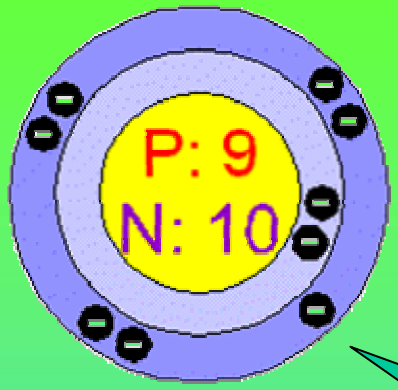
WHY DOES ALUMINUM AMPLIFY BIOLOGICAL and PHARMACOLOGICAL EFFECTS of FLUORIDE ?

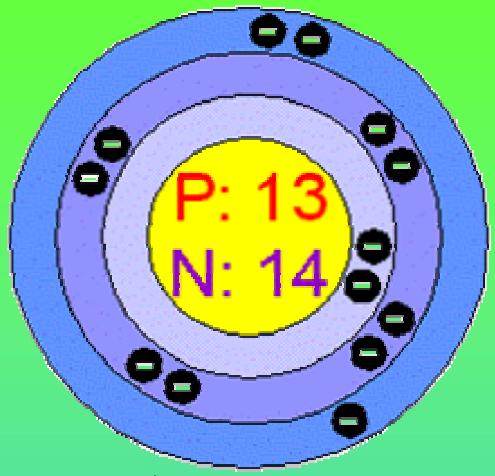
Anna Strunecká

Charles University Prague, Faculty of Science, Department of Physiology and Developmental Physiology, Vinicna 7, 128 00 Prague 2, Czech Republic

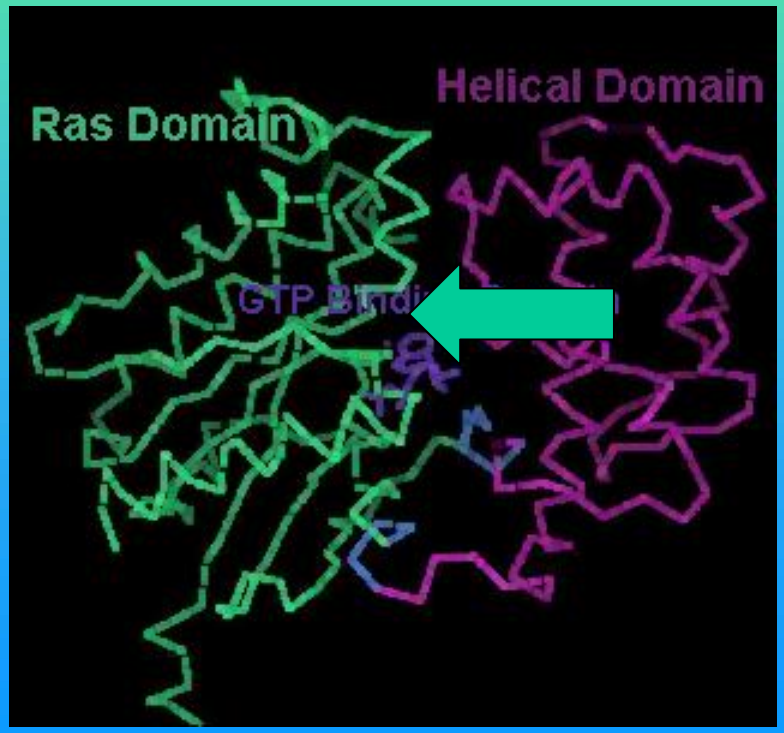
e-mail: strun@natur.cuni.cz



FLUORINE



ALUMINUM

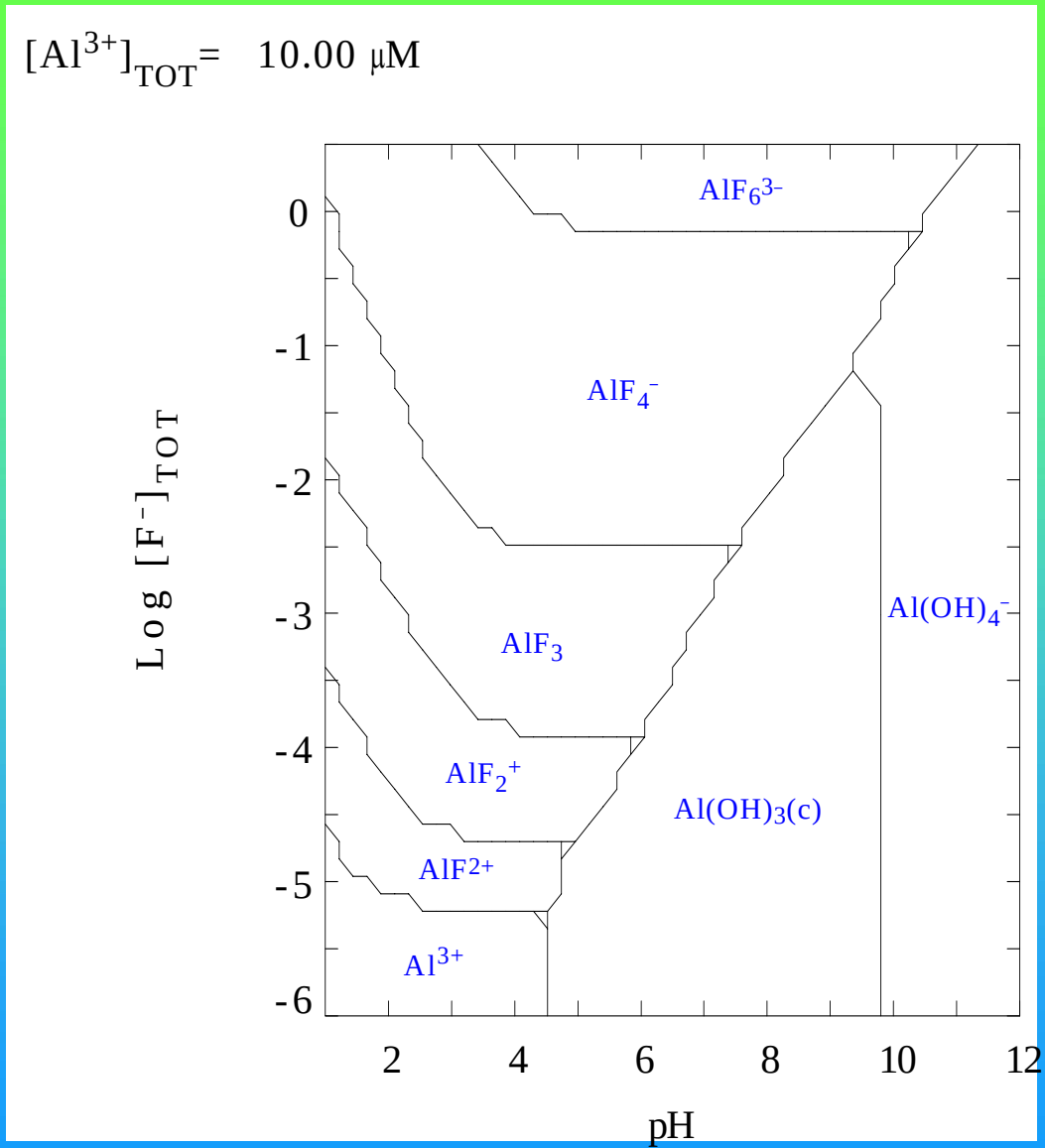


AlF_4^-

PO_4^{3-}

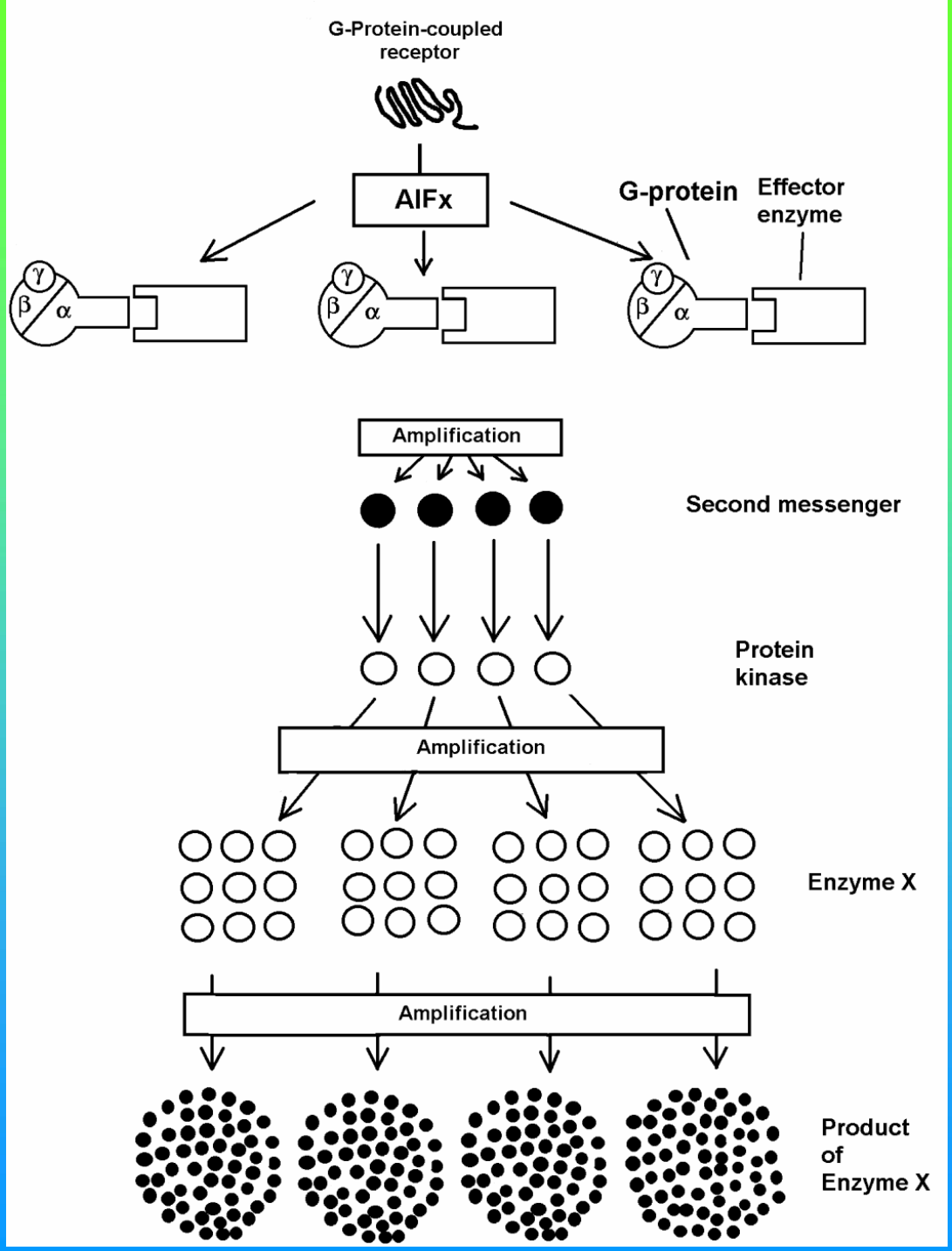
ALUMINUM – FLUORIDE PREDOMINANCE DIAGRAM

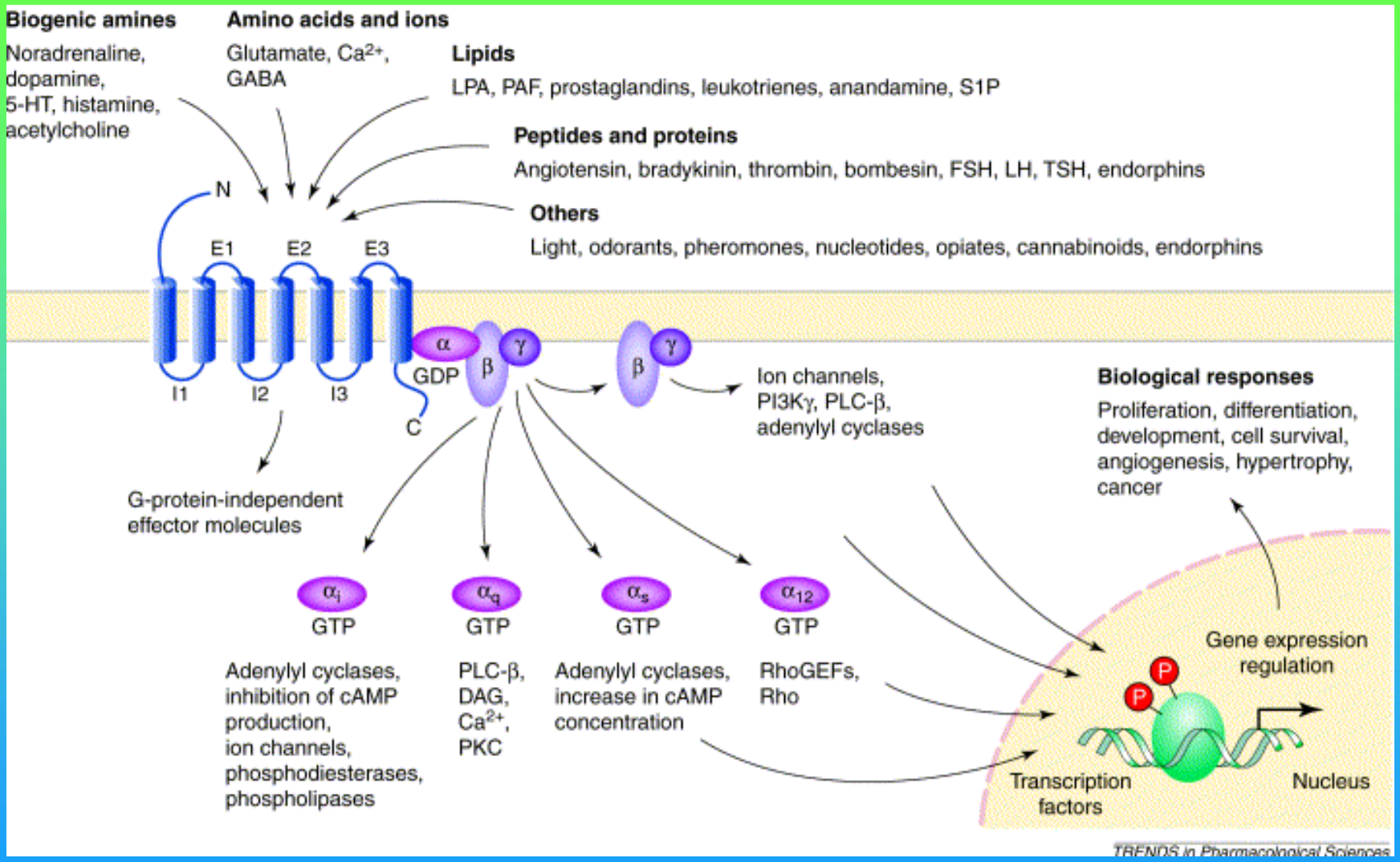
This diagram demonstrates HOW solubility of Al hydroxide is changing with pH or fluoride concentration.

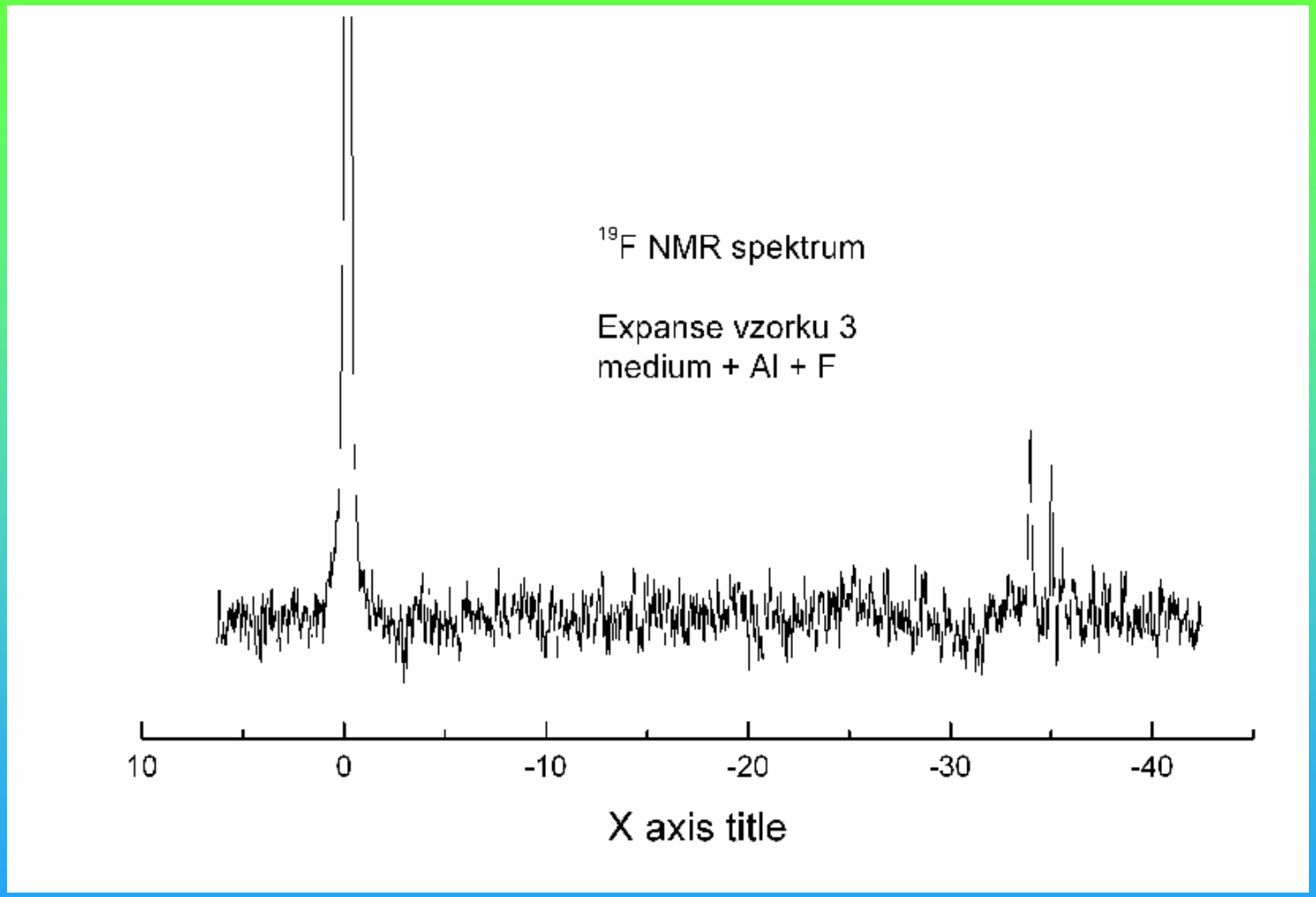


AlF_x MESSENGER of FALSE INFORMATION

Its message is greatly amplified



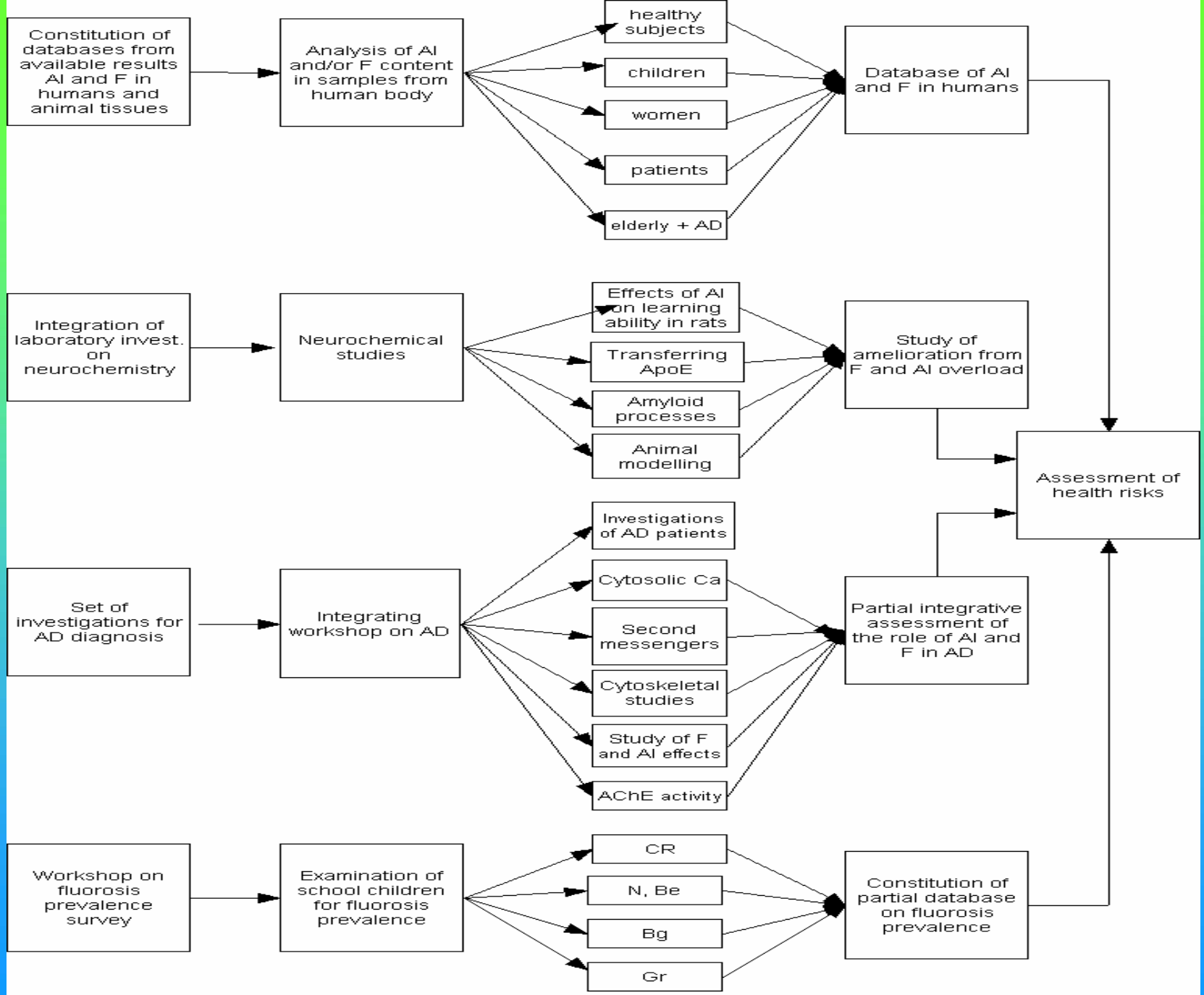

Biogenic amines
Noradrenaline, dopamine, 5-HT, histamine, acetylcholine
Amino acids and ions
Glutamate, Ca2+, GABA
Lipids
LPA, PAF, prostaglandins, leukotrienes, anandamine, S1P
Peptides and proteins
Angiotensin, bradykinin, thrombin, bombesin, FSH, LH, TSH, endorphins
Others
Light, odorants, pheromones, nucleotides, opiates, cannabinoids, endorphins
N
E1
E2
E3
I1
I2
I3
C
α
β
γ
GDP
Ion channels, PI3Kγ, PLC-β, adenylyl cyclases
Biological responses
Proliferation, differentiation, development, cell survival, angiogenesis, hypertrophy, cancer
G-protein-independent effector molecules
αi GTP
αq GTP
αs GTP
α12 GTP
Adenylyl cyclases, inhibition of cAMP production, ion channels, phosphodiesterases, phospholipases
PLC-β, DAG, Ca2+, PKC
Adenylyl cyclases, increase in cAMP concentration
RhoGEFs, Rho
Gene expression regulation
P
P
Transcription factors
Nucleus
TRENDS in Pharmacological Sciences



First peak represents free fluoride. Chemical shift of free fluoride was taken as zero and the peaks at – 34 ppm were identified as an alumino-fluoride complexes.

Some effects of AlF_x observed in laboratory investigations

CELL TISSUE	BIOCHEMICAL RESPONSE	FUNCTIONAL RESPONSE
Liver - hepatocytes	Ca^{2+}↑ IP3 ↑ cAMP↓	Activation of glycolysis, Fatty acid oxidation Activation of catabolic processes
Kidney	Ca^{2+}↑ cAMP↑ ion channels affected	Glomerular hypercellularity and distortions Renal mesangial proliferation
Platelets	Ca^{2+}↑↓ IP3 ↑↓	Agreggation
Red blood cells	IP3 ↑	Shape changes Disorganization of cytoskeleton
Fibroblasts	Ca^{2+}↑ IP3 ↑ cAMP↓	Growth, movement Production of extracel. matrix
Osteoblasts	PG synthesis ↑ Tyrosine phosphorylation ↑ Phosphate transport↑	Mitogenic effect proliferation↑ Life span ↑ Anabolic action ↑
Osteoclasts	cAMP Ca^{2+}↑	Inhibition of bone resorption Cellular retraction
Neurons	IP3 ↑ Ca^{2+}↑	Spike amplitude
Brain	IP3 ↑ Ca^{2+}↑	Enhancement of synaptic transmission and spike amplitude
Pars tuberalis	Ca^{2+}↑ Inositol phosphates↑	Binding of iodomelatonin ↓


Constitution of databases from available results Al and F in humans and animal tissues
Analysis of Al and/or F content in samples from human body
healthy subjects
children
women
patients
elderly + AD
Database of Al and F in humans
Integration of laboratory invest. on neurochemistry
Neurochemical studies
Effects of Al on learning ability in rats
Transferring ApoE
Amyloid processes
Animal modelling
Study of amelioration from F and Al overload
Assessment of health risks
Set of investigations for AD diagnosis
Integrating workshop on AD
Investigations of AD patients
Cytosolic Ca
Second messengers
Cytoskeletal studies
Study of F and Al effects
AChE activity
Partial integrative assessment of the role of Al and F in AD
Workshop on fluorosis prevalence survey
Examination of school children for fluorosis prevalence
CR
N, Be
Bg
Gr
Constitution of partial database on fluorosis prevalence

European Fluoride and Aluminum Network of Excellence

May 2002 – February 2003

37 participants – 17 countries
354 researchers

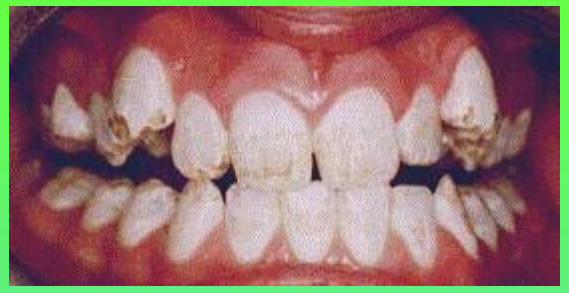
EU Member States, Bulgaria,
Turkey, India, China, Chile, Israel

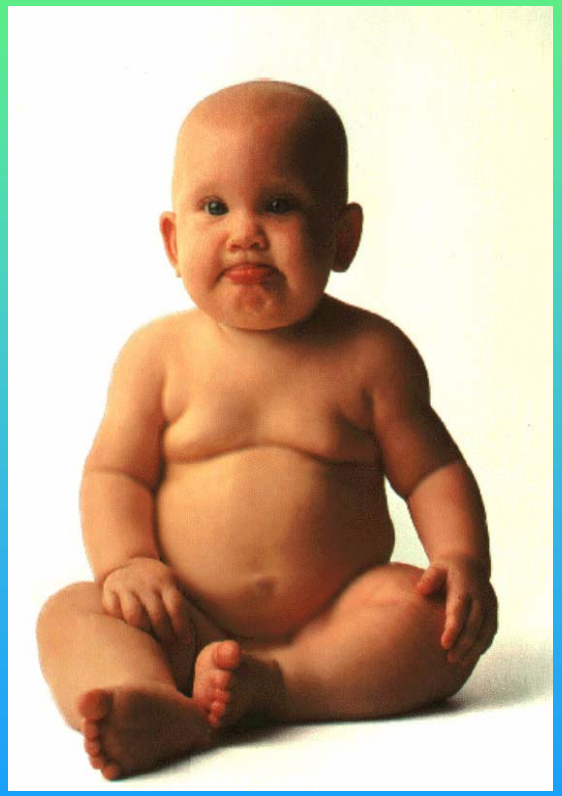
F + Al = aberration of G proteins

- How many children and our friends…???

CONCLUSIONS

AlFx is a molecule giving false information, which is amplified by processes of signal transmission. Biological signaling pathways interact with one another to form complex networks. Yet, it seems that we shall not probably find any physiological process, which is not potentially influenced by AlFx. The synergistic action of fluoride and aluminum in the environment, water, and food chains, can evoke various and multiple pathological symptoms. AlFx might induce the alterations of homeostasis, metabolism, growth, and differentiation of the living organism.





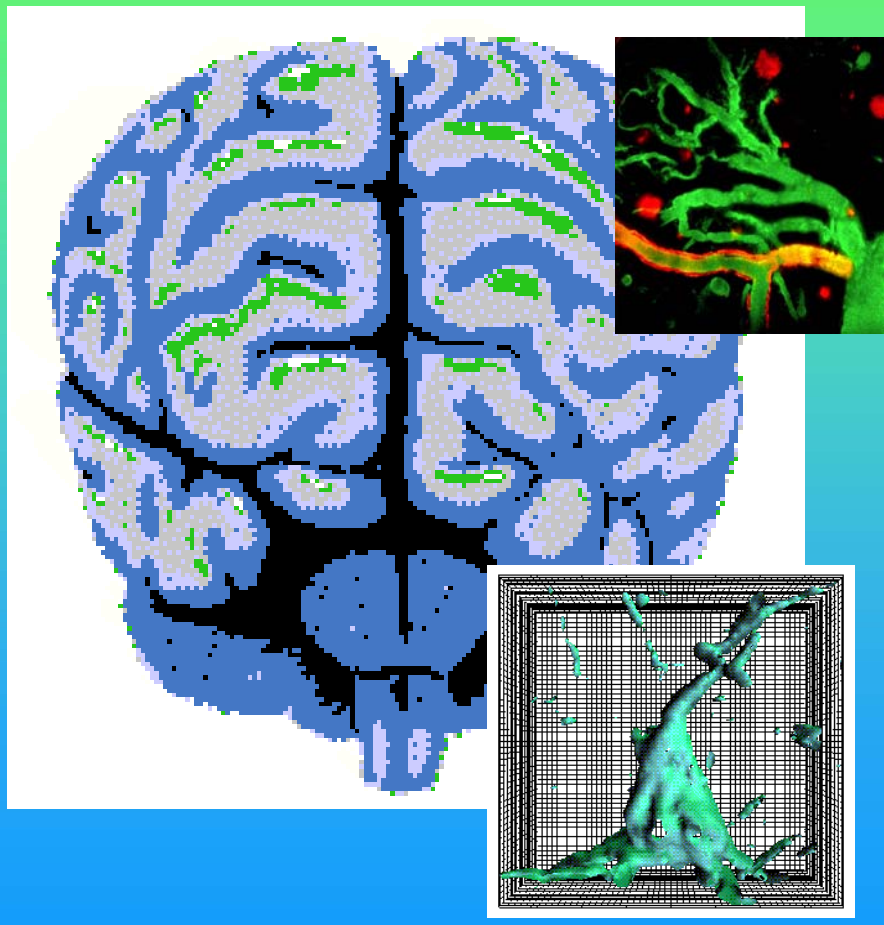
How long will science wait to admit evidence about the destructive actions of fluoride plus aluminum on the human race?

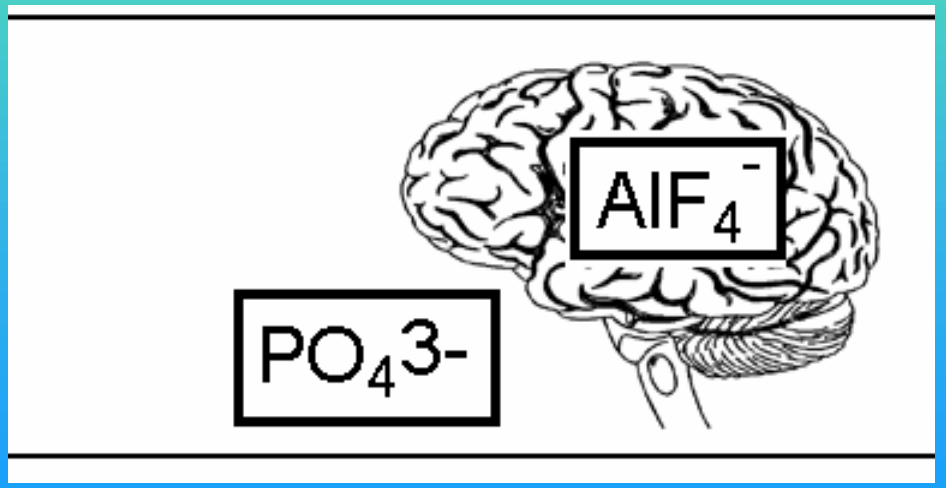
How many children and our friends shall we need for a overwhelming study?

	F concentrations used in laboratory
1 mM F^- ≅ 19 ppm	20 μM – 50 mM
1 ppm ≅ 53 μM F^-	0.4 ppm – 950 ppm

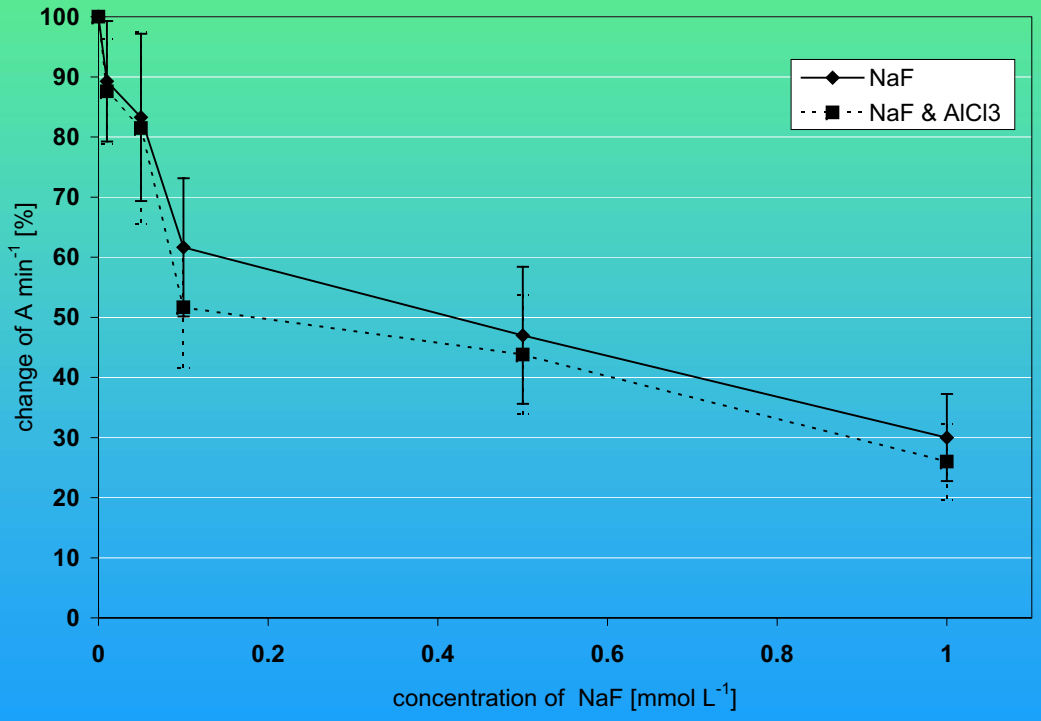
area	Serum F (μM)	Serum F (ppb)
<1 ppm	0. 63	12
1 ppm	1.00	19
4 ppm	4. 00	76
Peak (children)	76	1,450

Senile plaques and neurofibrillary tangles in brains of AD patients





Acetylcholinesterase activity of human RBC



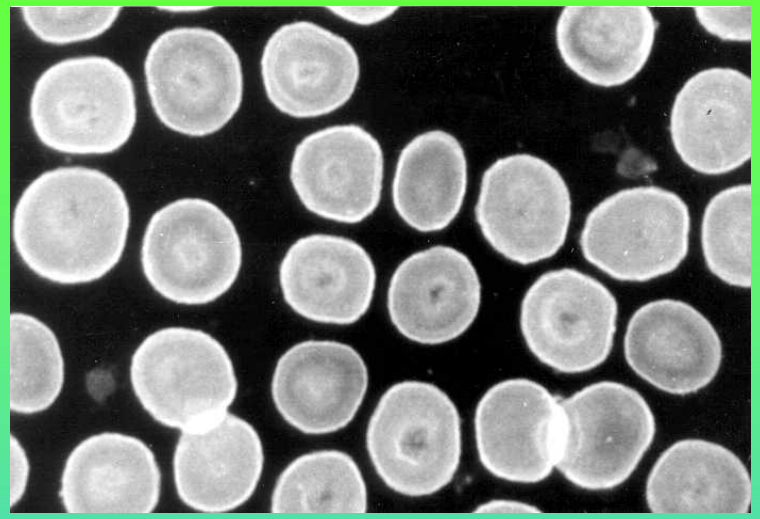
Cytosolic calcium level (nM) in platelets

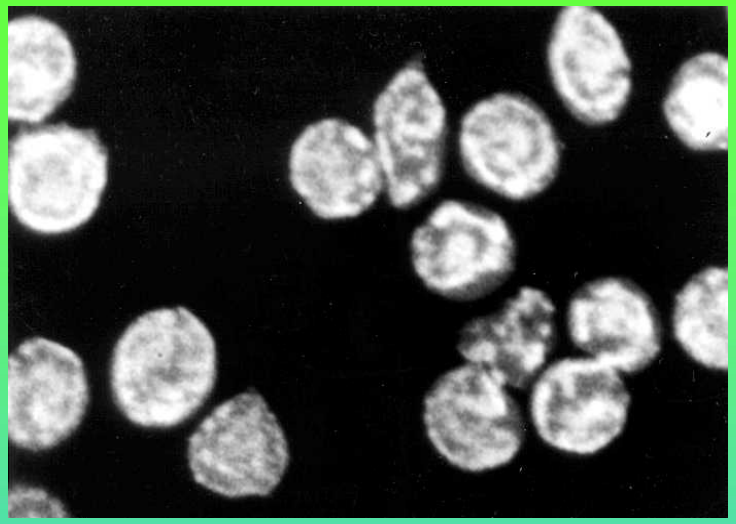
means ± SEM

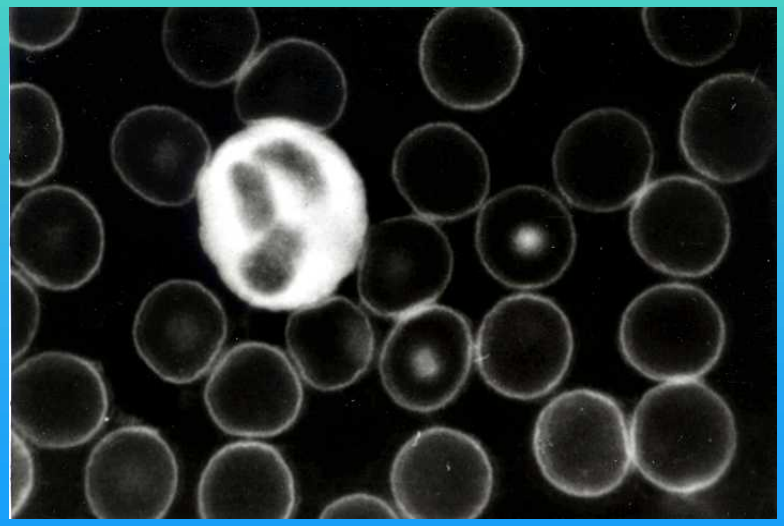
Young controls	AM controls	Schizophr. patients	AD patients
n=33	n=18	n=6	n=41
96.2± 4.1	**120± 4.8***	**190±10****	**92 ± 6.1***
84.5 ± 3.8	**103 ± 6.1**	**109± 8****	**91 ± 5.8**

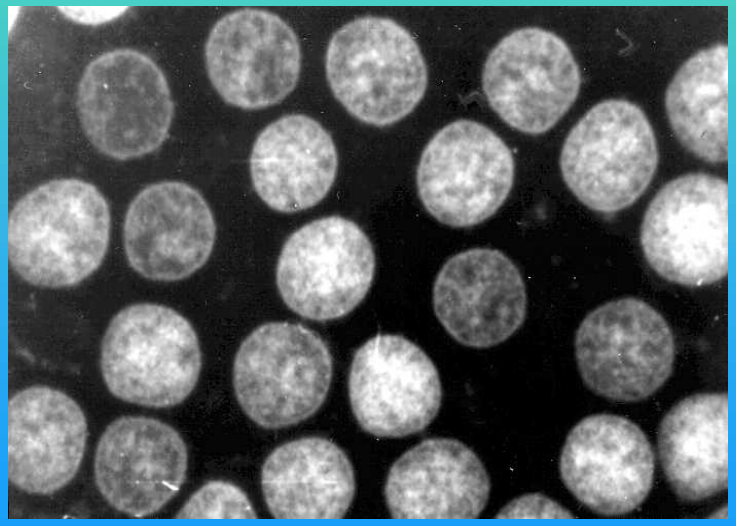
* P<0.01 YC versus AMC; AMC versus AD; AMC versus Sch; **P< 0.001 YC versus Sch; AD versus Sch. ; ANOVA for all groups P< 0.0001, df=3, 94, F=20.21

AlFx % 88 86 57.6 98.5

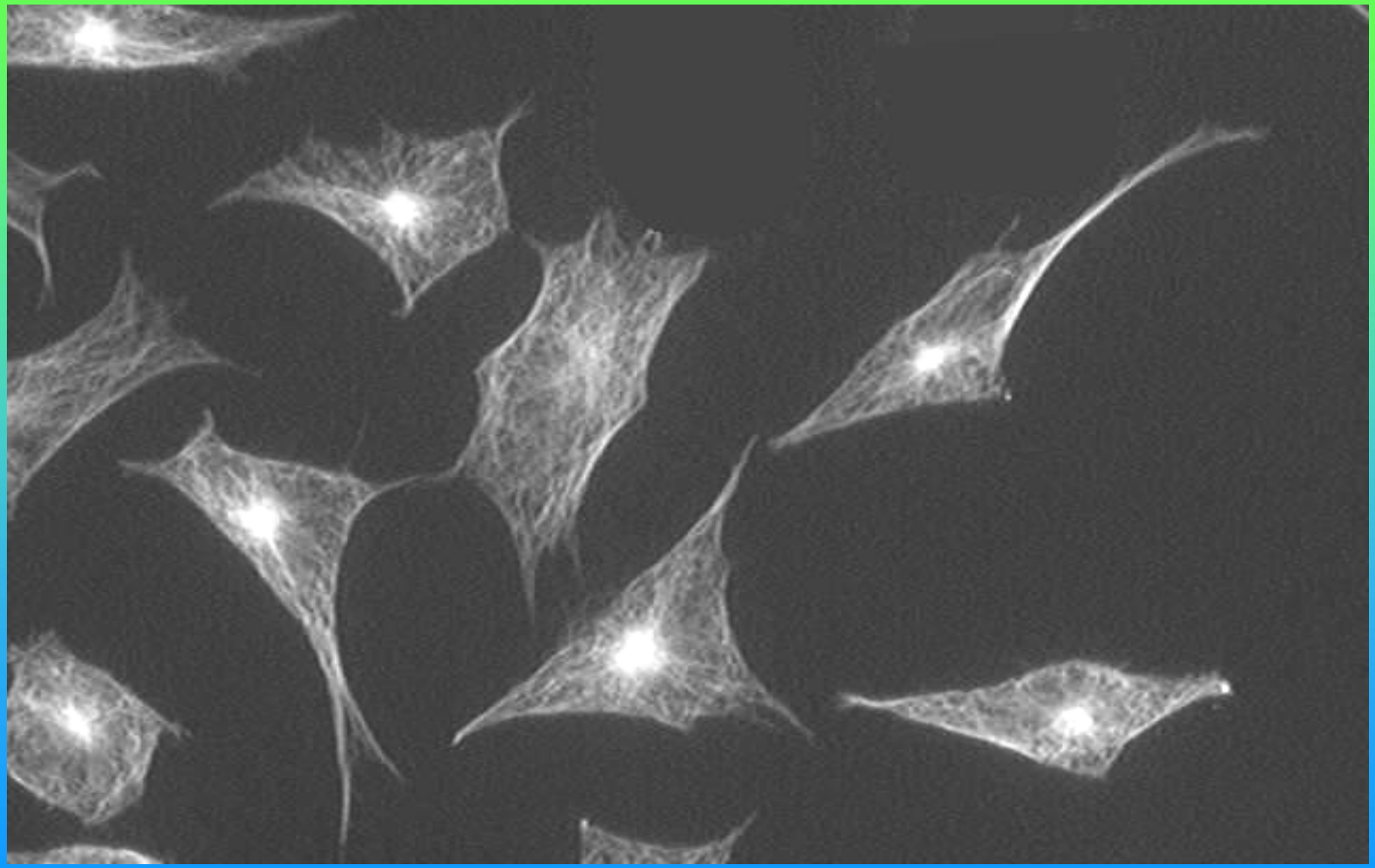








Tubulin in fibroblasts (control)



Incubation 60´ AlF_x