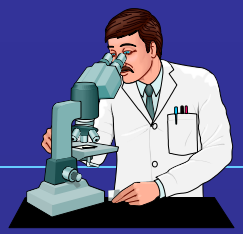
Anti-IgE
(Medium doses)



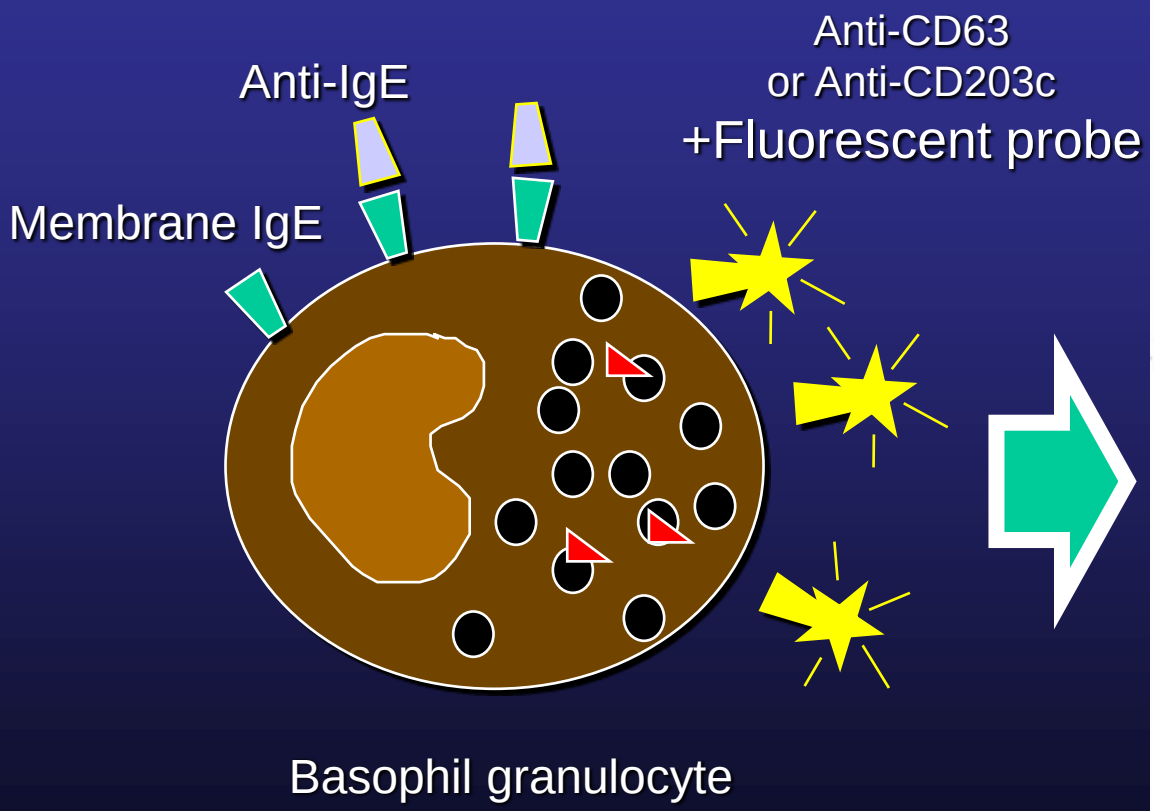
Resting cell

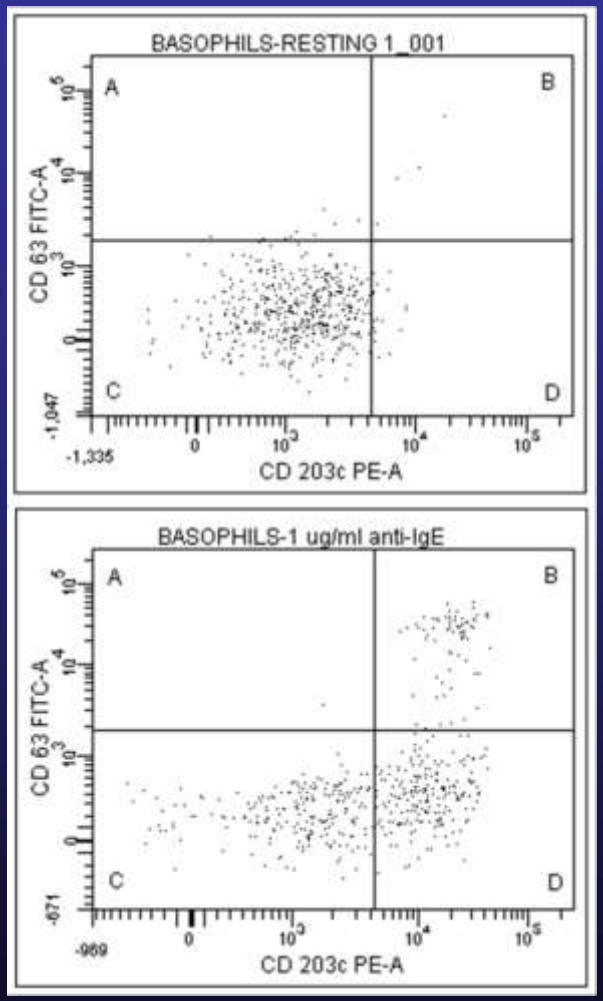
Inhibition of response to Anti-IgE

THE MODEL OF BASOPHIL ACTIVATION: Immunofluorescence



(Sainte-Laudy, Belon, Ennis, Bellavite, Mannaioni)

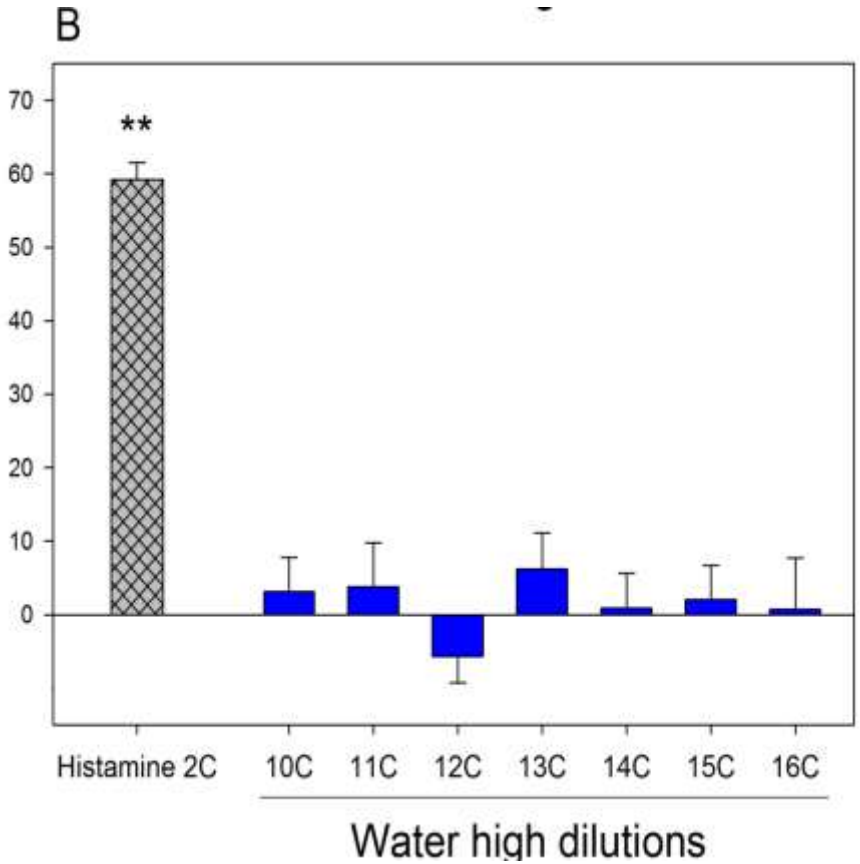




Cytofluorimetric detection

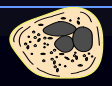
EFFECTS OF HISTAMINE AND WATER DILUTION ON CD203c

Chirumbolo , Bellavite et al., Inflammation Research 2009



Reports concerning the effect of highly diluted/succussed histamine on human basophils published in the mainstream literature (part 1 of 2)

	MAIN METHODOLOGICAL ASPECTS				RESULTS	
1st author/year (ref.)	Dilution Dynamization	Protocol of succussion	Control with dynamized water (yes/no)	Protocol/ Parameters	Effective molecular doses	Corresponding potencies
Cherruault 1989 ([1])	4C-20C (10^{-8} M-10^{-40} M), water not specif.	Not specif.	Not reported	Optical microscopy	10^{-10}-10^{-17} M e 10^{-30}-10^{-38} M	5C-9C e 15C-19C
Sainte-Laudy 1993 ([2])	10^{-14} M-10^{-38} M, water not specif.	Not specif.	Not reported	Optical microscopy	10^{-16}-10^{-22} M e 10^{-36} M	Not reported
Sainte-Laudy, 1996 ([3])	1C-20C, distilled water	Vortex	Not reported	CD63%	10^{-2} M, 10^{-4} M, 10^{-22} M, 10^{-34} M	Not reported
Belon, 1999 ([4]) (Multicentre)	15C-19C, distilled water	Vortex	Yes but not detailed	Optical microscopy	Not reported	15C-19C
Sainte-Laudy, 2000 ([5])	10C-20C, tap water	Vortex	Not reported	CD63%	10^{-30} M-10^{-34} M	15C-17C
Sainte-Laudy 2001 ([6])	13C-14C, water not specif.	Not specif.	Not reported	CD63%	Not reported	Stimulation 13C
Brown and Ennis 2001 ([7])	10^{-2} M-10^{-40} M, water not specif.	Not specif.	Not reported	CD63%	10^{-2}-10^{-6} M, 10^{-14} M, 10^{-18}-10^{-20} M, 10^{-26} M	Not reported
Lorenz 2003 ([8])	D0-D34 water for injectable use; brandy	Not specif.	Not reported	CD63-MFI	10^{-22} M, 10^{-23} M, 10^{-25}, 10^{-26} M	D10-D14



Reports concerning the effect of highly diluted/succussed histamine on human basophils published in the mainstream literature (part 2 of 2)

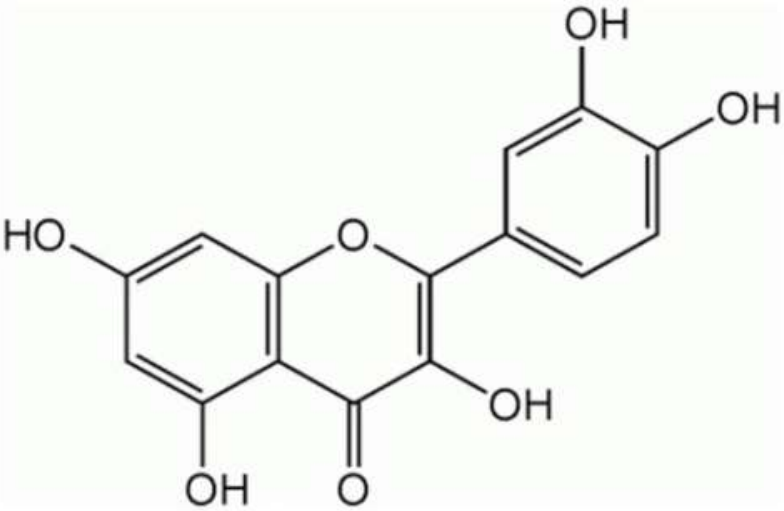
	MAIN METHODOLOGICAL ASPECTS				RESULTS	
1st author/year (ref.)	Dilution Dynamization	Protocol of succussion	Control with dynamized water (yes/no)	Protocol/ Parameters	Effective molecular doses	Corresponding potencies
Belon 2004 ([9]) (Multicentre)	2C-20C, water not specif.	Hand succussed	Not reported	Optical microscopy, CD63%	10^{-28} M-10^{36} M	14C,15C, 16C, 17C, 18C
Guggisberg 2005 ([10])	10^{-2} M-10^{-40} M distilled water	Vortex	Not reported	CD63%	10^{-2} M (and 10^{-22} M)	Not reported
Sainte-Laudy 2006 ([11])	2C-18C, deionized water	Vortex 10 sec	Yes, but not detailed	CD63%, CD203c MFI, ratio MFI 203c	10^{-4}M, 10^{-30} M e 10^{-32} M	2C, 15C, 16C
Sainte-Laudy 2006 ([12])	10^{-2} M-10^{-40} M (2C-20C),	Vortex 10 sec	Not reported	CD63%, CD203c MFI	10^{-4} M, 10^{-30} M, 10^{-32} M	2C, 15C, 16C
Sainte-Laudy 2008 ([13])	2C-16C, water deionized	Vortex 15 sec	Yes, but not detailed	CD203c index	10^{-4} M, 10^{-32} M	2C, 16C
Sainte-Laudy 2009 ([14])	2C-18C water, not specified	Not specif.	Not reported	CD203c MFI	10^{-4} M, 10^{-32} M, 10^{-34} M	2C, 16C, 17C
Chirumbolo Bellavite 2009 ([15])	2C+10C-16C distilled water (ultrapure)	Vertical succussion	Yes, detailed	CD203c MFI	10^{-4} M, 10^{-24} M, 10^{-28} M, 10^{-30} M, 10^{-32} M	2C, 12C, 14C, 15C, 16C
Mannaioni 2010(adrenaline and histamine)	2C+10C-16C distilled water (ultrapure)	Vertical succussion	Yes, detailed	CD203c, CD63 MFI	10^{-4} M, 10^{-24} M, 10^{-28} M, 10^{-30} M, 10^{-32} M	2C, 12C, 14C, 15C, 16C

Reports concerning the effect of highly diluted/succussed histamine on human basophils published in the mainstream literature

- IN SUMMARY:

- **15 publications (2 multicentre studies)**
  4 independent laboratories involved
- **13 papers with positive results**
- **1 negative**
- **1 uncertain**

QUERCETIN: A NATURAL FLAVONOL



Quercetin
(2-(3,4-diidrossifenil)- 3,5,7- triidrossi -4H- cromen-4-chetone)

Levistico (sedano di monte)
Levisticum officinalis L.

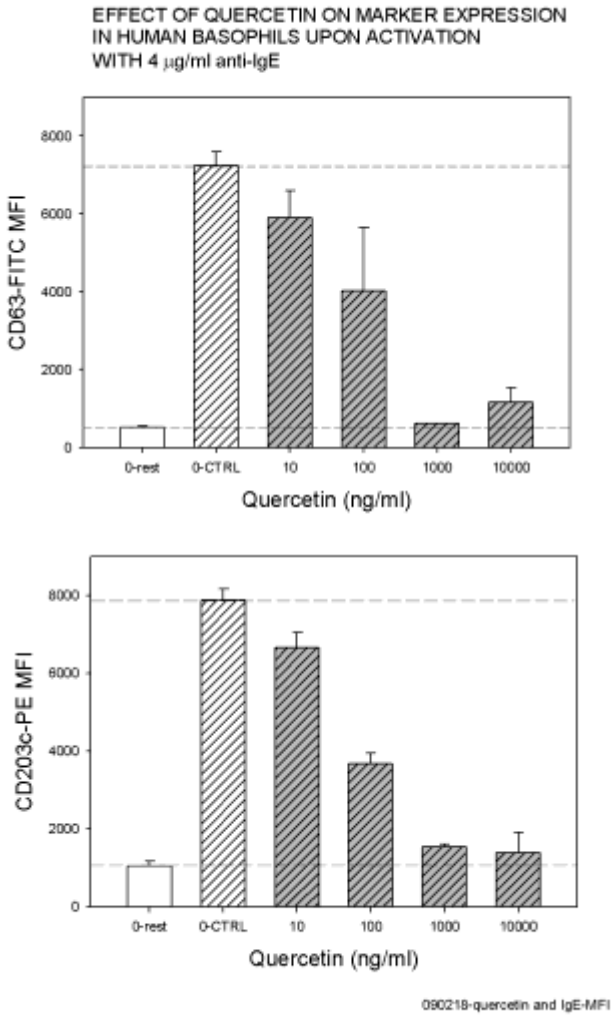
Cappero
Capparis spinosa L.

Mela
Malus communis L.

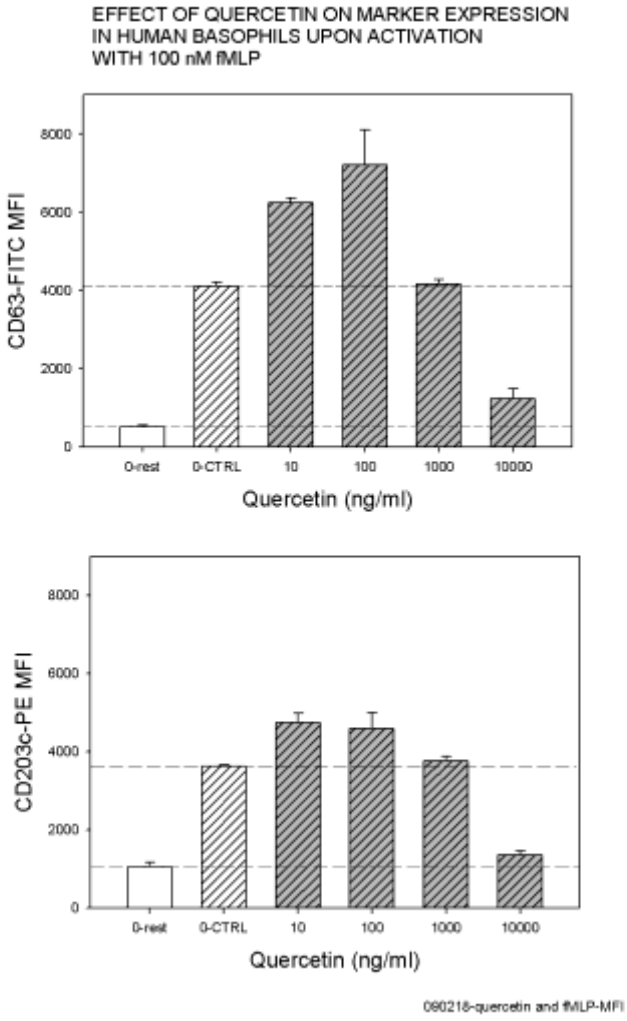
Abundant in onion (185-634 mg/kg), turnip(110-130 mg/kg), broccoli (10-68 mg/kg) e lettuce(5-30 mg/kg). Present also in apple, orange, green tea

EFFECT OF DIFFERENT DOSES OF QUERCETIN IN HUMAN BASOPHILS

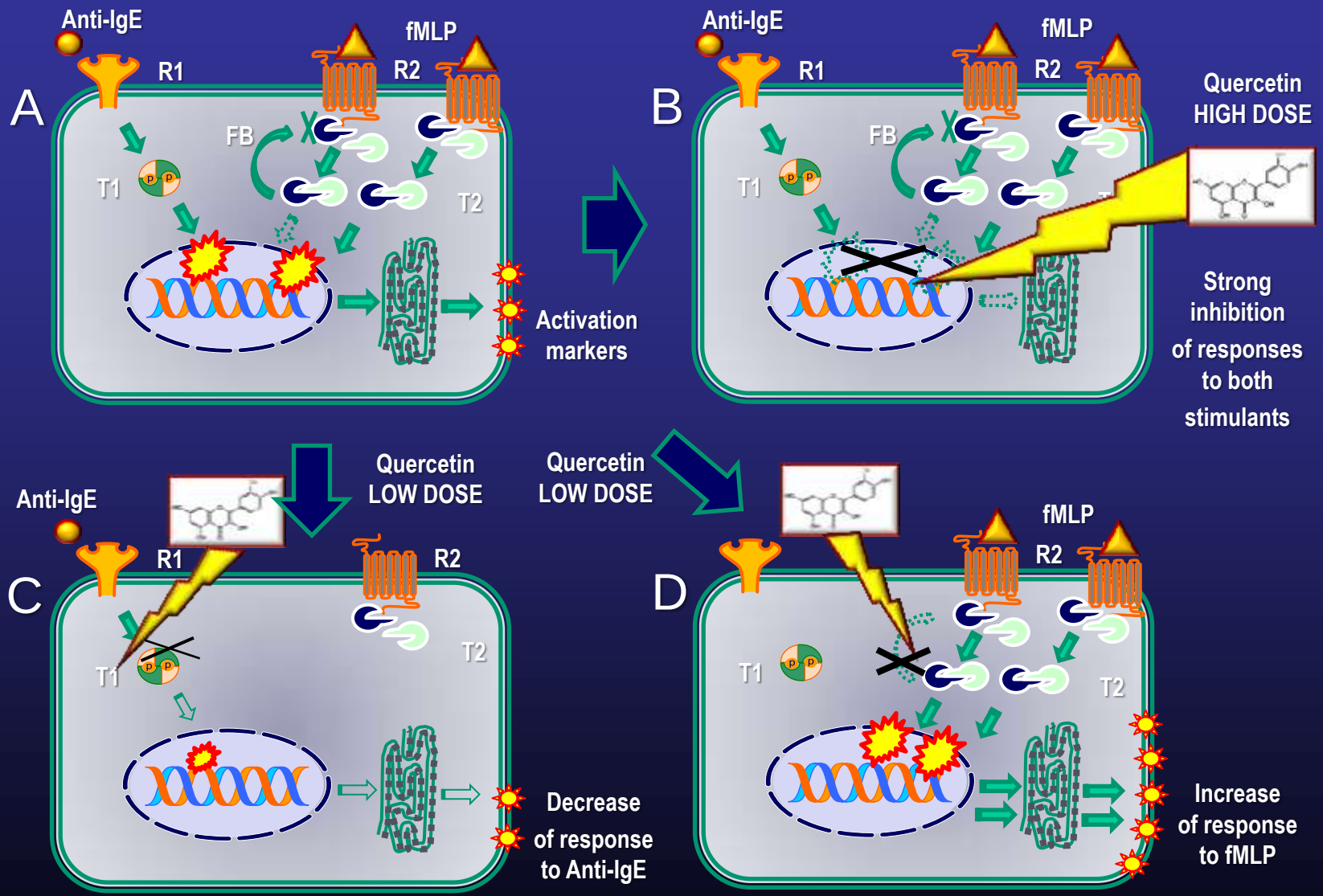
ALLERGY MODEL



INFECTION MODEL

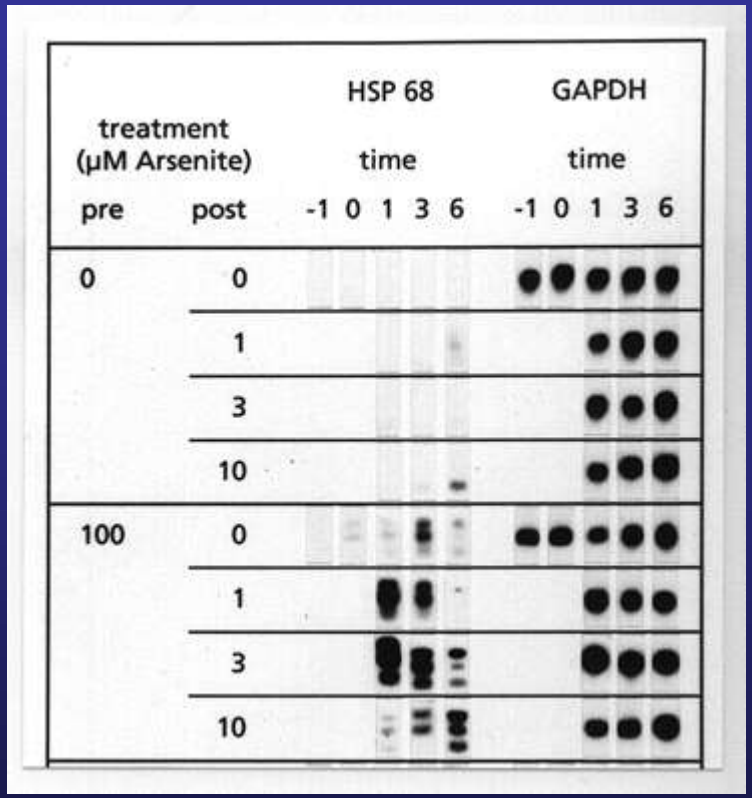


AGONIST-DEPENDENT EFFECTS OF QUERCETIN ON HUMAN BASOPHILS

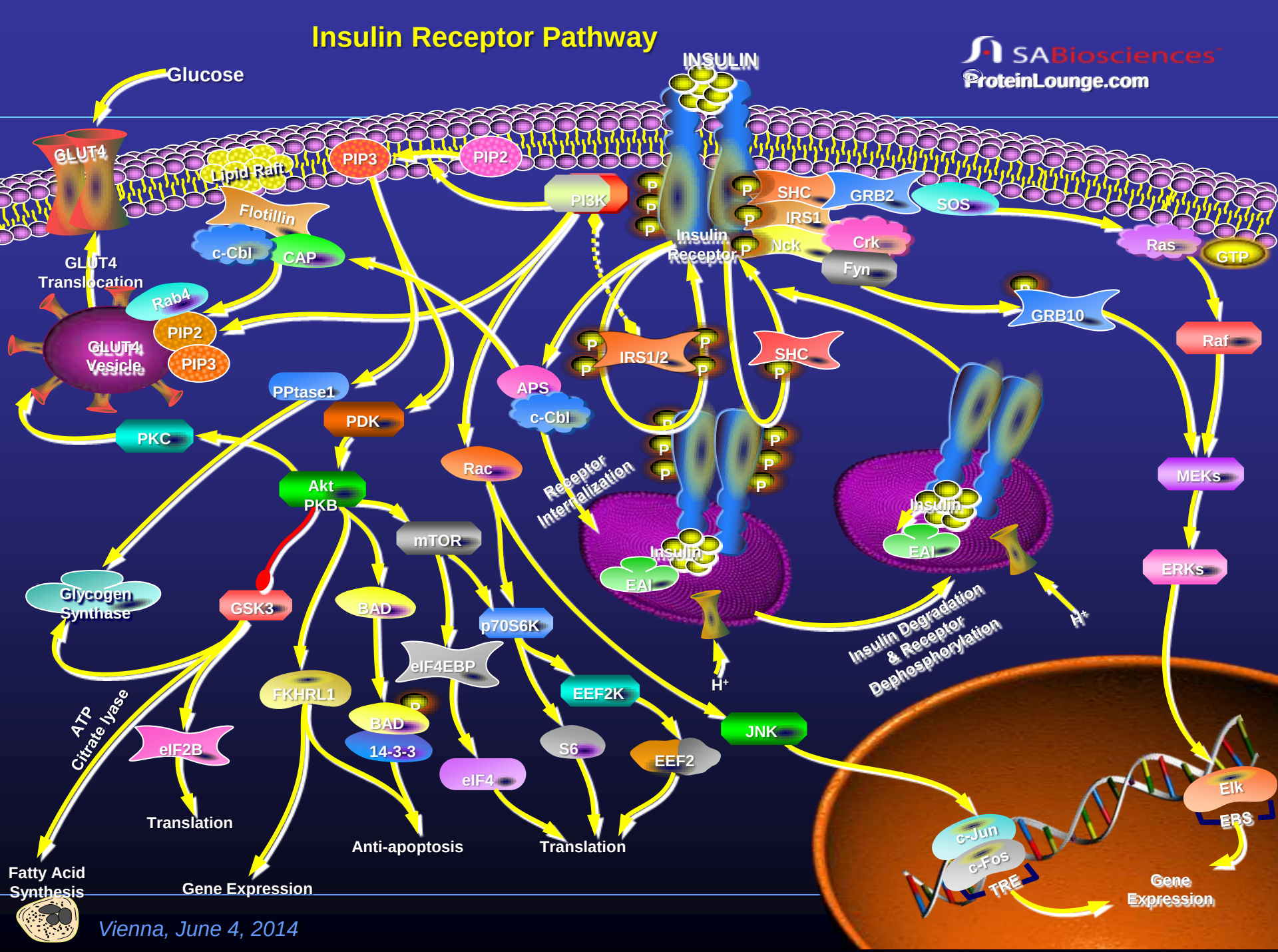


Roeland van Wijk

STIMULATION OF SELF-RECOVERY BY LOW DOSES OF ARSENITE IN ARSENITE-INTOXICATED CELLS. F.A.C. WIEGANT, R. VAN WIJK et al.

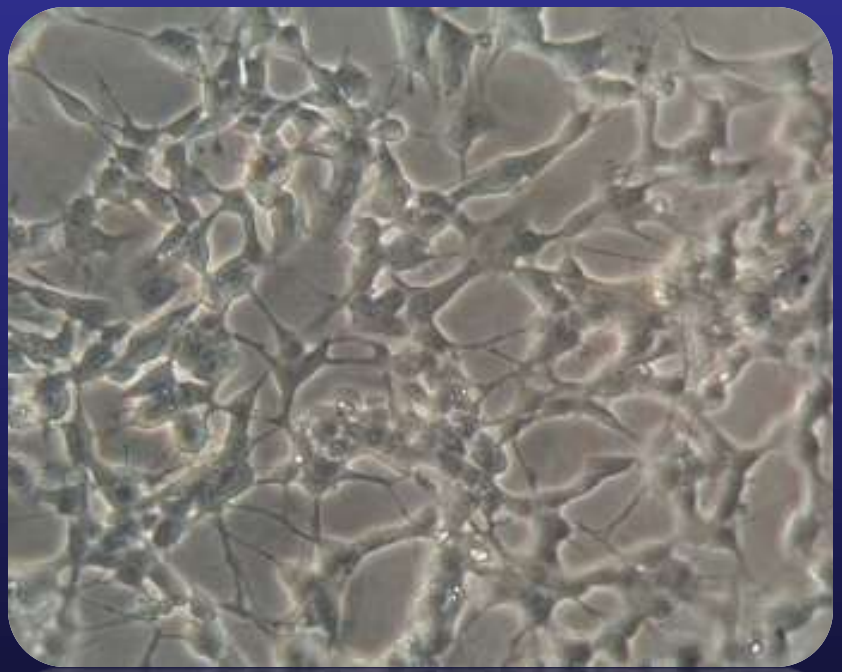


- The influence of a step-down arsenite treatment on the induction of hsp68-mRNA. H35 hepatoma cells were pretreated with 0 or 100 μM arsenite from 1 to 6 h, thoroughly washed and subsequently incubated in 0, 1, 3 or 10 μM arsenite. At the indicated times, RNA samples were prepared and processed by northern blotting and autoradiography. Autoradiograms are shown from a representative experiment made after hybridization with a radioactive hsp68 probe and a GAPDH probe.

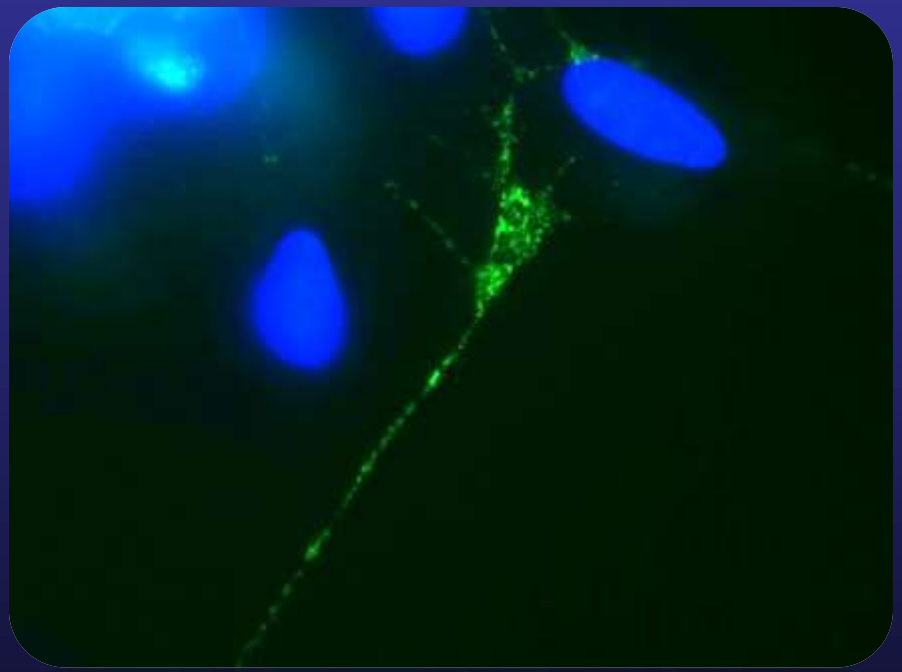

Insulin Receptor Pathway
SABiosciences
ProteinLounge.com
INSULIN
Glucose
GLUT4
Lipid Raft
Flotillin
c-Cbl
CAP
PIP3
PIP2
PI3K
Insulin Receptor
SHC
GRB2
SOS
IRS1
Nck
Crk
Fyn
Ras
GTP
GRB10
Raf
MEKs
ERKs
GLUT4 Translocation
GLUT4 Vesicle
Rab4
PIP2
PIP3
PPtase1
PDK
PKC
Akt PKB
mTOR
Rac
APS
c-Cbl
IRS1/2
SHC
Receptor Internalization
Insulin
EAI
Insulin Degradation & Receptor Dephosphorylation
H+
Glycogen Synthase
GSK3
BAD
p70S6K
eIF4EBP
FKHRL1
BAD
14-3-3
EEF2K
S6
EEF2
eIF4
JNK
ATP Citrate lyase
eIF2B
Translation
Anti-apoptosis
Translation
Fatty Acid Synthesis
Gene Expression
c-Jun
c-Fos
TRE
Elk
ERS
Gene Expression
Vienna, June 4, 2014

Neurocyte model system

SHSY5Y neurocytes-human neuroblastoma cells



Inverted microscope image



Confocal immunofluorescent image

Marzotto et al. BMC Complementary and Alternative Medicine 2014, 14:104
http://www.biomedcentral.com/1472-6882/14/104

BMC Complementary & Alternative Medicine

RESEARCH ARTICLE Open Access

Extreme sensitivity of gene expression in human SH-SY5Y neurocytes to ultra-low doses of *Gelsemium sempervirens*

Marta Marzotto[1], Debora Olioso[1], Maurizio Brizzi[2], Paola Tononi[3], Mirco Cristofoletti[1] and Paolo Bellavite[1*]

Abstract

Background: *Gelsemium sempervirens* L. (*Gelsemium s.*) is a traditional medicinal plant, employed as an anxiolytic at ultra-low doses and animal models recently confirmed this activity. However the mechanisms by which it might operate on the nervous system are largely unknown. This work investigates the gene expression of a human neurocyte cell line treated with increasing dilutions of *Gelsemium s.* extract.

Methods: Starting from the crude extract, six 100 × (centesimal, c) dilutions of *Gelsemium s.* (2c, 3c, 4c, 5c, 9c and 30c) were prepared according to the French homeopathic pharmacopoeia. Human SH-SY5Y neuroblastoma cells were exposed for 24 h to test dilutions, and their transcriptome compared by microarray to that of cells treated with control vehicle solutions.

Results: Exposure to the *Gelsemium s.* 2c dilution (the highest dose employed, corresponding to a gelsemine concentration of 6.5×10^{-9} M) significantly changed the expression of 56 genes, of which 49 were down-regulated and 7 were overexpressed. Several of the down-regulated genes belonged to G-protein coupled receptor signaling pathways, calcium homeostasis, inflammatory response and neuropeptide receptors. Fisher exact test, applied to the group of 49 genes down-regulated by *Gelsemium s.* 2c, showed that the direction of effects was significantly maintained across the treatment with high homeopathic dilutions, even though the size of the differences was distributed in a small range.

Conclusions: The study shows that *Gelsemium s.*, a medicinal plant used in traditional remedies and homeopathy, modulates a series of genes involved in neuronal function. A small, but statistically significant, response was detected even to very low doses/high dilutions (up to 30c), indicating that the human neurocyte genome is extremely sensitive to this regulation.

Microarray analysis of gene expression changes in human neurocytes

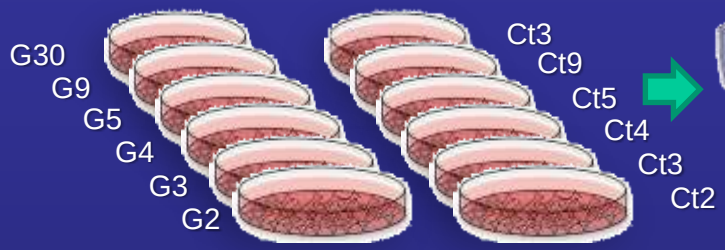
Extreme sensitivity of gene expression in human SH-SY5Y neurocytes to ultra-low doses of Gelsemium sempervirens

BMC Complement Altern Med. 2014 Mar 19;14(1):104.

Marta Marzotto, Debora Olioso, Maurizio Brizzi, Paola Tononi, Mirco Cristofoletti,Paolo Bellavite

Microarray analysis of gene expression changes in human neurocytes

24h



Gelsemium s. dilutions (G)

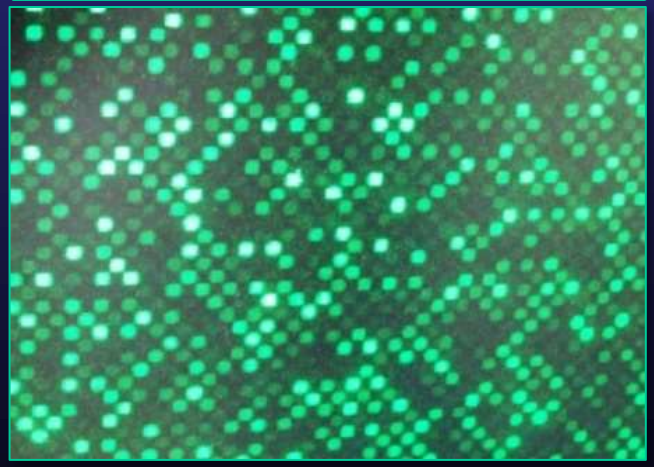
Control Dilutions (Ct)

RNA →cDNA

12-samples microarray chip

4 independent replicate experiments

- **NimbleGen chip**
- Entire human transcriptome **(45034 genes!)**



Scanning and data analysis

BMC-Complementary Alternative Medicine March 2014

Exposure to the Gelsemium s. 2CH promoted the significant down-expression of 49 while 7 genes were overexpressed

	Gene ID	Transcript ID	Symbol	Log2 fold change			p^1	Description
DOWN	7940	AF000424	LST1	-0.84	±	0.14	0.04	leukocyte specific transcript 1
	390113	NM_001004726	OR4X1	-0.83	±	0.06	0.01	olfactory receptor, family 4, subfamily X, member 1
	23746	AJ830742	AIPL1	-0.82	±	0.16	0.04	aryl hydrocarbon receptor interacting protein-like 1
	284498	AL833920	C1orf167	-0.80	±	0.17	0.05	chromosome 1 open reading frame 167
	221191	AK058068	Klkbl4	-0.79	±	0.12	0.04	plasma kallikrein-like protein 4
	26658	NM_012377	OR7C2	-0.77	±	0.07	0.01	olfactory receptor, family 7, subfamily C, member 2
	112401	BC039318	BIRC8	-0.76	±	0.11	0.00	baculoviral IAP repeat-containing 8
	2848	NM_005298	GPR25	-0.75	±	0.15	0.02	G protein-coupled receptor 25
	55803	NM_018404	ADAP2	-0.75	±	0.11	0.02	ArfGAP with dual PH domains 2
	386676	NM_198690	KRTAP10-9	-0.73	±	0.12	0.04	keratin associated protein 10-9
	4353	X04876	MPO	-0.72	±	0.15	0.04	Myeloperoxidase
	N/A	AY358413	N/A	-0.71	±	0.18	0.02	Homo sapiens clone DNA59853 trypsin inhibitor
	392391	NM_001001923	OR5C1	-0.71	±	0.05	0.04	olfactory receptor, family 5, subfamily C, member 1
	N/A	AK094115	N/A	-0.70	±	0.11	0.04	Homo sapiens cDNA FLJ36796 fis, clone ADRGL2006817
	55287	BC020658	TMEM40	-0.70	±	0.15	0.02	transmembrane protein 40
	54209	NM_018965	TREM2	-0.69	±	0.10	0.02	triggering receptor expressed on myeloid cells 2
	150365	AK097834	RP5-821D11.2	-0.68	±	0.17	0.02	similar to mouse meiosis defective 1 gene
	400934	NM_207478	FLJ44385	-0.68	±	0.09	0.04	FLJ44385 protein
	255061	NM_170685	TAC4	-0.67	±	0.14	0.01	tachykinin 4 (hemokinin)
	644065	XM_931993	LOC644065	-0.65	±	0.23	0.04	hypothetical protein LOC644065
	1339	NM_005205	COX6A2	-0.64	±	0.17	0.01	cytochrome c oxidase subunit VIa polypeptide 2
	N/A	AK128093	N/A	-0.63	±	0.09	0.04	Homo sapiens cDNA FLJ46214 fis, clone TESTI4012623.
	53841	AY358368	CDHR5	-0.63	±	0.11	0.04	mucin-like protocadherin
	9332	NM_004244	CD163	-0.63	±	0.18	0.03	CD163 molecule
	441239	XM_499305	LOC441239	-0.63	±	0.22	0.05	hypothetical gene supported by BC063653
	7164	NM_001003397	TPD52L1	-0.62	±	0.09	0.02	tumor protein D52-like 1
	11136	NM_014270	SLC7A9	-0.62	±	0.09	0.04	solute carrier family 7 member 9
	389084	NM_206895	UNQ830	-0.62	±	0.11	0.04	ASCL830
	400224	XM_375090	FLJ44817	-0.62	±	0.20	0.04	similar to pleckstrin homology domain protein (5V327)
	647240	XM_934559	LOC647240	-0.60	±	0.06	0.00	hypothetical protein LOC647240
	846	BC104999	CASR	-0.59	±	0.06	0.00	calcium-sensing receptor
	116123	NM_138784	RP11-45J16.2	-0.58	±	0.09	0.04	flavin-containing monooxygenase pseudogene
	644280	XM_497769	LOC644280	-0.58	±	0.06	0.05	hypothetical protein LOC644280
	57452	AB032956	GALNTL1	-0.57	±	0.17	0.05	alpha-D-galactosamine N-acetylgalactosaminyltransferase
	414301	NM_001001711	DDI1	-0.56	±	0.11	0.04	DDI1, DNA-damage inducible 1, homolog 1 (*S. cerevisiae*)
	116535	BC016964	MRGPRF	-0.55	±	0.17	0.01	MAS-related GPR, member F
	8811	NM_003857	GALR2	-0.55	±	0.07	0.04	galanin receptor 2
	10880	NM_006686	ACTL7B	-0.55	±	0.12	0.04	actin-like 7B
	6368	NM_145898	CCL23	-0.55	±	0.11	0.05	chemokine (C-C motif) ligand 23
	64581	BC071746	CLEC7A	-0.54	±	0.08	0.04	C-type lectin domain family 7, member A
	644003	XM_927256	LOC644003	-0.54	±	0.11	0.04	similar to Mucin-2 precursor (Intestinal mucin 2)
	643514	XM_931594	LOC643514	-0.54	±	0.10	0.03	hypothetical protein LOC643514
	374569	XM_935431	LOC374569	-0.54	±	0.07	0.04	Similar to Lysophospholipase
	84504	BC101635	NKX6-2	-0.53	±	0.13	0.03	NK6 transcription factor related, locus 2 (Drosophila)
	732	NM_000066	C8B	-0.53	±	0.06	0.05	complement component 8, beta polypeptide
	146336	NM_182510	FLJ32252	-0.52	±	0.03	0.01	hypothetical protein FLJ32252
	150763	BC042847	LOC150763	-0.51	±	0.10	0.04	hypothetical protein LOC150763
	2020	NM_001427	EN2	-0.51	±	0.08	0.04	engrailed homolog 2
	646258	XM_929203	LOC646258	-0.51	±	0.11	0.04	hypothetical protein LOC646258
UP	154872	NM_001024603	LOC154872	0.51	±	0.10	0.03	hypothetical LOC154872
	400866	NM_001001789	C21orf24	0.52	±	0.12	0.05	chromosome 21 open reading frame 24
	9457	NM_020482	FHL5	0.55	±	0.19	0.04	four and a half LIM domains 5
	55816	NM_018431	DOK5	0.56	±	0.04	0.03	docking protein 5
	1446	NM_001890	CSN1S1	0.57	±	0.09	0.04	casein alpha s1
	285600	AK130941	KIAA0825	0.63	±	0.06	0.01	KIAA0825 protein
	57538	NM_020778	ALPK3	0.76	±	0.10	0.01	alpha-kinase 3

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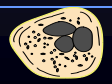
Top enriched annotation terms associated with the 56 genes differentially expressed upon exposure to *Gelsemium s.* 2c in SH-SY5Y cells.

Many of these 56 genes belong to:

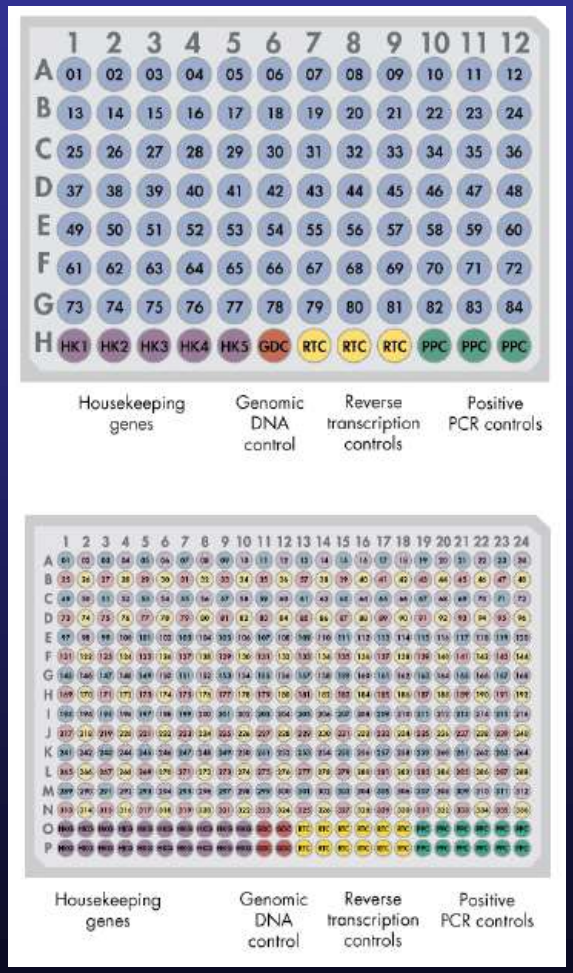
- neuropeptide/receptor systems
- calcium signalling
- G-protein coupled transduction systems
- inflammatory pathways

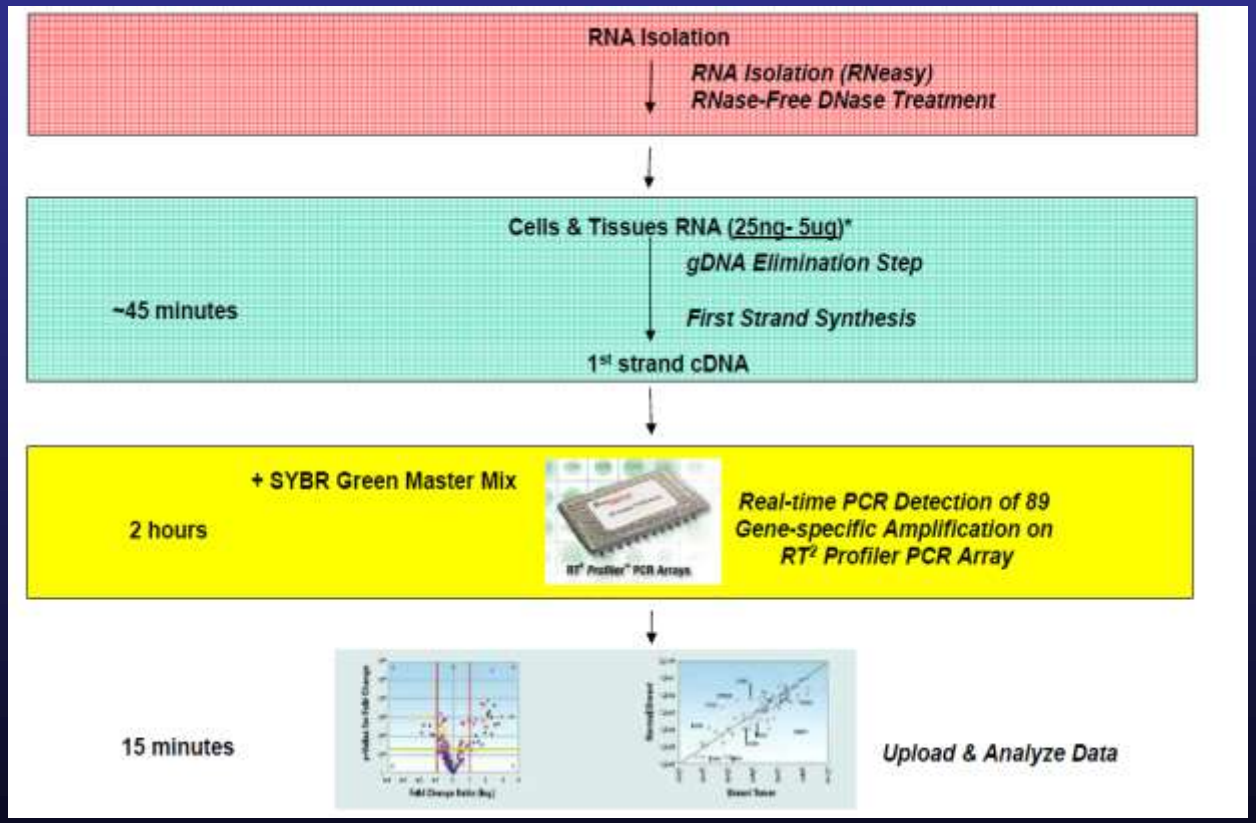
Category	Annotation Term	P value	Genes	Fold Enrichment
SP_PIR_KEYW	receptor	8.32E-11	AIPL1, OR4X1, CASR, OR5C1, GPR25, GALR2, OR7C2, MRGPRF, CLEC7A, TREM2	3.68
GOTERM_BP_FAT	GO:0007186~G-protein coupled receptor protein signalling pathway	6.60E-11	OR4X1, CASR, OR5C1, CCL23, GPR25, GALR2, OR7C2, MRGPRF, TAC4	4.17
GOTERM_BP_FAT	GO:0007166~cell surface receptor linked signal transduction	0.001	OR4X1, CASR, OR5C1, CCL23, DOK5, GPR25, GALR2, OR7C2, MRGPRF, CLEC7A, TAC4	0.08
GOTERM_BP_FAT	GO:0051606~detection of stimulus	0.02	AIPL1, CASR, CLEC7A	13.23
INTERPRO	IPR017452:GPCR, rhodopsin-like superfamily	0.009	OR4X1, OR5C1, GPR25, GALR2, OR7C2, MRGPRF	4.44
KEGG_PATHWAY	hsa04740:Olfactory transduction	0.09	OR4X1, OR5C1, OR7C2	5.31
GOTERM_BP_FAT	GO:0006954~inflammatory response	0.02	C8B, CCL23, CLEC7A, CD163	6.40
GOTERM_BP_FAT	GO:0006952~defense response	0.02	C8B, CCL23, MPO, CLEC7A, CD163	4.23
GOTERM_BP_FAT	GO:0006955~immune response	0.03	C8B, CCL23, LST1, CLEC7A, TREM2	3.77
GOTERM_BP_FAT	GO:0006874~cellular calcium ion homeostasis	0.04	CASR, CCL23, GALR2	8.53
GOTERM_BP_FAT	GO:0030182~neuron differentiation	0.04	LST1, NKX6-2, GALR2, EN2	4.75
GOTERM_CC_FAT	GO:0005886~plasma membrane	0.02	CASR, OR5C1, SLC7A9, MRGPRF, CDHR5, CD163, C8B, OR4X1, ADAP2, GALR2, GPR25, OR7C2, CLEC7A, TREM2	1.65



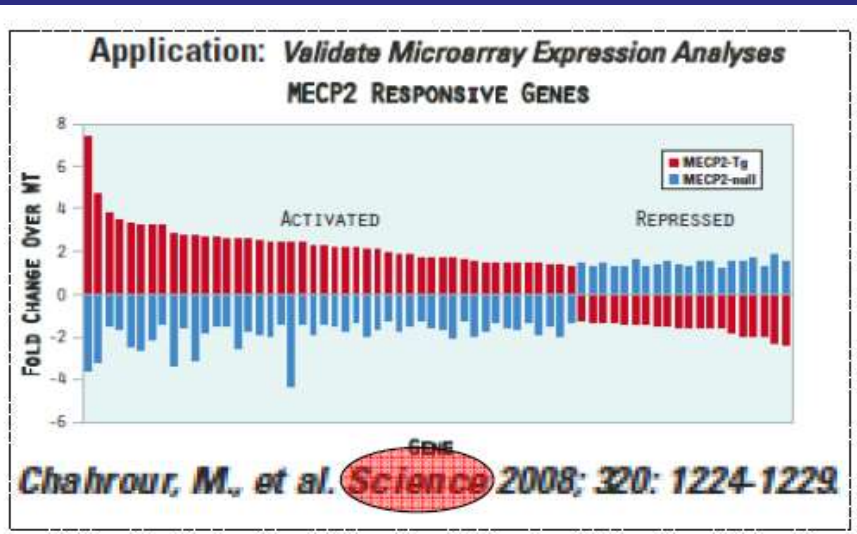
RT-ARRAY TECHNIQUE

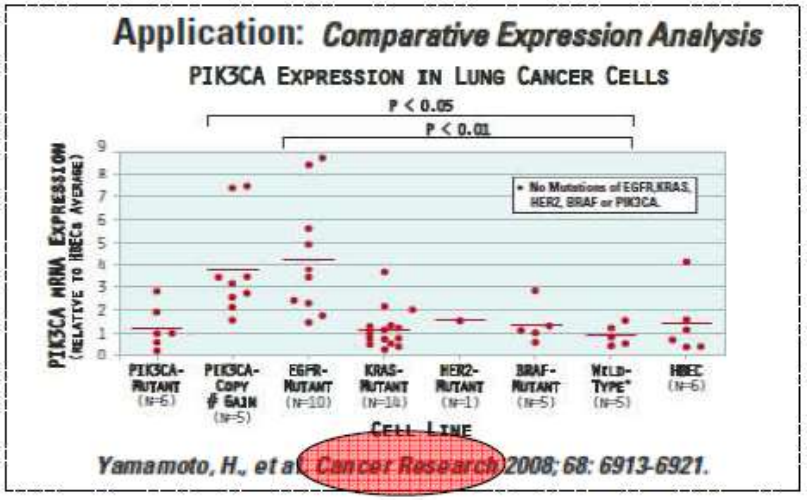
Real-time PCR is the gold standard for gene expression analysis studies





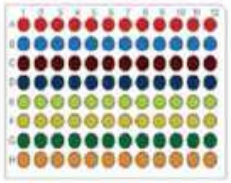
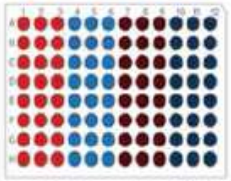
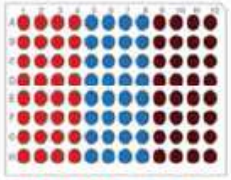
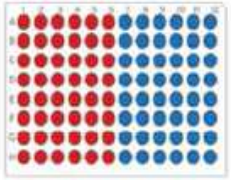
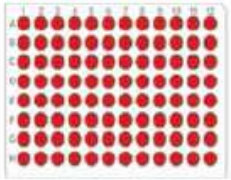
Real-time PCR is the gold standard for gene expression analysis studies



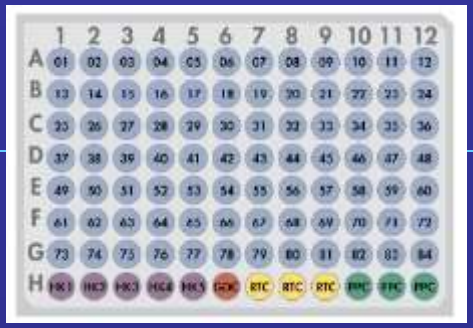


Plates custom

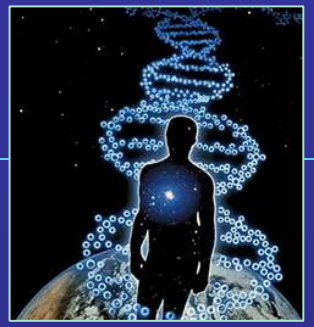
• Choose any gene from the Human, Mouse, Rat, Drosophila, Rhesus macaque, or Dog Genomes

	96-well	384-well
12 Genes : 8 Samples		
24 Genes : 4 Samples		
32 Genes : 3 Samples		
48 Genes : 2 Samples		
96 Genes : 1 Sample		

- Analyze the Genes Most Important To *Your* Research
- Available for any real-time PCR instrument.
- Wet-Bench Validated design & performance.
- 2 to 3 week turn around time first order
- 2 to 3 DAY turn around on re-order
- Same Data Analysis as Catalogued Arrays

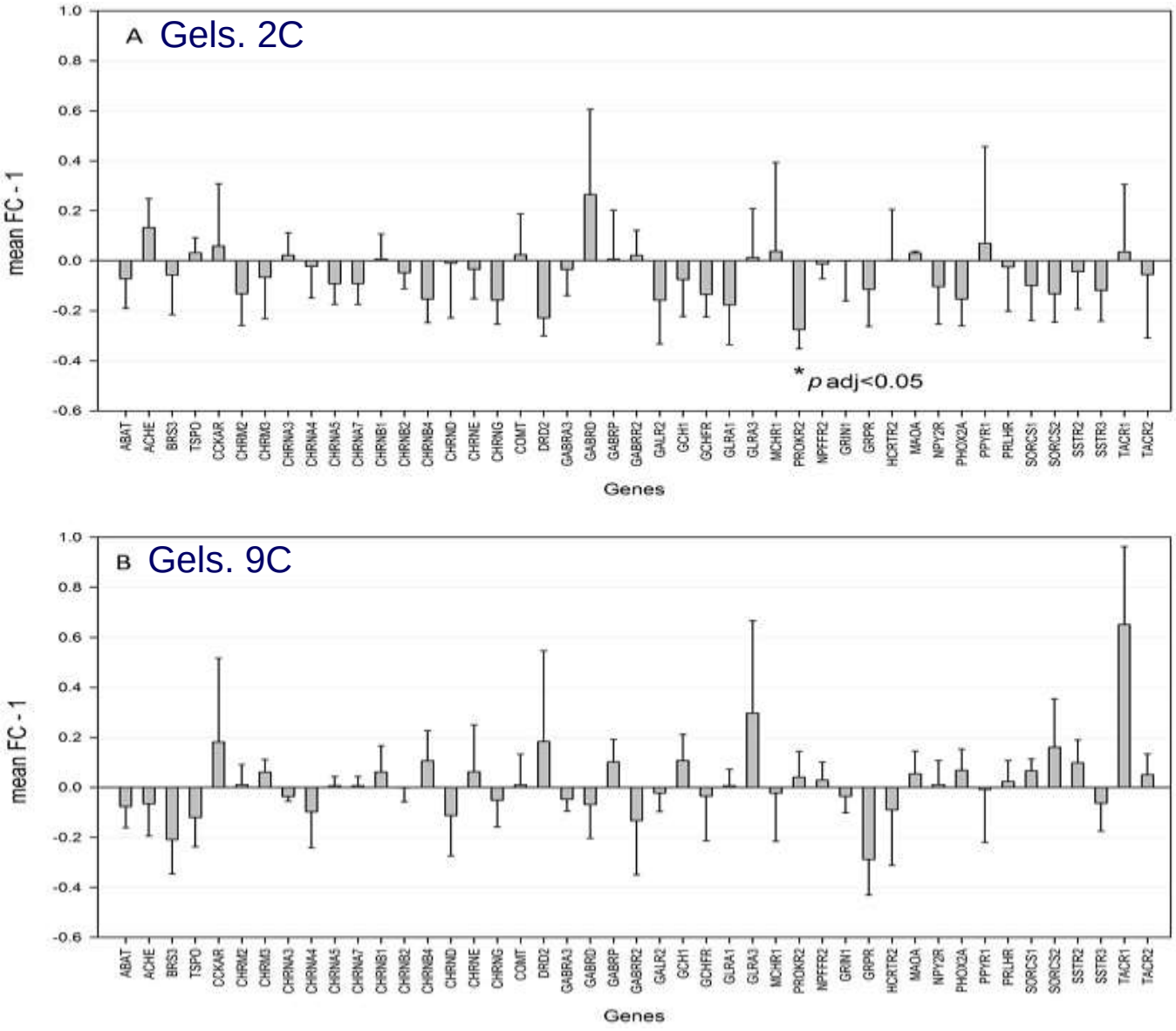


Typical examples of RT-Arrays of gene expression profiles



- **Cancer PathwayFinder** RT² Profiler PCR Array profiles the expression of 84 genes representative of 9 different biological pathways involved in transformation and tumorigenesis
- **Neurotransmitter Receptors** RT² Profiler™ PCR Array profiles the expression of 84 genes involved in modulating the biological processes of neurotransmitter biosynthesis, uptake, transport and signaling through neurotransmitter receptors.
- **Inflammatory Cytokines & Receptors** RT² Profiler PCR Array profiles the expression of 84 key genes mediating the inflammatory response.
- **Allergy & Asthma** RT² Profiler PCR Array profiles the expression of 84 key genes central to allergic responses. CD4+ T cells differentiate into multiple subtypes during immune responses. An overrepresentation of the T helper 2 (Th2) cell subtype and the IgE antibody isotype commonly characterizes allergic inflammation, and both the cell and the molecule play central roles in allergic disease mechanisms.
- **Stress & Toxicity PathwayFinder** RT² Profiler PCR Array profiles the expression of 84 key genes regulated during cellular responses to stress and toxic compounds.
- **Human Aging** RT² Profiler PCR Array profiles the expression of 84 genes altered during aging, a major biological process and a risk factor for many diseases.

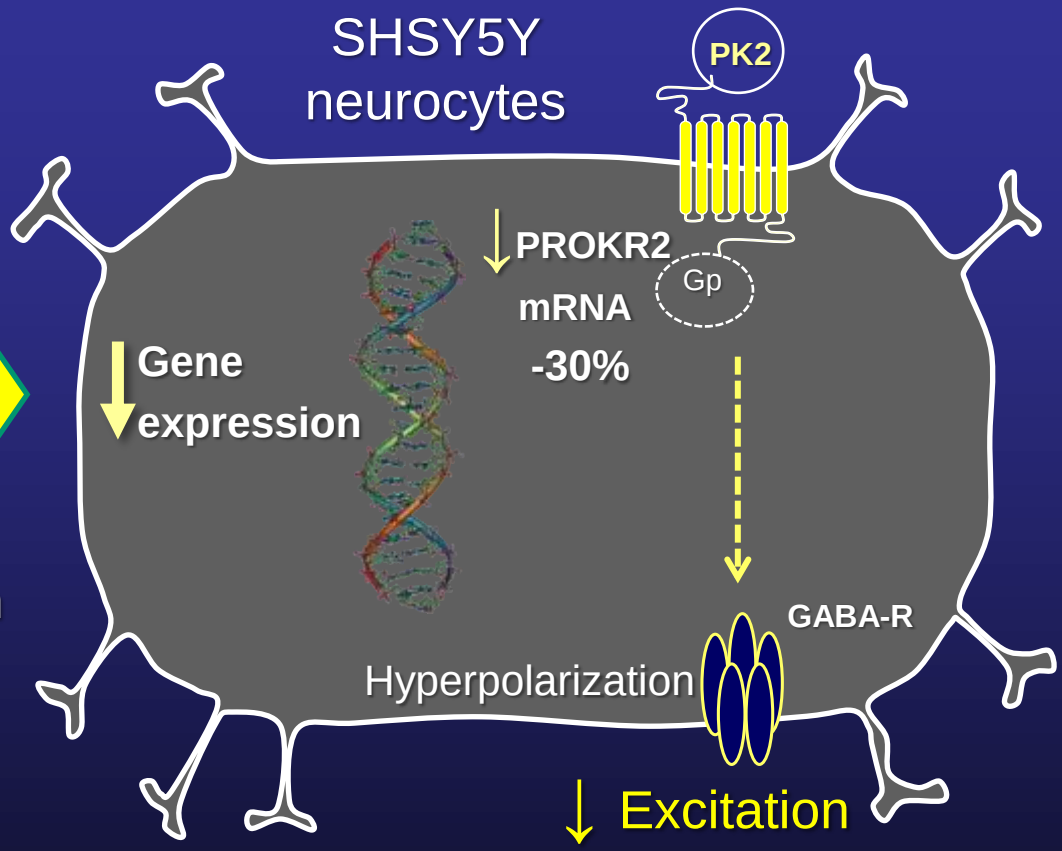
RT-Array sy panel di geni di recettori

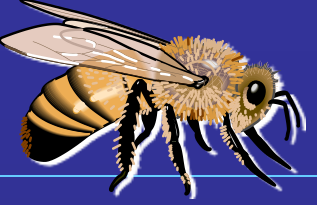


RT-Array on

Gelsemium sempervirens L.

2c
24 h





Developments of experimental studies on APIS M.

1975--1990

- High dilutions (7C-9C) of bee venom (*Apis mellifica* and *Apium virus*, which are currently used in homeopathy to treat skin manifestations with edema, erythema and pruritus) have a protective and curative effect on about 50% of X-ray induced erythema in albino guinea pig (BASTIDE1975, BILDET1989, 1990, POITEVIN1988)

1993

- Our group studied the effects of homeopathic preparations of *Apis mellifica* (and *Histamin)* on rat paw edema induced by the injection of inflammatory doses of histamine. It was observed that high dilutions of up to 30D had a small but significant inhibitory effect on the development of edema (Conforti et al.,1993).

2004

- We confirmed a small regulating effect of *Apis mellifica* (4 D, oral drops) in the carrageenan-induced edema in rats but could not reproduce it in blind trial (Conforti et al., 2004) probably for technical reasons (animals with different treatment in the same cage)

2014

- Bigagli and coworkers (2014) showed with microarray techniques that *Apis mellifica* TM modifies expression of hundreds of genes in human prostate epithelial cells; dynamized dilutions (3C, 5C and 7C) still exert significant effects on genes involved in inflammation and oxidative stress

OMICS AND HOMEOPATHY

The rapid development of new technology platforms provides a methodological basis for deep understanding the action mechanisms and targets of homeopathic remedies.

Its widespread use would significantly advance the field by bridging the gap between homeopathy and Western medicine.

Homeopathic experimental studies. Proposals - 2014

- Study of the effects of specific **homeopathic drugs on well-established experimental systems** (in vitro and in laboratory animals). Low and high dilutions.

- E.g.: **Arsenic** (stress defense systems), **Arnica** (wound healing), **Belladonna** (immunological models, inflammation), **Zinc** (immunological models, stress defense system)

- Cell models of **toxicity/hormesis** (neurocytes, macrophages), **Inflammation** (THP-1, MAC 6, lymphocytes), **allergy** (basophils, mastcells), **healing** (fibroblasts)

- Systematic adoption of "**Omics**" techniques

- Perspectives: **database of homeodrug effects**
  - Organismic level (proving/clinical verification)
  - Effects on animal models
  - Cellular and molecular level
  - Active principles and active dilutions
  - Physicochemical state (nanoparticles?)

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