

# **Fluoride and Aluminum Interactions: AlFx as the Magic Bullets Producing Aberration of G Proteins**

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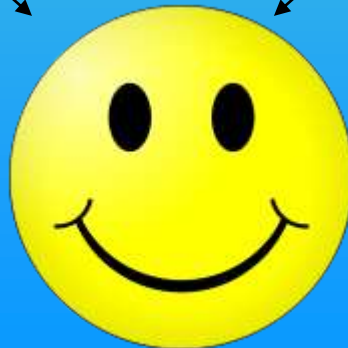
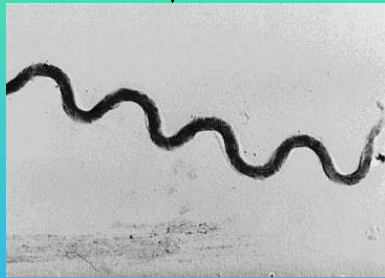
**1st Faculty of Medicine, Charles University  
Prague, Czech Republic**



# MAGIC BULLETS

606 SALVARSAN

FLUORIDE



# MAGIC BULLETS

FLUORIDE



- **AlFx as laboratory tools**
- **F and Al ions in living environment**
- **Prediction of health risks**
- **Effects of AlFx on CNS**

Strunecka et al. Fluoride interactions.

*Curr. Signal Transd. Therapy* 3, 190–213, 2007.



# **The use of fluoride (mM) in laboratory investigations helped in the discovery of glycolytic pathways**

**F inhibits 20 metabolic enzymes**

**8 have Al requirement**

**F activates 10 metabolic enzymes**

**14 have Al requirement**

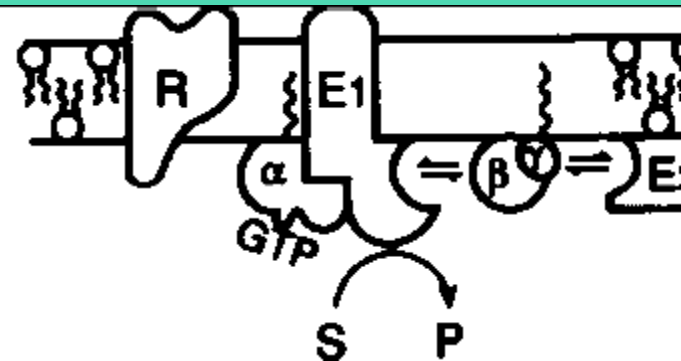
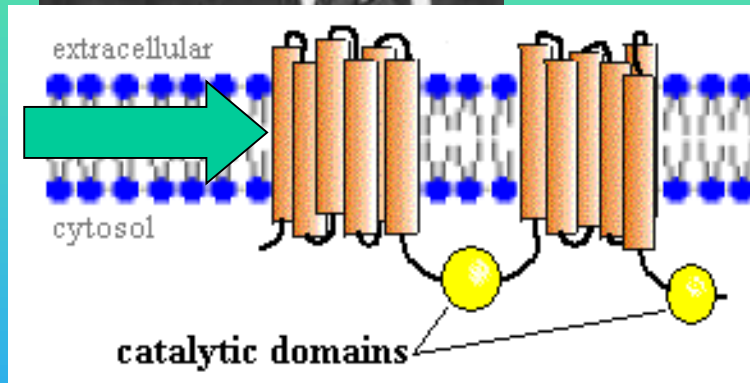
A.G.  
Gilman



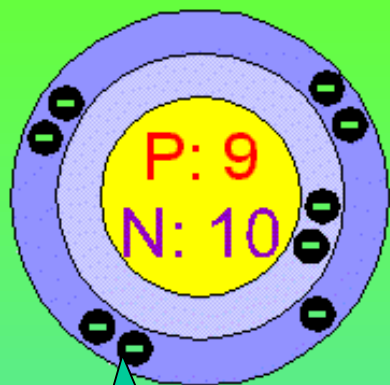
Nobel  
Prize  
1994



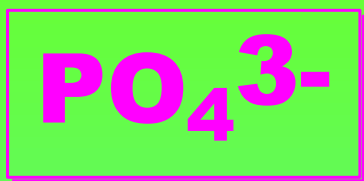
M. Rodbell



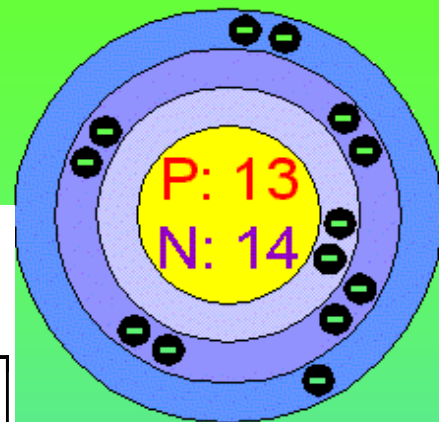
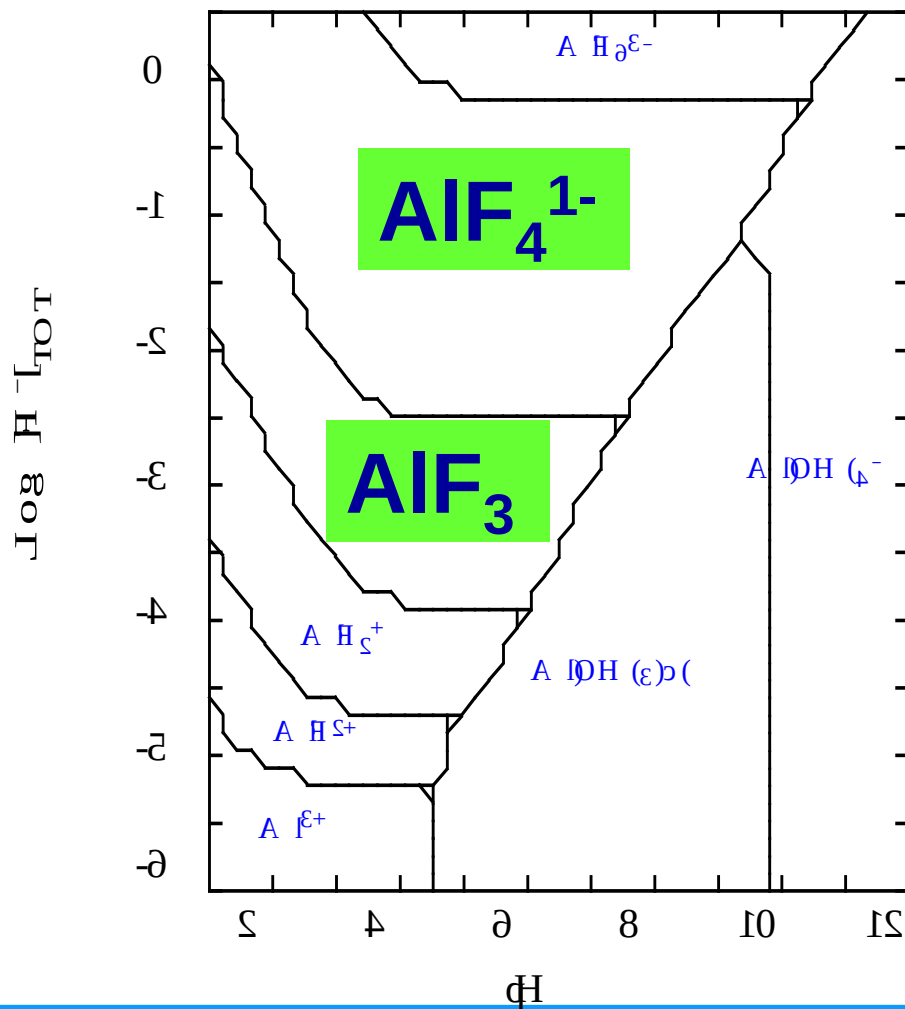
**Aluminum is a requirement for  
activation of adenylylcyclase by F**



FLUORINE

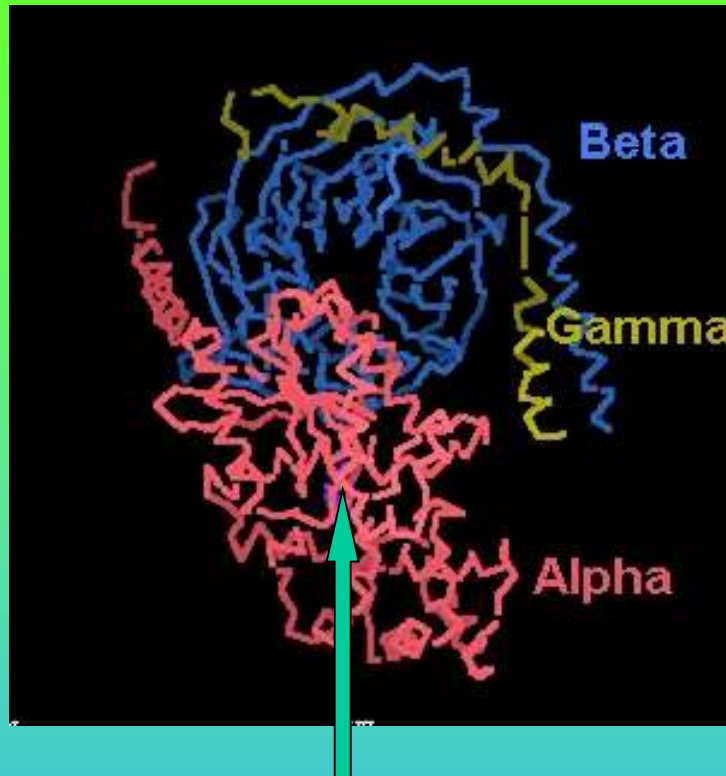


$$A \text{ } I^{\varepsilon+} L_{\text{TOT}} = 10.00 \text{ M}$$

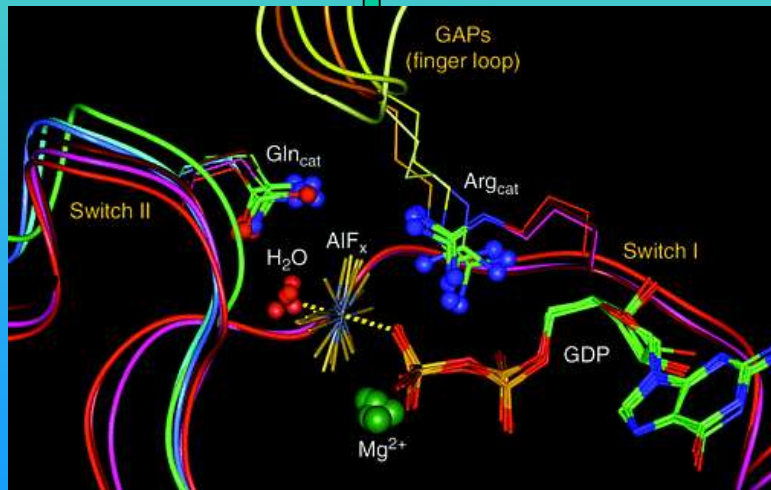


ALUMINUM

$\text{AlF}_x$



**AlFx is a general  
pharmacological  
activator of all  
G-proteins**



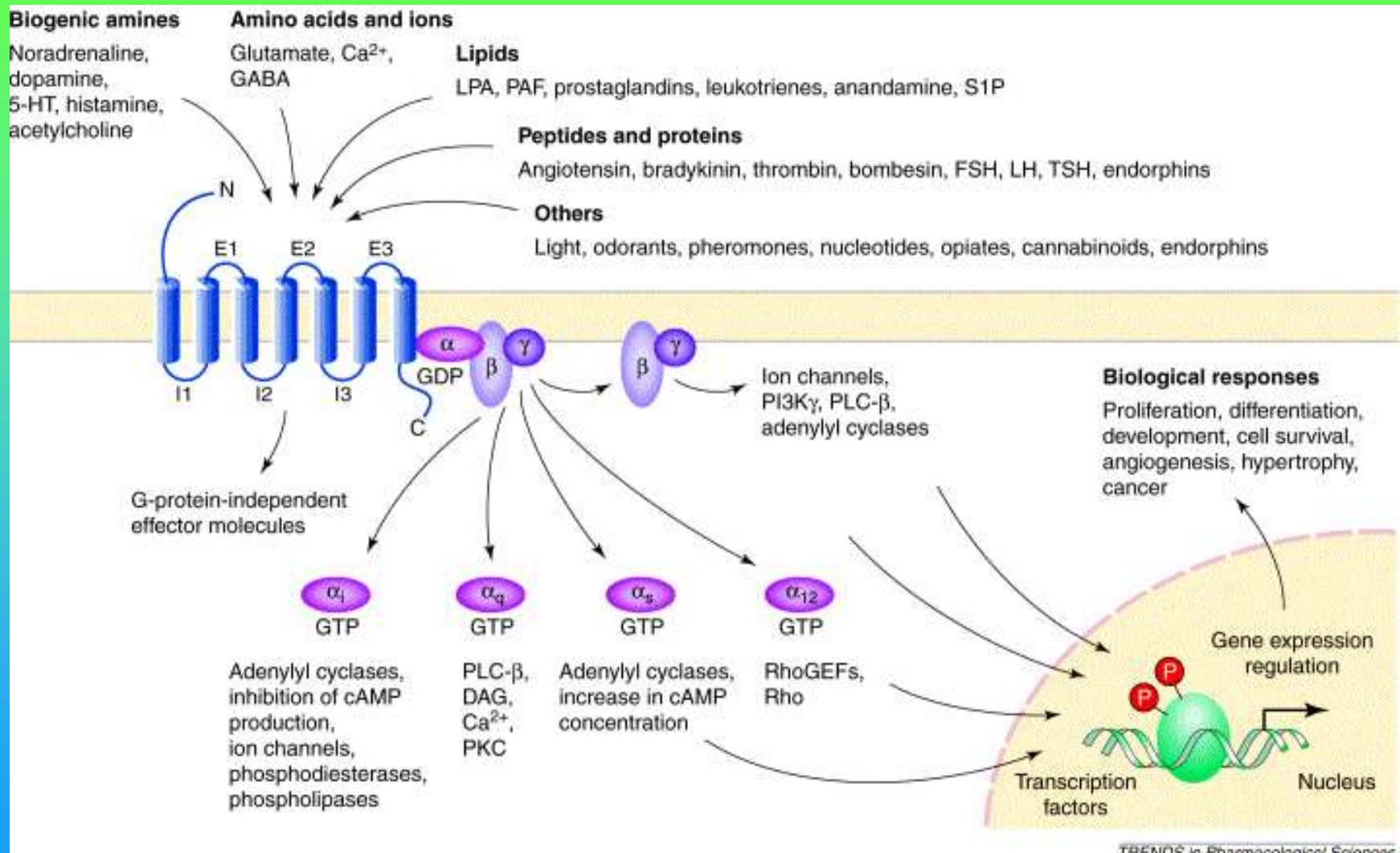
**AlFx acts as a  
transition-state  
analog**



It seems that we shall not find any physiological process, which is not potentially influenced by AIFx

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

# General scheme of G protein-mediated transmembrane signaling

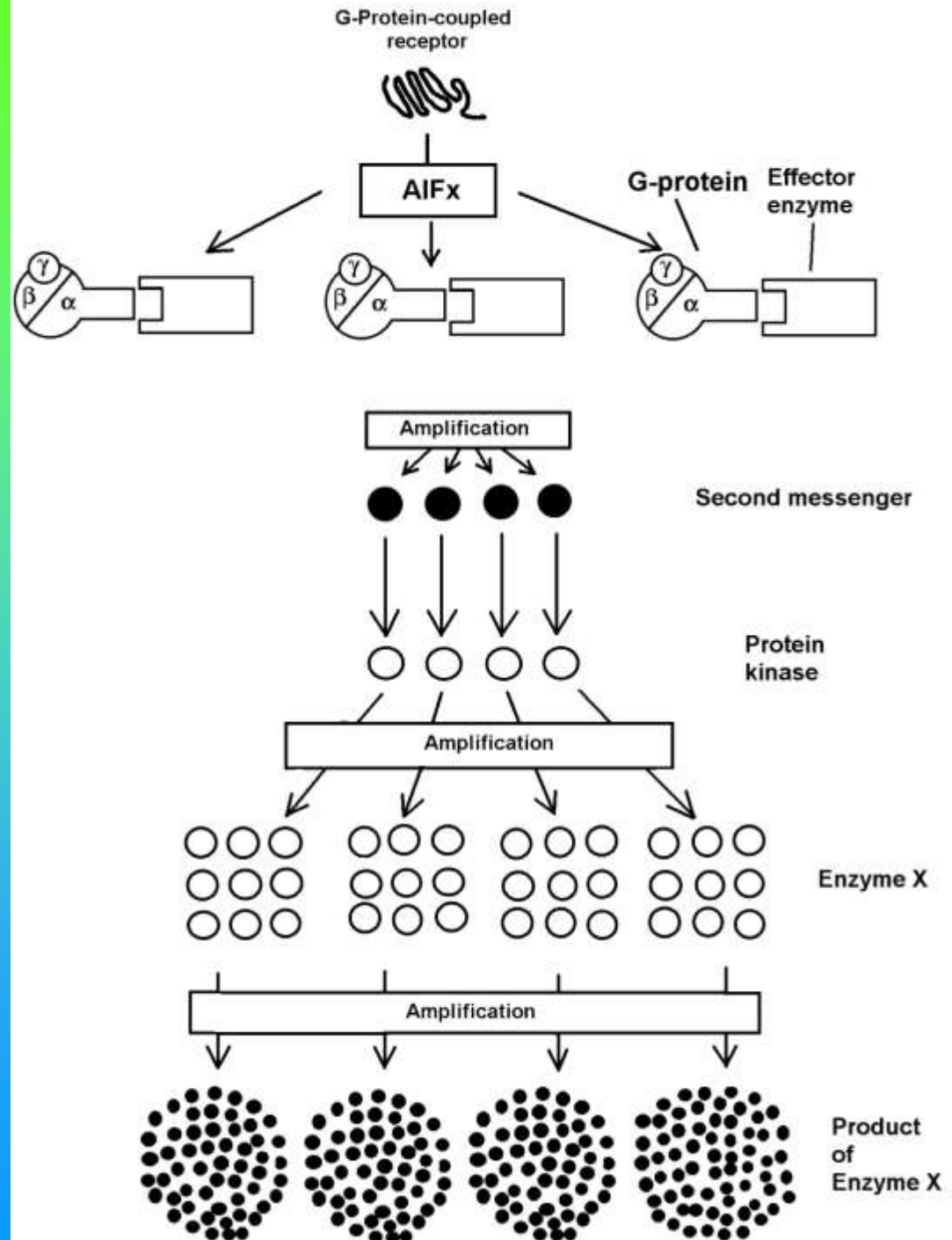


TRENDS in Pharmacological Sciences

Marinissen and Gutkind, 2001

# $AIF_x$ MESSENGER of FALSE INFORMATION

Its message  
is greatly  
amplified



**Pharmacologists estimate that up to 60% of all medicines used today exert their effects through G protein signaling pathways.**

**Gilman said in his Nobel Prize lecture:**

*"The ultimate dream is to design drugs that will prevent aberrant G protein action."*

**AlFx are man-made Magic Bullets that produce aberration of G proteins.**



# Fluoride plus Al



Drinking water, soil and air, food, beverages (e.g. tea, mineral waters), tabs, fluorinated drugs



| <b>Blood serum</b> | <b>ppb</b>     | <b><math>\mu\text{mol/ L}</math><br/>1-2</b> |
|--------------------|----------------|----------------------------------------------|
| Europe             | 13- 57         | 0.7- 3                                       |
| China              | 41             | 2.2                                          |
| India              | 19-300         | 1-16                                         |
| <b>F areas</b>     | <b>81- 410</b> | <b>4.3 - 21.6</b>                            |

**Millions of people live in endemic fluorosis area**

**Dental fluorosis is endemic in 25 countries;**

**14-86% children are affected (36% in the USA)**



**9 millions of people  
suffer  
with skeletal fluorosis**



**AlFx might induce the alterations of  
homeostasis, metabolism, growth, cognition,  
and behavior of the living organism.**

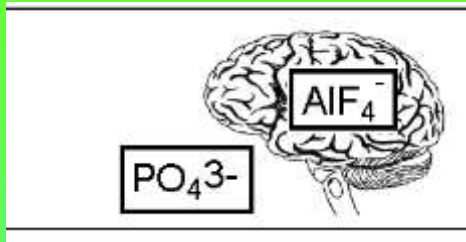


# Effects of AIFx on CNS in children

**ASD**

- Impaired development of fetal brain
  - 6 studies
- A lowering of IQ ( $\leq 80$ )- 18 human studies
- Hypothyroidism
- Pineal gland – melatonin inhibition
- Hypomagnesemia
- Hypocalcemia





# Effects of AlFx on CNS in adults Alzheimer's disease

- Alterations in neurotransmission
- $\beta$ -amyloid production
- Cytoskeletal abnormalities
- Dysregulation of calcium homeostasis
- Protein tau hyperphosphorylation

Strunecka A, Patocka J. Aluminofluoride Complexes in the Etiology of Alzheimer's disease. *Structure and Bonding* 104, 139-181, 2003.

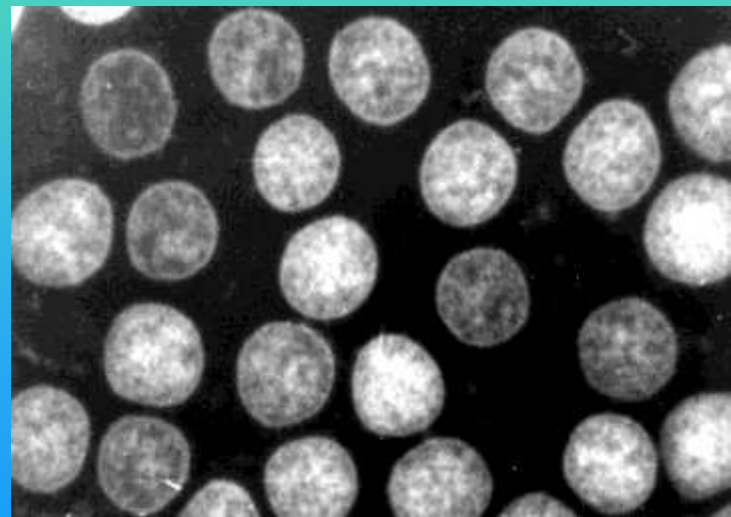
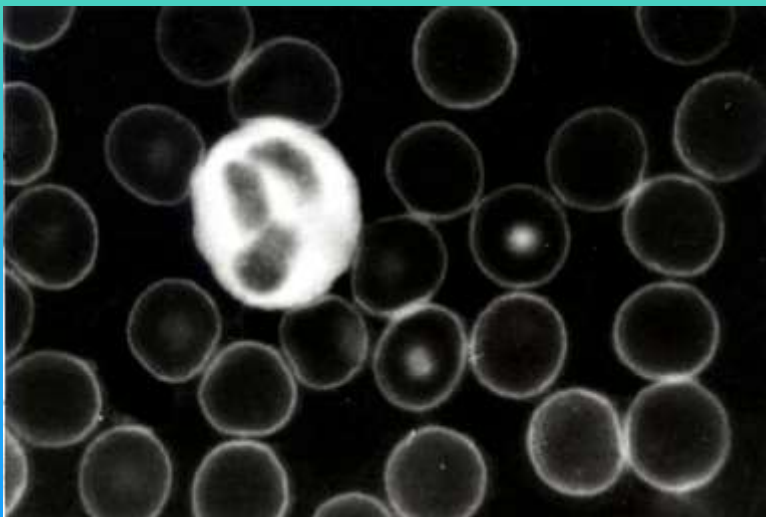
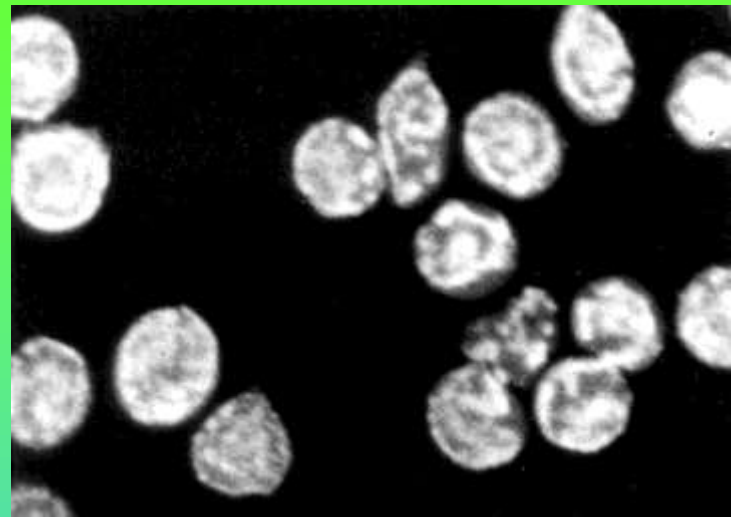
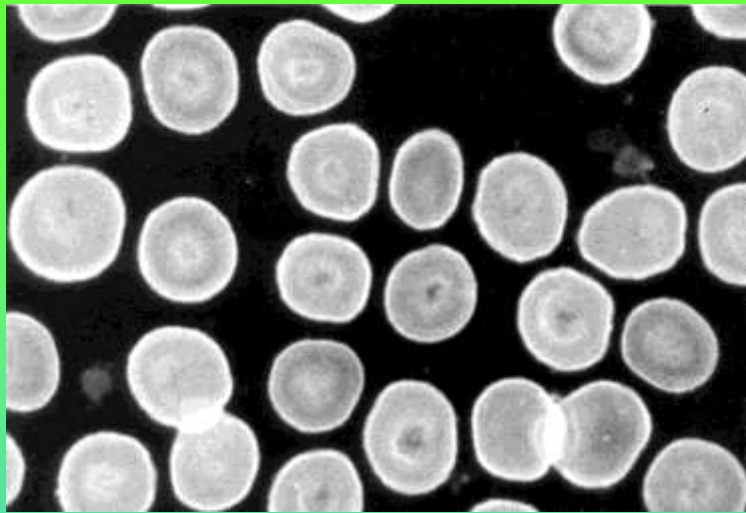


# AChE activity

While **20  $\mu\text{M}$   $\text{AlCl}_3$**  increases the AChE activity in RBC of investigated subjects to **158 - 285 %** AlFx inhibit the AChE activity.

| Subjects | AD             | AM – HS        | YS             |
|----------|----------------|----------------|----------------|
| n        | 29             | 30             | 26             |
|          | $16.3 \pm 5.5$ | $18.9 \pm 4.2$ | $17.1 \pm 2.3$ |

The effect of 1 mM NaF + 20  $\mu\text{M}$   $\text{AlCl}_3$ . Data are expressed in percentage of the AChE activity in the absence of Al and F ions.



# CONCLUSIONS



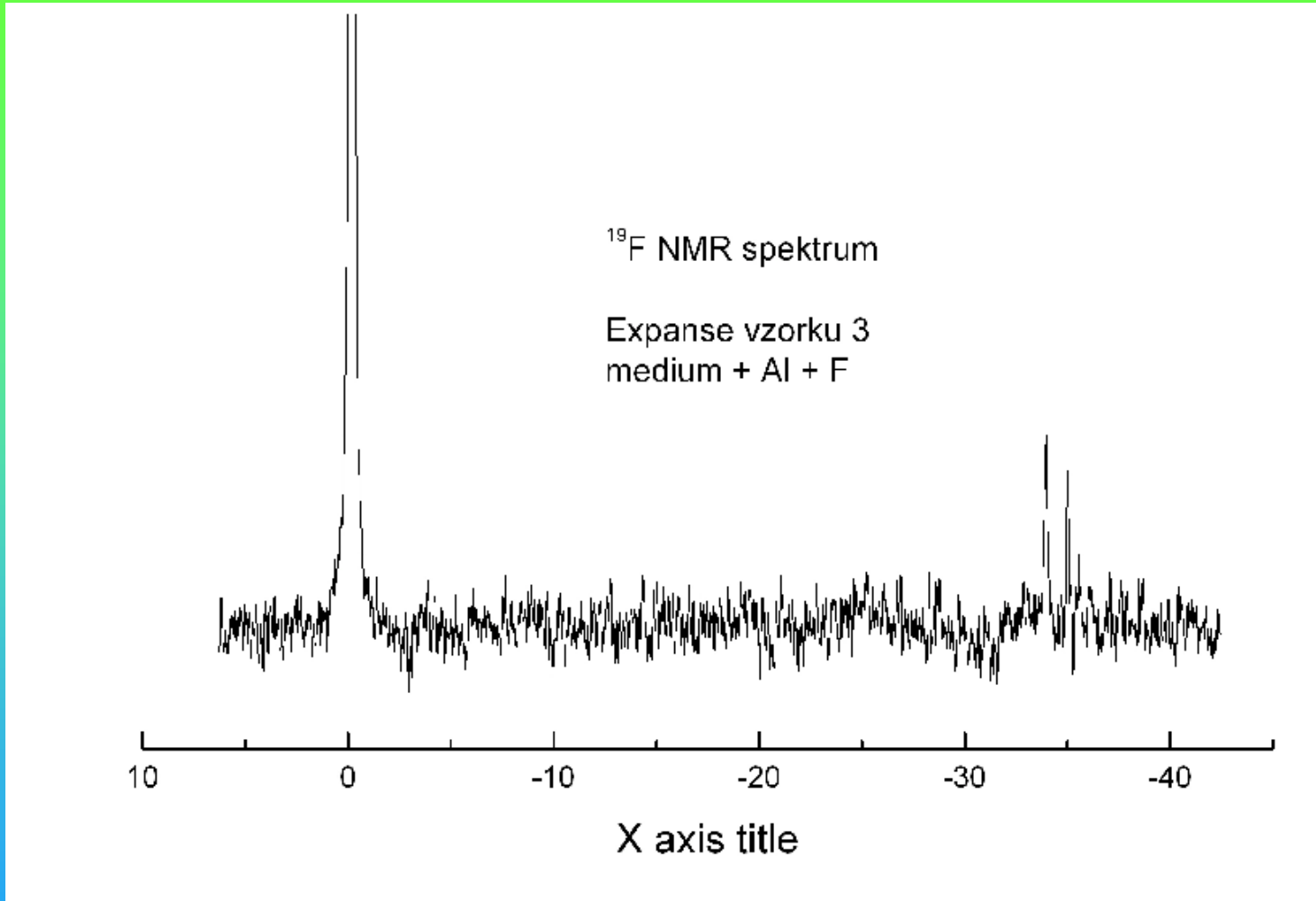
- 1) The definition of a safe concentration of F for humans must consider that the dose is much lower in the presence of  $\text{Al}^{3+}$ .
- 2)  $\text{AlFx}$  is a molecule giving false information, which is amplified by processes of signal transmission.
- 3) The interactions of F and  $\text{Al}^{3+}$  in the environment, water, and food chains, can evoke various and multiple pathological symptoms.

**Thank you for your attention**



**Supported by MSM 0021620806**

# F



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.