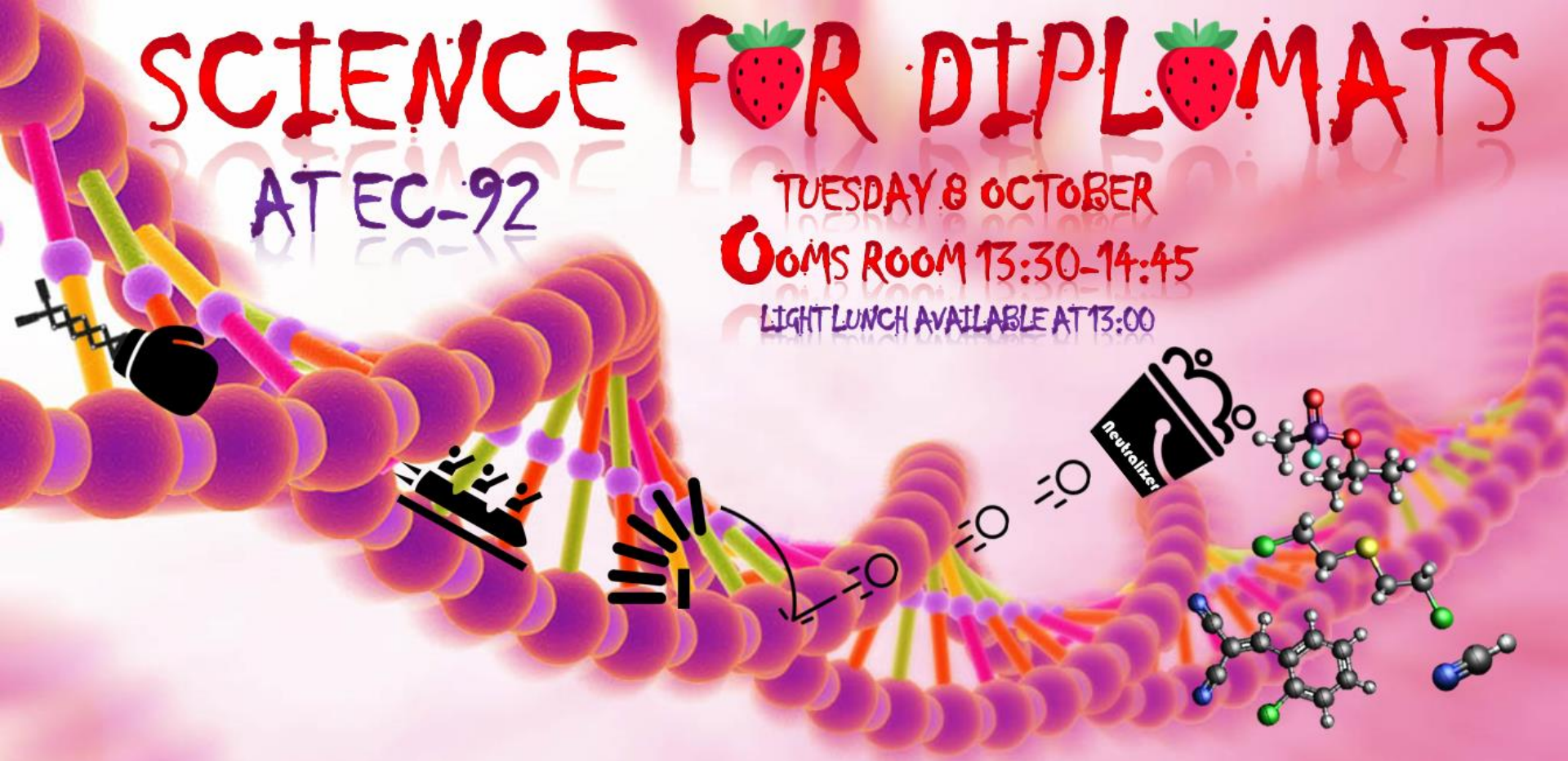
SCIENCE FOR DIPLOMATS

AT EC-92

TUESDAY 8 OCTOBER

OOMS ROOM 13:30-14:45

LIGHT LUNCH AVAILABLE AT 13:00



CHEMICAL ACTION ON LIFE PROCESSES

An exploration of the systems biology of toxic chemicals with a hands-on DNA experience!

OPCW

OPCW

Organisation for the Prohibition of Chemical Weapons

Chemical Action on Life Processes

An exploration of the systems biology of toxic chemicals and a hands on DNA experience

Science for Diplomats at EC-92
The Hague, 8 October 2019

Dr Christophe Curty, 2019 Scientific Advisory Board Vice-Chair/2020 Chair
Ms Andrea Dymytrova, Special Guest
Dr Jonathan E. Forman, Science Policy Adviser/Secretary to the SAB
Mr Bernhardt Fourie, Office of Confidentiality and Security
Ms Giovanna Pontes, Office of Strategy and Policy
Ms Julieta Schneider, Office of Strategy and Policy
Mr Cheng Tang, 2019 Scientific Advisory Board Chair

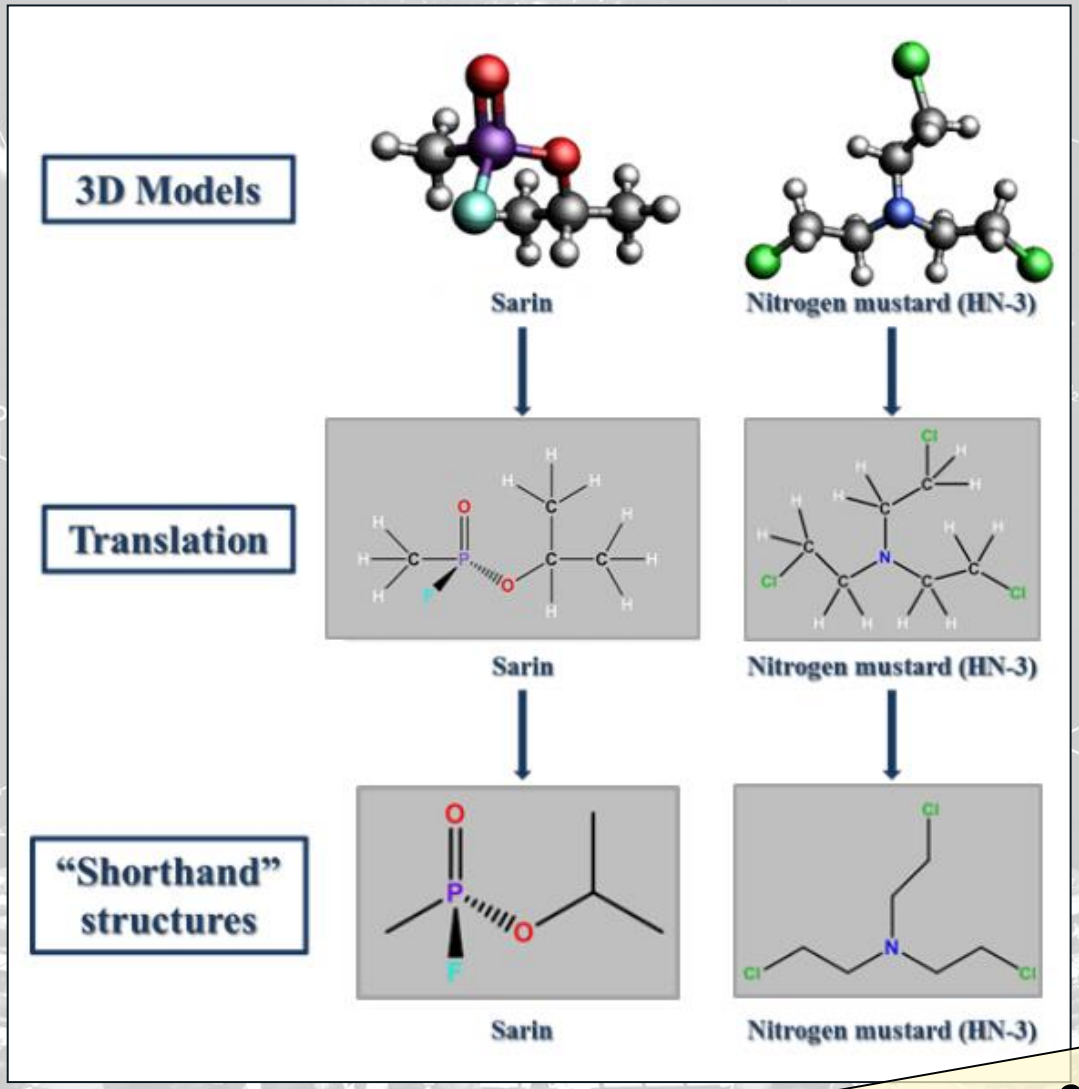
Let us Know You are Here!

Collect your Periodic Table magnet outside the Ooms Room

Before We Begin...

Please do not eat the strawberries!

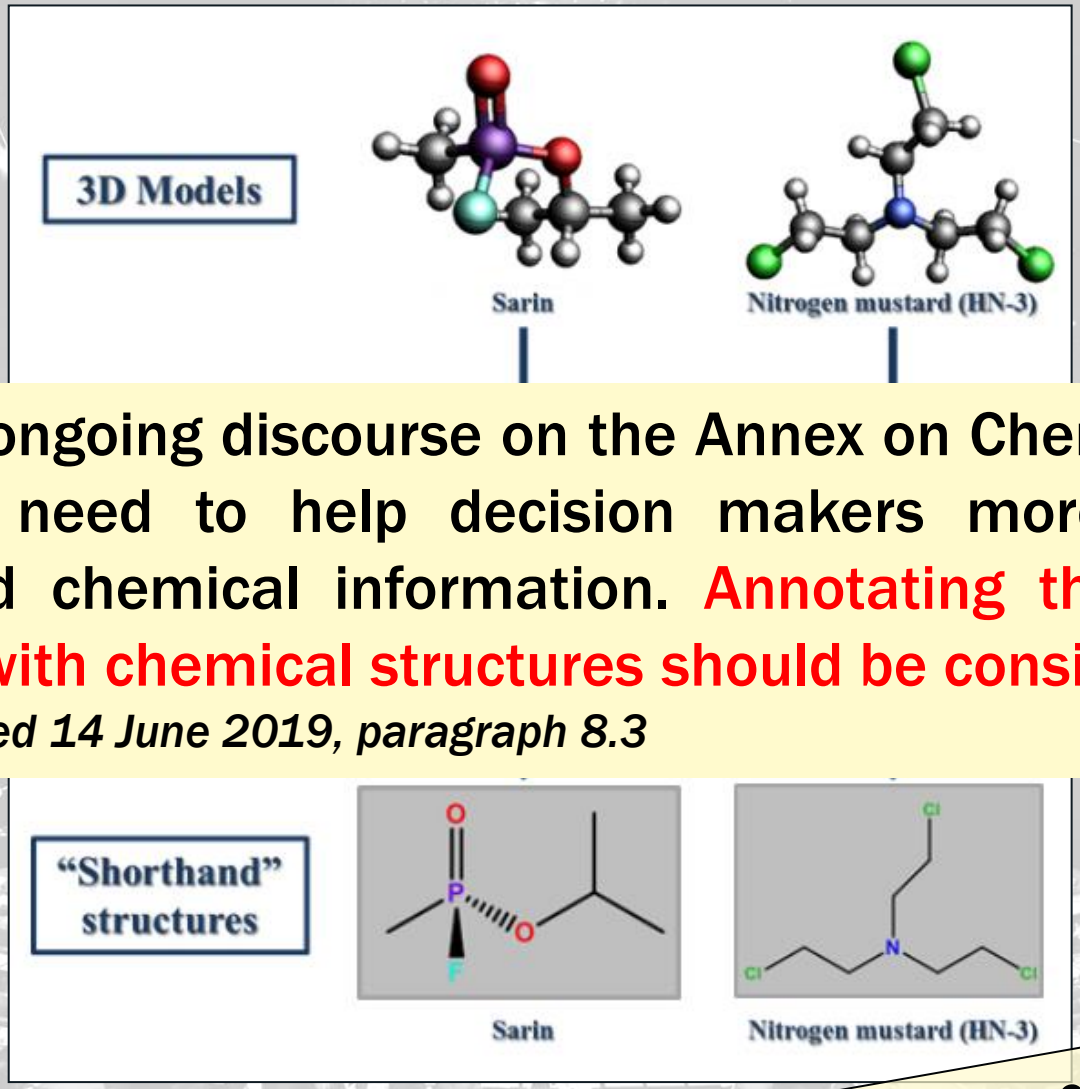
Where we left off…



The language of chemistry is written in connected atoms

OPCW

Where we left off…



"…with the ongoing discourse on the Annex on Chemicals, there is a great need to help decision makers more effectively comprehend chemical information. Annotating the Annex on Chemicals with chemical structures should be considered."

- SAB-28/1, dated 14 June 2019, paragraph 8.3

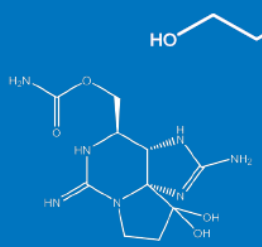
The language of chemistry is written in connected atoms

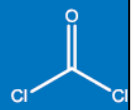
Where we left off...

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

THE "SCIENCE FOR DIPLOMATS" ANNEX ON CHEMICALS

A user friendly and scientifically annotated version of the Chemical Weapons Convention Annex on Chemicals





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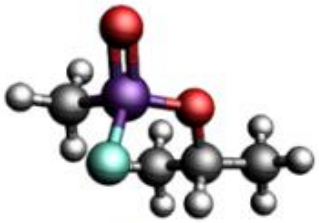
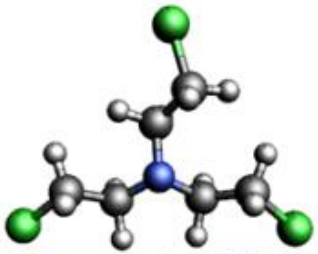


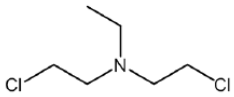
Sarin

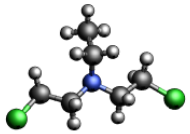


Nitrogen mustard (HN-3)

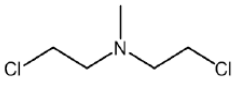
(6) Nitrogen mustards:

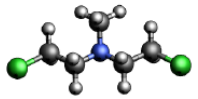
HN1: Bis(2-chloroethyl)ethylamine (538-07-8)
(IUPAC Name: 2-chloro-N-(2-chloroethyl)-N-ethylethanamine)
Scientific Advisory Board recommendation: including corresponding protonated salts.





HN2: Bis(2-chloroethyl)methylamine (51-75-2)
(IUPAC Name: 2-chloro-N-(2-chloroethyl)-N-methylethanamine)
Scientific Advisory Board recommendation: including corresponding protonated salts.





HN3: Tris(2-chloroethyl)amine (555-77-1)
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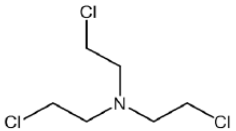
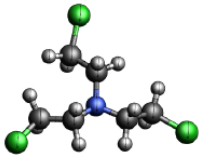
Scientific Advisory Board recommendation: including corresponding protonated salts.

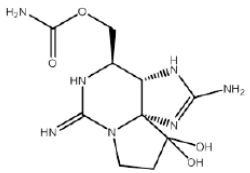


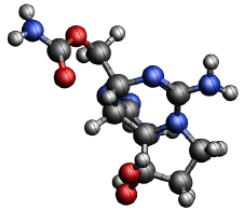


15

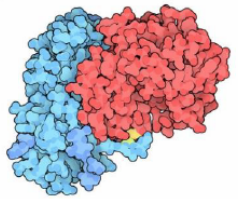
(7) Saxitoxin (35523-89-8)

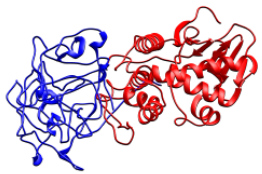
(IUPAC Name: [(3aS,4R,10aS)-2,6-diamino-10,10-dihydroxy-3a,4,8,9-tetrahydro-1H-pyrrolo[1,2-c]purin-4-yl]methyl carbamate)
Scientific Advisory Board recommendation: including corresponding protonated salts.





(8) Ricin (9009-86-3)





Ricin is a protein composed of toxic (A-chain) and cell-targeting (B-chain) subunits, illustrated in red (A-chain) and blue (B-chain) in the structure on the left. The right structure is an interactive ribbon model of the ricin molecule.[8]

[8] E. Rutenber, B. J. Katzin, S. Ernst, E. J. Collins, M. P. Ready, J. D. Robertus; Crystallographic refinement of ricin to 2.5 Angstroms; *Proteins*;, 1991, 10, 240-250. DOI: 10.1002/prot.340100308. Protein Data Bank structure 2AA1. Available at: https://www.rcsb.org/structure/2AAI.

16

Where we left off…

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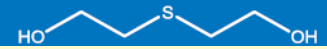
A user friendly and scientifically annotated version of the Chemical Weapons Convention Annex on Chemicals



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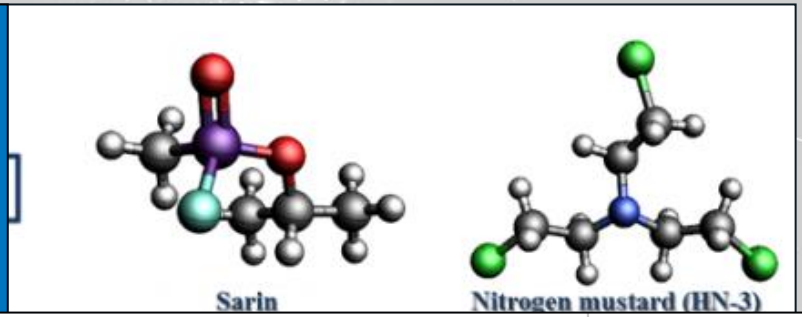

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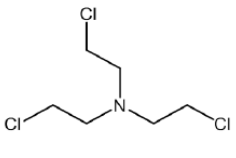

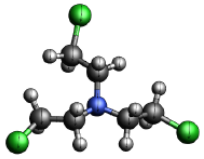

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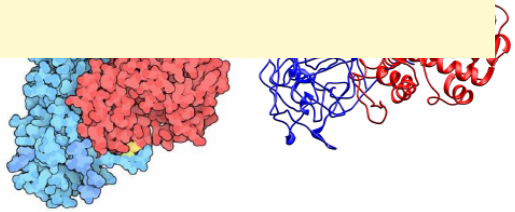

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16

"**The Director-General supports the SAB's view** that annotating the Annex on Chemicals with chemical structures would better equip decision makers to understand and draw upon key chemistry concepts in their discourse."

- EC-92/DG.12, dated 9 September 2019, paragraph 15

written

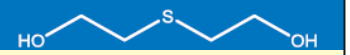
OPCW

Where we left off…

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEA

THE "SCIENCE FOR DIPLOMAT
ANNEX ON CHEMICALS

A user friendly and scientifically annotated vers
Chemical Weapons Convention Annex on Ch

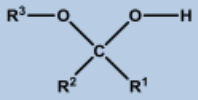
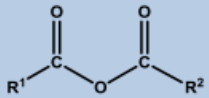
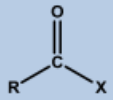


"The Director-Ge
the Annex on Ch
equip decision
chemistry concep
- EC-92/DG.12, dated 9

OPCW

F. ORGANIC CHEMICAL FUNCTIONAL GROUPS

Chemicals are defined by the functional groups they contain within their molecular structures. A functional group is a particular group of atoms in a molecule that defines reactivity, and influences chemical properties and behaviour. Complex molecules can contain multiple types of functional groups. This table provides descriptions of many of the types of functional groups found in organic chemistry, it is not intended to be comprehensive.

Functional Group Nomenclature	General Structure	Substructures	Description
Acetal [substructure: *-al dialkyl acetal*]		R^1 = hydrogen atom or alkyl group R^2, R^3 = alkyl group	Acetals are chemical structures containing a carbon atom connected to two oxygen atoms (which serve as bridges to alkyl groups), and to either two hydrogen atoms or to a hydrogen atom and an alkyl group.
Acid Anhydride [substructure: *-oic anhydride*]		R^1, R^2 = hydrogen atom or alkyl group	Acid anhydrides are chemical structures in which an oxygen atom serves as a bridge between two carbonyl groups (a carbon connected to an oxygen atom through a double bond), each of which is further connected to a hydrogen atom or alkyl group.
Acyl Halide [substructure: *-oyl halide* (e.g. fluoride, chloride, bromide, iodide, astatide)]		R = hydrogen atom or alkyl group X = halogen atom	Acyl Halides are chemical structures containing a carbon atom connected to a hydrogen atom or an alkyl group, a halogen and an oxygen atom through a double bond.
Alcohol [substructure: *-ol*]		R = alkyl group	Alcohols are chemical structures that contain a hydroxyl group (an oxygen atom attached to a hydrogen atom) connected to an alkyl group, and has no other [illegible] attached to the hydroxyl attached

(35523-89-8)

[(3aS,4R,10aS)-2,6-diamino-10,10-dihydroxy-3a,4,8,9-tetrahydro-1H-purin-4-yl]methyl carbamate)

hat annotating
s would better
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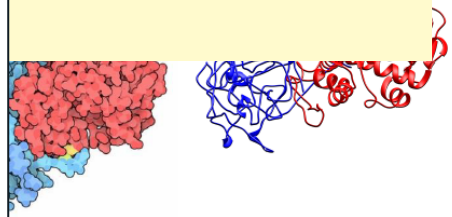

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D. Roberts; Crystallographic
of ricin to 2.5 A. DOI: 10.1002/prot.340100308.
http://www.rcsb.org/structure/1AAI.

Chemical properties are all about the "functional groups"!

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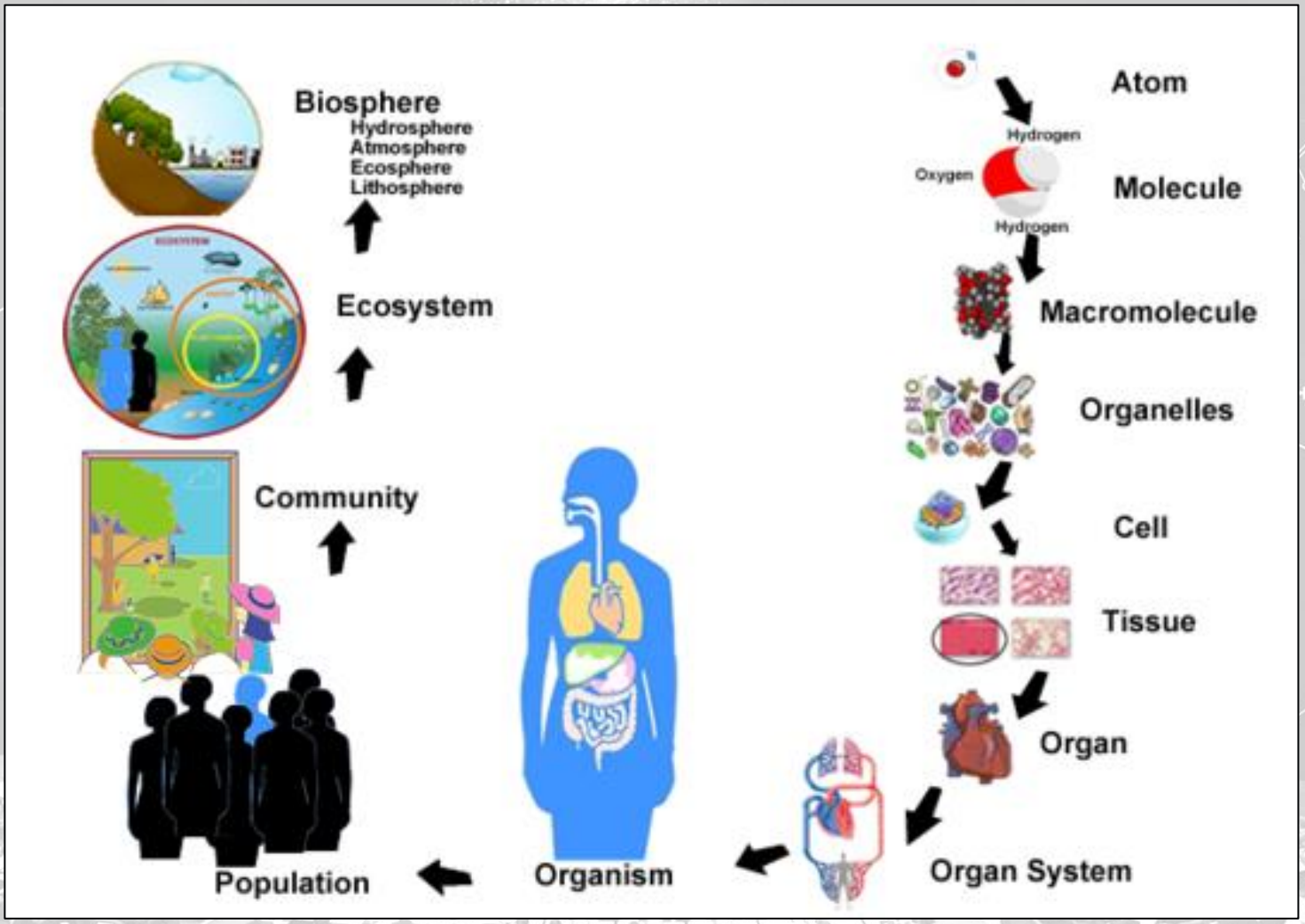
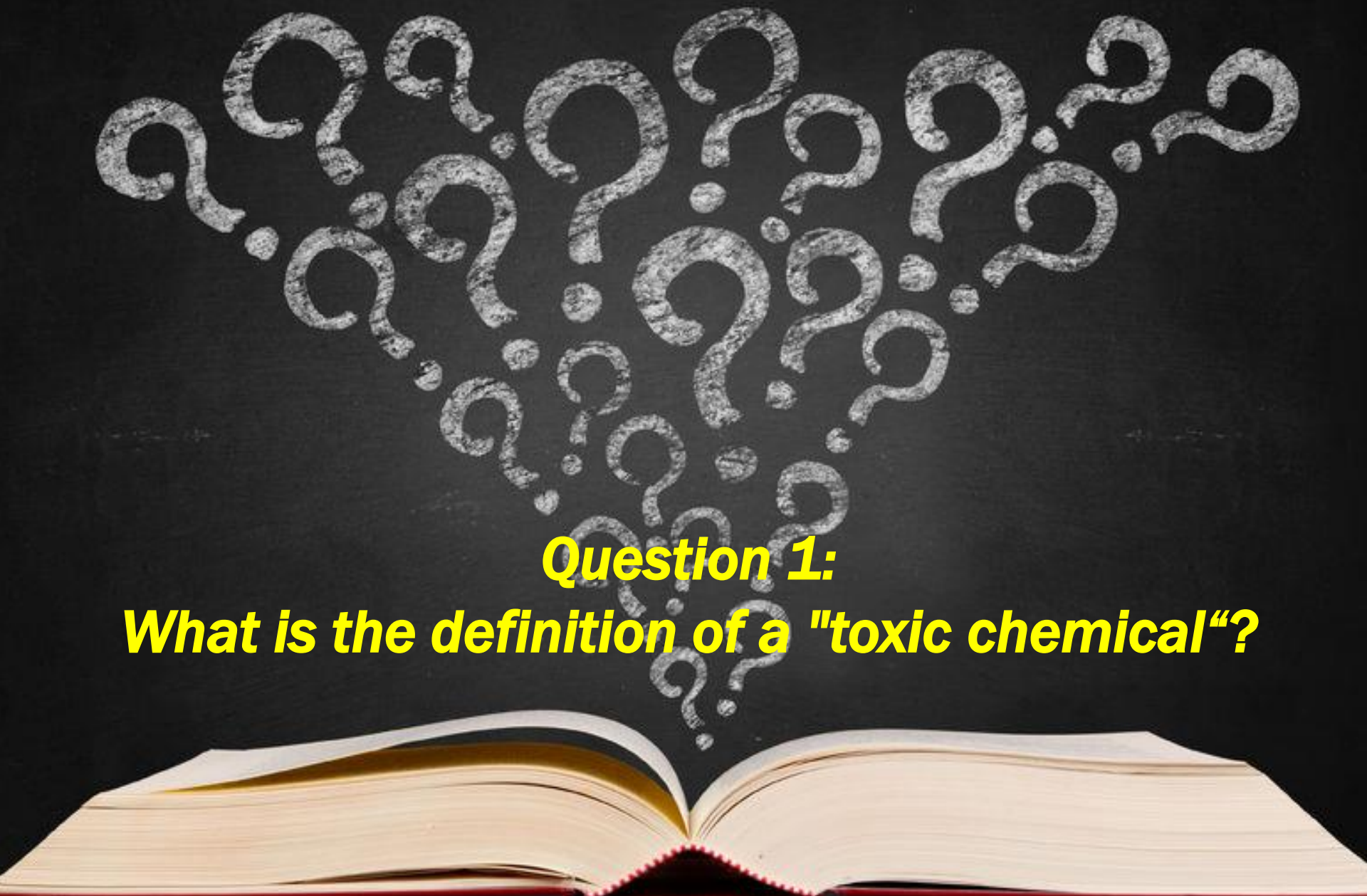
How Do Atoms and Molecules Connect to our Priorities?



http://cms.gavirtualschool.org/Shared/Science/Biology17/WelcomeToBiology/Biology_WelcomeToBiology_Shared4.html

A “Science of the Chemical Weapons Convention” Quiz



Question 1:
What is the definition of a "toxic chemical“?

Answers from the Audience (22 Responses)

Mentimeter

What is the definition of a "toxic chemical"?

- It means so there is a skull on the bottle
- It kills or hurt you
- A chemical which is toxic.
- Poisonous substance
- Incurs a chemical reaction detrimental to human health
- Chemical which causes harm
- hazardous substance
- Whatever the CWC says it means
- All chemicals
- Chemical that do harm to human body
- Non-edible
- A chemical liked by britney spears
- Poison
- Frenemy
- Poison
- Harmful chemical not classified as CW
- A chemical with an adverse effect'
- Kills living beings in a nasty manner
- A chemical that is toxic
- Any chemical which through its chemical action on life processes can cause death or permanent harm to humans or animals
- All Chemicals

22

Toxicology

"The study of the adverse effects of chemicals on living organisms"

GHS hazard pictograms

Basic assumption of toxicology

"The dose makes the poison"
(Latin: ***sola dosis facit venenum***)

"Alle Ding' sind Gift und nichts ist ohn' Gift; allein die Dosis macht, dass ein Ding kein Gift ist."

All things are poison, and nothing is without poison, the dosage alone makes it so a thing is not a poison.

Paracelsus (1493-1541)

Basic assumption of toxicology

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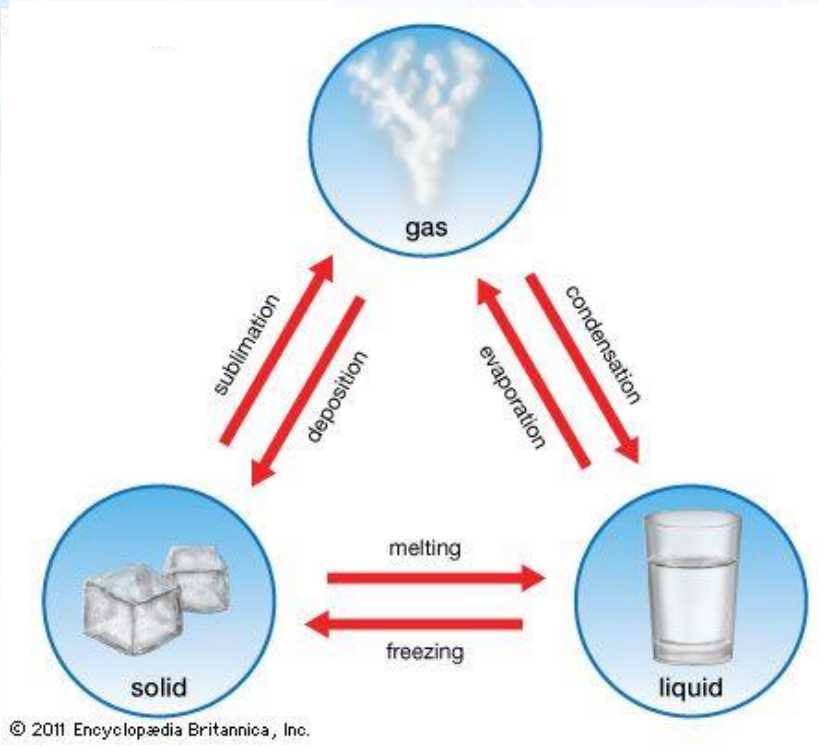
Paracelsus (1493-1541)

Individual Response to Exposure

Individual sensitivity

Routes of Exposure



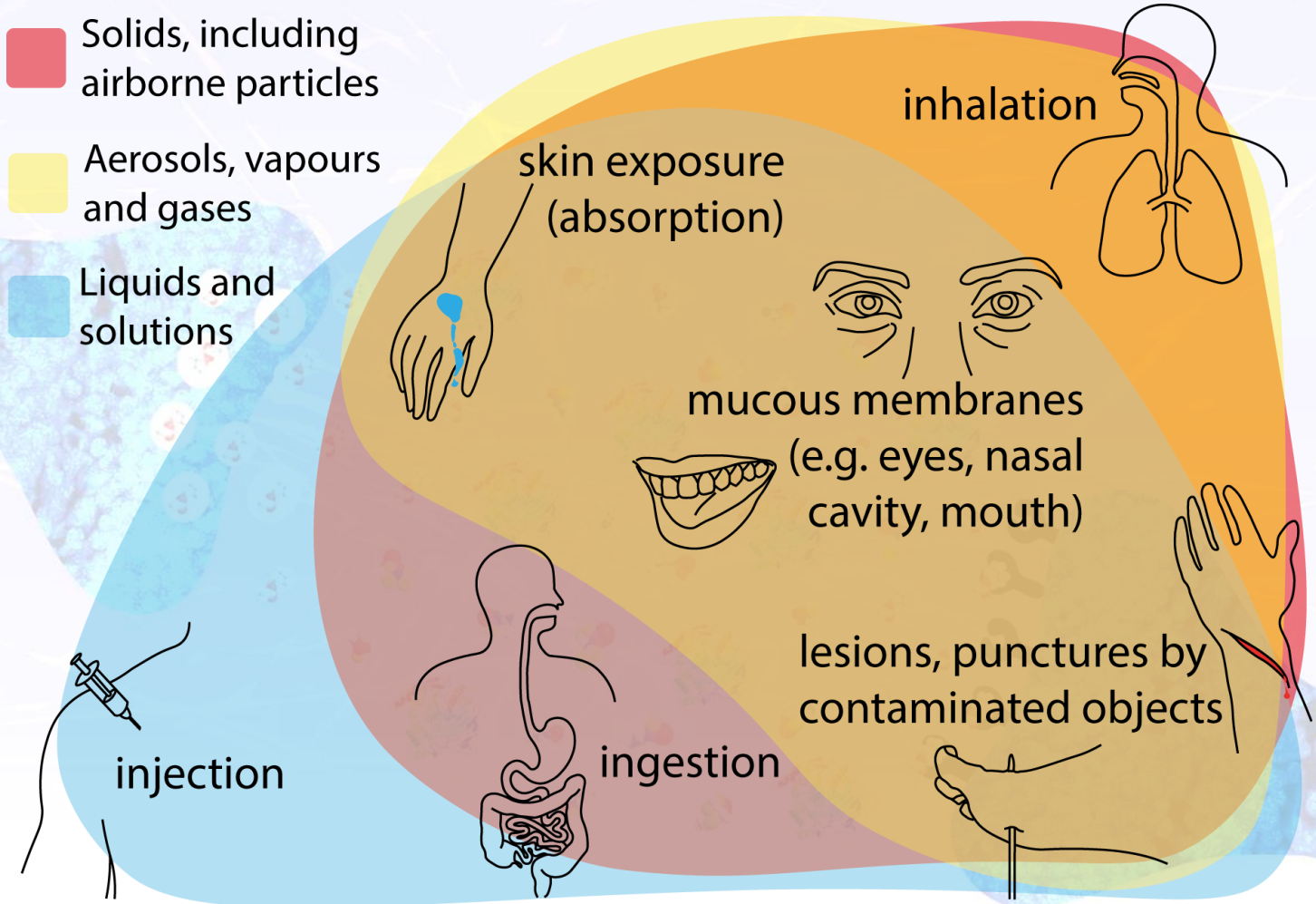
Inhalation

Ingestion

Skin absorption

Duration of exposure

Routes of Exposure and Physical State of Chemical Agent



Routes of Exposure

Acute

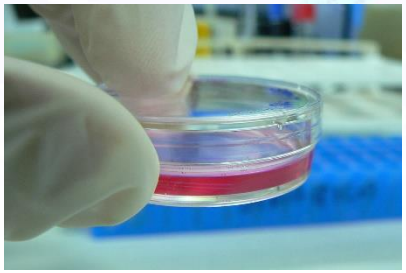
Single short-term exposure

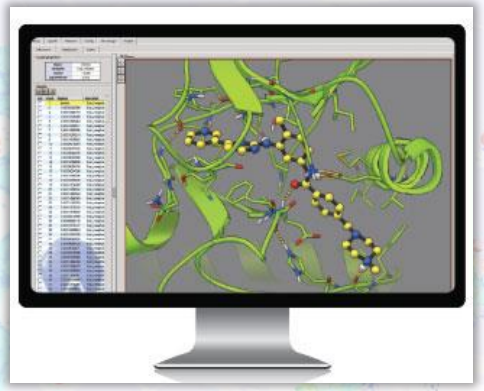
Chronic

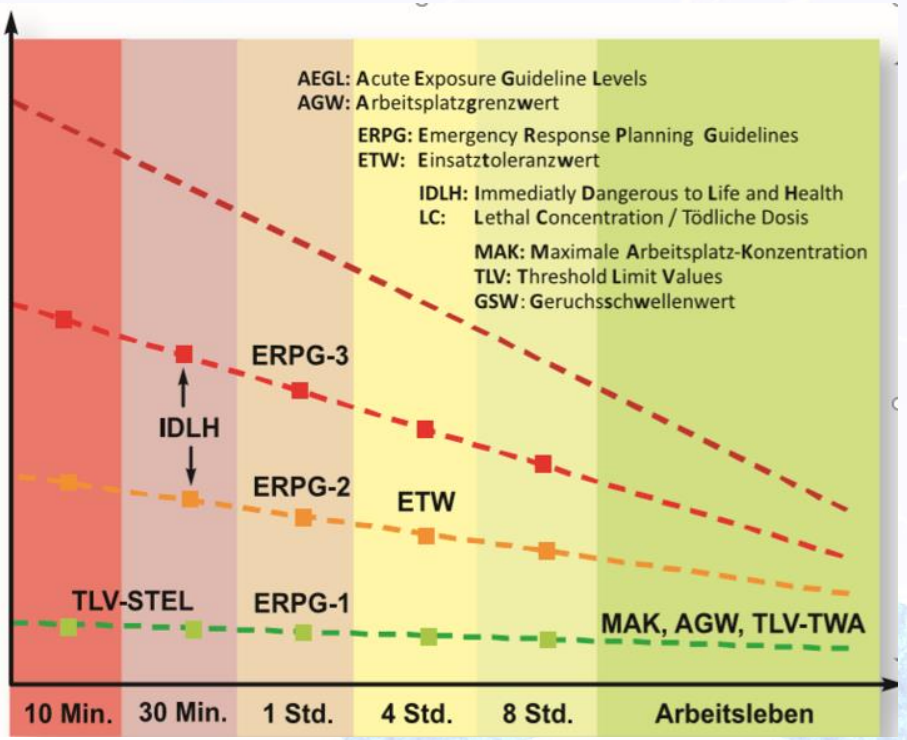
Repeated or continuous exposure

How much of a chemical is required to cause death?

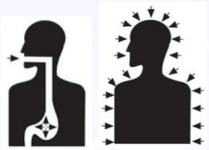
Testing for Toxicity







Dosage Units



- **Median Lethal Dose** (LD_{50})

  The "dose of a chemical expected to be lethal to 50% of the members of an exposed population."

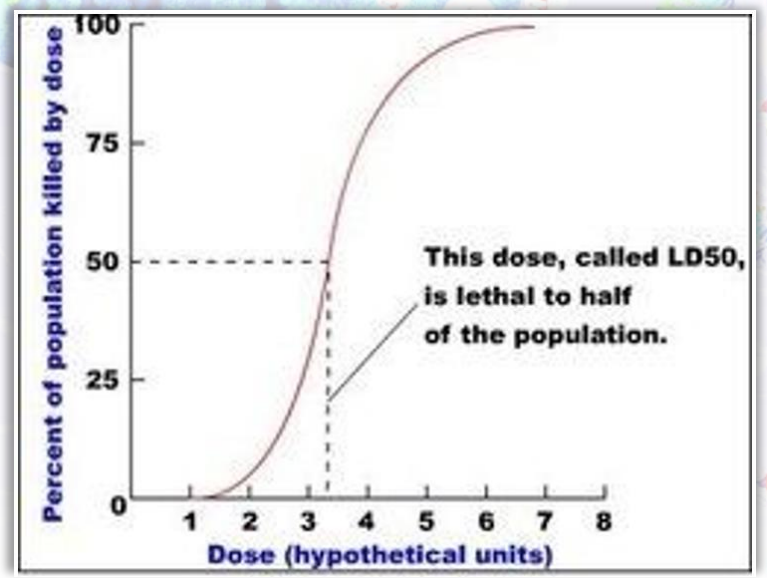
  [mg/kg body weight]

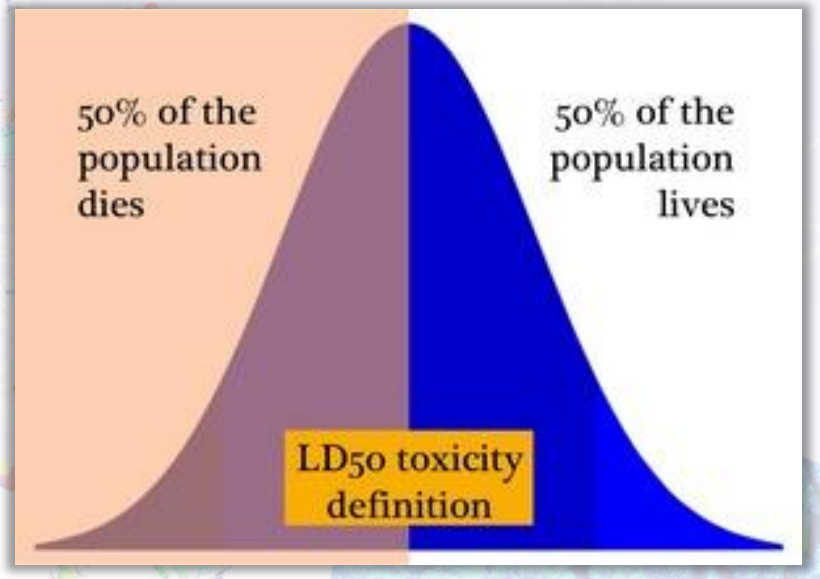
- **Median Lethal Concentration as a function of time** (LCt_{50})

  The "concentration of a chemical (in vapor phase) expected to be lethal to 50% of the members of an exposed population for a specified period of time."

  [mg·min/m^3]

Dosage Units





Example: Dichlorovos

Insecticide commonly used in household pesticide strips

- Oral LD_{50} (rat): 56 mg/kg
- Dermal LD_{50} (rat): 75 mg/kg
- Intraperitoneal LD_{50} (rat): 15 mg/kg
- Inhalation LC_{50} (rat): 1.7 ppm (15 mg/m3); 4-hour exposure
- Oral LD_{50} (rabbit) 10 mg/kg
- Oral LD_{50} (pigeon:): 23.7 mg/kg

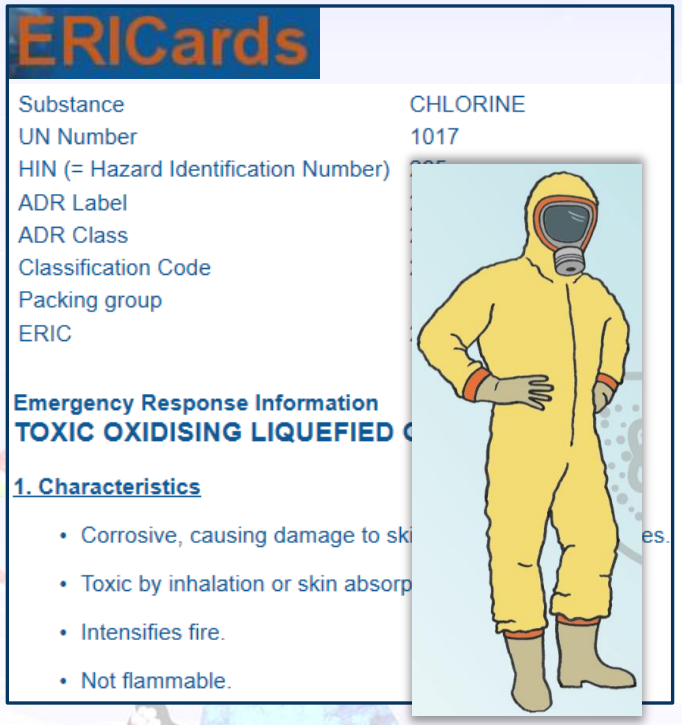
Toxicity classes



Toxicity Classes: Hodge and Sterner Scale					
		Routes of Administration			
		Oral LD_{50}	Inhalation LC_{50}	Dermal LD_{50}	
Toxicity Rating	**Commonly Used Term**	**(single dose to rats) [mg/kg]**	**(exposure of rats for 4 hours) [ppm]**	**(single application to skin of rabbits) [mg/kg]**	**Probable Lethal Dose for Man**
1	Extremely Toxic	1 or less	10 or less	5 or less	1 grain (a taste, a drop)
2	Highly Toxic	1-50	10-100	5-43	4 ml (1 tsp)
3	Moderately Toxic	50-500	100-1000	44-340	30 ml (1 fl. oz.)
4	Slightly Toxic	500-5000	1000-10,000	350-2810	600 ml (1 pint)
5	Practically Non-toxic	5000-15,000	10,000-100,000	2820-22,590	1 litre (or 1 quart)
6	Relatively Harmless	15,000 or more	100,000	22,600 or more	1 litre (or 1 quart)

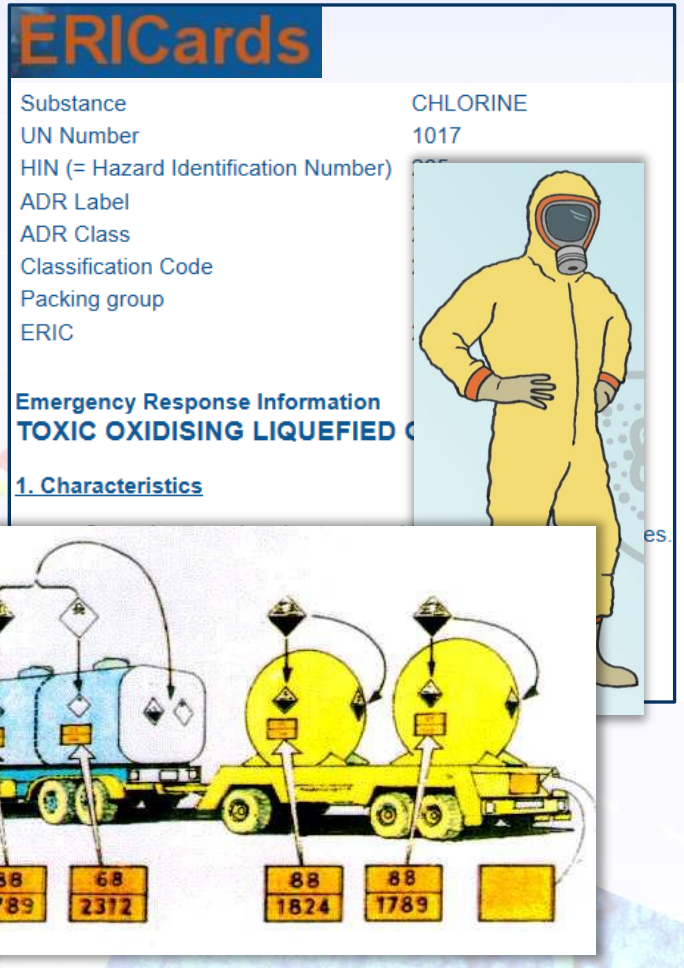
For what?

- Emergency procedures
- Safety clothing and equipment guidelines



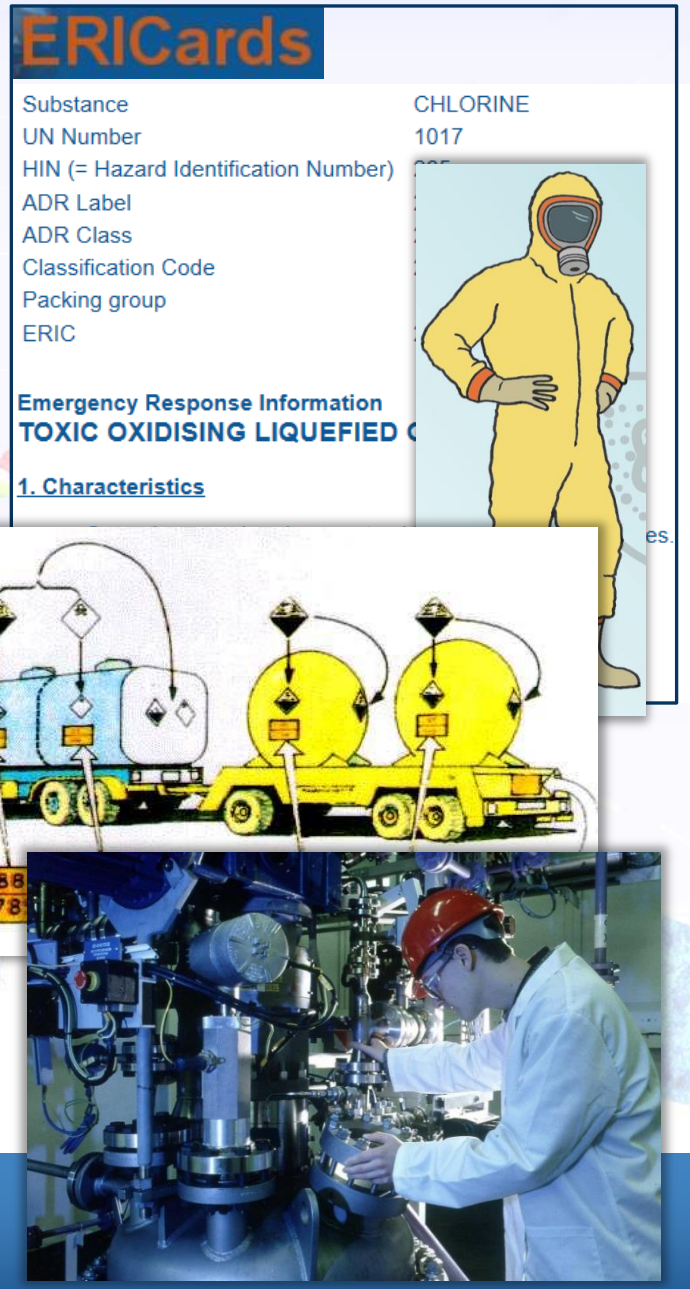
For what?

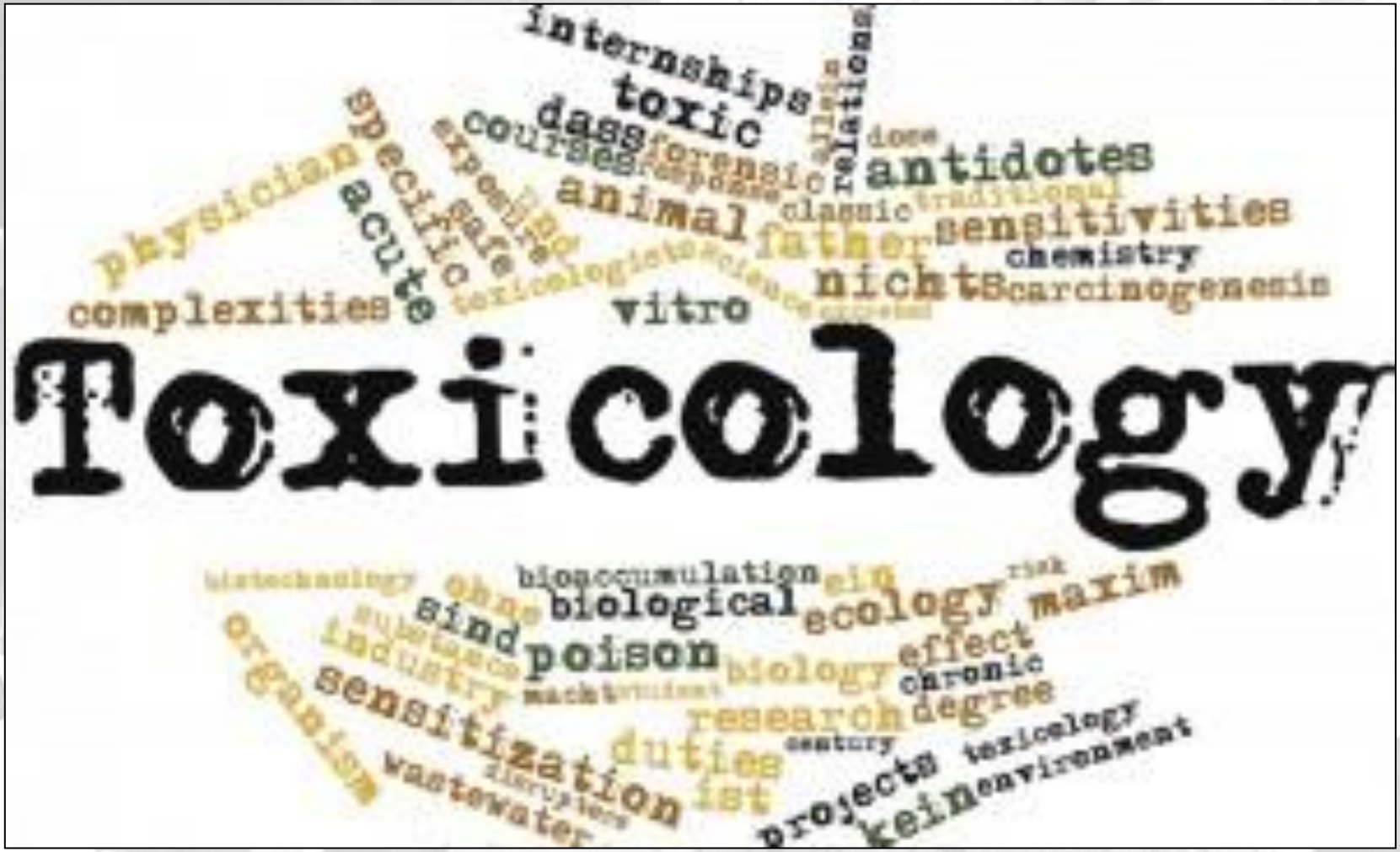
- Emergency procedures
- Safety clothing and equipment guidelines
- Transportation regulations



For what?

- Emergency procedures
- Safety clothing and equipment guidelines
- Transportation regulations
- Occupational exposure limits





Environmental Toxicology: https://www.slideshare.net/misteraugie/hlth104chapter03

What is a LD_{50} and LC_{50}? https://www.ccohs.ca/oshanswers/chemicals/ld50.html

A “Science of the Chemical Weapons Convention” Quiz Answer

Any chemical which through its ***chemical action on life processes*** can cause death, temporary incapacitation or permanent harm to humans or animals. This includes all such chemicals, regardless of their origin or of their method of production, and regardless of whether they are produced in facilities, in munitions or elsewhere

- Chemical Weapons Convention Article II, Paragraph 2

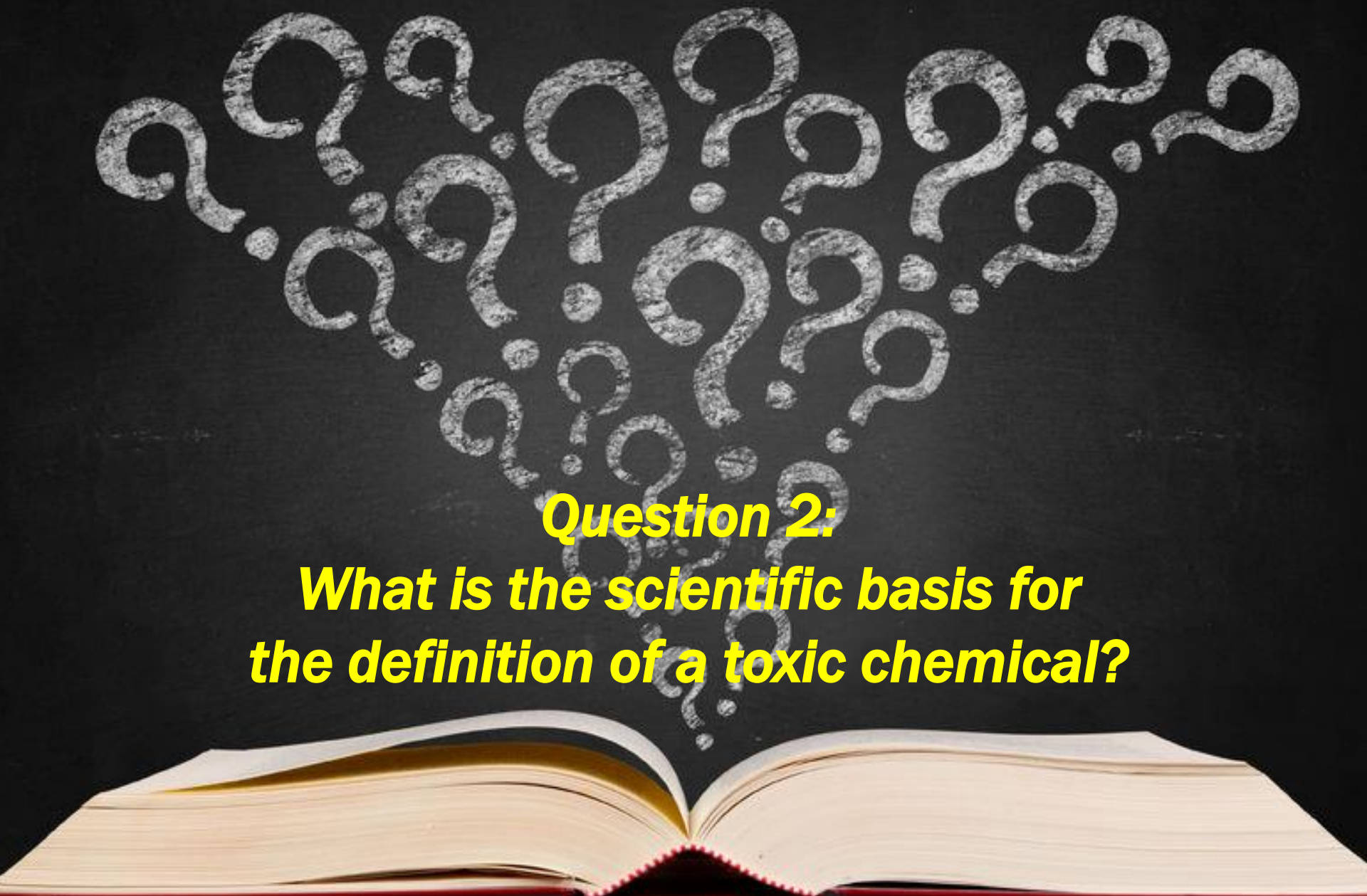
Question 1:
What is the definition of a "toxic chemical“?

What is a “Life Process”?

(*this is not defined in the Convention*)

OPCW

A “Science of the Chemical Weapons Convention” Quiz



Question 2:
What is the scientific basis for the definition of a toxic chemical?

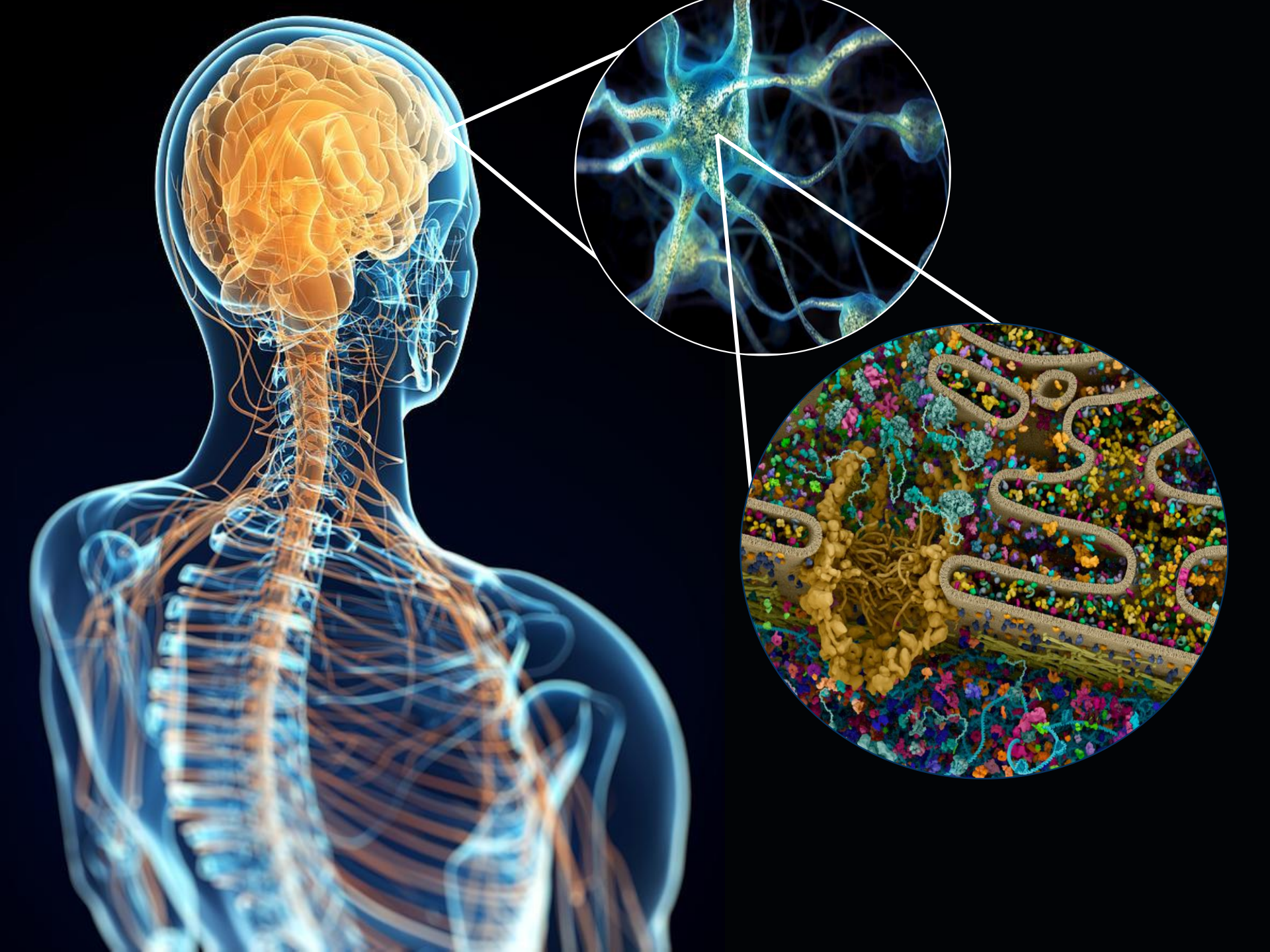
Answers from the Audience (9 Responses)

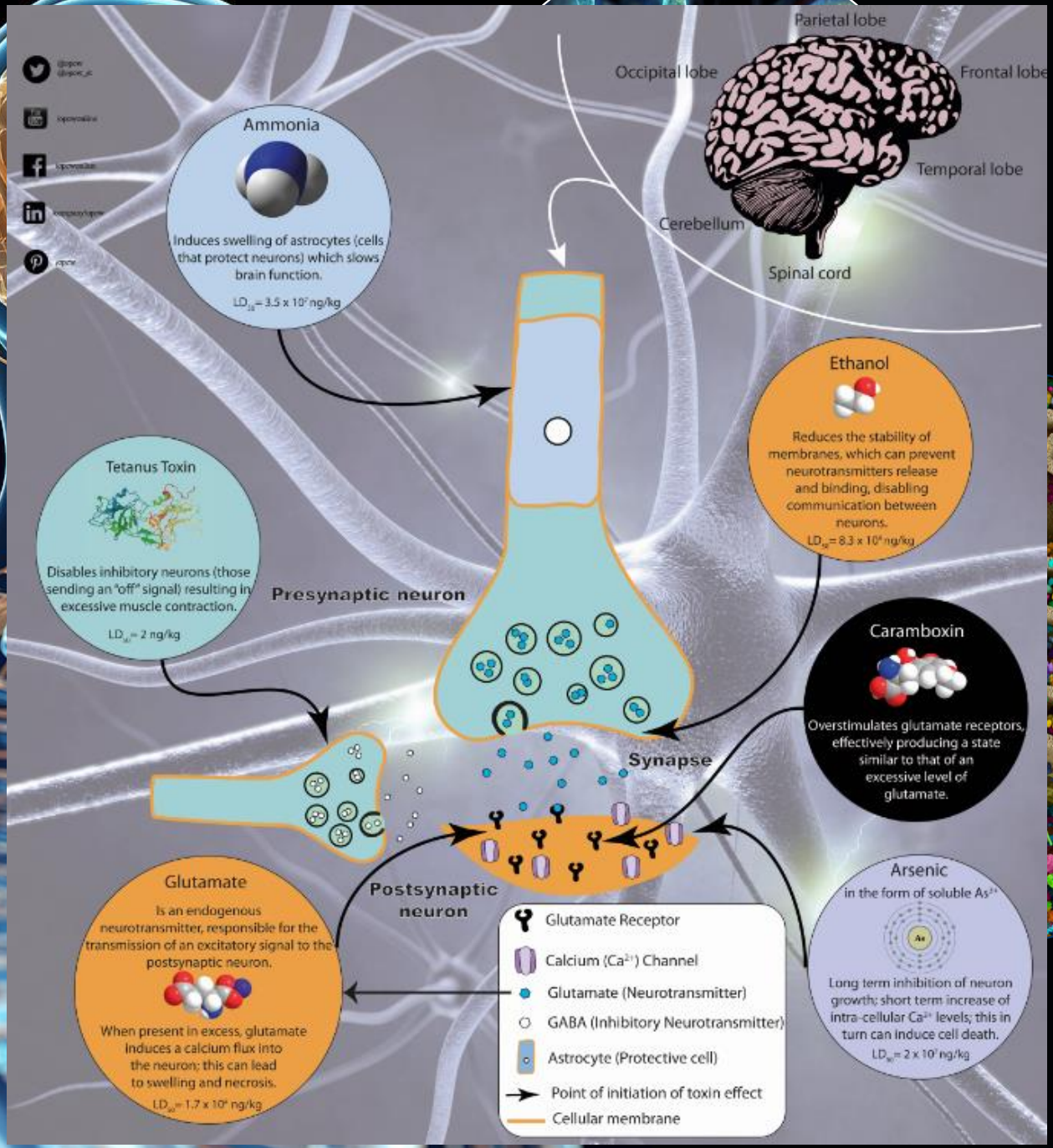
Mentimeter

What is the scientific basis for the definition of a toxic chemical?

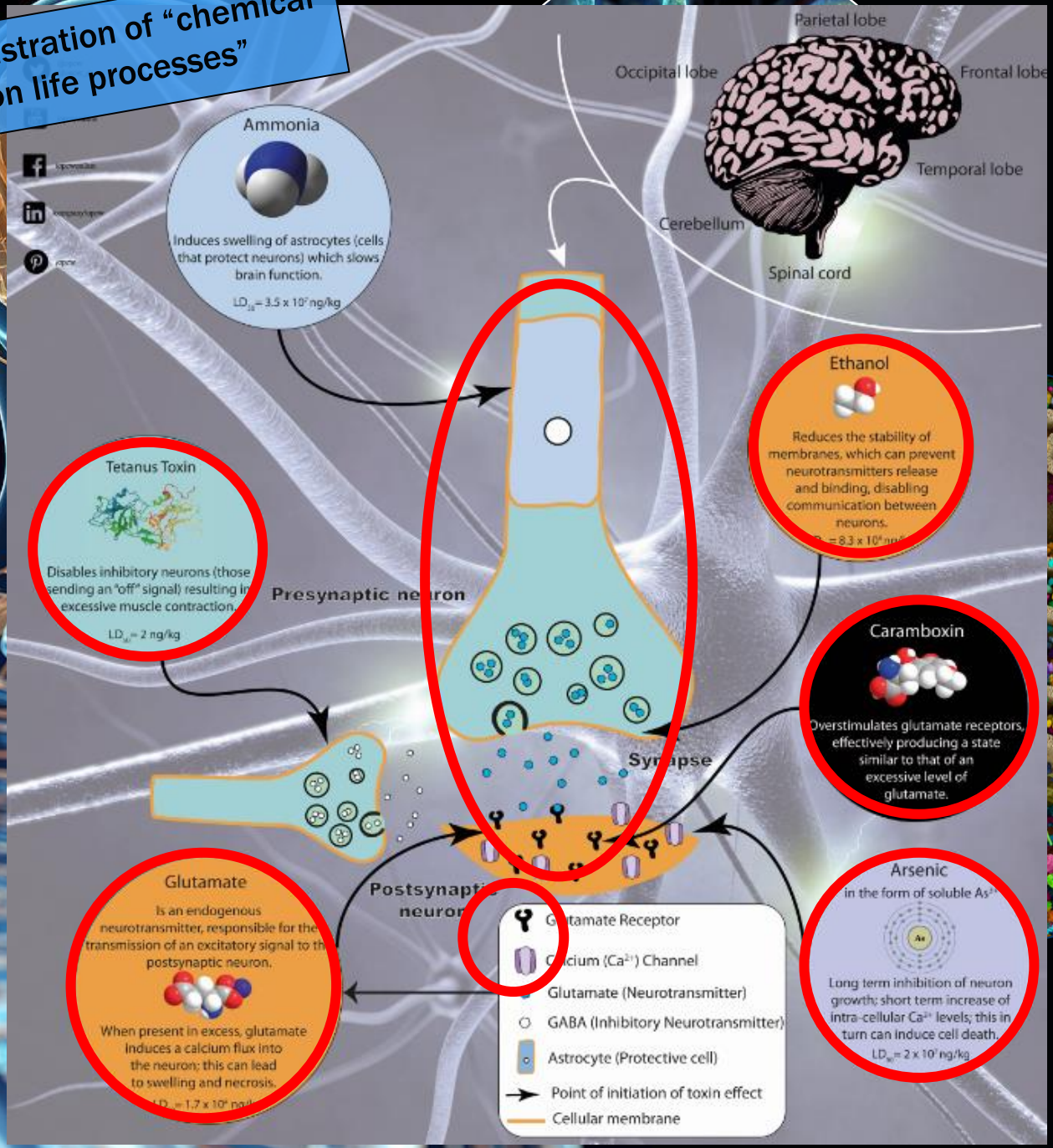
Tests	it has a certain LD50	Toxicology
A chemical with adverse effects on human , animals...	Chemistry	Biochemistry
Chemical testing	What is the procedure to die	Art II adverse Affekts on Action on Life processes

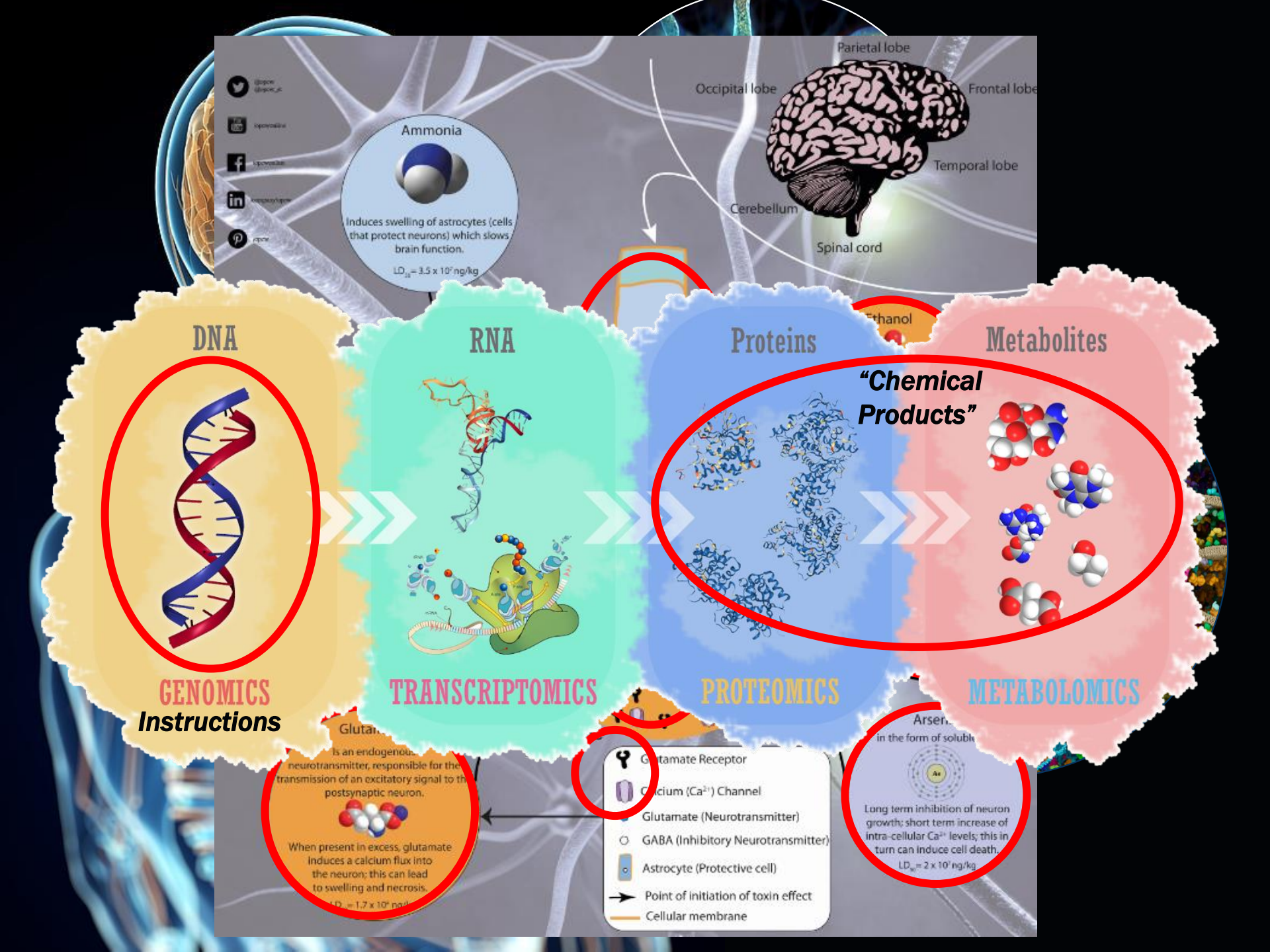
9

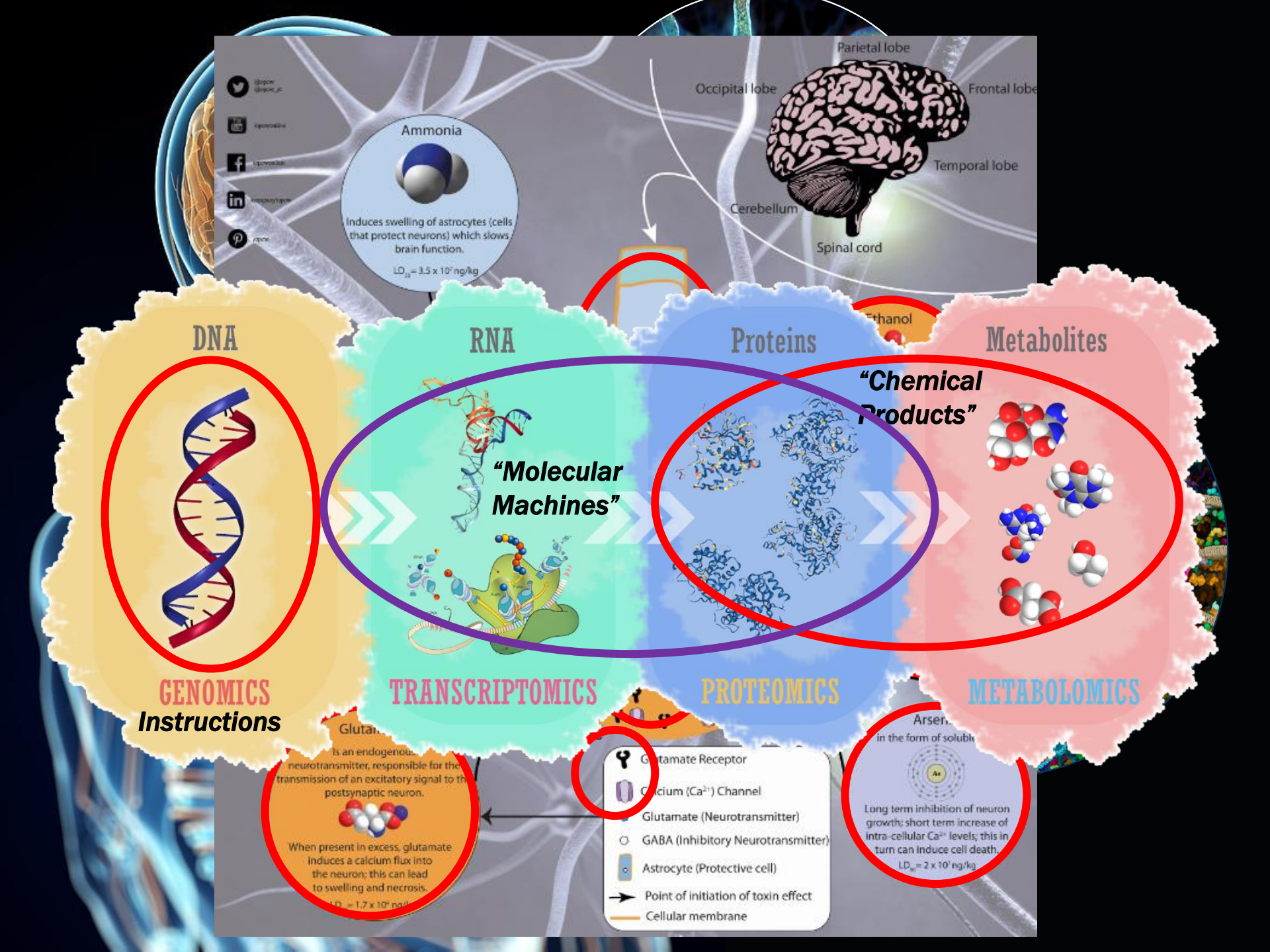



Parietal lobe
Occipital lobe
Frontal lobe
Temporal lobe
Cerebellum
Spinal cord
Ammonia
Induces swelling of astrocytes (cells that protect neurons) which slows brain function.
LD_{50} = 3.5 x 10⁷ ng/kg
Ethanol
Reduces the stability of membranes, which can prevent neurotransmitters release and binding, disabling communication between neurons.
LD_{50} = 8.3 x 10⁸ ng/kg
Tetanus Toxin
Disables inhibitory neurons (those sending an "off" signal) resulting in excessive muscle contraction.
LD_{50} = 2 ng/kg
Presynaptic neuron
Caramboxin
Overstimulates glutamate receptors, effectively producing a state similar to that of an excessive level of glutamate.
Synapse
Glutamate
Is an endogenous neurotransmitter, responsible for the transmission of an excitatory signal to the postsynaptic neuron.
When present in excess, glutamate induces a calcium flux into the neuron; this can lead to swelling and necrosis.
LD_{50} = 1.7 x 10⁸ ng/kg
Postsynaptic neuron
Arsenic
in the form of soluble As^{3+}
Long term inhibition of neuron growth; short term increase of intra-cellular Ca^{2+} levels; this in turn can induce cell death.
LD_{50} = 2 x 10⁷ ng/kg
Glutamate Receptor
Calcium (Ca^{2+}) Channel
Glutamate (Neurotransmitter)
GABA (Inhibitory Neurotransmitter)
Astrocyte (Protective cell)
Point of initiation of toxin effect
Cellular membrane

This is an illustration of "chemical action on life processes"




Parietal lobe
Occipital lobe
Frontal lobe
Temporal lobe
Cerebellum
Spinal cord
Ammonia
Induces swelling of astrocytes (cells that protect neurons) which slows brain function.
DNA
RNA
Proteins
Metabolites
"Chemical Products"
GENOMICS
Instructions
TRANSCRIPTOMICS
PROTEOMICS
METABOLOMICS
When present in excess, glutamate induces a calcium flux into the neuron; this can lead to swelling and necrosis.
Glutamate Receptor
Glutamate (Neurotransmitter)
GABA (Inhibitory Neurotransmitter)
Astrocyte (Protective cell)
Point of initiation of toxin effect
Cellular membrane
Long term inhibition of neuron growth; short term increase of intra-cellular Ca2+ levels; this in turn can induce cell death.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https://www.cellsignal.com/contents/science-cellular-landscapes/cellular-landscapes-vesicle-trafficking/science-landscapes-vesicle-trafficking#

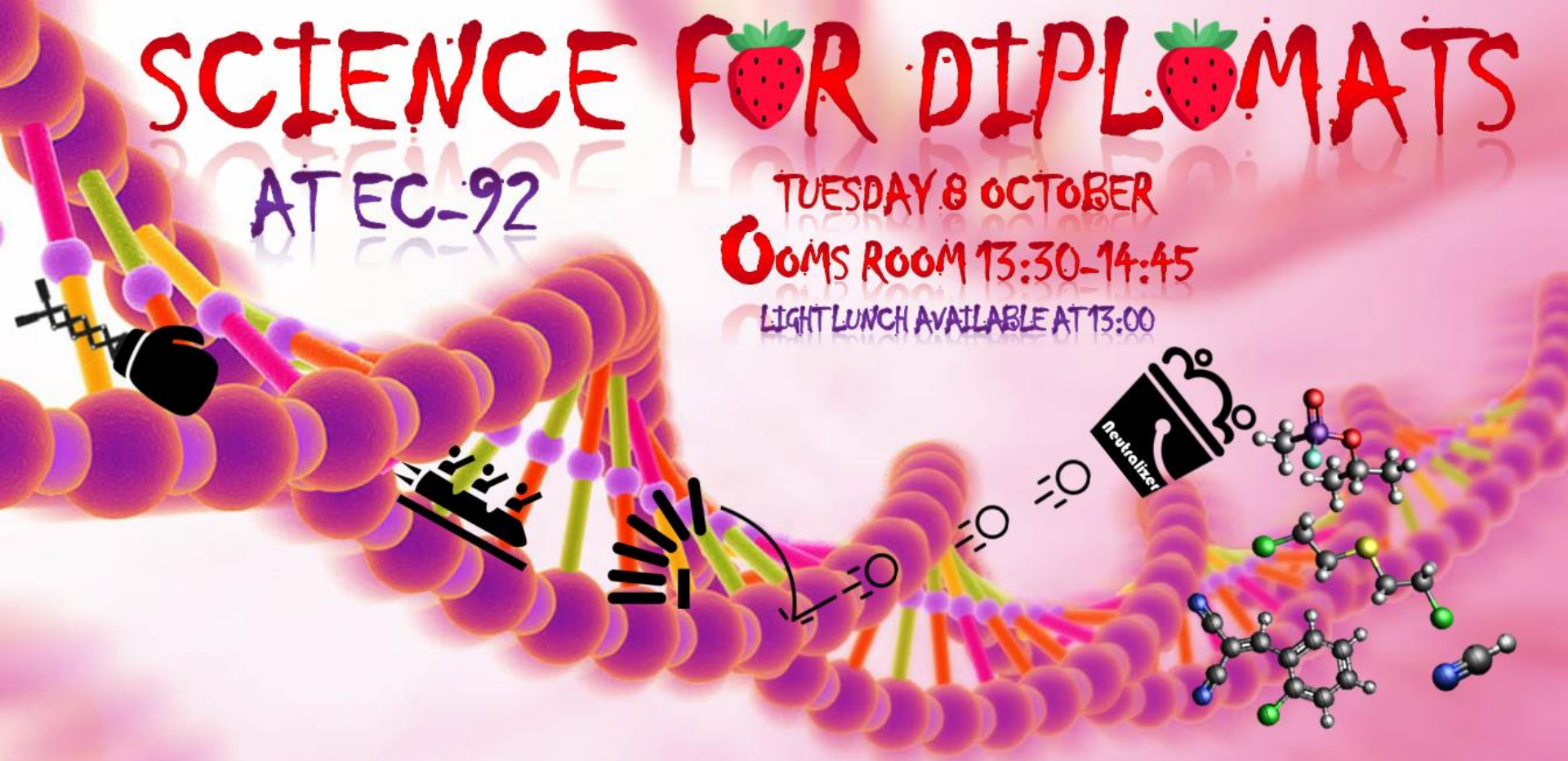
SCIENCE FOR DIPLOMATS

AT EC-92

TUESDAY 8 OCTOBER

OOMS ROOM 13:30-14:45

LIGHT LUNCH AVAILABLE AT 13:00

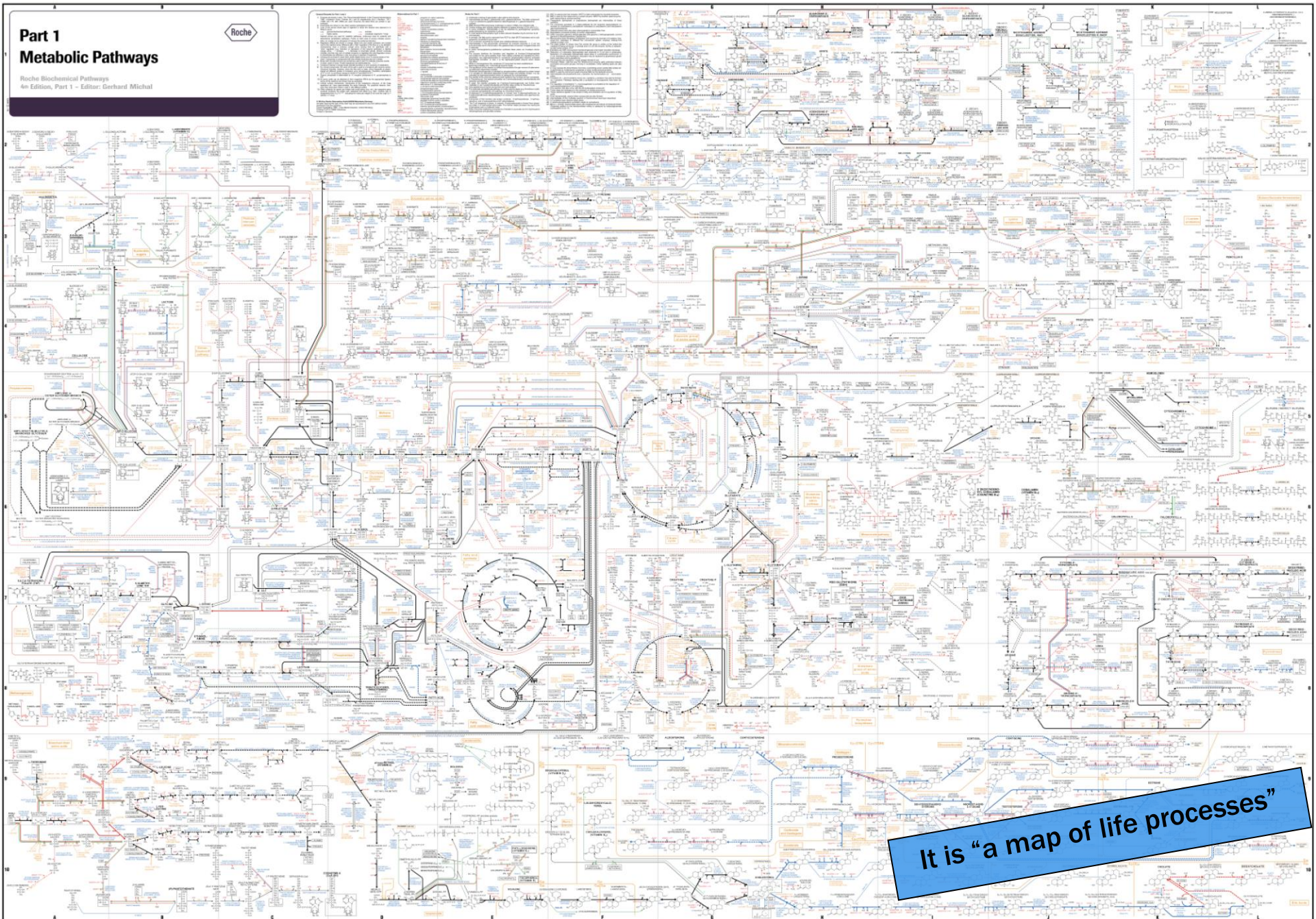


CHEMICAL ACTION ON LIFE PROCESSES

An exploration of the systems biology of toxic chemicals with a hands-on DNA experience!

OPCW

This is NOT a UN Org Chart!



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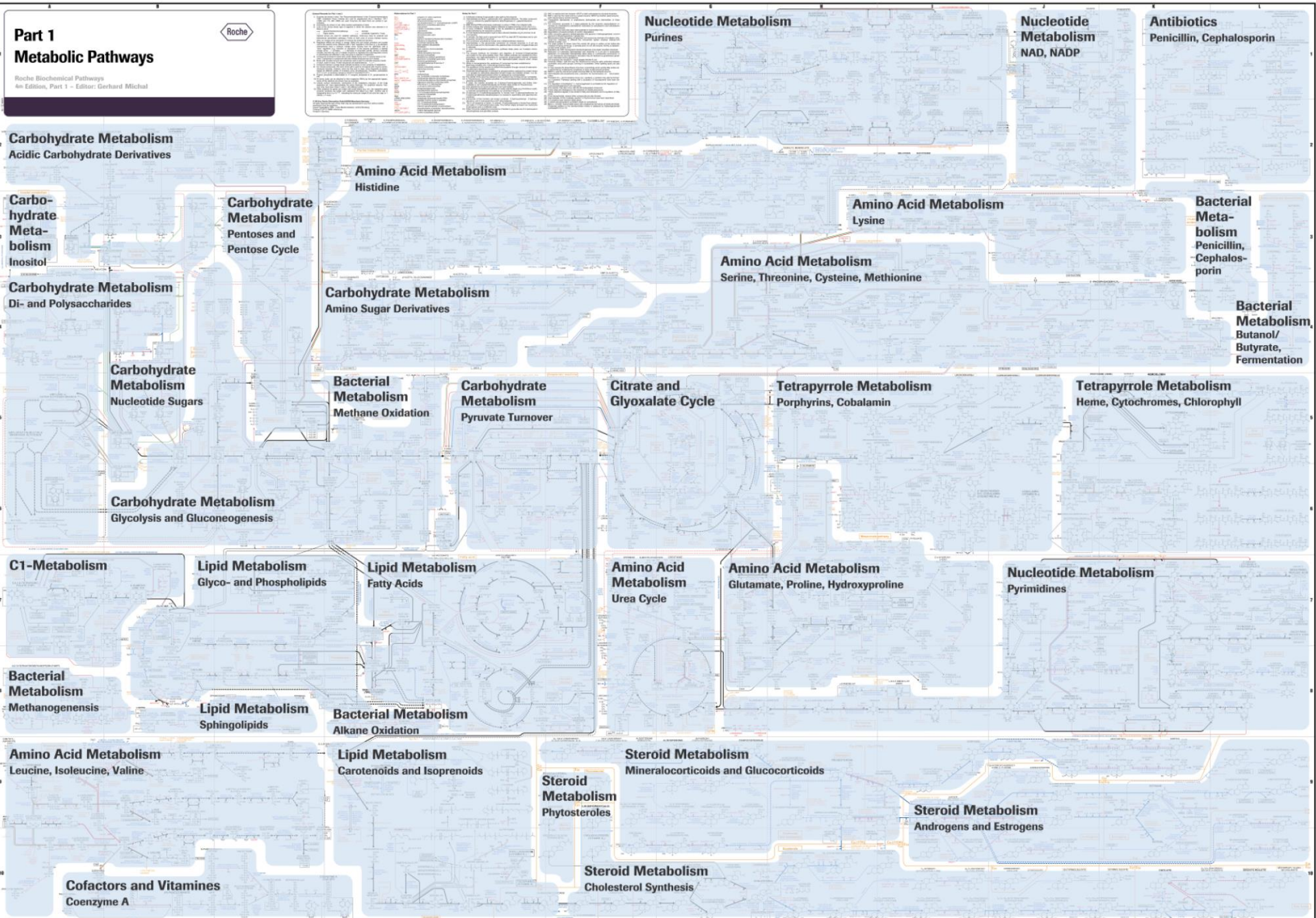

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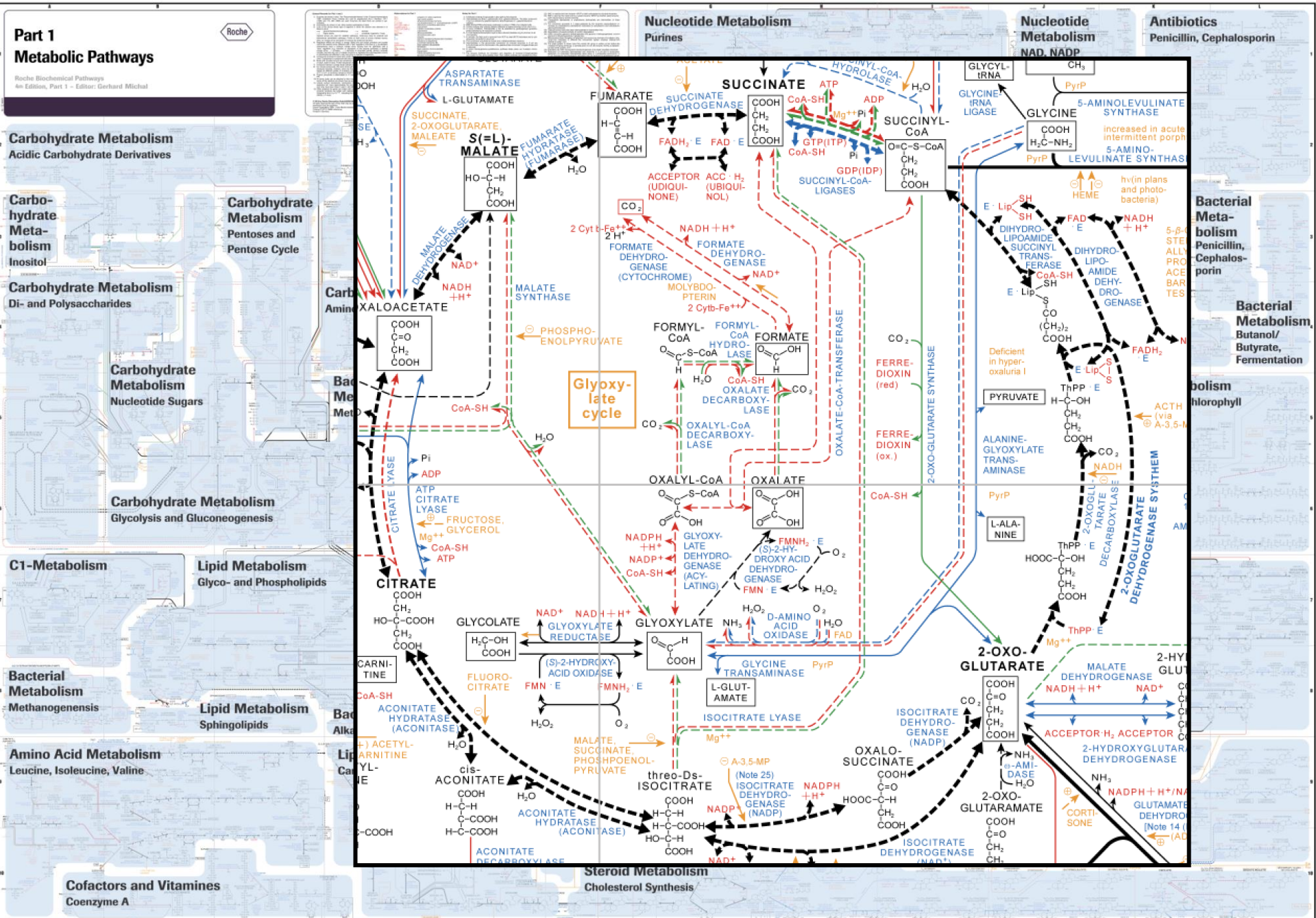
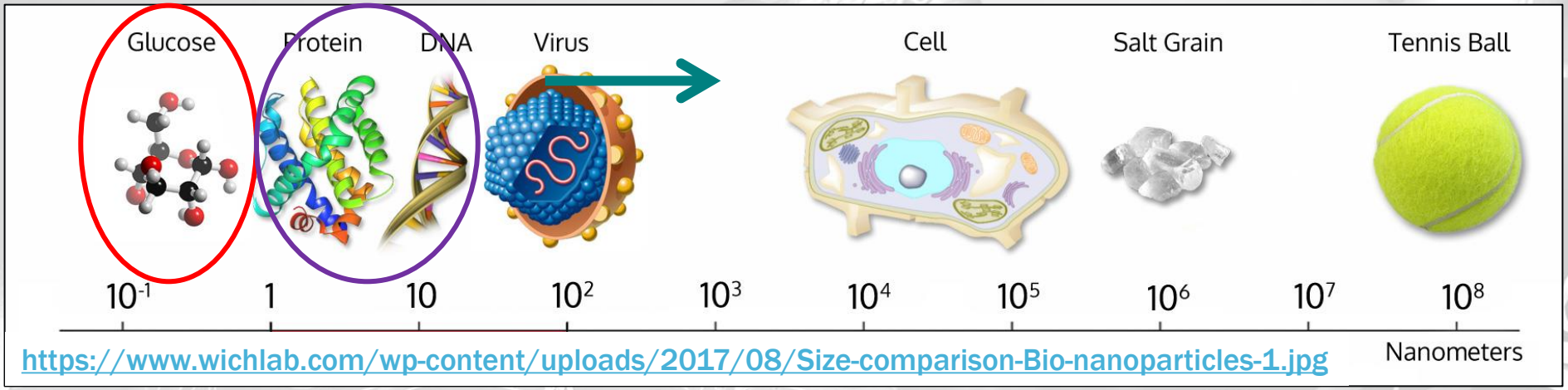


Just Like Chemistry, Molecular Biology is also About Molecules…

The molecules are just very large…



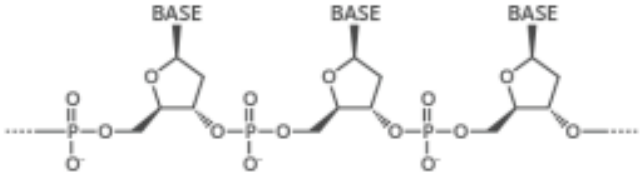
https://www.wichlab.com/wp-content/uploads/2017/08/Size-comparison-Bio-nanoparticles-1.jpg

Similar size to a number of classical chemical warfare agents

Proteins and DNA can be ~10 – 100 times larger

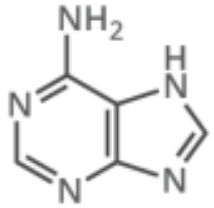
THE CHEMICAL STRUCTURE OF DNA

THE SUGAR PHOSPHATE 'BACKBONE'

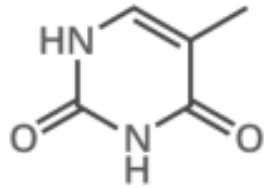


DNA is a polymer made up of units called nucleotides. The nucleotides are made of three different components: a sugar group, a phosphate group, and a base. There are four different bases: adenine, thymine, guanine and cytosine.

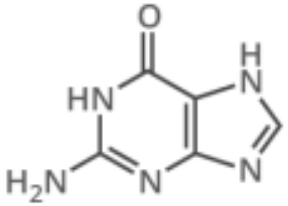
A ADENINE



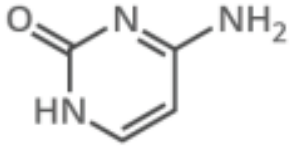
T THYMINE



G GUANINE

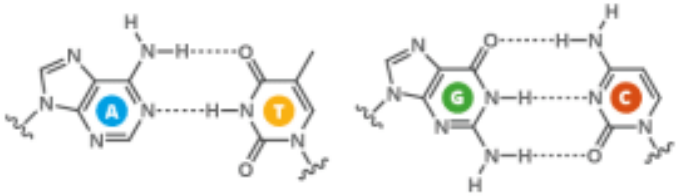


C CYTOSINE



WHAT HOLDS DNA STRANDS TOGETHER?

DNA strands are held together by hydrogen bonds between bases on adjacent strands. Adenine (A) always pairs with thymine (T), while guanine (G) always pairs with cytosine (C). Adenine pairs with uracil (U) in RNA.



FROM DNA TO PROTEINS

The bases on a single strand of DNA act as a code. The letters form three letter codons, which code for amino acids - the building blocks of proteins.

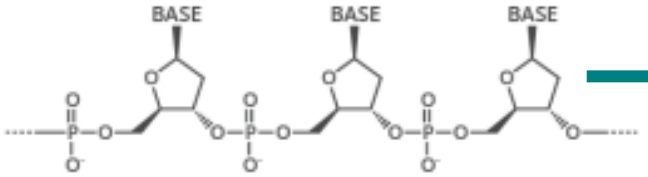
An enzyme, RNA polymerase, transcribes DNA into mRNA (messenger ribonucleic acid). It splits apart the two strands that form the double helix, then reads a strand and copies the sequence of nucleotides. The only difference between the RNA and the original DNA is that in the place of thymine (T), another base with a similar structure is used: uracil (U).

In multicellular organisms, the mRNA carries genetic code out of the cell nucleus, to the cytoplasm. Here, protein synthesis takes place. 'Translation' is the process of turning the mRNA's 'code' into proteins. Molecules called ribosomes carry out this process, building up proteins from the amino acids coded for.

THE CHEMICAL STRUCTURE OF DNA

"Shape"

THE SUGAR PHOSPHATE 'BACKBONE'



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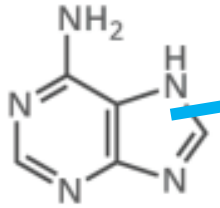
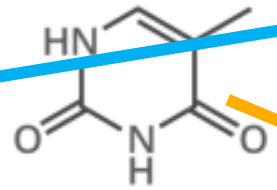
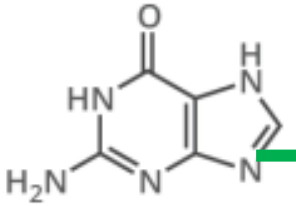


T THYMINE



G GUANINE



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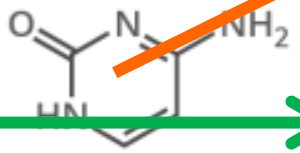

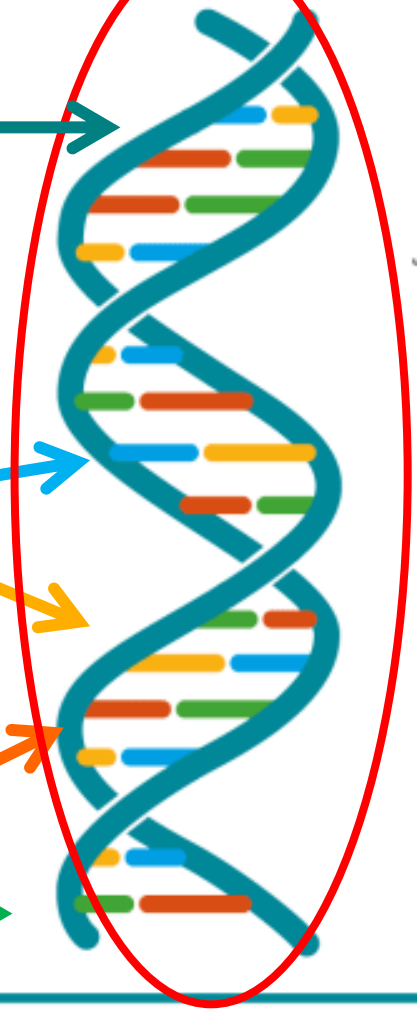

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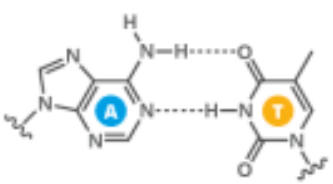

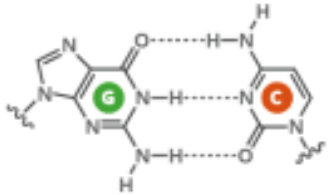

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DNA → (TRANSCRIPTION) → RNA → (TRANSLATION) → PROTEIN

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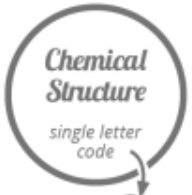
"Short-hand"

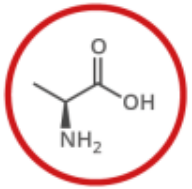
In multicellular organisms, the mRNA carries genetic code out of the cell nucleus, to the cytoplasm. Here, protein synthesis takes place. 'Translation' is the process of turning the mRNA's 'code' into proteins. Molecules called ribosomes carry out this process, building up proteins from the amino acids coded for.

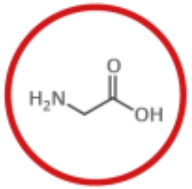
A GUIDE TO THE TWENTY COMMON AMINO ACIDS

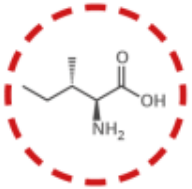
AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS CAN BE SYNTHESISED IN THE BODY.

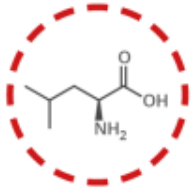
Chart Key: ALIPHATIC · AROMATIC · ACIDIC · BASIC · HYDROXYLIC · SULFUR-CONTAINING · AMIDIC · NON-ESSENTIAL · ESSENTIAL

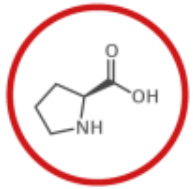


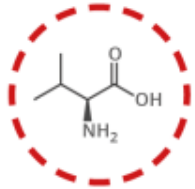

ALANINE A
Ala
GCT, GCC, GCA, GCG

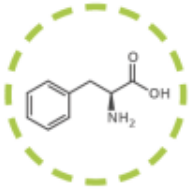

GLYCINE G
Gly
GGT, GGC, GGA, GGG

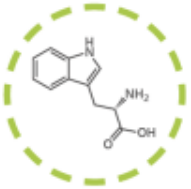

ISOLEUCINE I
Ile
ATT, ATC, ATA

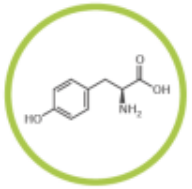

LEUCINE L
Leu
CTT, CTC, CTA, CTG, TTA, TTG

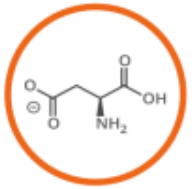

PROLINE P
Pro
CCT, CCC, CCA, CCG

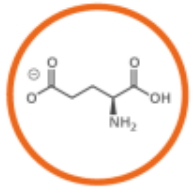

VALINE V
Val
GTT, GTC, GTA, GTG

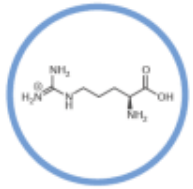

PHENYLALANINE F
Phe
TTT, TTC

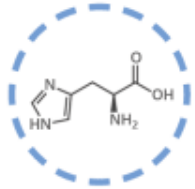

TRYPTOPHAN W
Trp
TGG

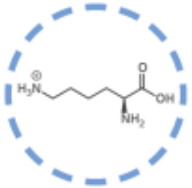

TYROSINE Y
Tyr
TAT, TAC

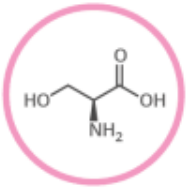

ASPARTIC ACID D
Asp
GAT, GAC

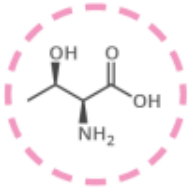

GLUTAMIC ACID E
Glu
GAA, GAG

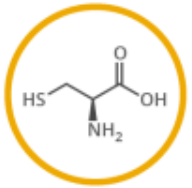

ARGININE R
Arg
CGT, CGC, CGA, CGG, AGA, AGG

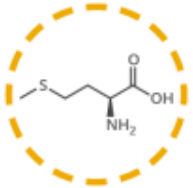

HISTIDINE H
His
CAT, CAC

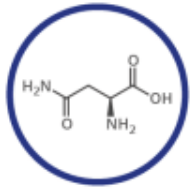

LYSINE K
Lys
AAA, AAG

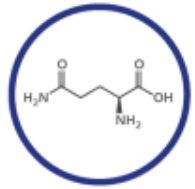

SERINE S
Ser
TCT, TCC, TCA, TCG, AGT, AGC


THREONINE T
Thr
ACT, ACC, ACA, ACG


CYSTEINE C
Cys
TGT, TGC

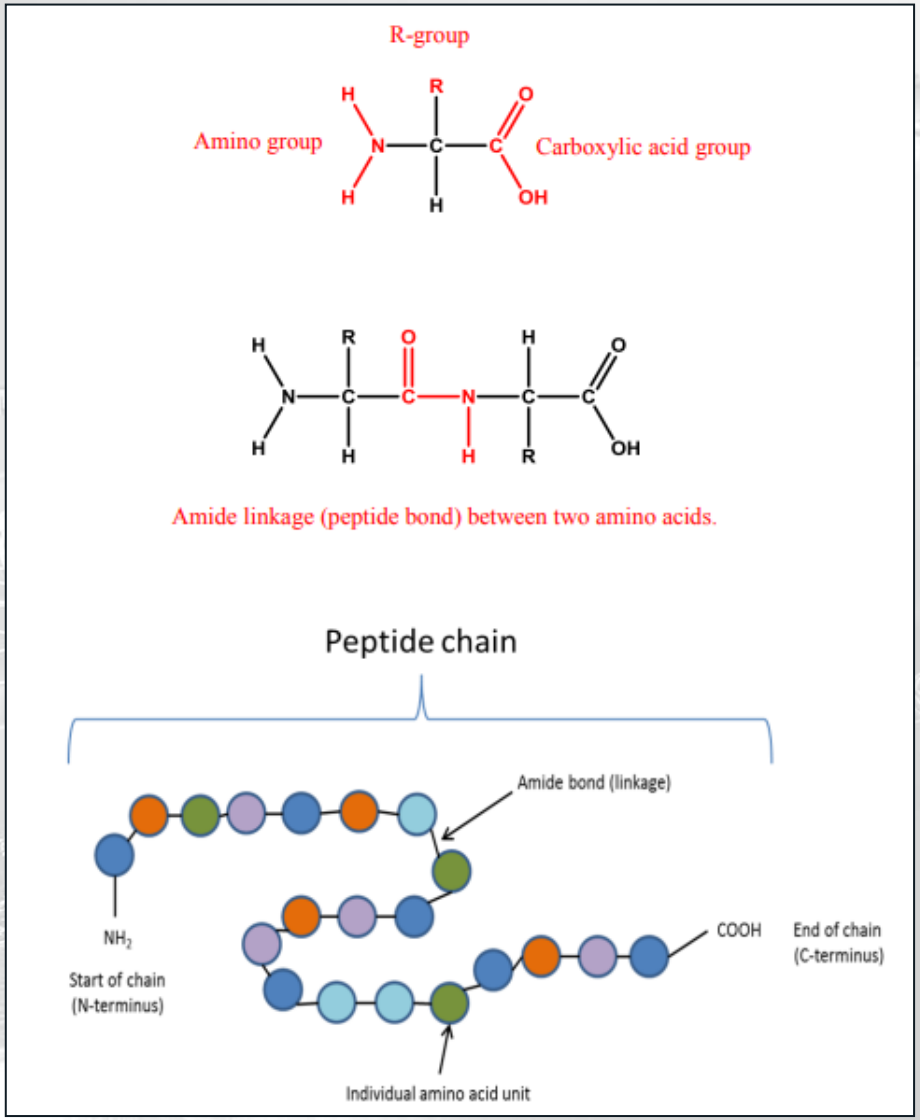

METHIONINE M
Met
ATG


ASPARAGINE N
Asn
AAT, AAC


GLUTAMINE Q
Gln
CAA, CAG

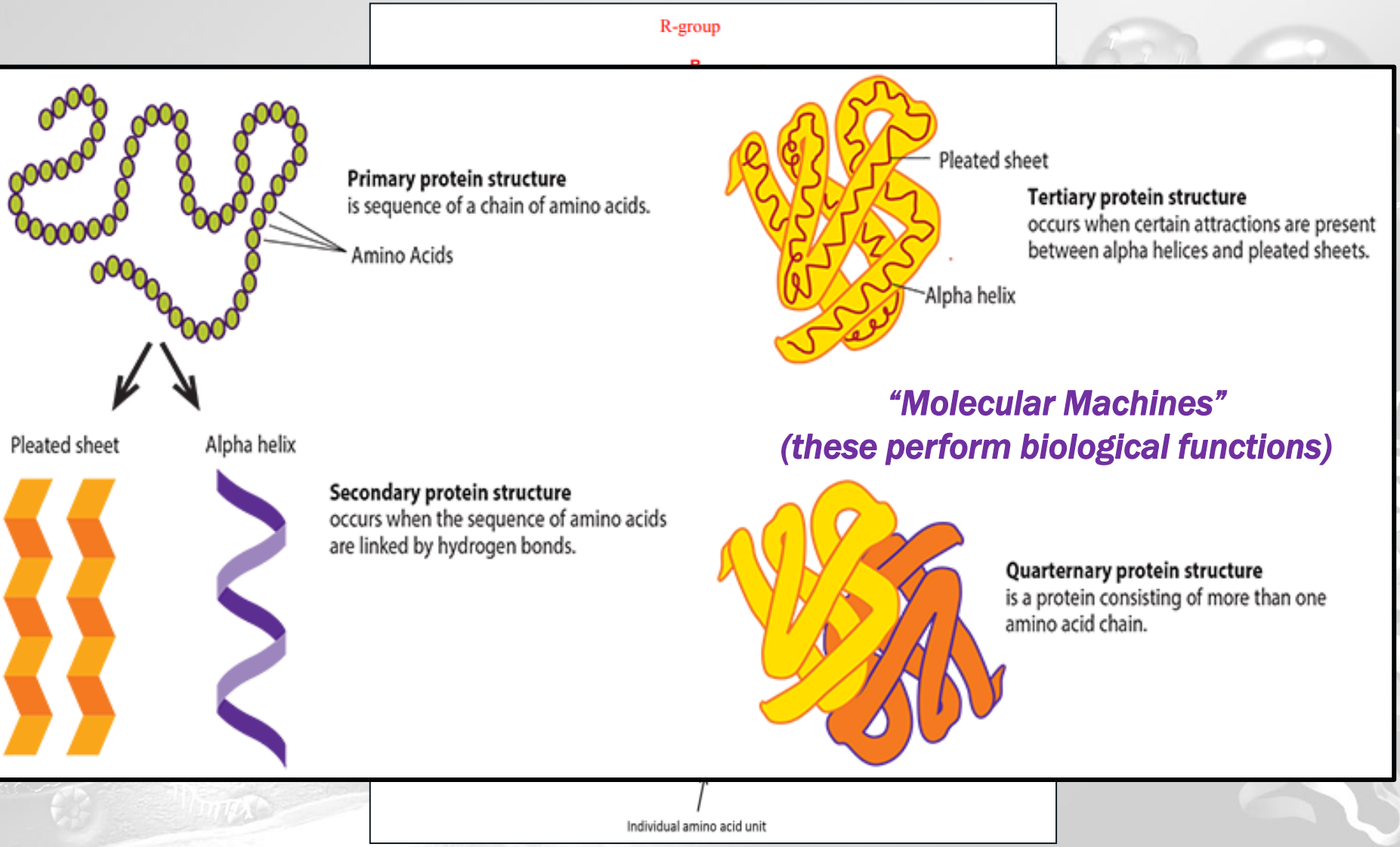
Note: This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.

Proteins are Sequences of Connected Amino Acids

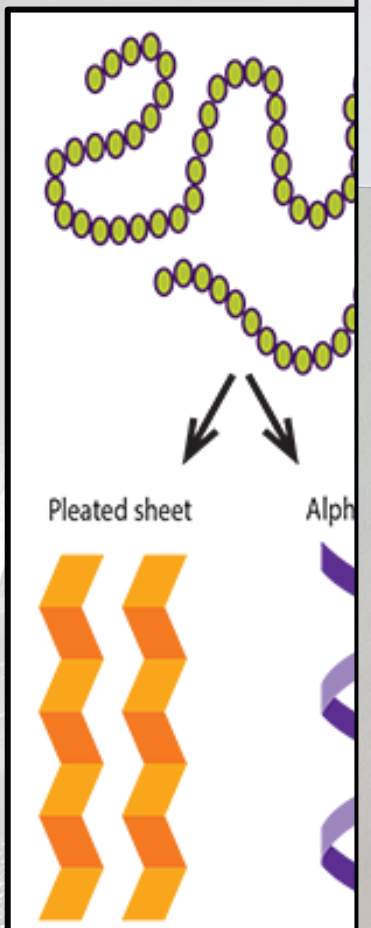


OPCW

Proteins are Sequences of Connected Amino Acids



Pr



structure
tain attractions are present
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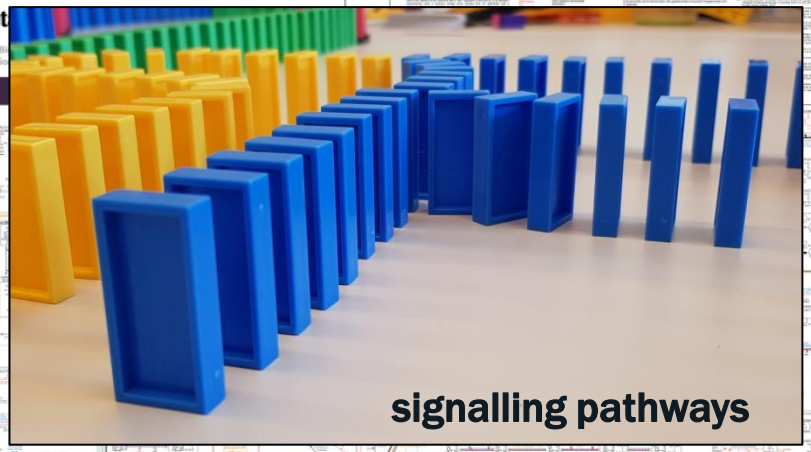
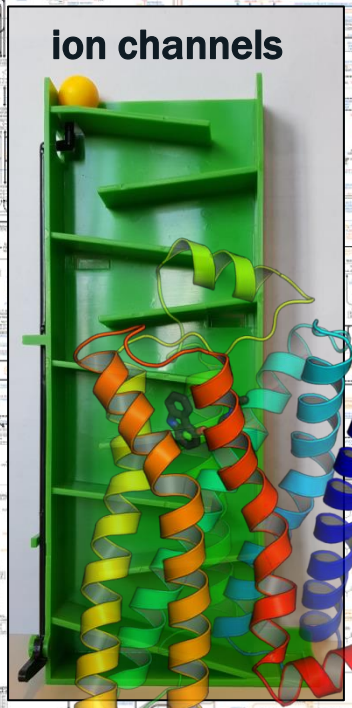
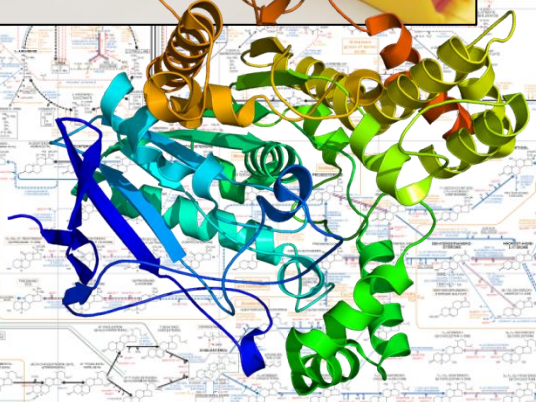
OPCW

To Help Understand This, We Built a Model…







To Help Understand This, We Built a Model...

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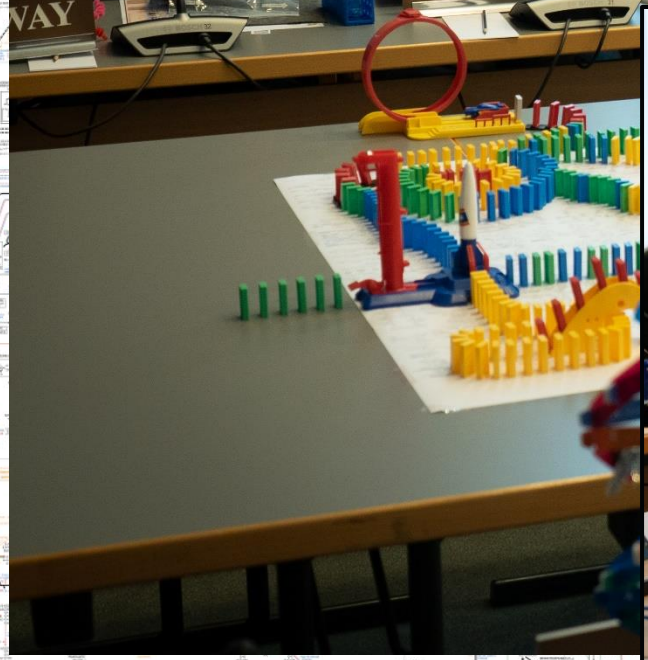
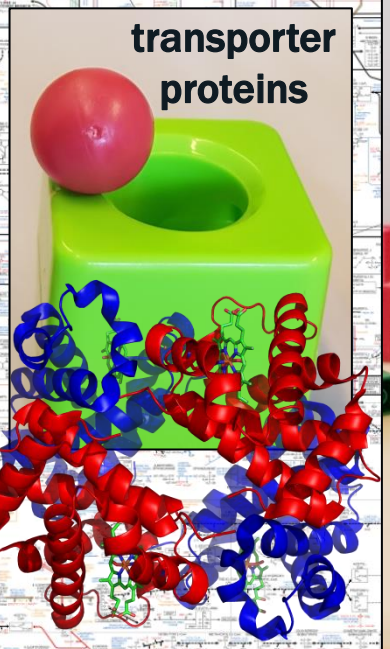
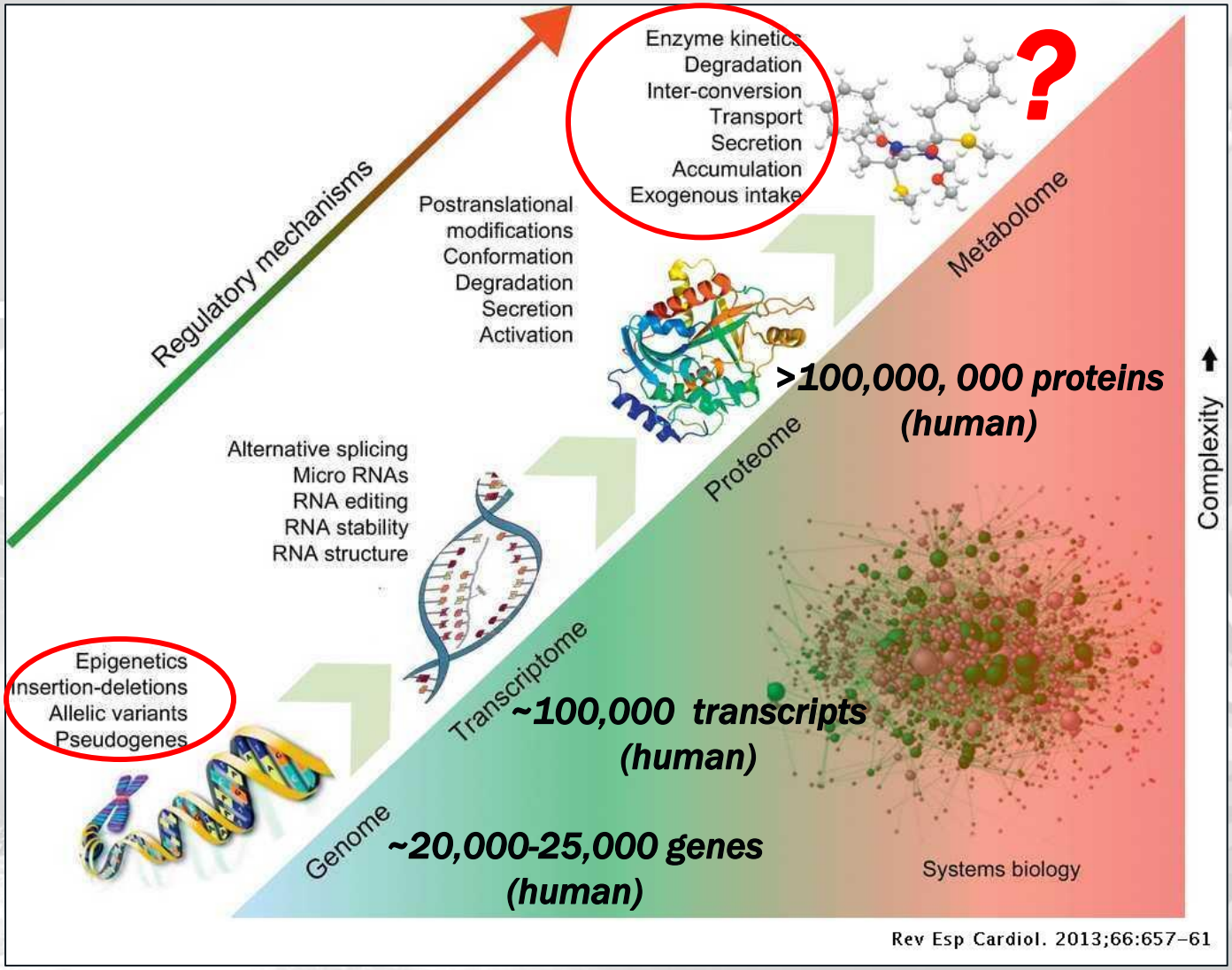


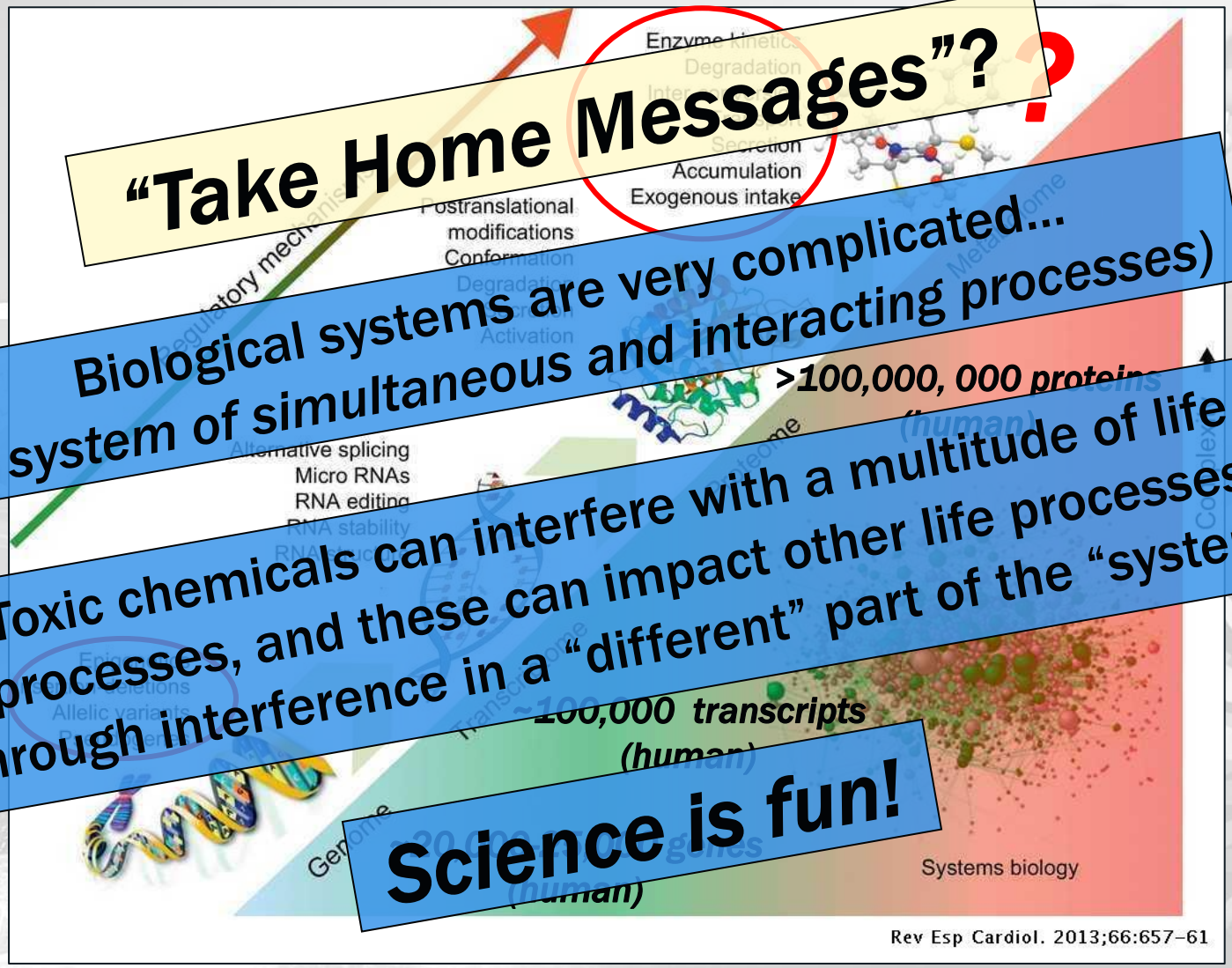
To Help Understand This, We Built a Model…



Living Systems Enjoy Broad Molecular Diversity



Living Systems Enjoy Broad Molecular Diversity



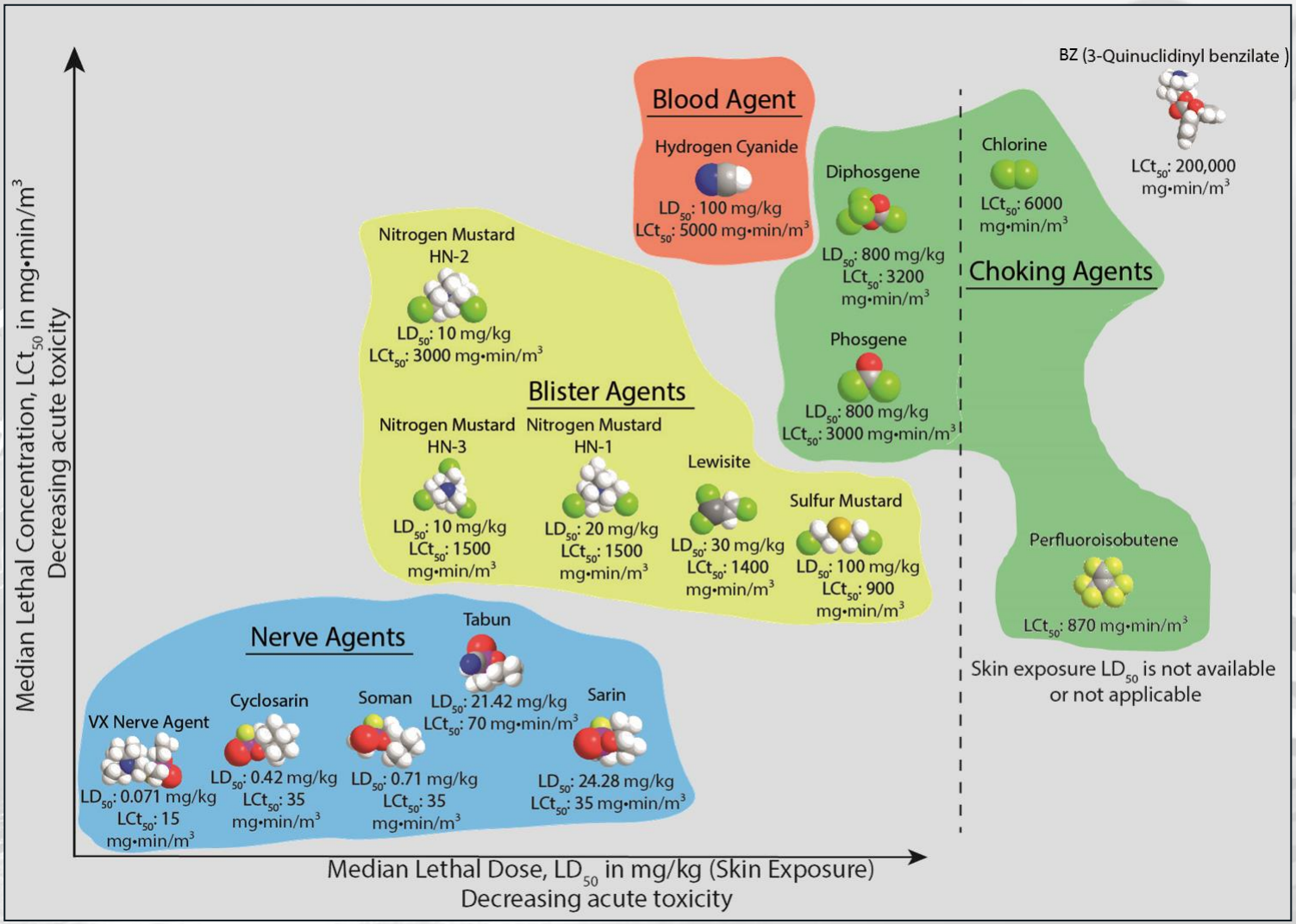
"Take Home Messages"?

Biological systems are very complicated...
(a system of simultaneous and interacting processes)

Toxic chemicals can interfere with a multitude of life processes, and these can impact other life processes through interference in a "different" part of the "system"

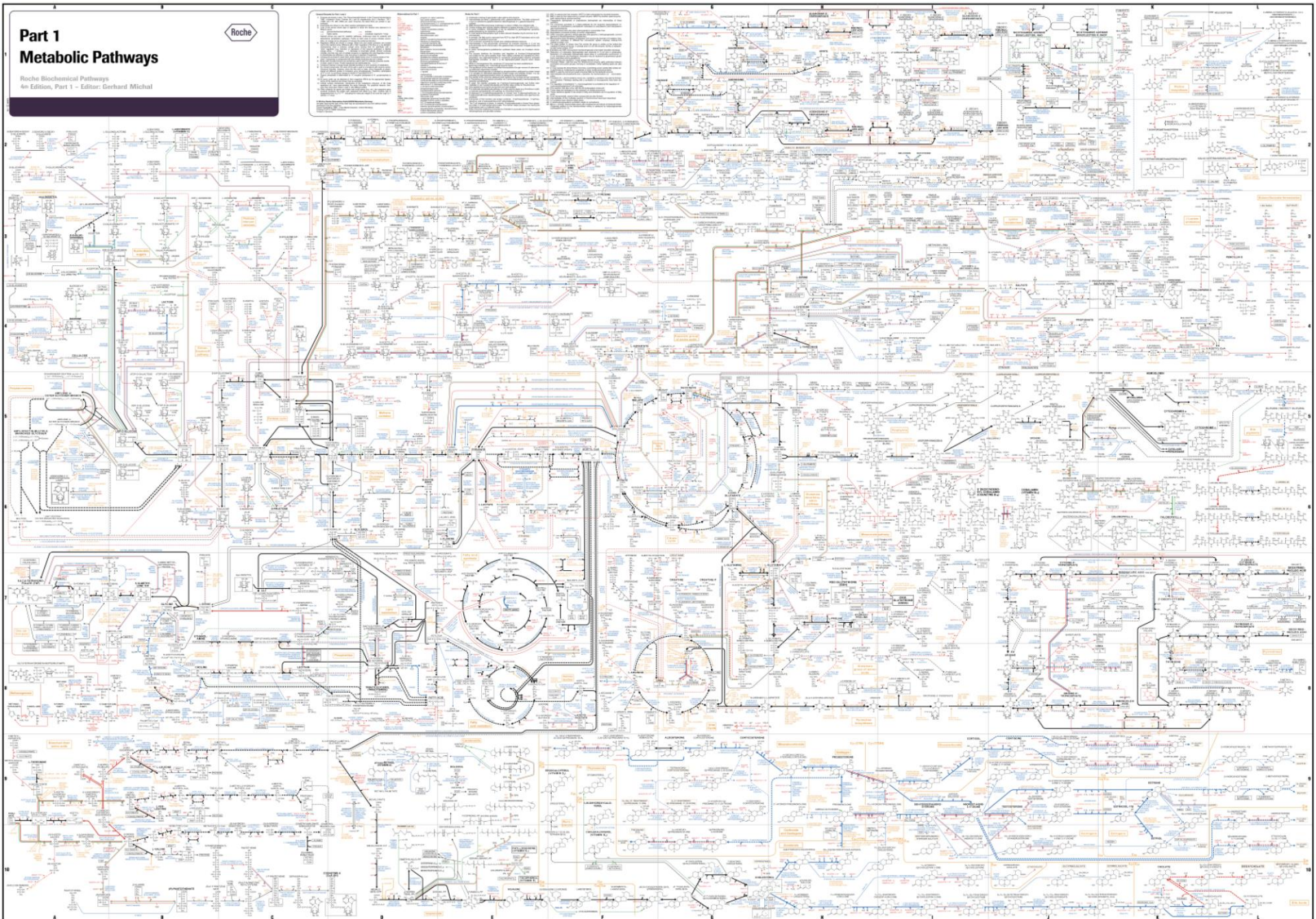
Science is fun!

Why are Some Chemicals are "More Toxic" Than Others

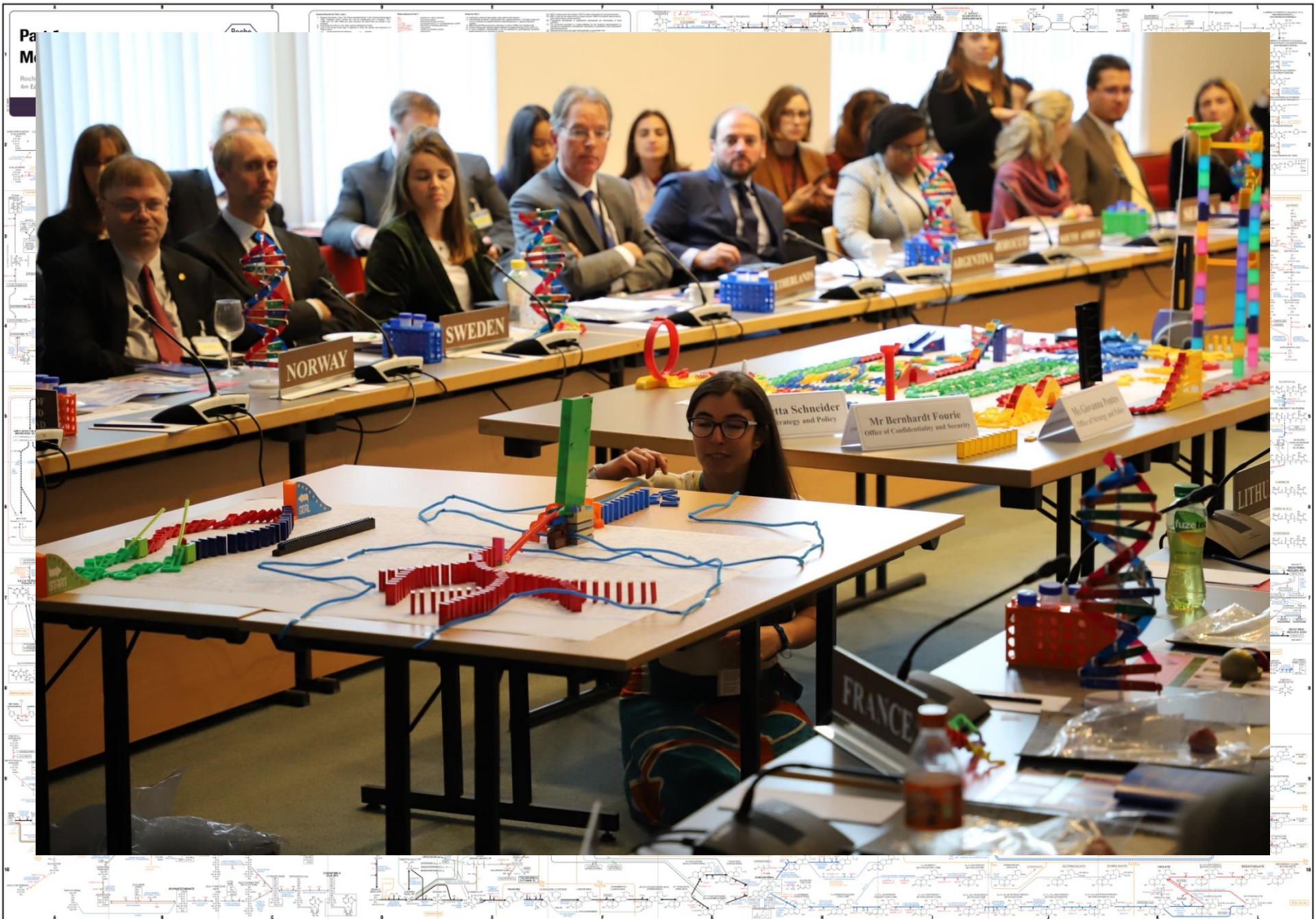


OPCW

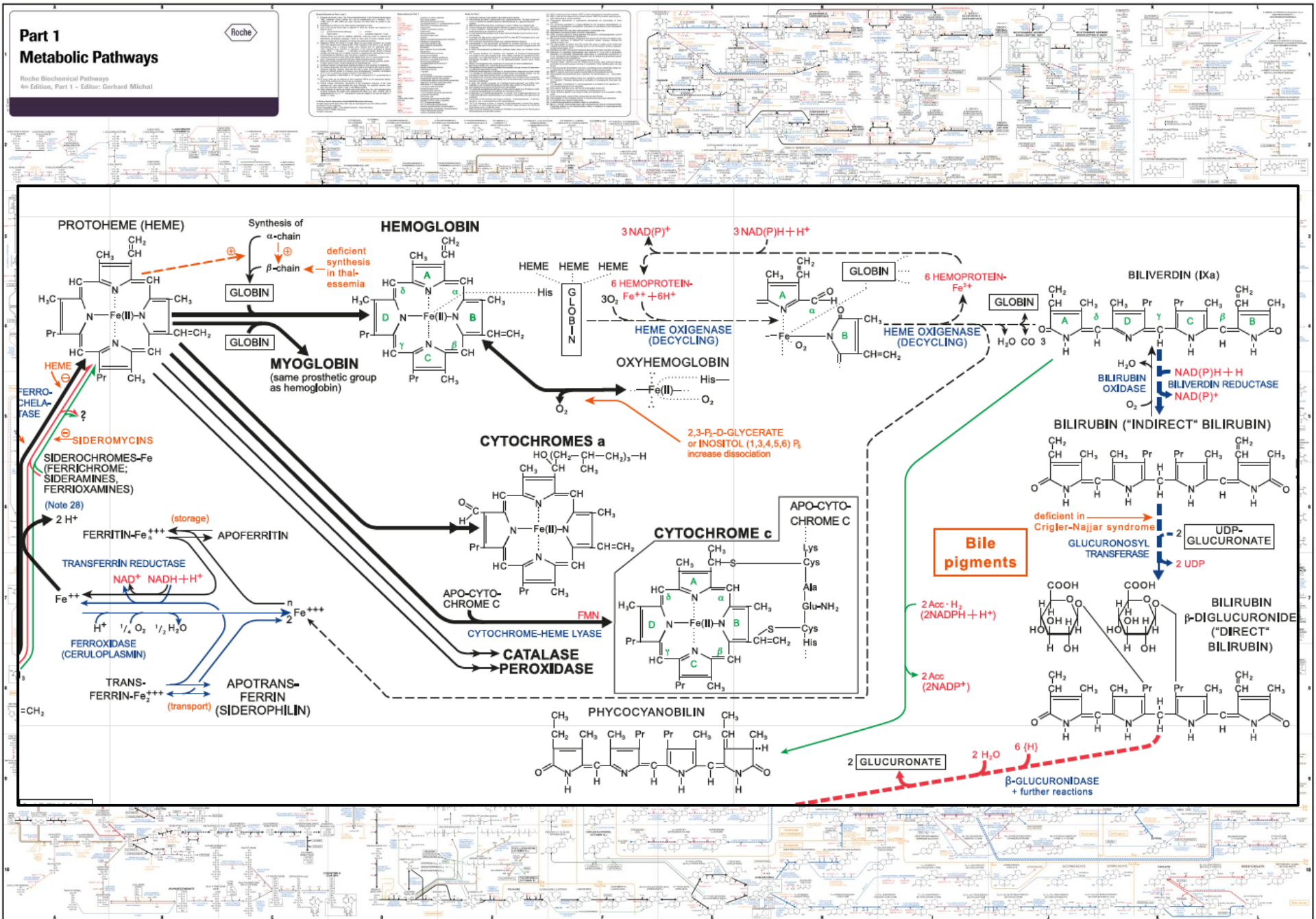
Chemical Action on Life Processes: Some Examples



Chemical Action on Life Processes: Some Examples



Chemical Action on Life Processes: Some Examples



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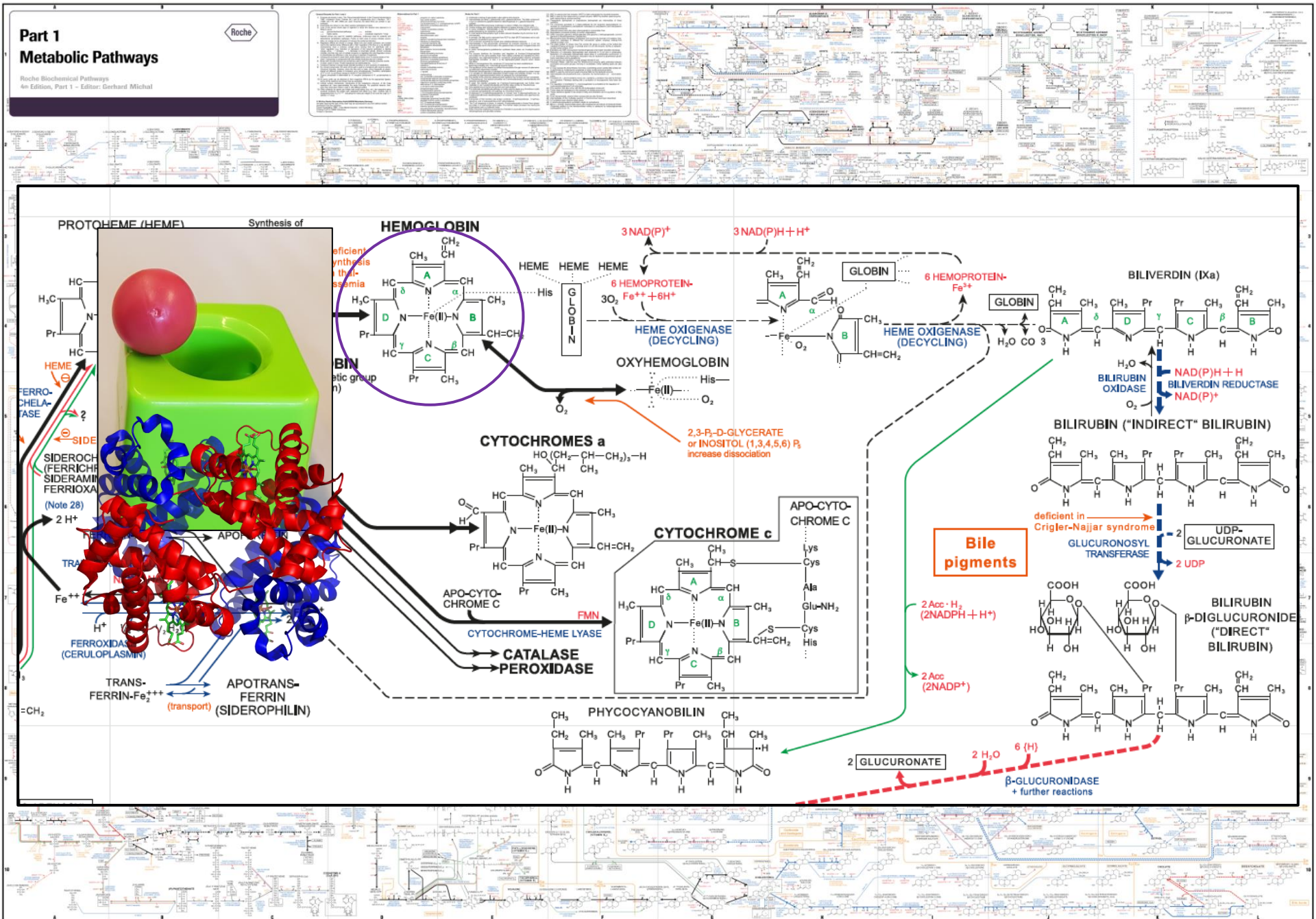
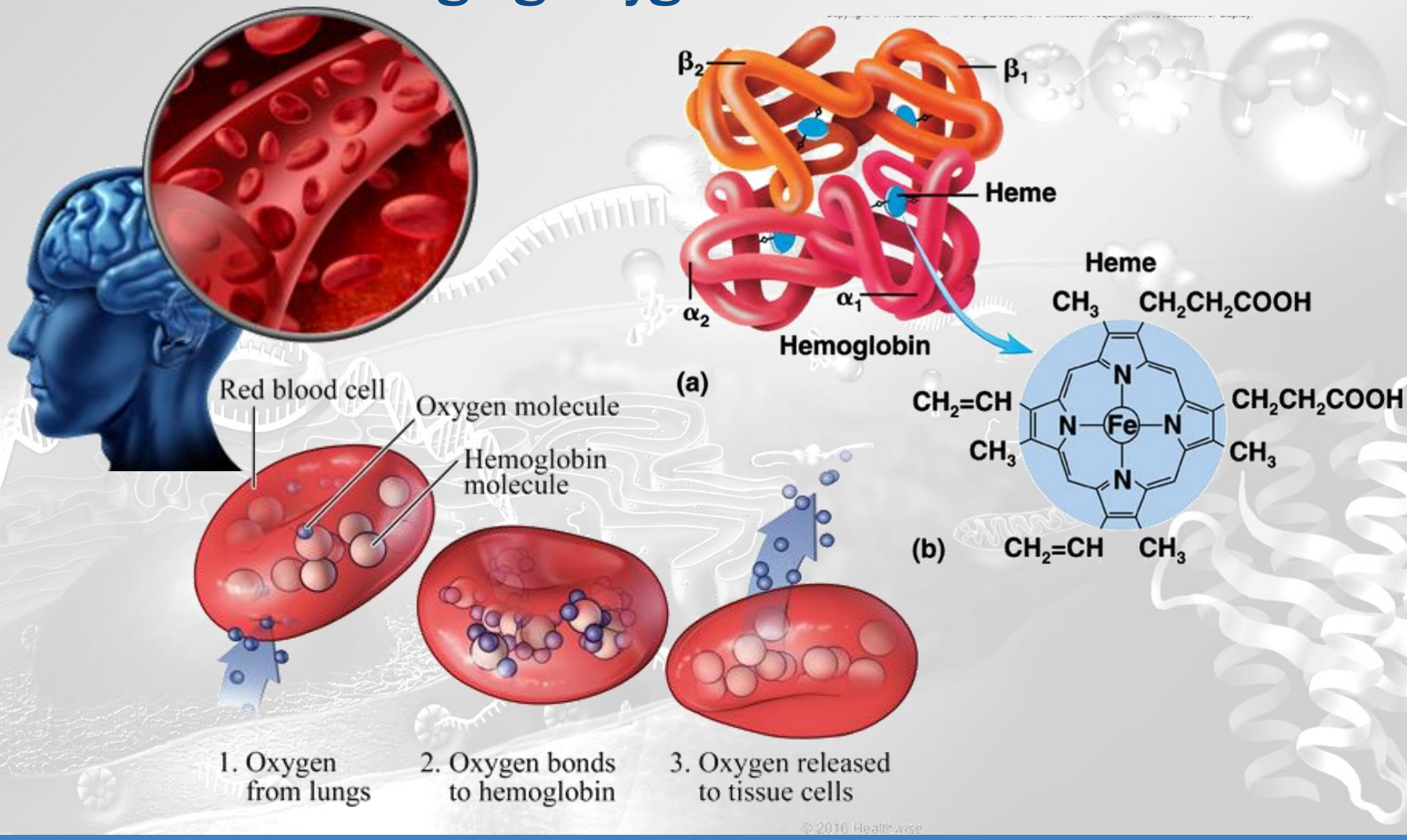


Bringing Oxygen to the Brain



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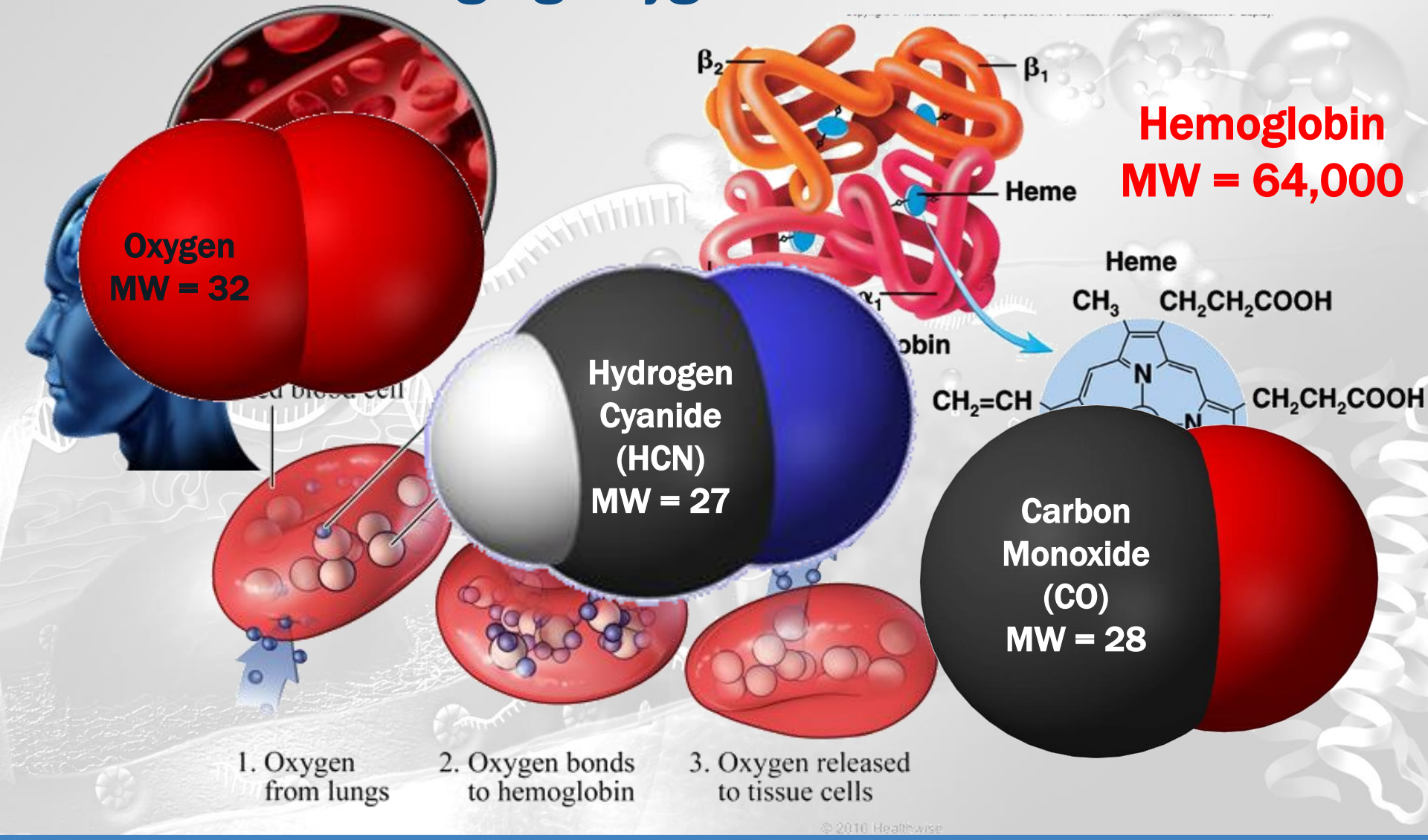


Bringing Oxygen to the Brai

CN^- and CO bind to heme and do not let go…
Prevents oxygen transport to the brain

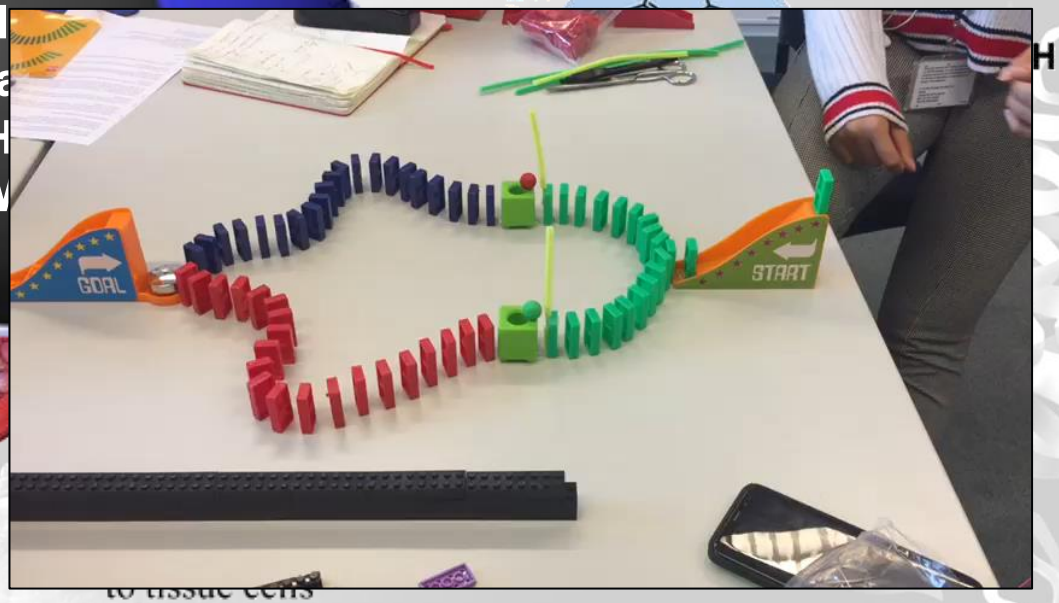
Toxic chemicals ~ 2,000 times smaller than the transporter protein, shut down a vital life process

emoglobin
= 64,000

Heme
CH_3 CH_2CH_2COOH

obin

Hyd
Cya
(H
MW

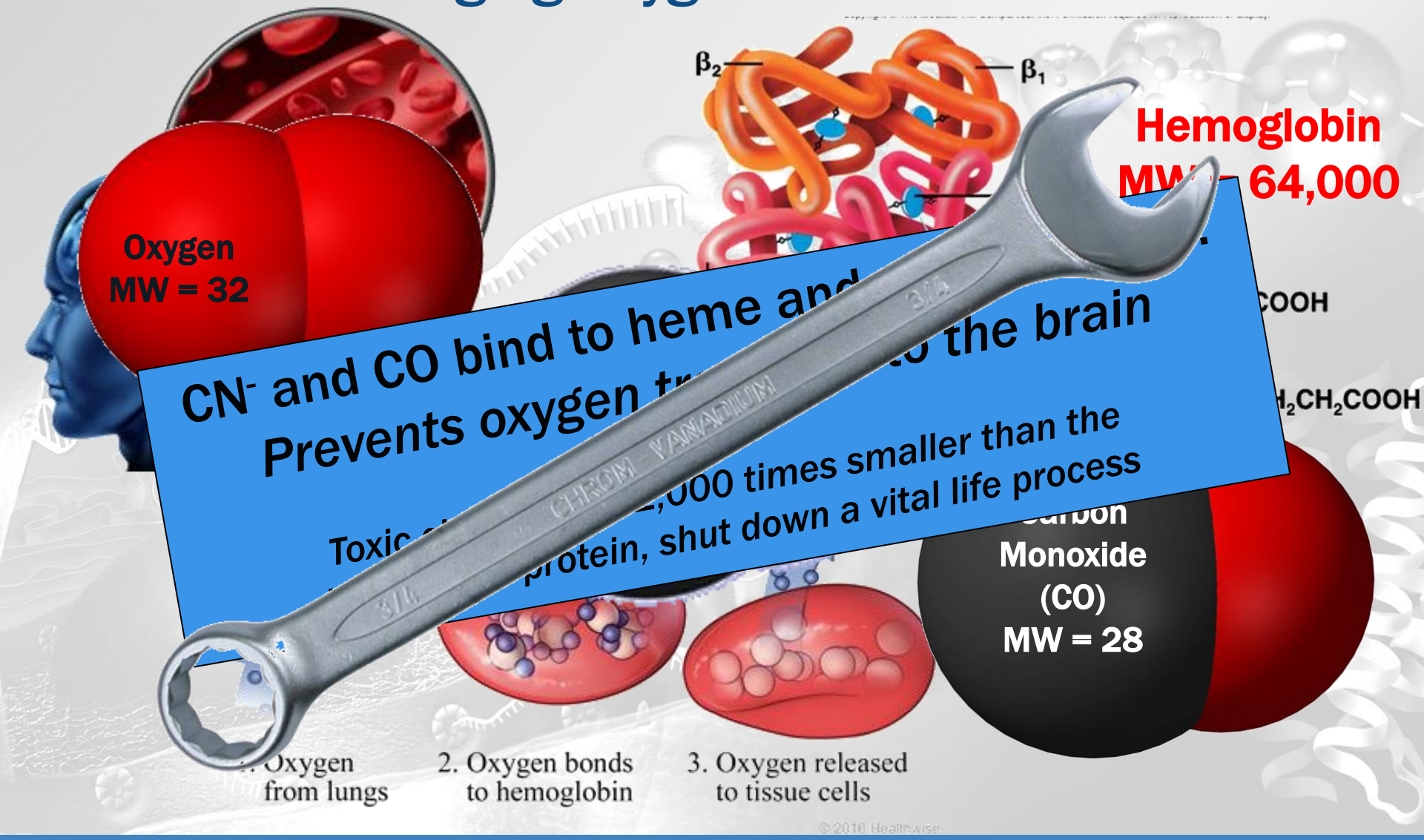


1. Oxygen from lungs

2. Oxygen bonds to hemoglobin

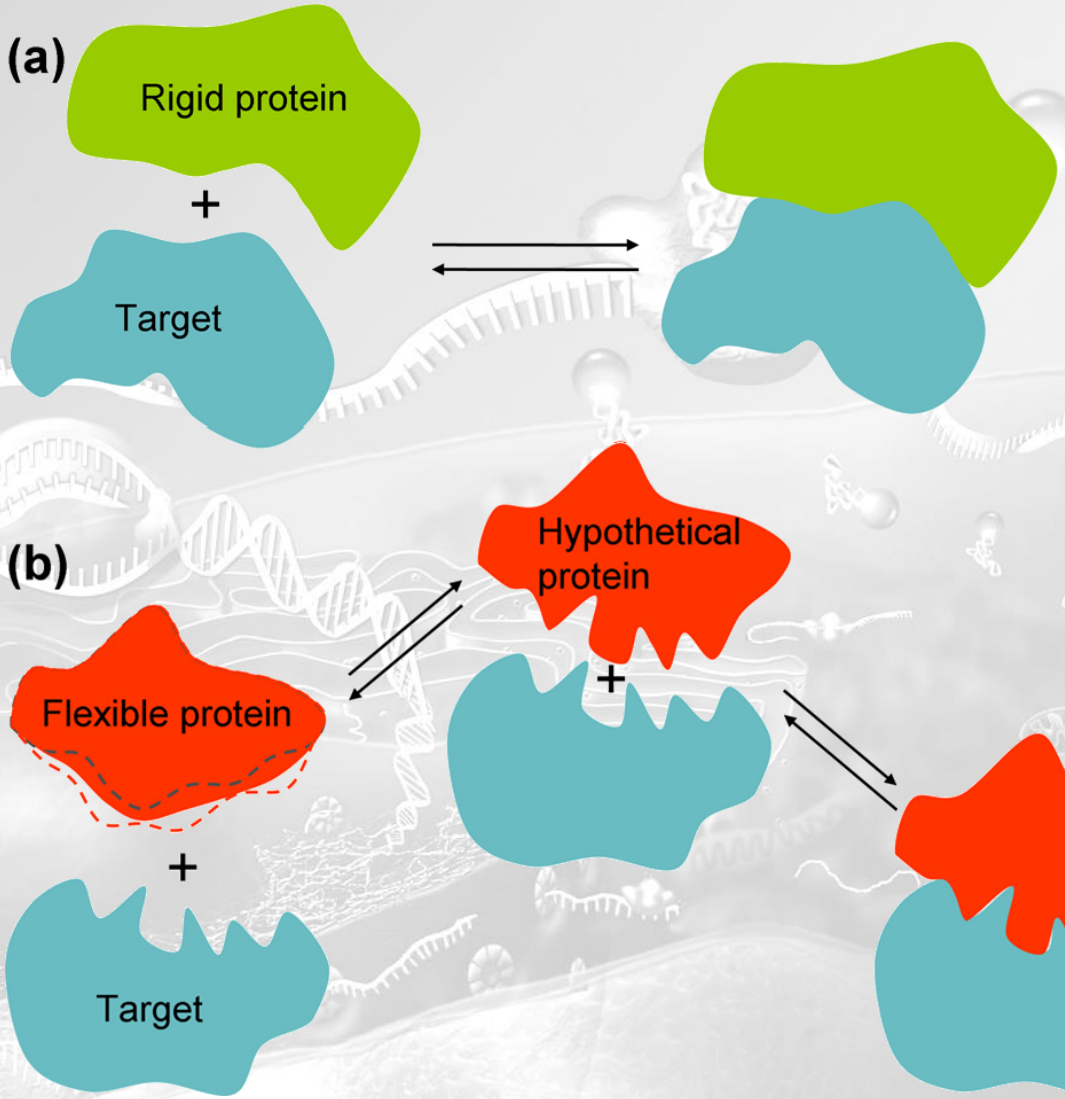
to tissue cells

Bringing Oxygen to the Brain



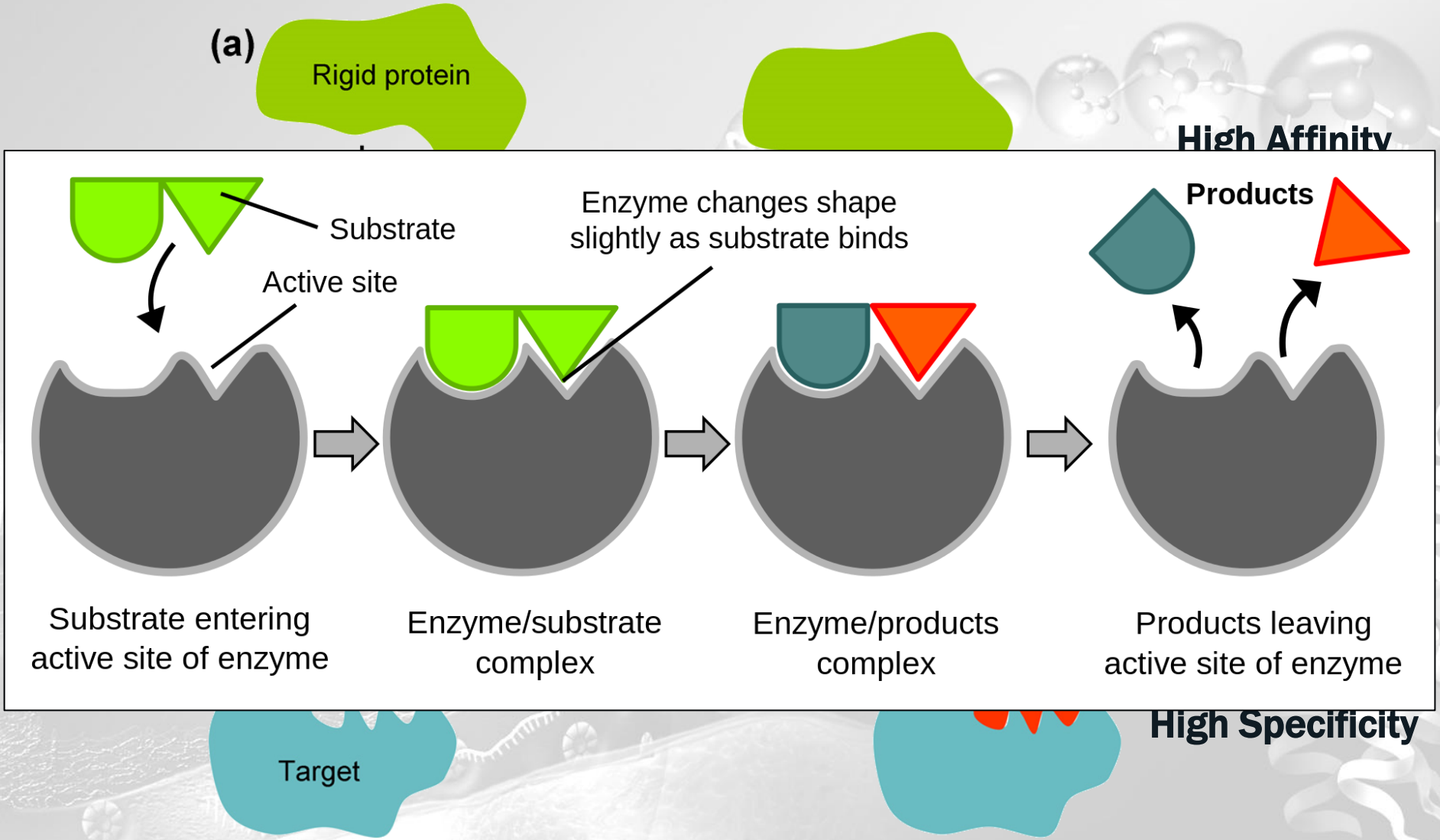
OPCW

Molecule to Molecule Interactions



Zhou, 2011; DOI:10.1016/j.tibs.2011.11.002

Molecule to Molecule Interactions



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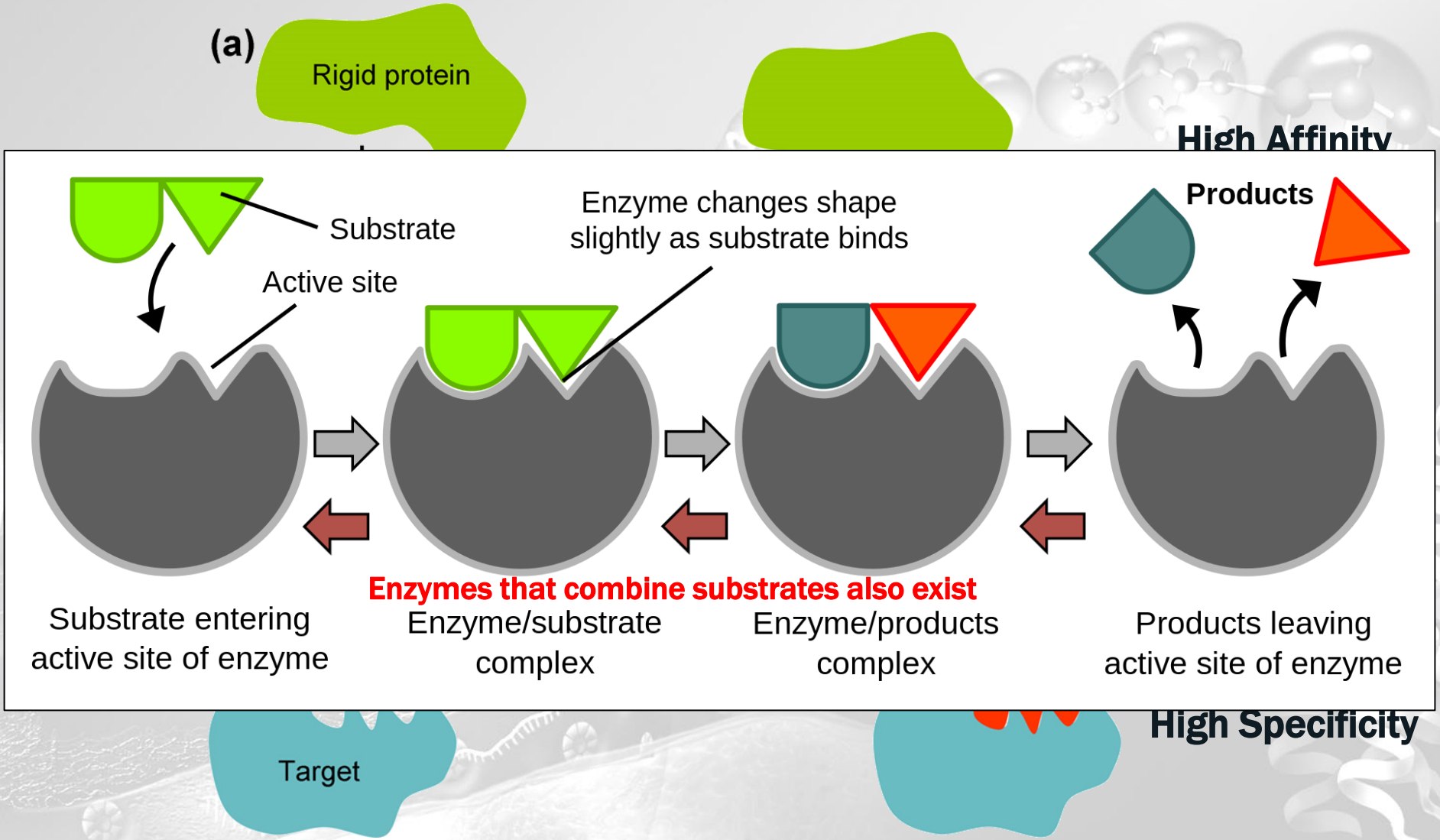
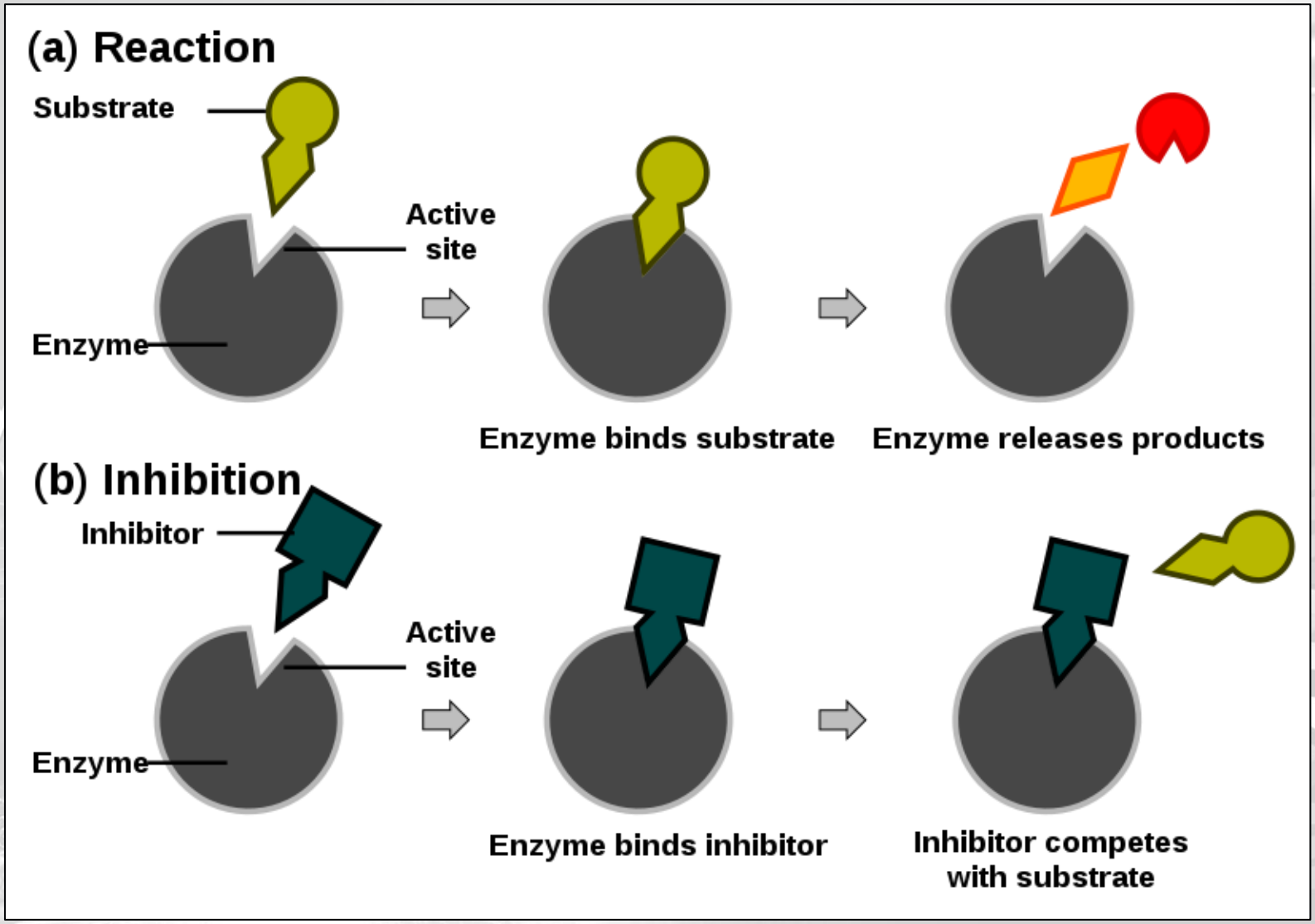
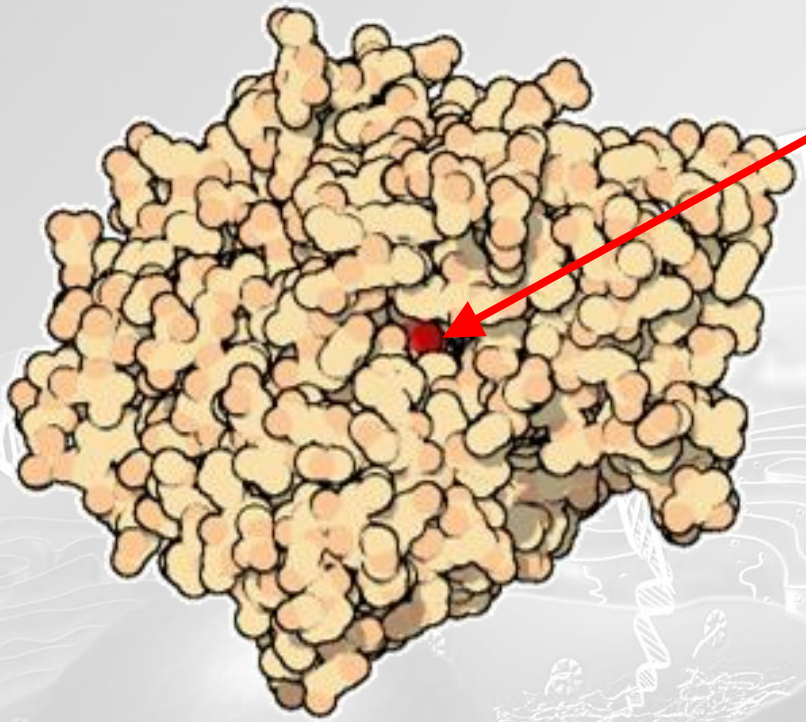


Zhou, 2011; DOI:10.1016/j.tibs.2011.11.002

Enzyme Inhibition: “Turning off a Life Process”

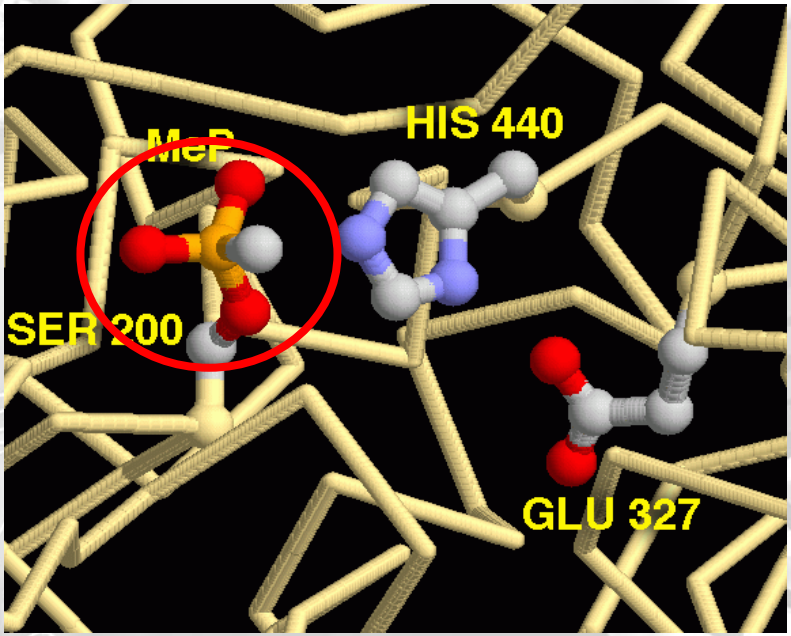


In Addition to Size and Shape – Chemical Functional Groups Still Matter



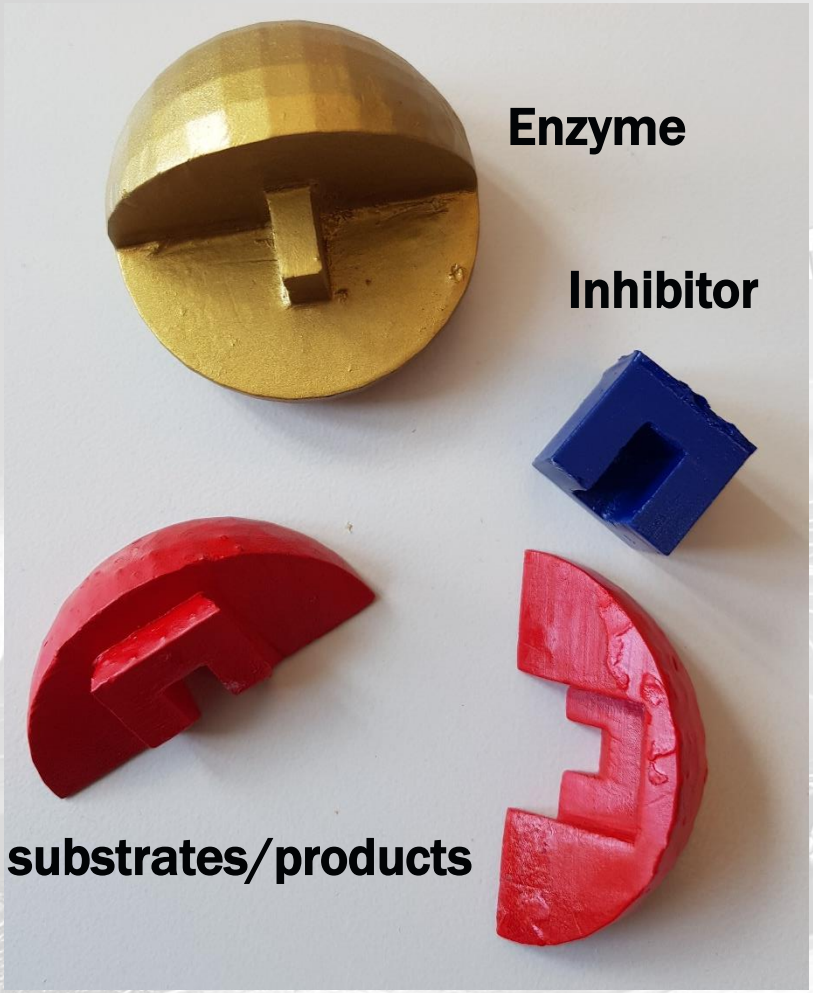
Binding pocket

Sarin adduct



From PDB Molecule of the Month, 2004
https://pdb101.rcsb.org/motm/54

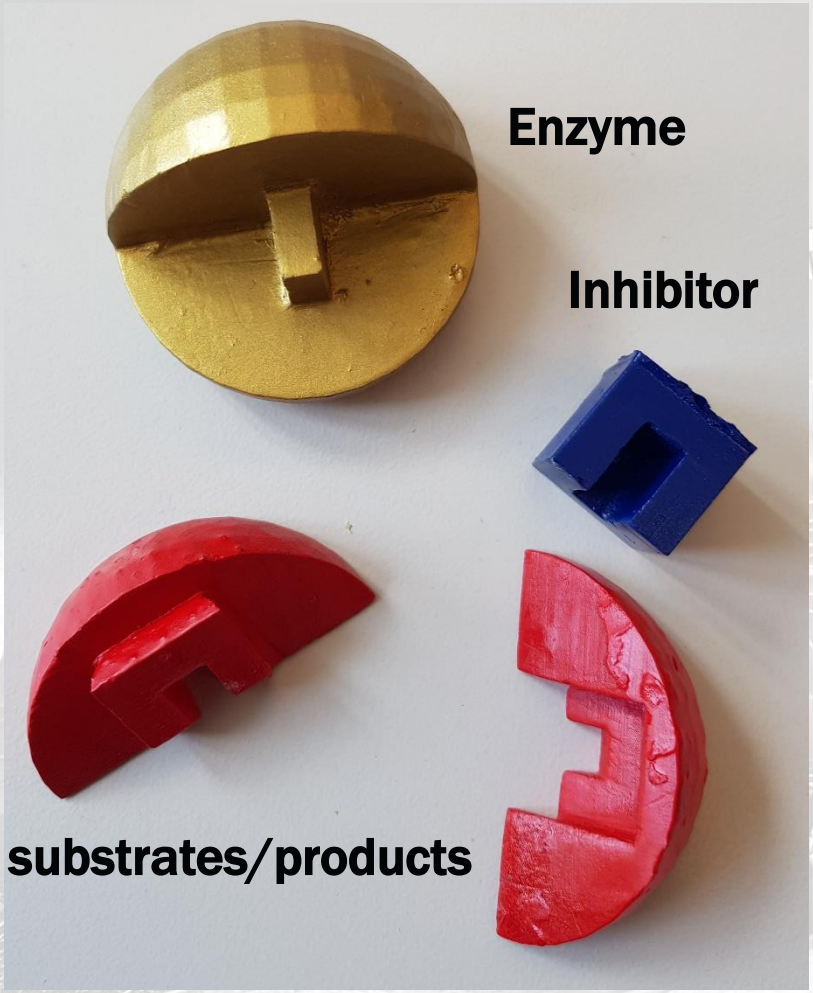
A Simple Shape and Spatial Orientation Excercise



Exercise #1:

Combine substrates inside
The enzyme (do not combine them
Before inserting into the enzyme)

A Simple Shape and Spatial Orientation Excercise



Exercise #1:

Combine substrates inside
The enzyme (do not combine them
Before inserting into the enzyme)

Orientation of parts matter!

Exercise #2:

Use enzyme to break apart the “wedge”
(do not pull apart outside enzyme)

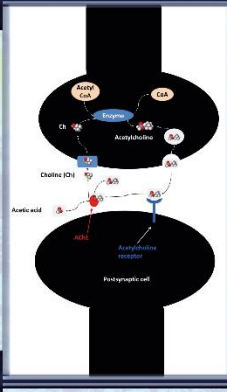
Exercise #3:

Inhibit the enzyme

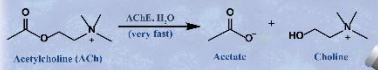
Acetylcholinesterase Inhibition

created by Sofía Sola Sancho and Maria Hemme

Acetylcholinesterase



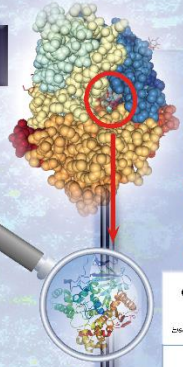
The primary **toxicity** of organophosphorus nerve agents results from the **inhibition** of the **enzyme Acetylcholinesterase (AChE)**.



AChE is responsible for breaking down the **neurotransmitter acetylcholine (ACh)**. This switches a nerve signal from on to off. If the enzyme is **inhibited**, ACh **accumulates** in the synapse and the signal **continues to transmit**.

Figure 1: Life Cycle of ACh.

Binding Site



The AChE **active site** is buried deep within the enzyme. It contains three amino acid residues **crucial for catalytic activity**: serine 200, histidine 440 and glutamate 327. The nerve agent binds to **serine 200**.

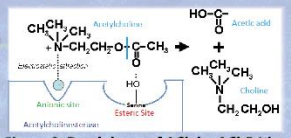


Figure 2: Breakdown of ACh by AChE (the normal function of the enzyme).

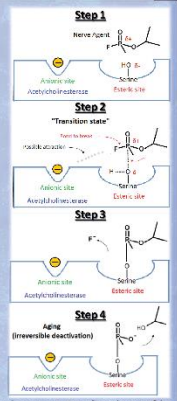
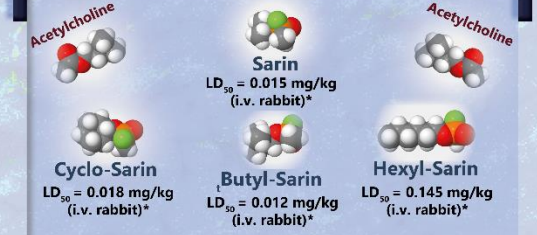
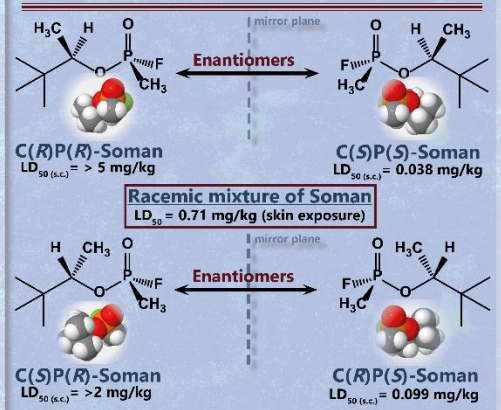


Figure 3: Mechanism of inhibition of AChE by Sarin.

Nerve Agent Molecular Shape and Size



Toxicity of an organophosphorus nerve agent depends on the ability to access the AChE binding site. **Size**, **shape** and **hydrophobicity** of the nerve agent exerts an effect. As alkyl substituents increase in size and degrees of freedom, toxicity decreases.



The **spatial orientation** (shape) of the molecule also matters, as illustrated by toxicity differences across the four stereoisomers of Soman.

Effects and Symptoms

Inhibition of AChE in muscarinic synapses (neuromuscular system) induces **cholinergic crisis**. Nicotinic synapses (central nervous system, e.g. brain) are also effected.

Symptoms include **sweating**, **salivation**, **miosis (pinpoint pupils)**, **paralysis**, **respiratory failure**, **seizures** and eventually **death**.

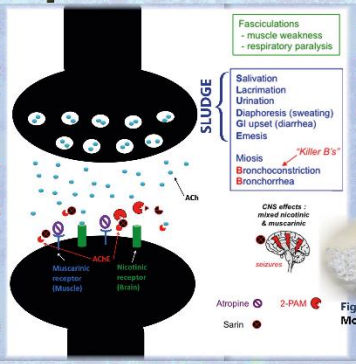
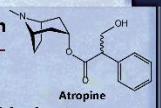


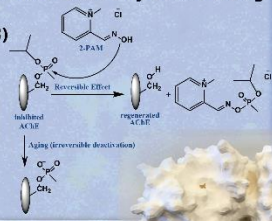
Figure 4: Inhibition of AChE by Sarin and Treatment with Atropine and 2-PAM.

Treatment

Atropine blocks the action of ACh at **muscarinic receptors** and treats **SLUDGE**.



Oximes such as **2-PAM** (pralidoxime) can reactivate inhibited AChE, but only before the aging process.
(Fig. 3, Step 3)



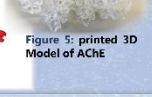


Figure 5: printed 3D Model of AChE

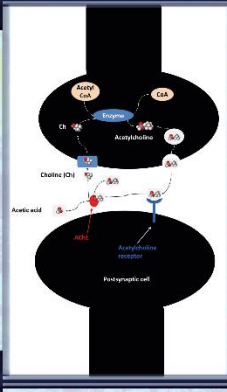
Figure 6: printed 3D Model of the AChE surface

* Black, R. M., & Harrison, J. M. (2009). The Chemistry of Organophosphorus Chemical Warfare Agents. PATAI'S Chemistry of Functional Groups. doi:10.1002/9780470682531.pat0070

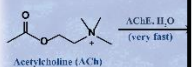
Acetylcholinesterase Inhibition

created by Sofía Sola Sancho and Maria Hemme

Acetylcholinesterase



The primary toxicity of organophosphorus nerve agents results the enzyme Acetylch

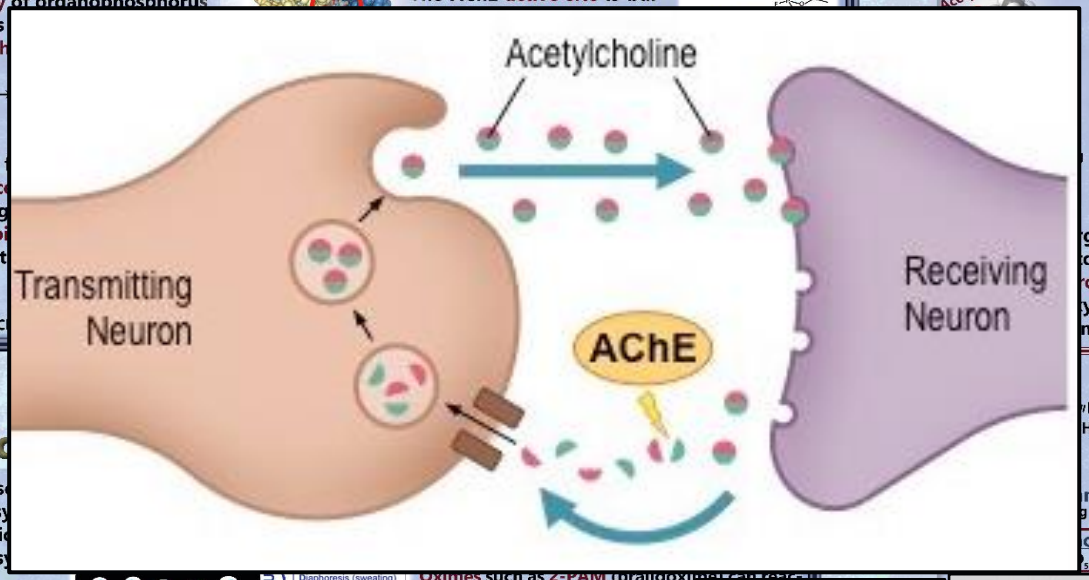


AChE is responsible f neurotransmitter ac switches a nerve sig the enzyme is inhibi in the synapse and t transmit.

Figure 1: Life Cycle of AC

Binding Site

The AChE active site is bur-



Effects and

Inhibition of AChE in mus synapses (neuromuscular sy induces cholinergic crisis. Ni synapses (central nervous sy

Diaphoresis (sweating)

Oximes such as 2-PAM (pralidoxime) can reac

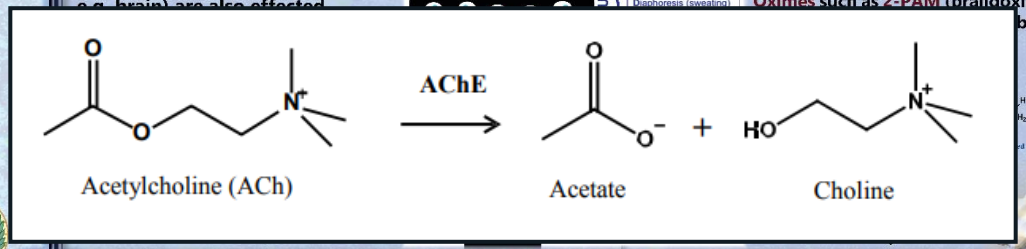
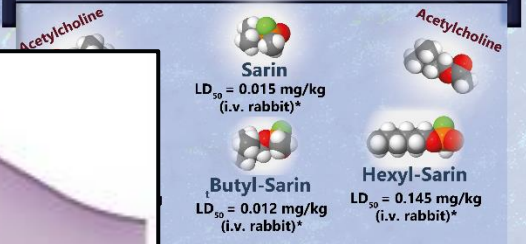


Figure 6: printed 3D Model of the AChE surface

Nerve Agent Molecular Shape and Size



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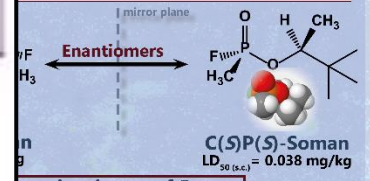

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50 = 0.71 mg/kg (skin exposure)

-Soman
.099 mg/kg

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across the

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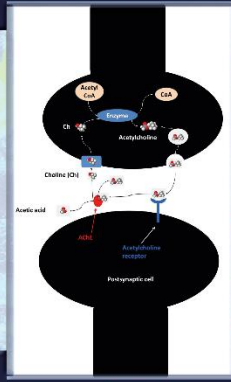
Acetylcholinesterase Inhibition

created by Sofía Sola Sancho and Maria Hemme

Acetylcholinesterase

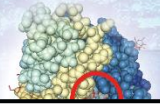


The primary toxicity of organophosphorus nerve agents results the enzyme Acetylch

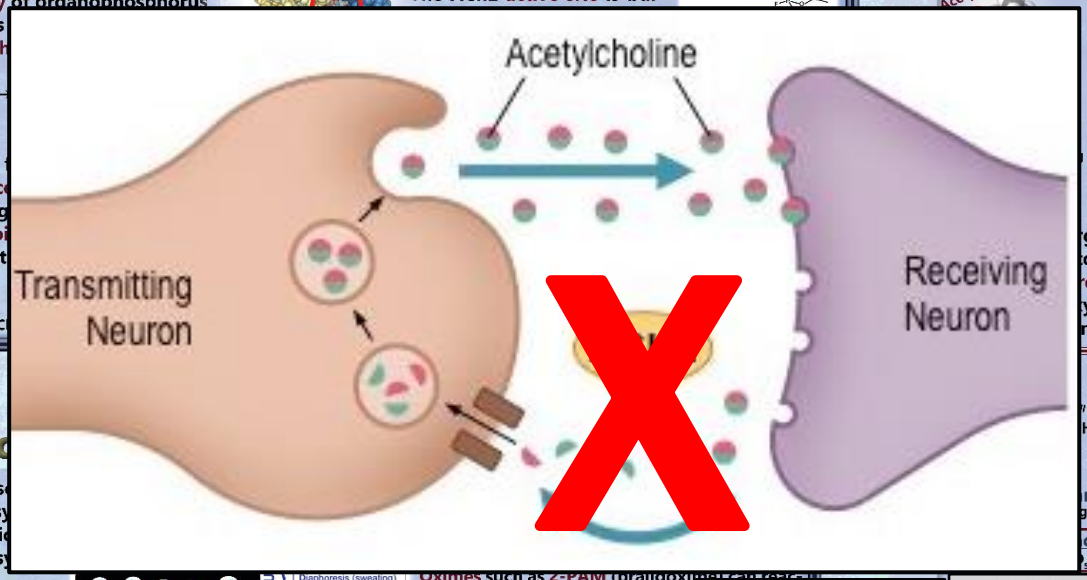
AChE is responsible neurotransmitter ac switches a nerve sig the enzyme is inhibi in the synapse and t transmit.

Figure 1: Life Cycle of AC

Binding Site



The AChE active site is bur-



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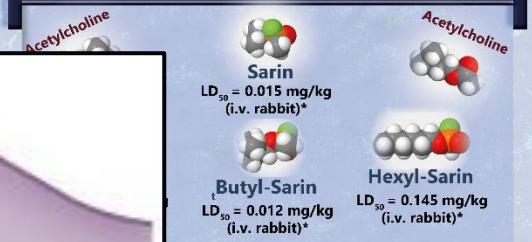

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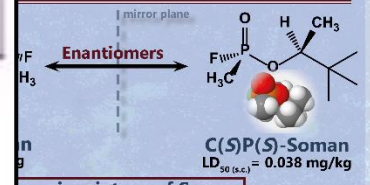

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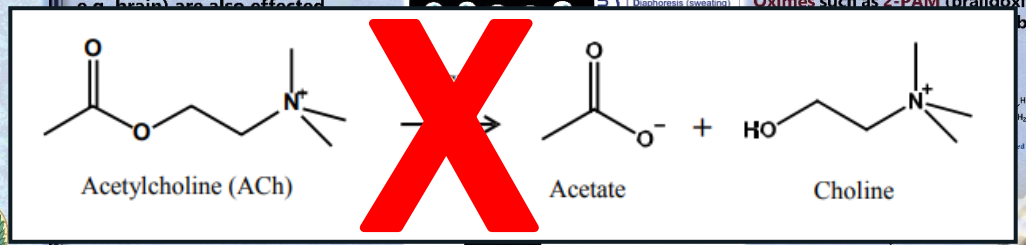
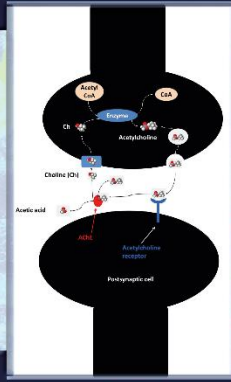


Figure 6: printed 3D Model of the AChE surface

A…erase

Acetylcholinesterase



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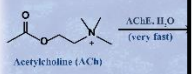

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switches a nerve sig…
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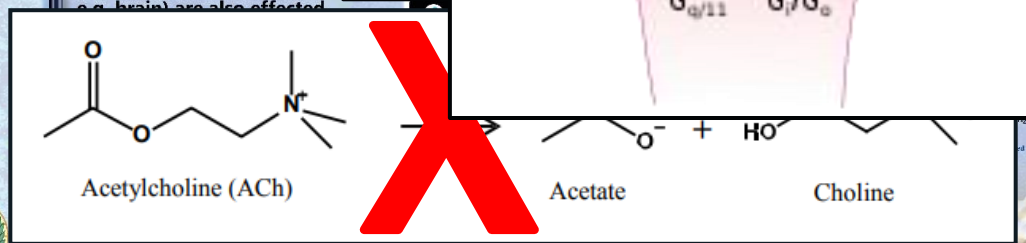
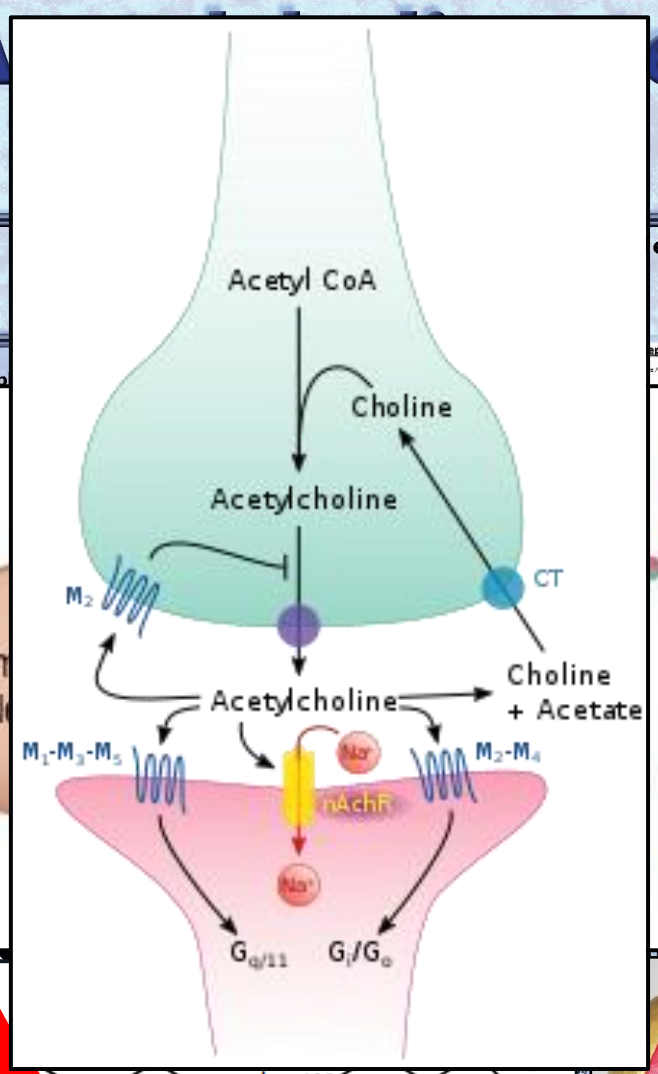
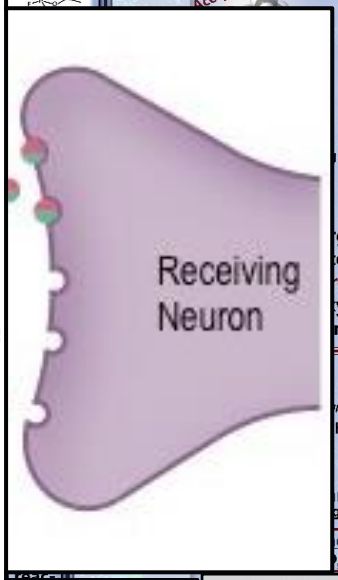
e.g. brain) are also affected.







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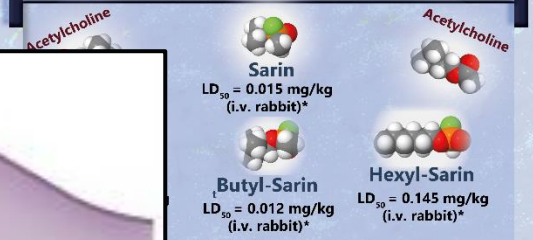

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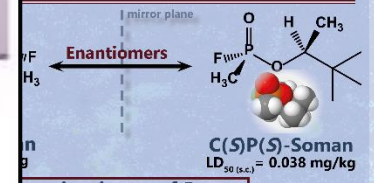

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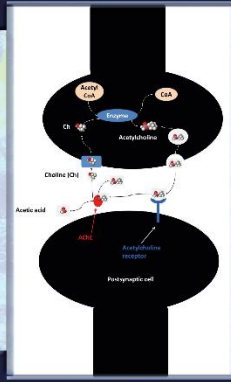

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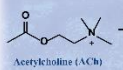

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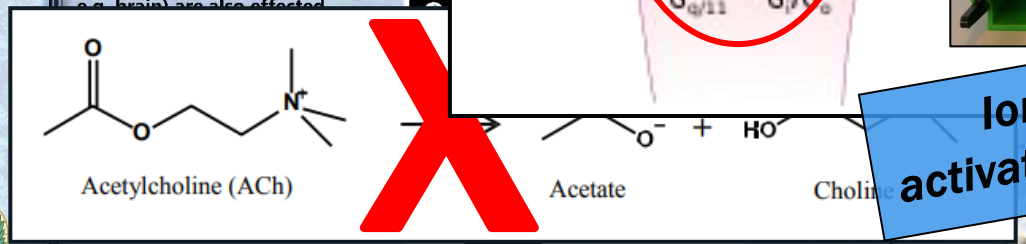


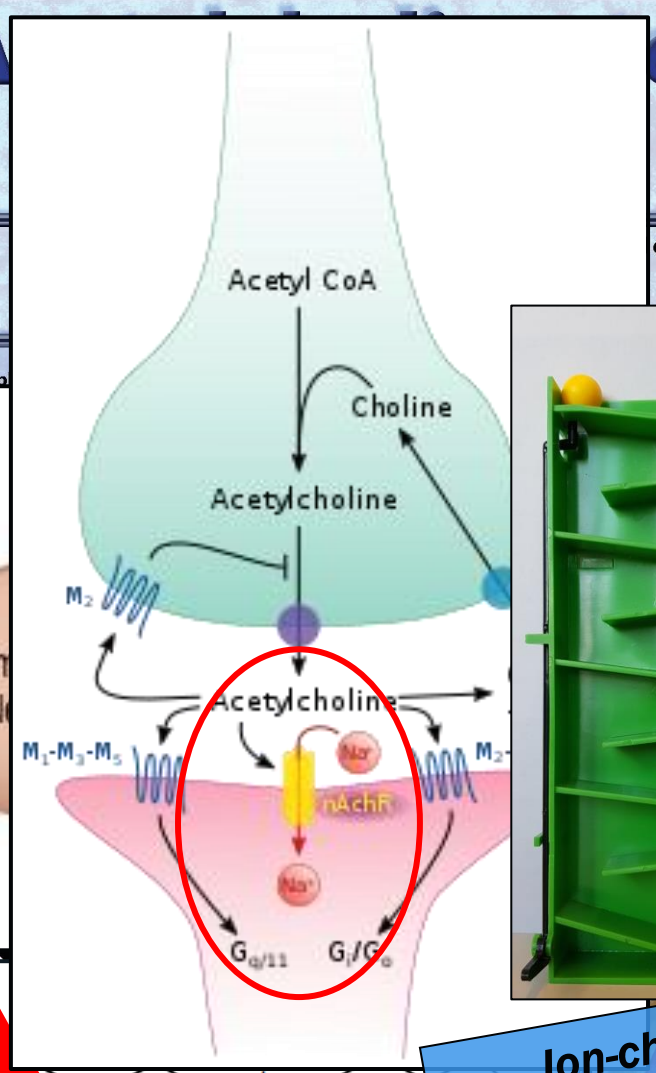
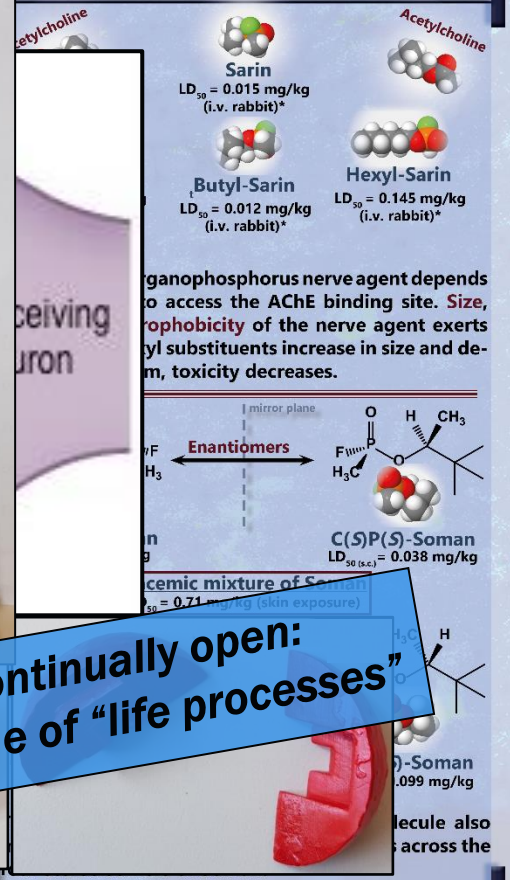


Figure 6: printed 3D Model of the AChE surface

Ion-channel continually open:
activates a cascade of "life processes"

…lerve Agent Molecular Shape and Size



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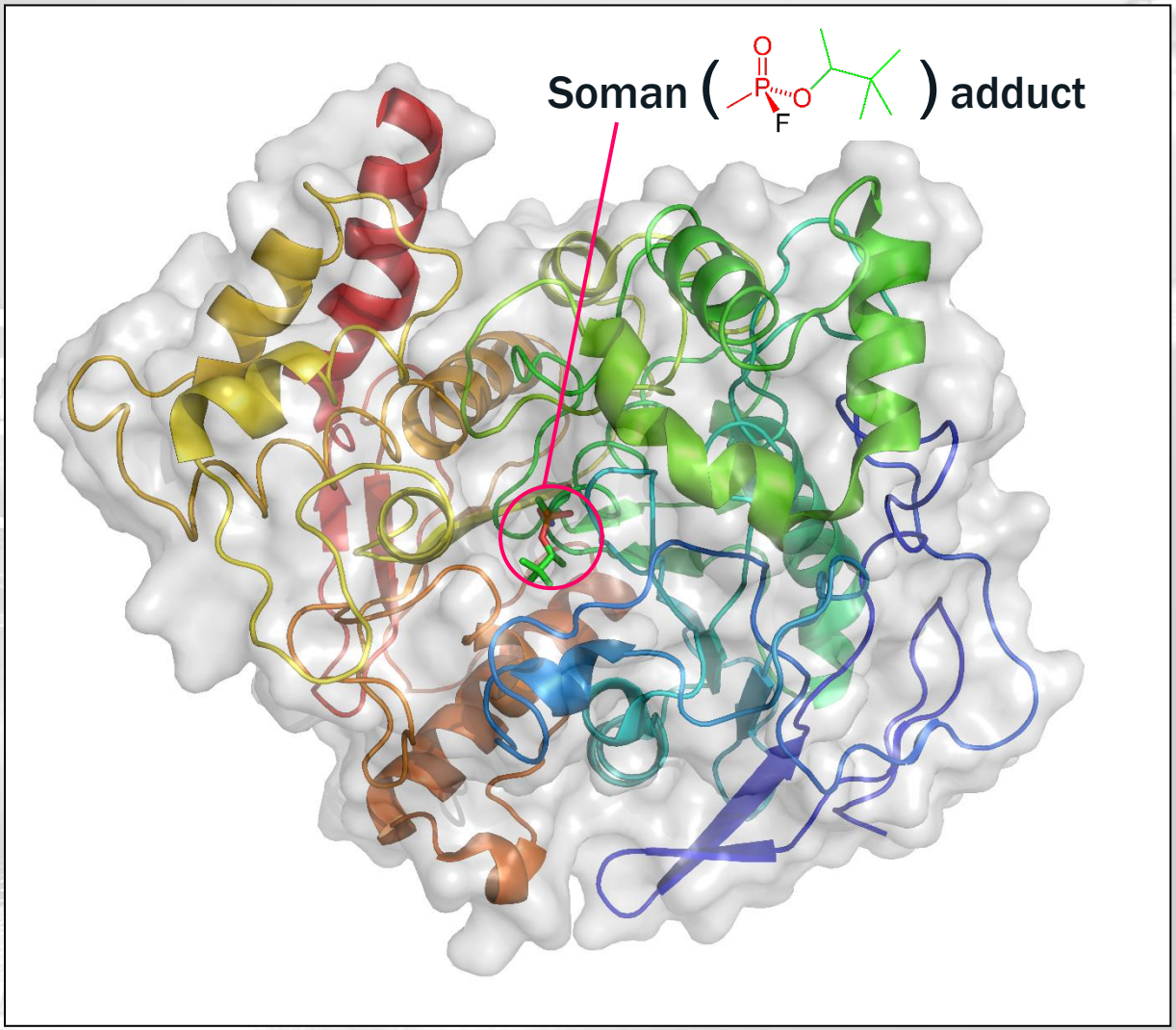
Acetylcholinesterase Inhibition: Nerve Agent Size, Shape and Orientation



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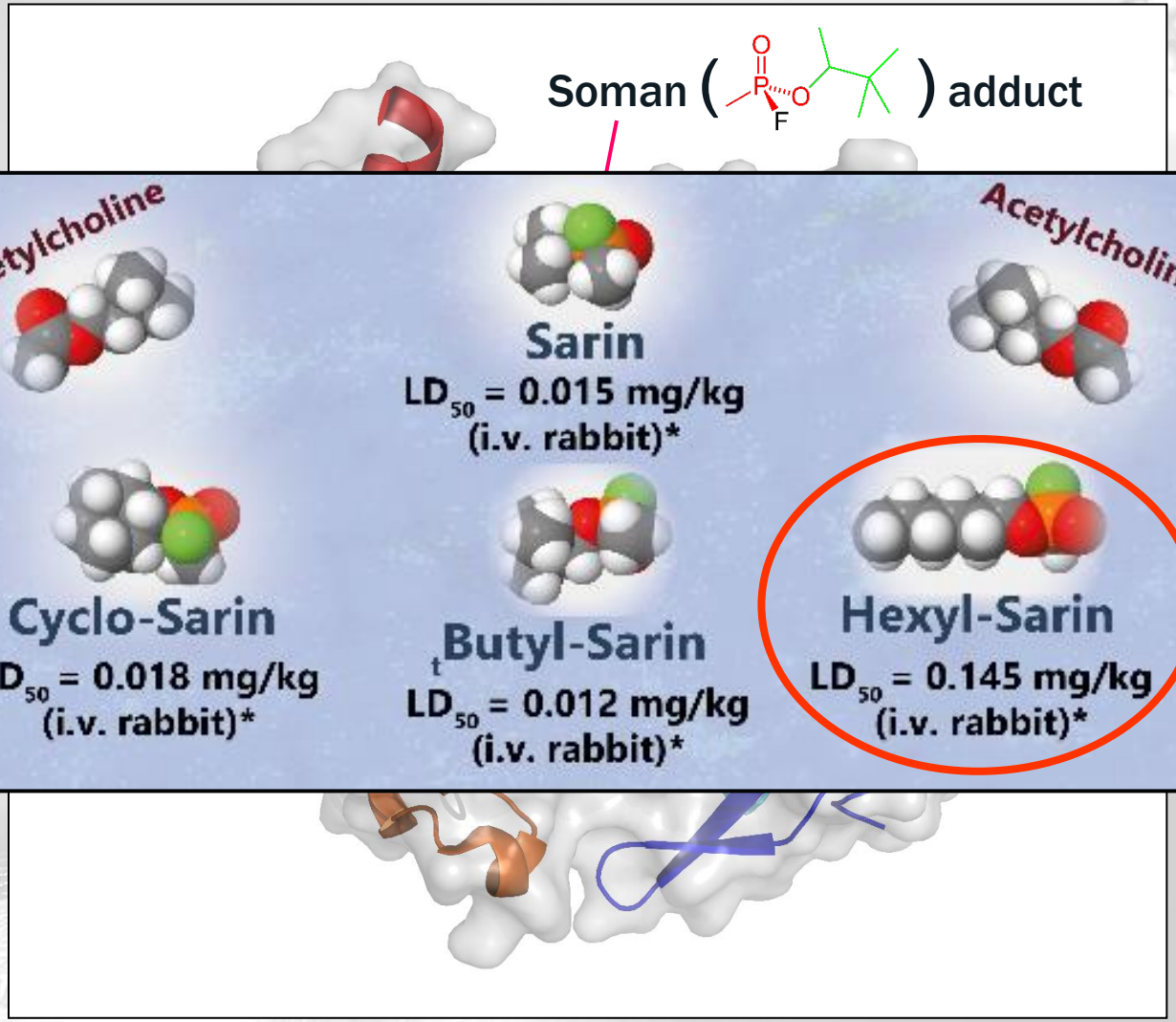

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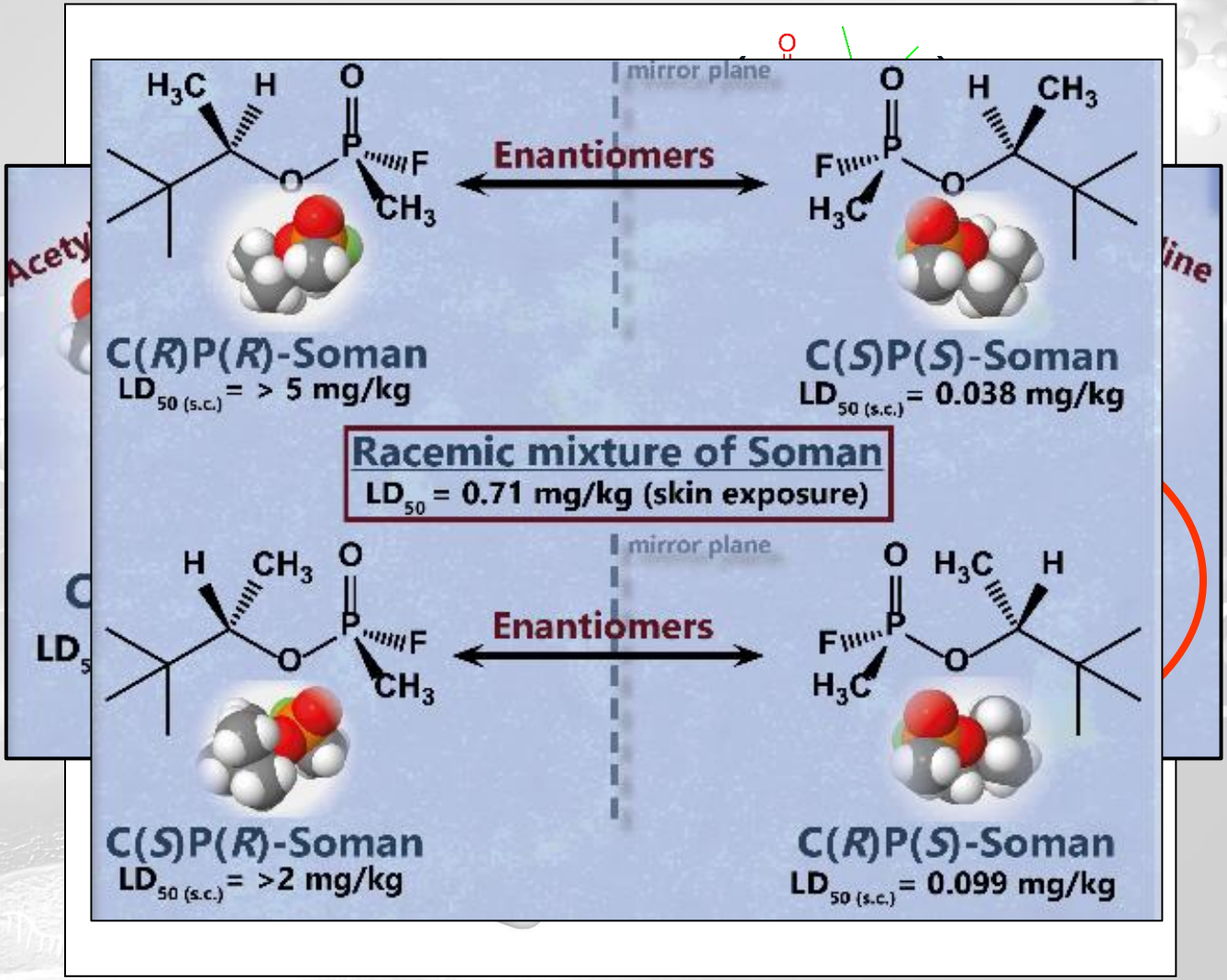
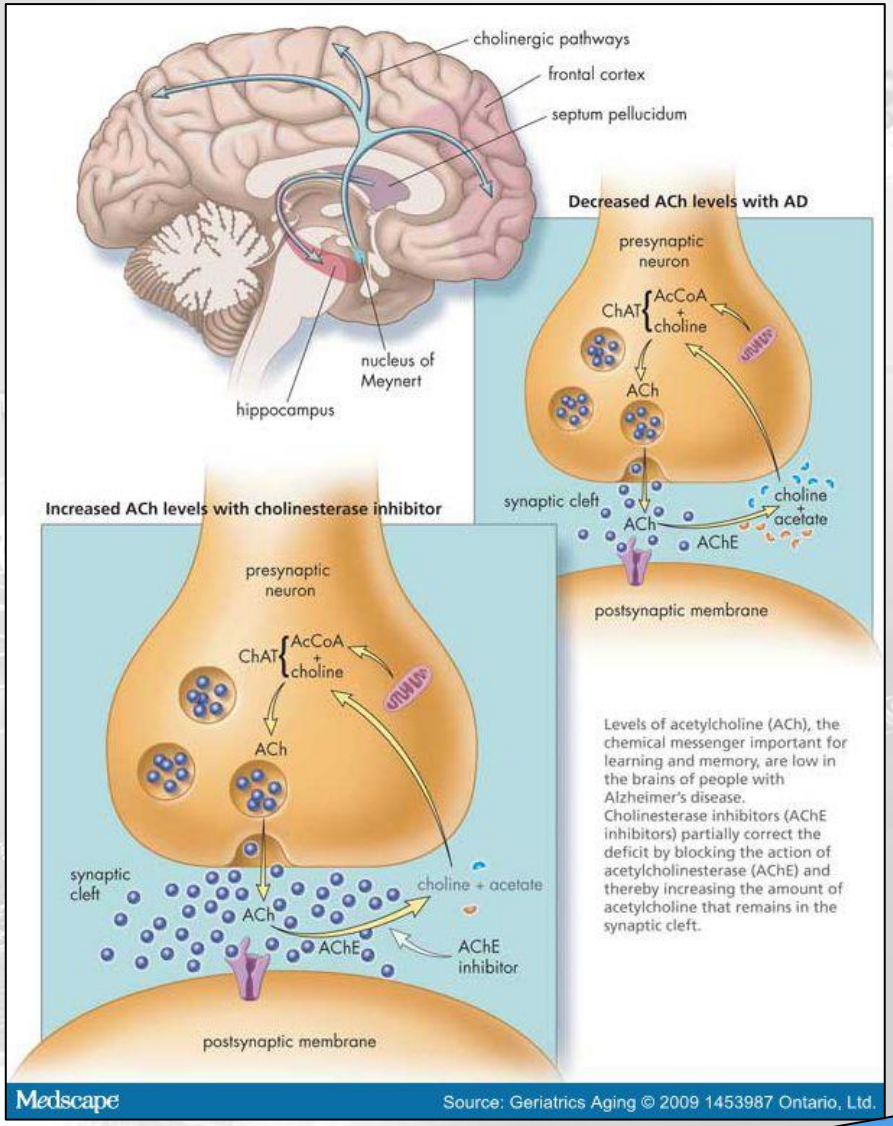


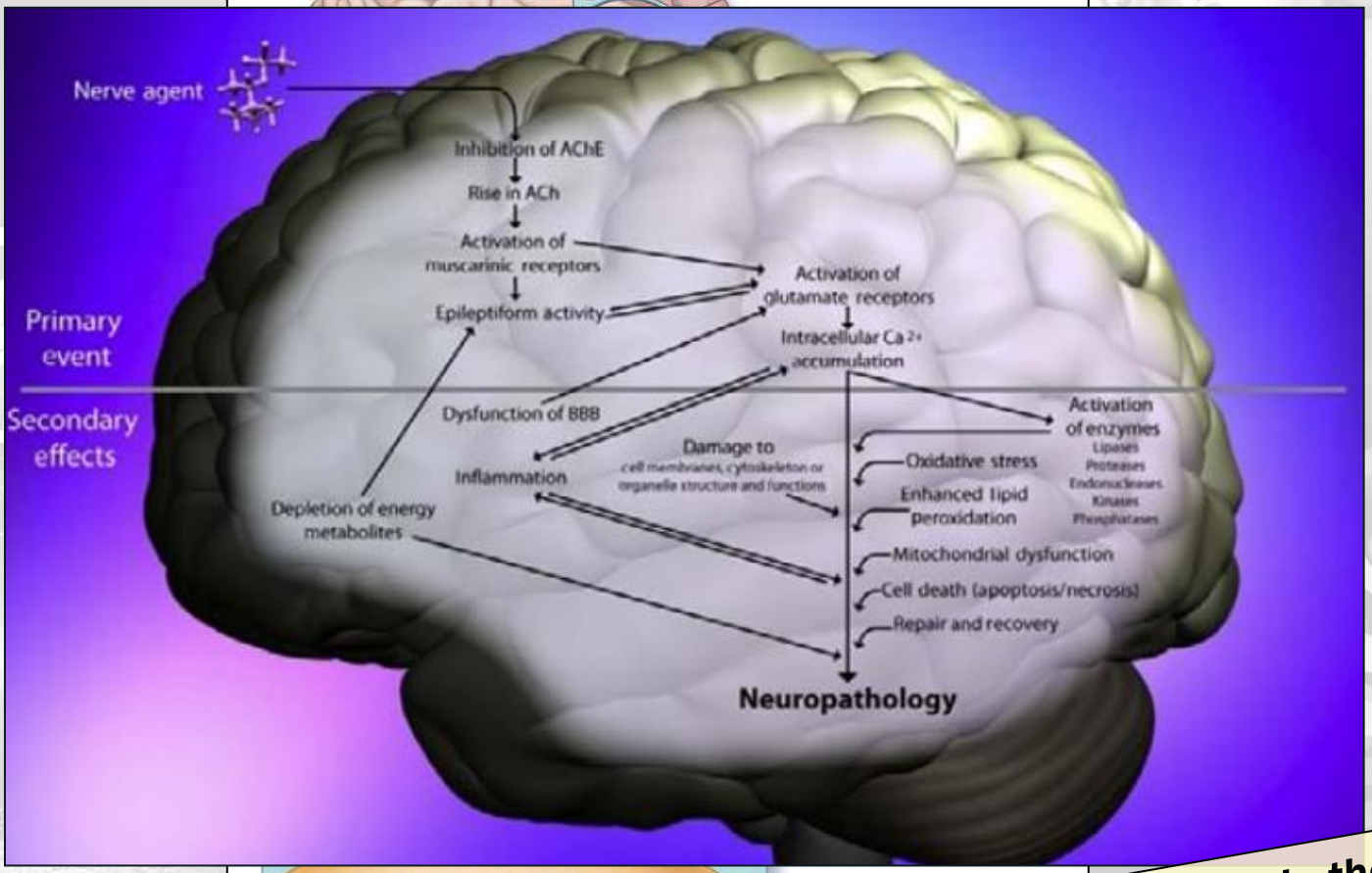
Acetylcholinesterase is also Found in the Brain...



AChE inhibitors are used in the treatment of Alzheimer's Disease! (but not Scheduled "nerve agents")

OPCW

Acetylcholinesterase is also Found in the Brain…

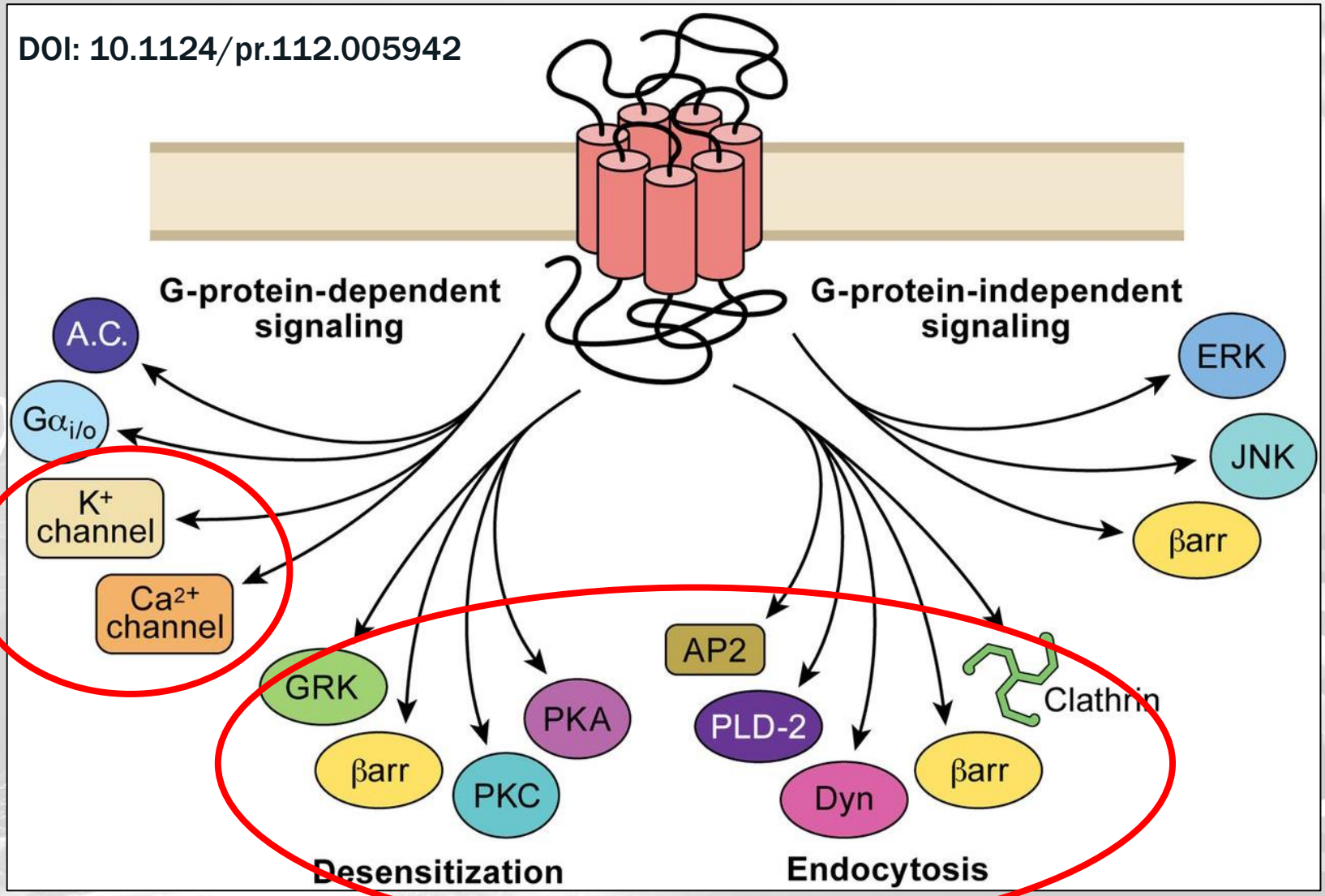


interference with life processes in the brain

- Nerve agent exposure can lead to long term post-exposure neurological conditions

Modulating Pain Response

Modulating Pain Response



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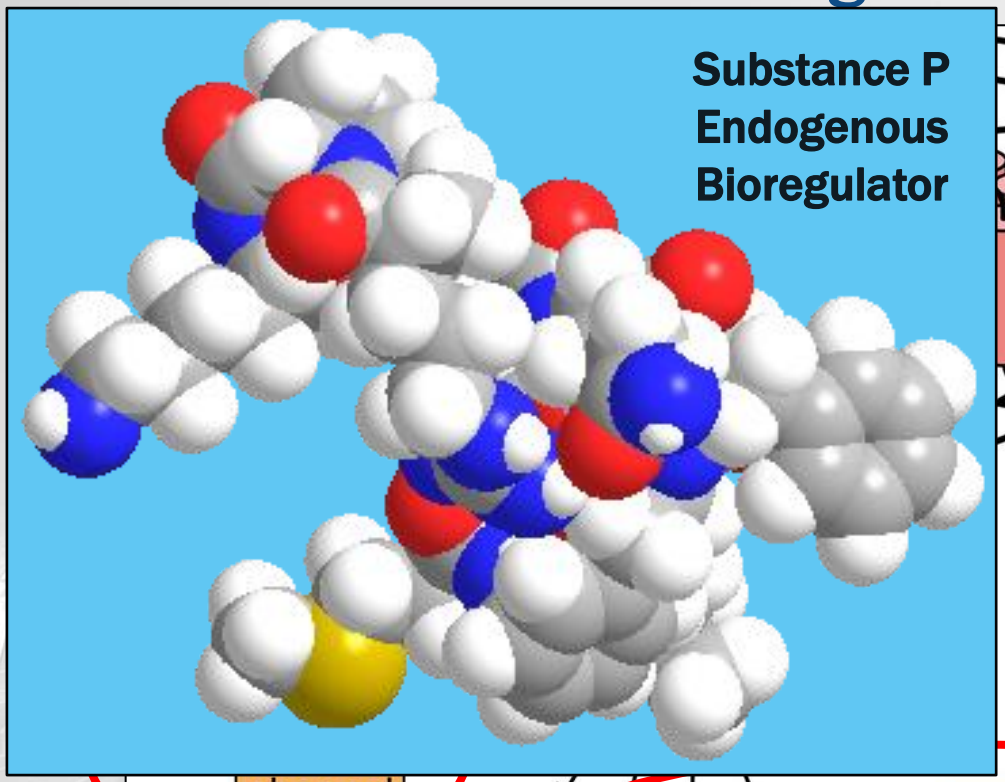
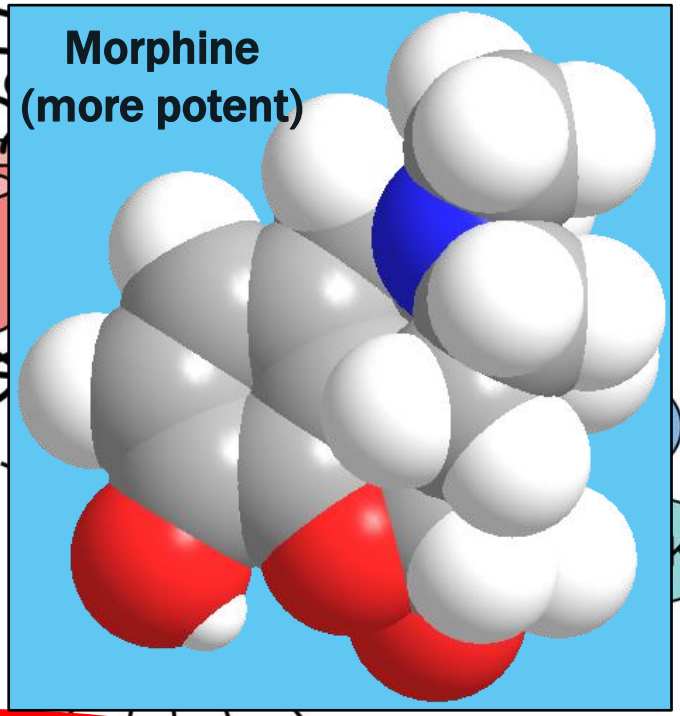
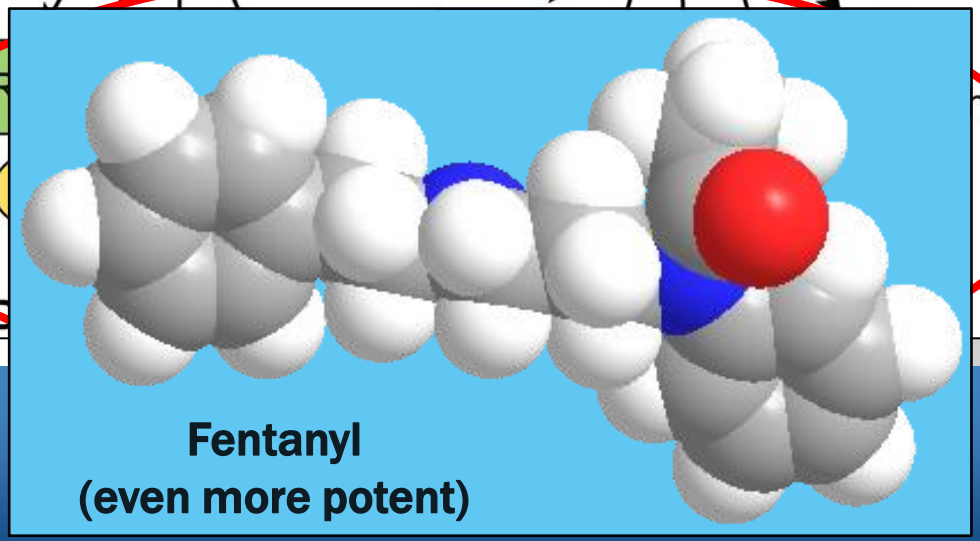






channel

OPCW

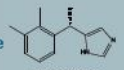
Central Nervous System (CNS)-Acting Chemicals

by Sofia Sola Sancho, Maria Hemme and Ayah wafi
Office of the Science Policy Advisor

Toxic chemicals that target the central nervous system (CNS). These chemicals can act as anaesthetics, sedatives, and analgesics. Specific CNS-acting chemicals discussed in the context of the Chemical Weapons Convention have included α2-adrenergic receptor agonists, inhaled anaesthetics, fentanils and the Schedule 2A.03* chemical BZ.

α2-adrenergic receptor agonist examples

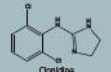
Dexmedetomidine



Mechanism of action:

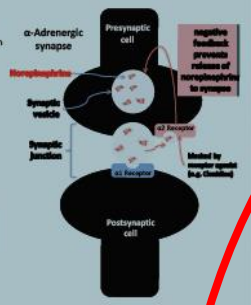
- Presynaptic activation of the α2-adrenoceptor, inhibiting norepinephrine release, preventing entry of the neurotransmitter into the synaptic junction (negative feedback).
- Postsynaptic activation of the α1-adrenoceptor
- inhibiting sympathetic activity. This results in decreased blood pressure and heart rate.
- Produces analgesic, sedative, and anxiolytic effects.
- Occupational exposure band (OEB) 5: control exposure to < 1 µg/m³.

Clonidine



Mechanism of action:

- Reduces release of noradrenaline at both central and peripheral sympathetic nerve terminals.
- Produces dose-related sedation, analgesia and anxiolysis.
- A reduction in the effective dose of other anaesthetic agents and opioids is also observed.
- LC_{50} (rat inh): 19.7 mg/m³/4 Hours
- LD_{50} (rat i.v.): 29 mg/kg

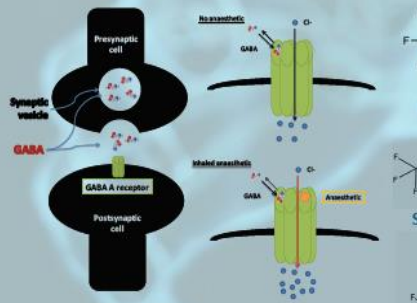


Mechanism of action of Dexmetomidine and Clonidine.

Inhaled anaesthetic examples

Mechanism of action:

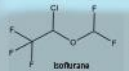
- Enhances γ-aminobutyric acid (GABA) binding to its chloride ion-channel receptor.
- The increase in intra-cellular chloride levels produces an inhibitory effect (anaesthesia).



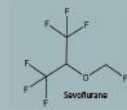
Mechanism of action of inhaled anaesthetics.

Halothane

Isoflurane



Sevoflurane



Toxicity Data	Oral LD_{50} (Human) (µL/kg)	Oral LD_{50} (rat)	Inhalation LC_{50} (rat) (ppm)	Oral LD_{50} (mouse) (µL/kg)	Inhalation LC_{50} (mouse) (ppm (3 hrs))
Halothane	-	5000 mg/kg	29000 (1h)	-	-
Isoflurane	1071	4770 µL/kg	16300 (1h)	5000	16000
Sevoflurane	-	10000 µL/kg	28000 (1h)	18200	28000

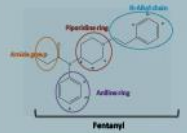
LD_{50}: the lowest dosage of a substance observed to cause a fatality within a specific subject population under a specific set of exposure conditions. LD_{50}: the median value of all the observed dosages of a substance resulting in a fatality within a specific subject population under a specific set of exposure conditions. LC_{50}: the median value of all the observed concentrations (based on an exposure time) of a substance resulting in a fatality within a specific subject population under specific set of exposure conditions. Lethal dose and lethal concentration values are statistics derived from specific populations and exposure conditions (typically controlled animal studies), they may not be representative of alternate populations and/or exposure conditions.

Fentanils

- Fentanils are a highly potent family of opioid narcotic analgesic drugs.
- The family includes fentanyl, a narcotic linked to an increased risk of overdose amongst opioid addicts.
- As of May 2018, there were 20 fentanil derivatives scheduled under the Single Convention on Narcotic Drugs

Properties

- Fentanyl and its analogues are solids that require aerosolisation for weaponisation purposes.
- Routes of exposure for fentanils include inhalation (aerosolized form), oral exposure or ingestion. Transdermal absorption is possible (for example, the use of transdermal patches), however as the process is slow, such that brief incidental exposures may not cause significant opioid toxicity.



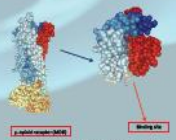
Structure and substitution positions for fentanyl and derivatives.

- Fentanyl and its analogues have higher potency than morphine and heroin.
- Poor drug dosage, poly-drug use and addiction are all contributors to the high rates of overdose, respiratory depres-

Fentanyl derivative	Amide group	Piperidine ring	N-Alkyl chain	Aniline ring
Sufentanil				
Carfentanil				
Ocfentanil				
Remifentanyl				
3-Fluorofentanyl				
Phenylfentanyl				
α'-methyl Butyrylfentanyl				
Cyclopentanylfentanyl				
Cyclopropylfentanyl				
para-chloro Valerylfentanyl				Cl
Valerylfentanyl				
Acetylfentanyl				
Furanylfentanyl				
4F-IBF				F
Tetrahydrofuranylfentanyl (THF-F)				
Methoxyacetylfentanyl				
ortho-methyl Cyclopropylfentanyl				
Acrylfentanyl				
2'-fluoro ortho-Fluorofentanyl				

Mechanism of action:

- In the CNS, fentanils bind to opioid receptors, specifically μ-receptors. These receptors are found predominantly in the brain and spinal cord
- They act to depress CNS function.
- Bioavailbility from inhalation exposure can range from 12-100%.



Crystal structure of the μ-opioid receptor bound to a morphinan antagonist (Protein Data Bank Structure 4DKL)

Effects:

- Loss of pain sensation
- Miosis
- Decreased intestinal paristalsis (constipation)
- Nausea and vomiting
- Dose-dependent respiratory depression (which can lead to death)
- Diminished mental alertness resulting in a feeling of drowsiness, euphoria, sleepiness, or unconsciousness

Antidotes: Naloxone hydrochloride (Narcan) or Naltrexone

- Opioid receptor antagonists.
- Bind to the opioid receptors more strongly than a fentanyl derivative, but do not activate the receptor.
- Quickly reverse signs and symptoms, especially life-threatening respiratory depression.
- Short half-life, symptoms may return in an apparently stabilized patient and antidotes might need to be readministered.
- 0.4 mg is the standard starting dose but for some fentanyl derivatives dose up to 2 mg have been required.

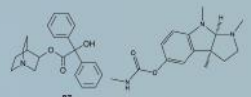
Time Weighted Average – Occupational Exposure Limits (OEL-TWA)	
Alfentanil	1 µg/m³
Fentanyl	0.1 µg/m³
Sufentanil	[illegible] µg/m³

BZ (3-quinuclidinyl benzilate)

BZ is a glycolate anticholinergic compound and is a only "CNS-acting chemical" found in the Annex of Chemicals of the Chemical Weapons Convention (Schedule 2A.03*).

Properties

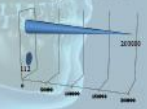
- Odourless crystalline powder with bitter taste.
- Persistent in soil and water and on most surfaces.
- Half-life in moist air ~ 3-4 weeks.



Antidote: Physostigmine

- Temporarily raises acetylcholine concentrations by binding reversibly to anticholinesterase.

Safety Ratio of BZ



The large difference between the median lethal concentration (LC_{50}) and the median incapacitating concentration (IC_{50}) allows for the onset of CNS-acting symptoms to appear at a dosage much lower than a lethal dose.

Dose in [mg.min/m³]

Mechanism of action:

- Acts as a competitive inhibitor of the neurotransmitter acetylcholine (ACh) in postsynaptic ACh receptors.
- As the concentration of BZ at these sites increases, the proportion of receptors available for binding to acetylcholine decreases, resulting in an understimulation of nerve signal transduction.
- When administered by inhalation (in aerosolised form), absorption to the bloodstream is more pronounced than with oral administration.

Mechanism of action of BZ.

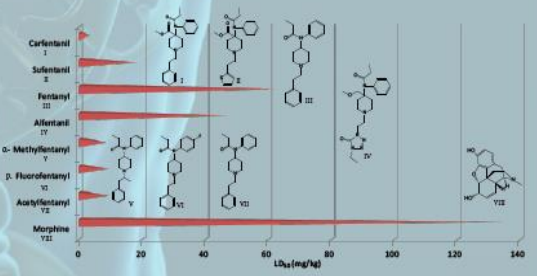
CNS effects:

- Stupor, ataxia, confusion, and confabulation. Induces concrete and panoramic illusions and hallucinations.

Peripheral effects:

- Mydriasis, blurred vision, dry mouth and skin, initially rapid heart rate; later, normal or slow heart rate.

Toxicity



Riot Control Agents

OPCW

Fauzia Nurul Izzati, Jonathan E. Forman and Christopher M. Timperley

What is the definition of a Riot Control Agent (RCA)?

From paragraph 7, Article II of the Chemical Weapons Convention:

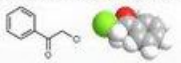
"Any chemical not listed in a Schedule, which can produce rapidly in humans sensory irritation or disabling physical effects which disappear within a short time following termination of exposure."

How do Riot Control Agents work?

RCAs produce irritation through binding to TRP (Transient Receptor Potential) receptors. This activates some of the same biochemical pathways that are triggered by eating horseradish or hot peppers.

What are Riot Control Agents?

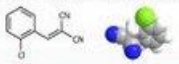
Chemicals that meet the criteria of an RCA include the following:



2-Chloroacetophenone (CN)

Synonyms:
Mace, CAP, Khlorketon (10% CN, 45% benzene, 40% carbon tetrachloride), CNC (30% CN, 70% chloroform), and CNS (23% CN, 38.4% chloropicrin, 38.4% chloroform).

Physical states:
White solid with odour of apple blossom
Melting Point 54-56 °C; Boiling Point 245 °C



2-Chlorobenzylidenemalononitrile (CS)

Synonyms:
2-Chlorobenzalmalononitrile, o-chlorobenzylidene malononitrile, K62 CS (pure), CS1 (95% CS, 5% silica aerogel), CS2 (CS and silica aerogel), CSX (1 g CS, 99 g tri-n-octyl phosphite). CS dissolved in methyl ethyl ketone is used in spray devices.

Physical states:
White solid with pungent peppery odour
Melting Point 93-95 °C;
Boiling Point 310-315 °C dec

Dibenzo[b,f][1,4]oxazepine (CR)

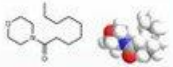
Synonym:
CR

Physical states:
Yellow stable powder
Melting Point 72 °C; Boiling Point 335 °C

2'-Chloroacetophenone

Synonyms:
o-chloroacetophenone

Physical states:
Colourless liquid
Boiling Point 229 °C



4-Nonanoylmorpholine

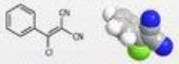
Synonyms:
MPA, MPK, pelargonic acid morpholide

Physical states:
Liquid
Boiling Point 310 °C

3'-Chloroacetophenone

Synonyms:
m-chloroacetophenone

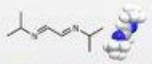
Physical states:
Colourless liquid
Boiling Point 228°C



α-Chlorobenzylidenemalononitrile

Synonym:
none

Physical states:
White solid
Melting Point 68-70 °C;
Boiling Point 126 °C/0.1 mmHg



N,N'-Bis(isopropylethylene)diimine

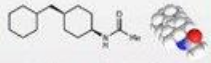
Synonym:
Diimine

Physical states:
Volatile tan-coloured solid
Melting Point 48-50 °C

N,N'-Bis(tert-butylethylene)diimine

Synonyms:
none

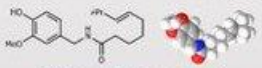
Physical states:
White solid
Melting Point 39-43 °C



Cis-4-Acetylaminocyclohexylmethane

Synonyms:
none

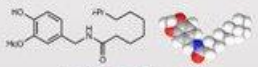
Physical states:
White solid
Melting Point 112 °C



8-Methyl-N-vanillyl-trans-6-nonenamide

Synonyms:
C, capsoicin, Moltin, Zacin

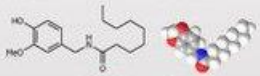
Physical states:
White solid
Melting Point 62-65 °C; Boiling Point 210-220 °C at 0.01 mmHg



8-Methyl-N-vanillylnonanamide

Synonyms:
Dihydrocapsaicin, DHC

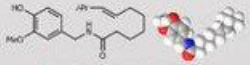
Physical states:
White solid
Physical data unavailable



N-Vanillylnonanamide

Synonyms:
N-(4-hydroxy-3-methoxy-benzyl)nonanamide, nonivamide, pseudo-capsaicin, pelargonic acid vanillylamide, PAVA

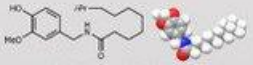
Physical states:
White solid with stinging odour
Melting Point 57 °C



N-Vanillyl-9-methyldec-7-(E)-enamide

Synonym:
homocapsaicin

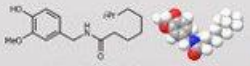
Physical states:
Lipophilic colourless odourless crystalline or waxy solid



N-Vanillyl-9-methyldecanamide

Synonym:
homodihydrocapsaicin

Physical states:
Lipophilic colourless odourless crystalline or waxy solid



N-Vanillyl-7-methyloctanamide

Synonym:
nordihydrocapsaicin

Physical states:
Lipophilic colourless odourless crystalline or waxy solid

Oleoresin capsicum (OC)

This is a mixture containing ≥ 8% capsaicins: capsaicin, dihydrocapsaicin, and nordihydrocapsaicin dissolved in an organic solvent.

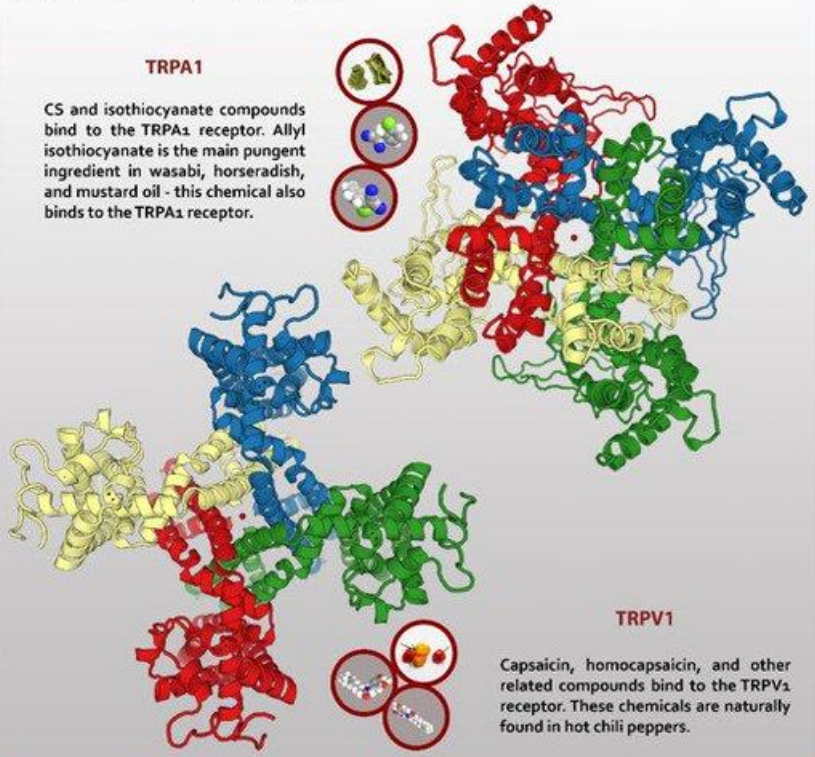
What are TRP Receptors?

TRP receptors are a family of ion channel receptors mainly located on cell membranes of multicellular organisms. TRP receptors are classified into seven subfamilies: TRPC (canonical or classical), TRPV (vanilloid), TRPM (melastatin), TRPA (ANKTM1 homologues), TRPP (polycystin), TRPML (mucolipin), and TRPN (NOMP-C homologues).

TRP receptor functions are diverse; the receptors serve as versatile sensors that allow individual cells and entire organisms to detect changes in their environment. This includes experiencing changes in temperature, touch, taste and other stimuli (including pain).

TRPA1

CS and isothiocyanate compounds bind to the TRPA1 receptor. Allyl isothiocyanate is the main pungent ingredient in wasabi, horseradish, and mustard oil - this chemical also binds to the TRPA1 receptor.



TRPV1

Capsaicin, homocapsaicin, and other related compounds bind to the TRPV1 receptor. These chemicals are naturally found in hot chili peppers.

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2-Chlorobenzyli

Synonyms:
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zylidene malononitri
(95% CS, 5% silica ae
silica aerogel), CSX (1
phosphite). CS dissolv
ketone is used in spray

Physical states:
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Melting Point 93-95 °C;
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Synonym:
m-chloroacetophenone

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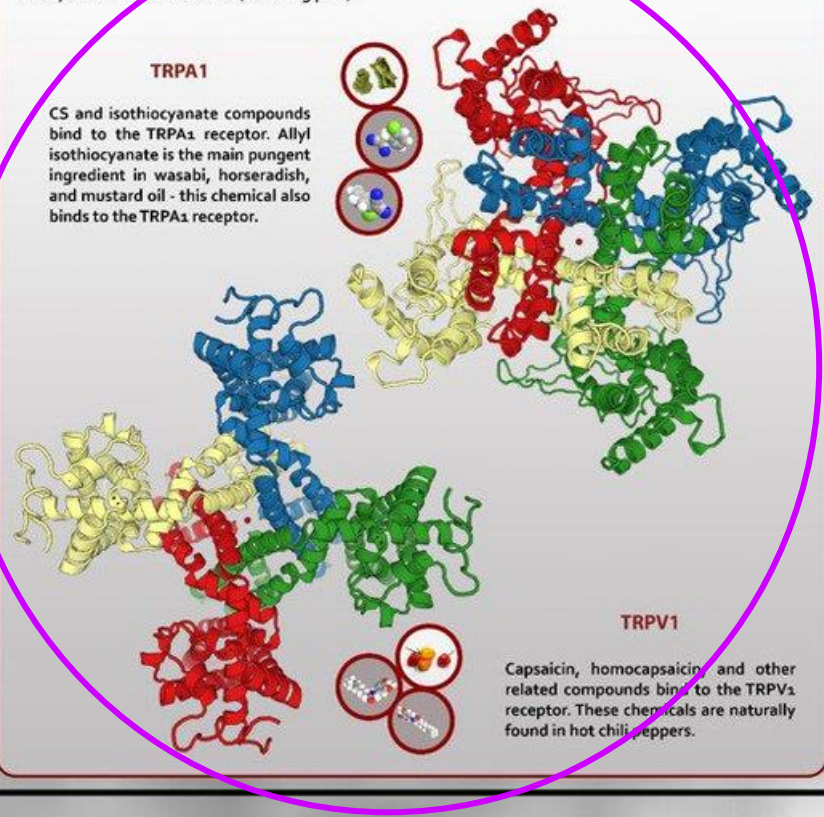
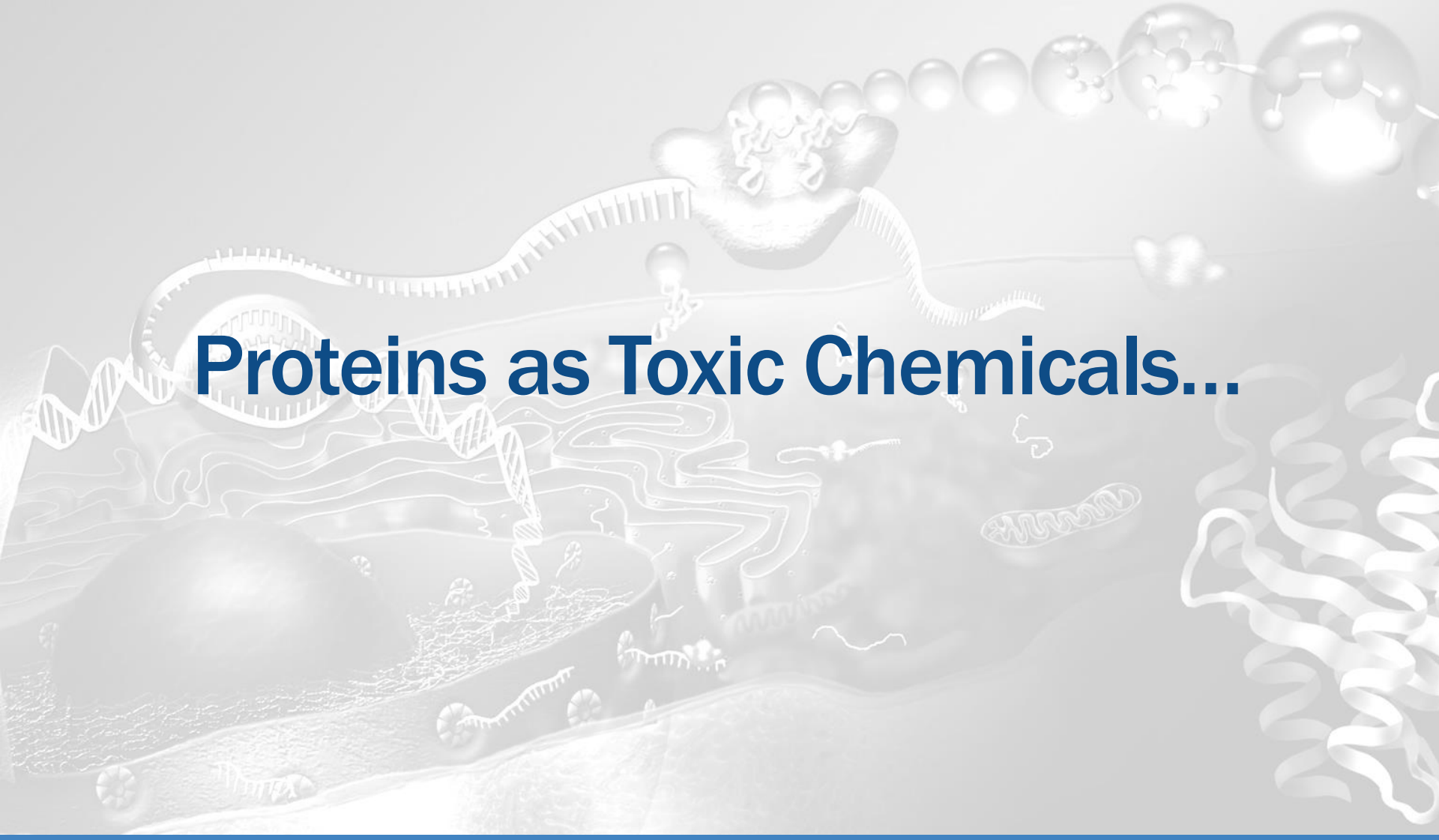


TRPV1

Capsaicin, homocapsaicin, and other related compounds bind to the TRPV1 receptor. These chemicals are naturally found in hot chili peppers.

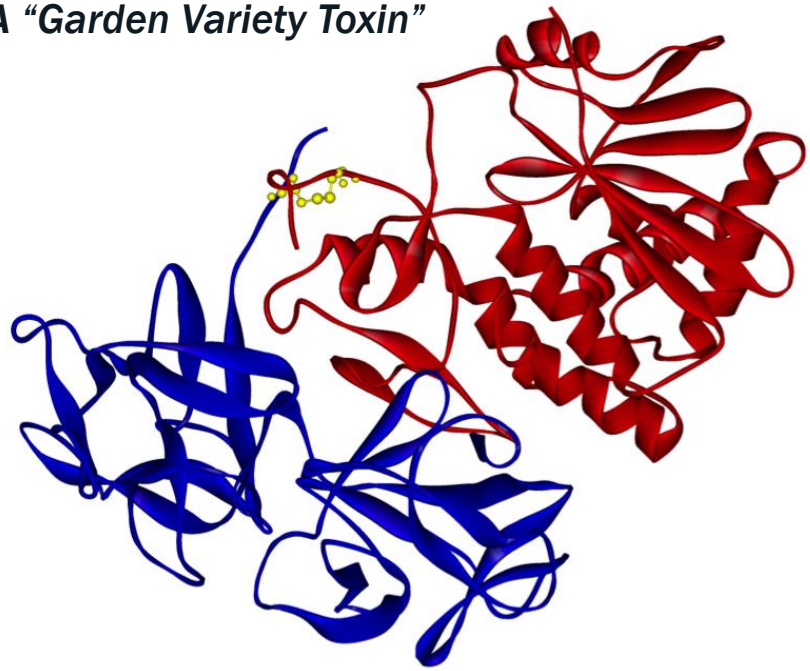
The 17 RCA's activate peripheral nervous system ion channel receptors (TRPA1, TRPV1) – these initiate an irritation response

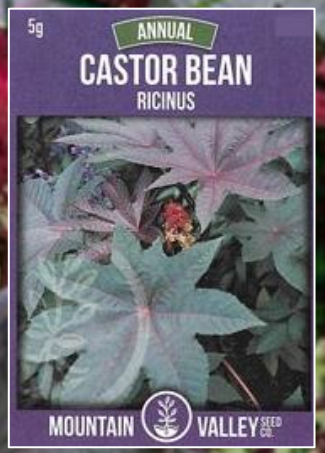
Proteins as Toxic Chemicals…

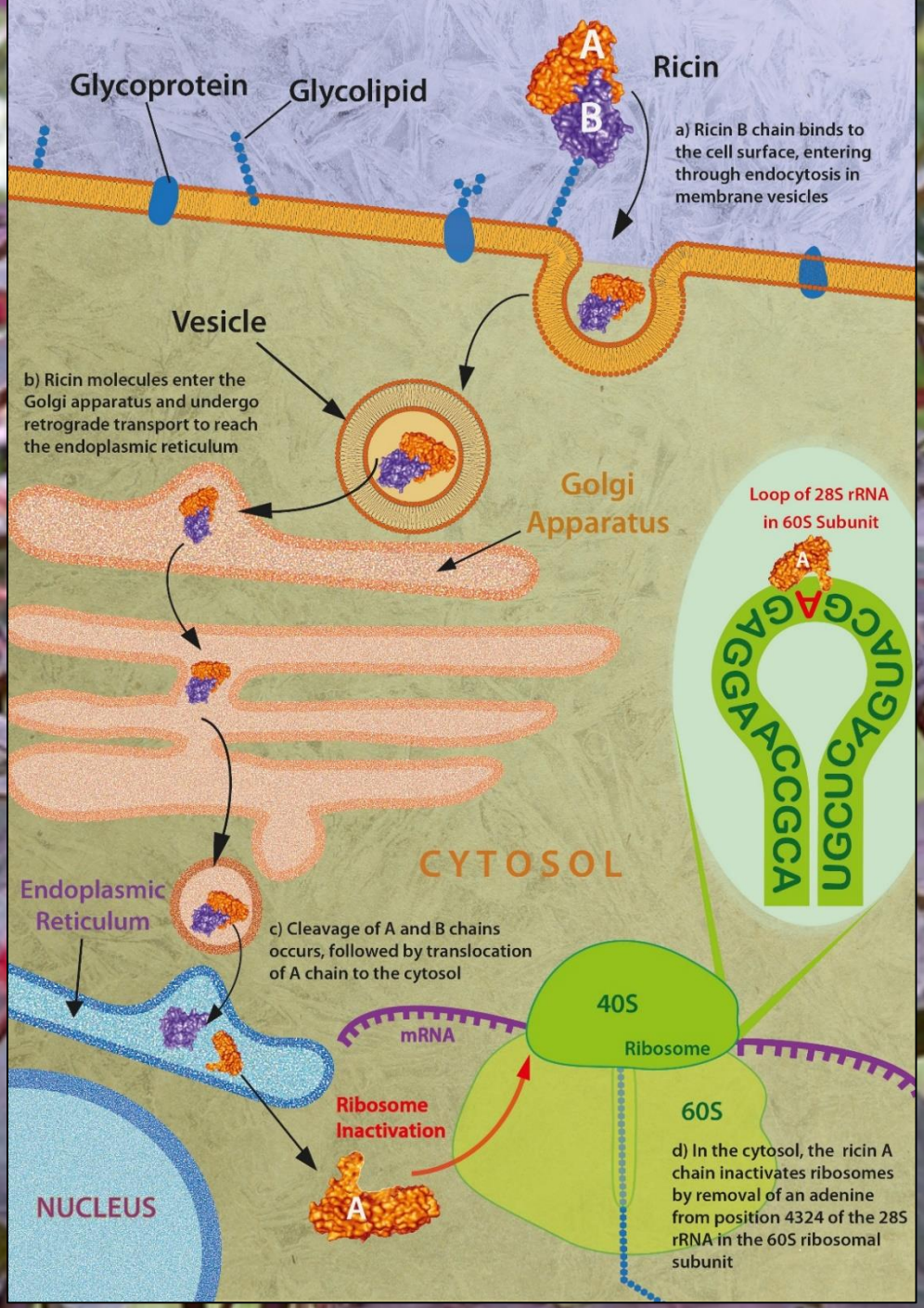


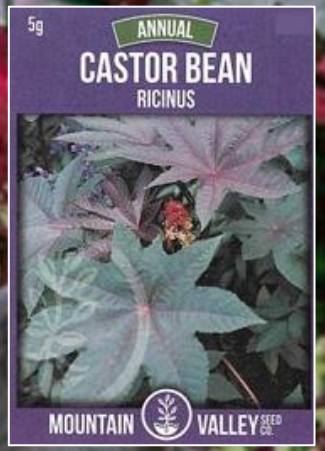

5g
ANNUAL
CASTOR BEAN
RICINUS
MOUNTAIN VALLEY SEED CO.

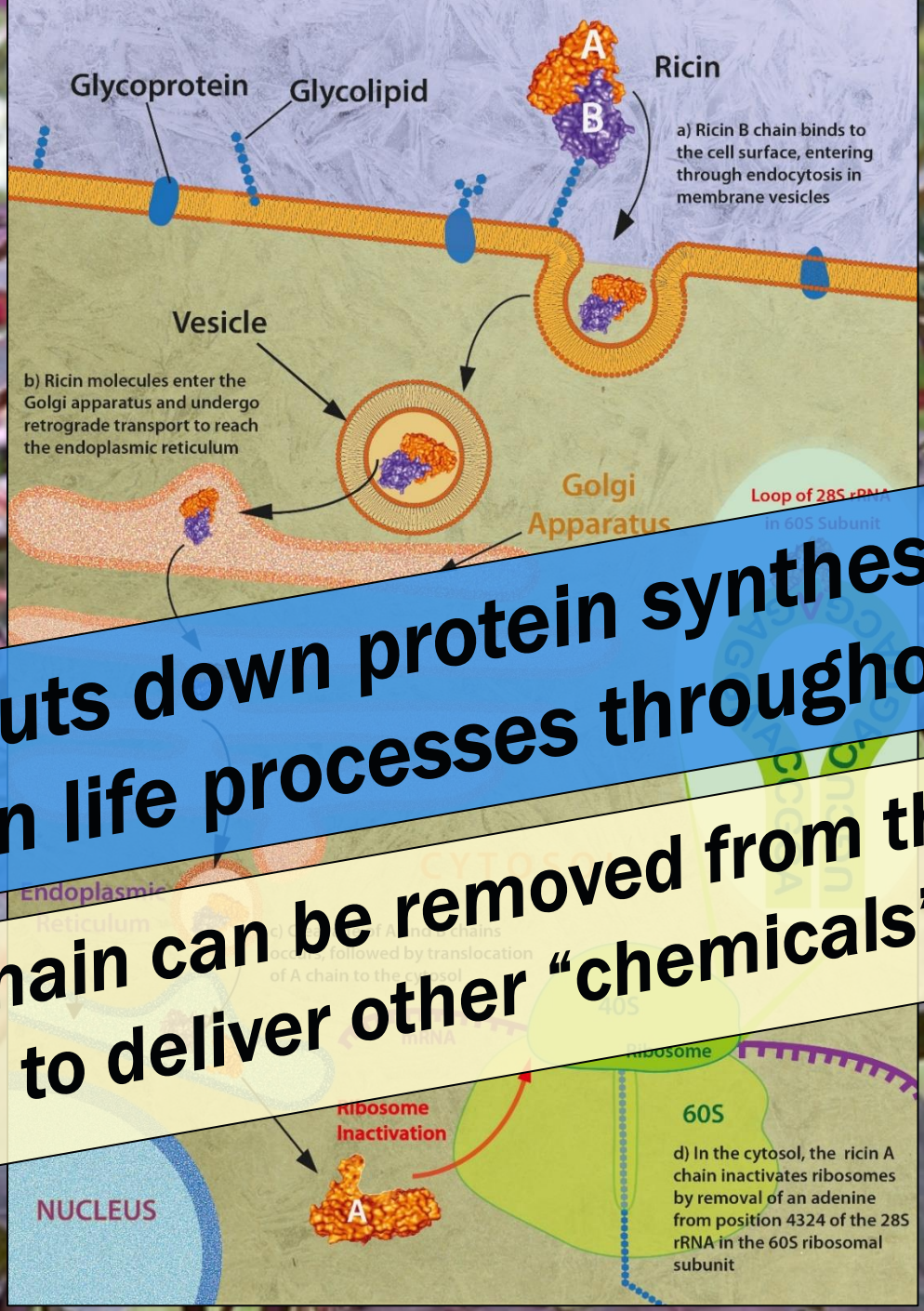
A “Garden Variety Toxin”






Glycoprotein
Glycolipid
A
B
Ricin
a) Ricin B chain binds to the cell surface, entering through endocytosis in membrane vesicles
Vesicle
b) Ricin molecules enter the Golgi apparatus and undergo retrograde transport to reach the endoplasmic reticulum
Golgi Apparatus
Loop of 28S rRNA in 60S Subunit
A
AGUACGAGGAACCGCA
UGCUCAGU
CYTOSOL
Endoplasmic Reticulum
c) Cleavage of A and B chains occurs, followed by translocation of A chain to the cytosol
40S
Ribosome
mRNA
60S
Ribosome Inactivation
A
NUCLEUS
d) In the cytosol, the ricin A chain inactivates ribosomes by removal of an adenine from position 4324 of the 28S rRNA in the 60S ribosomal subunit

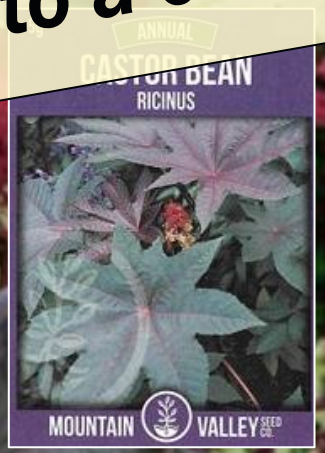

5g
ANNUAL
CASTOR BEAN
RICINUS
MOUNTAIN VALLEY SEED CO.



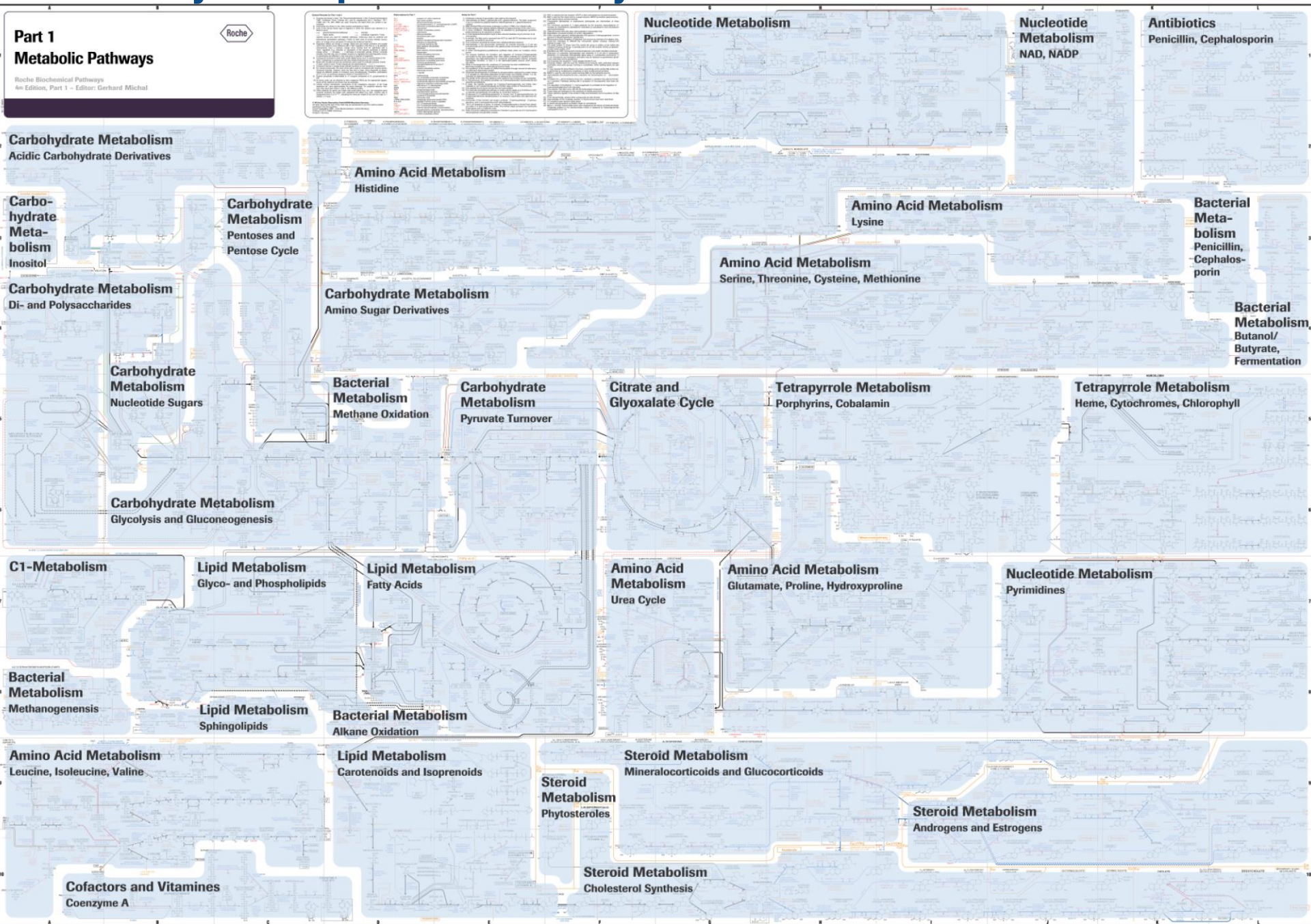
Shuts down protein synthesis.

Impacts on life processes throughout the cell.

Ricin B chain can be removed from the A chain and used to deliver other "chemicals" into a cell



Why its Important to Fully Understand Life Processes



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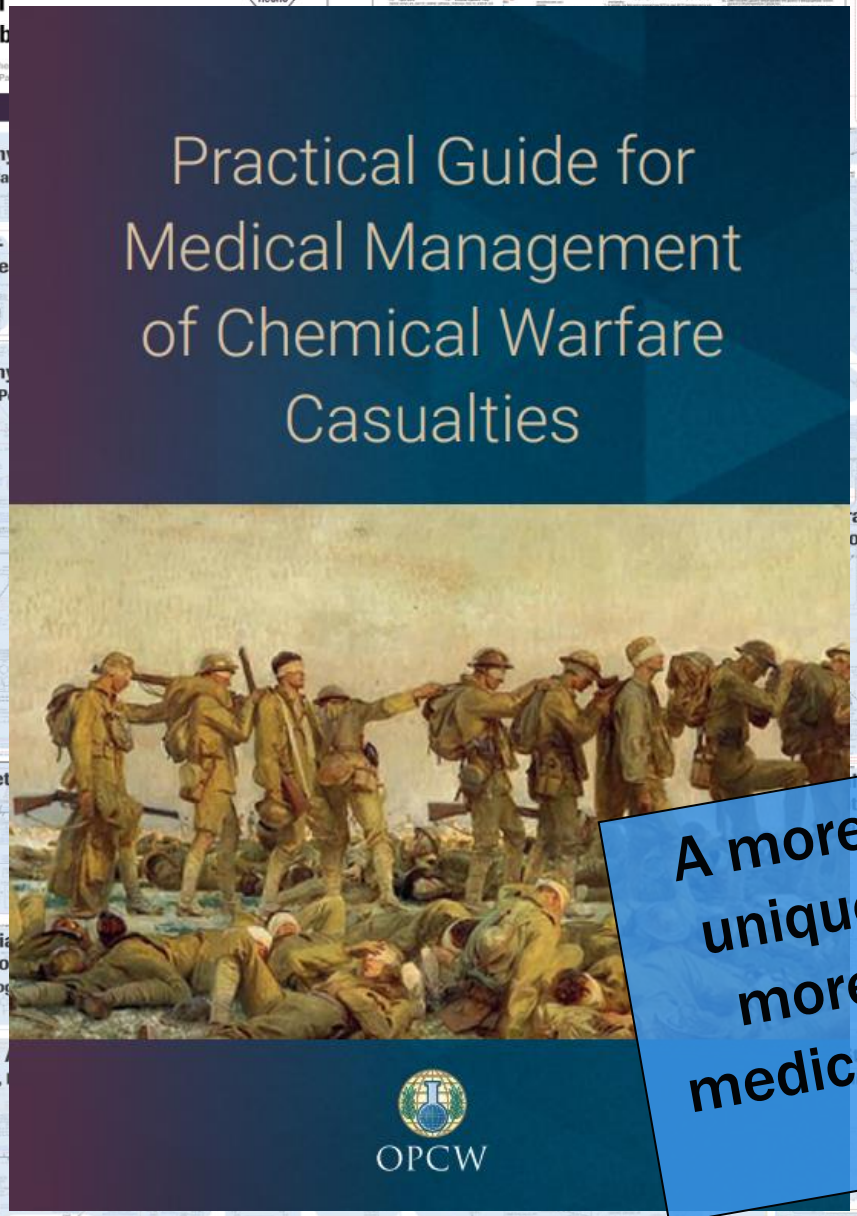
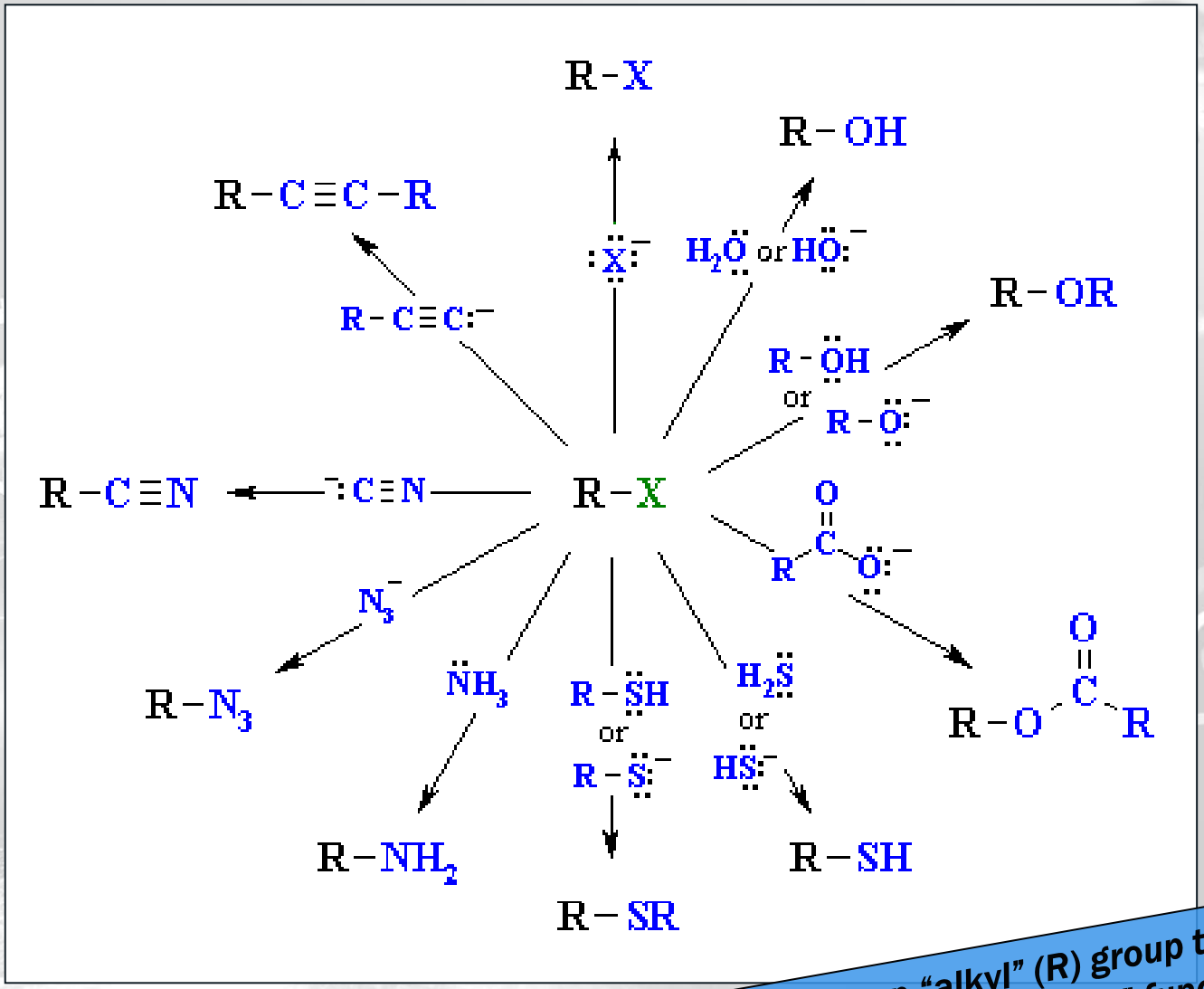


A more specific effect on a unique life process allows more targeted/effective medical countermeasures to be developed

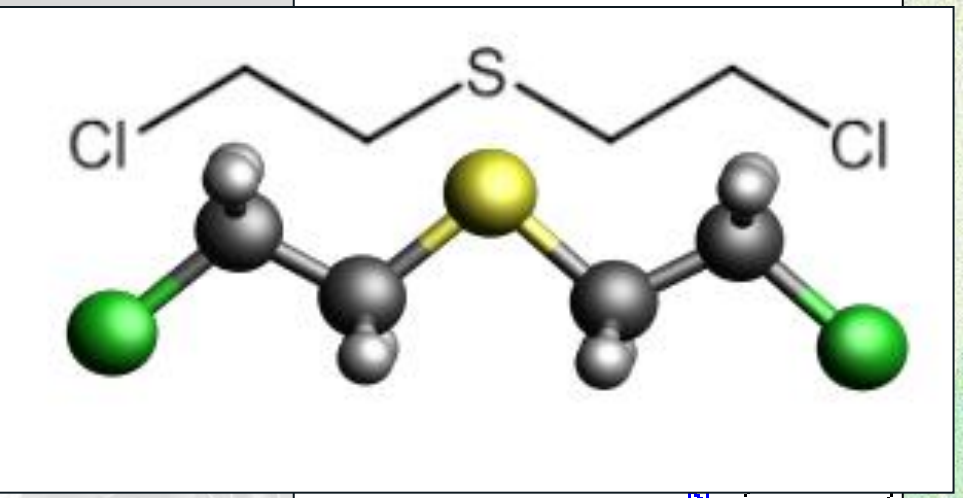
Chemical Action Does Not Always need to be So Complicated..

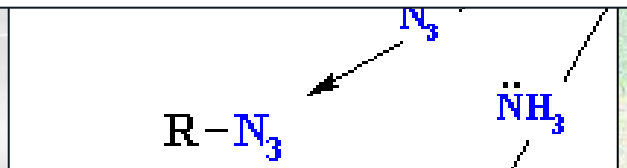


An alkyl halide will transfer an "alkyl" (R) group to another molecule through reaction with a "nucelphilic" functional group

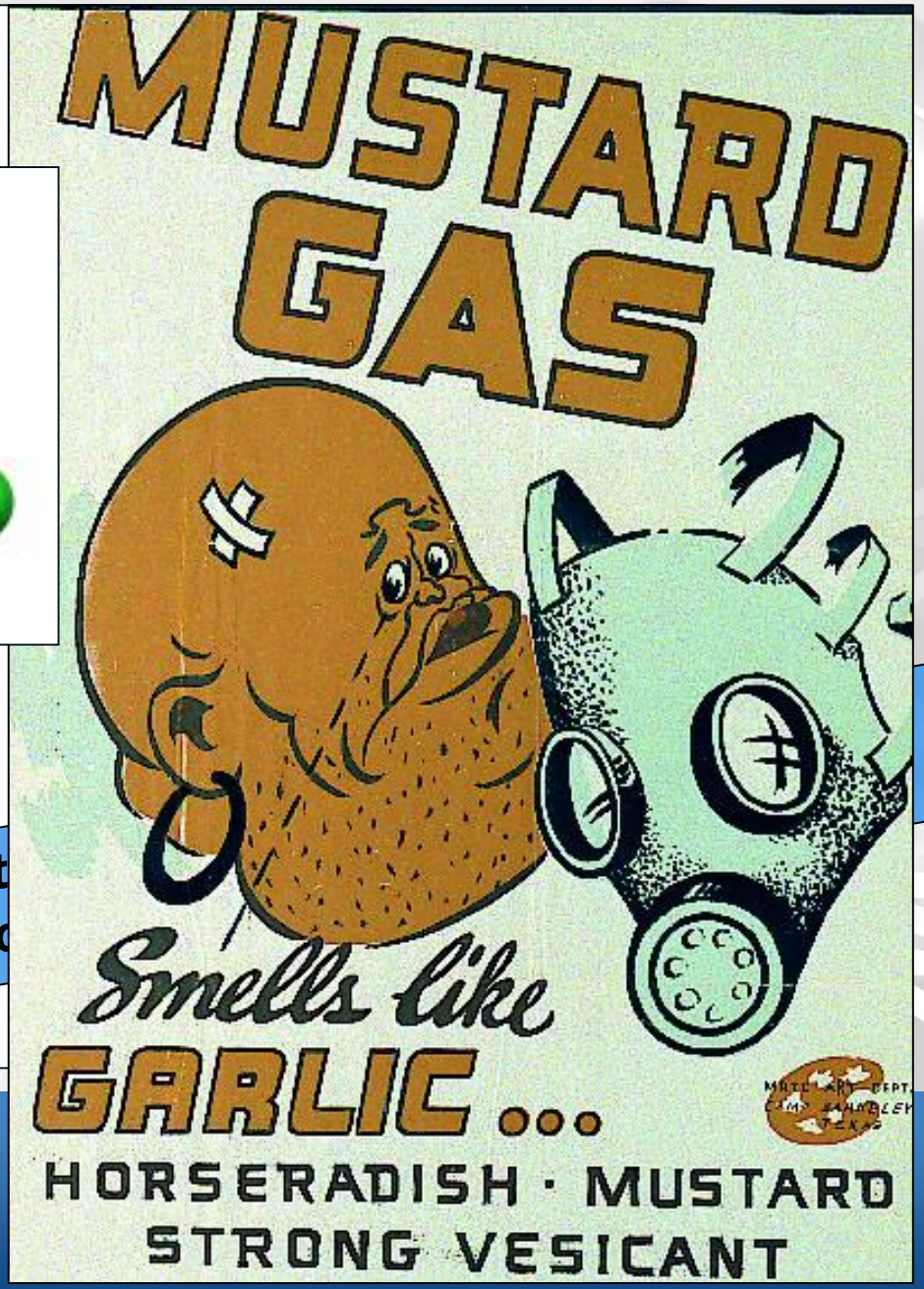
OPCW

Chemical Action Does Not Always need to be So Complicated..





An alkyl halide will t
molecule through reac



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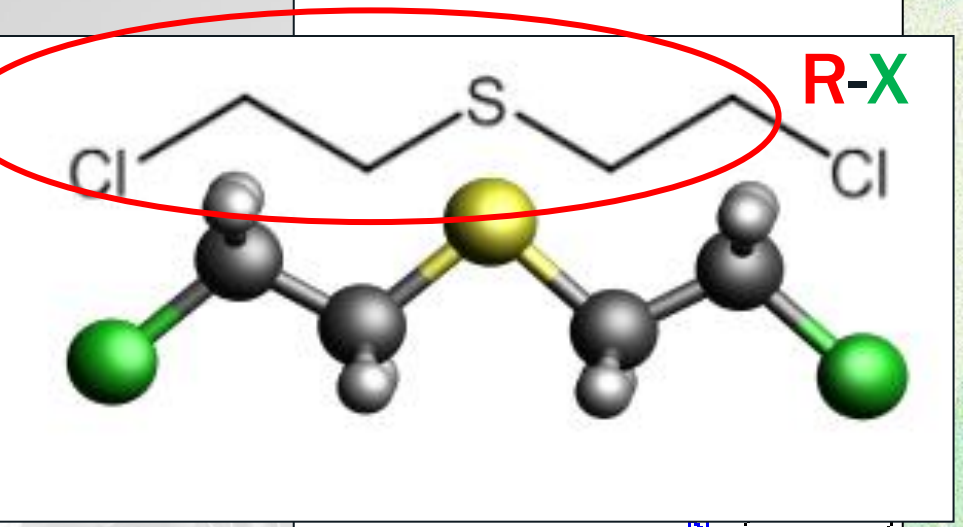
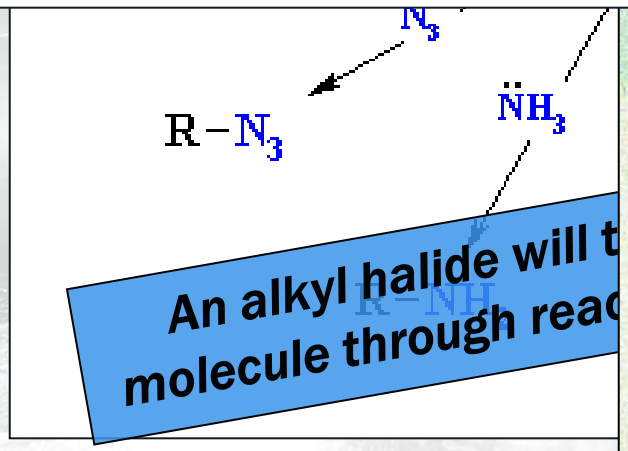
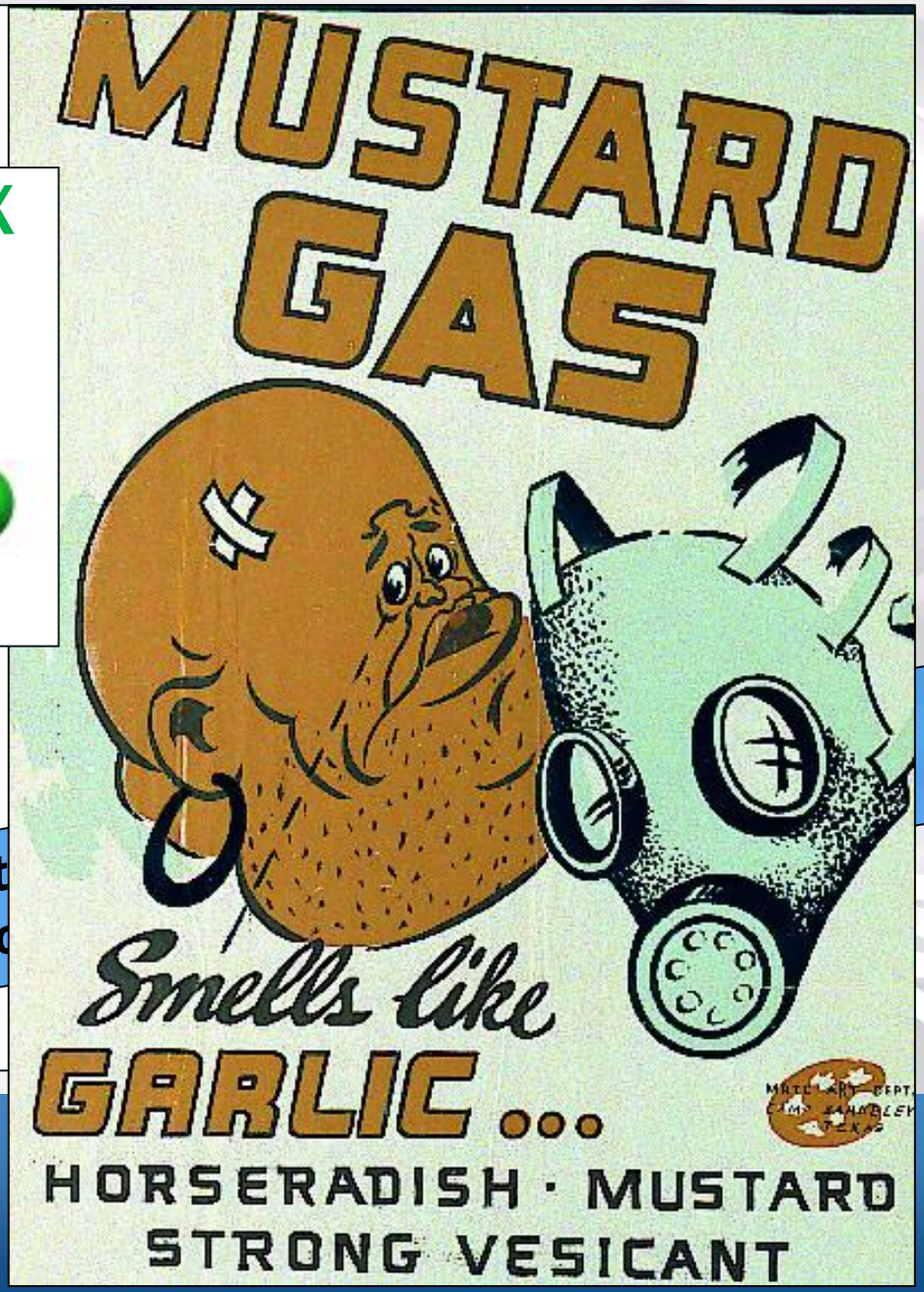




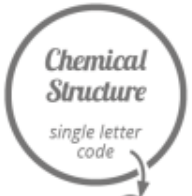


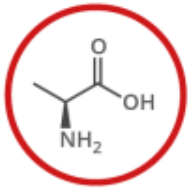
OPCW

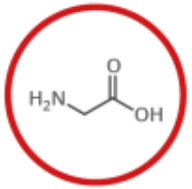
A GUIDE TO THE TWENTY COMMON AMINO ACIDS

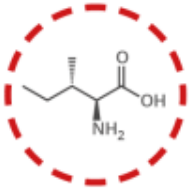
AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS CAN BE SYNTHESISED IN THE BODY.

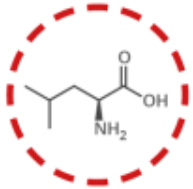
Chart Key: ALIPHATIC · AROMATIC · ACIDIC · BASIC · HYDROXYLIC · SULFUR-CONTAINING · AMIDIC · NON-ESSENTIAL · ESSENTIAL

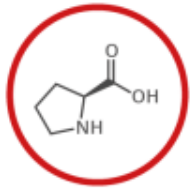


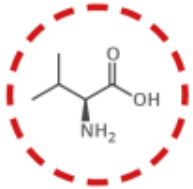

ALANINE A
Ala
GCT, GCC, GCA, GCG

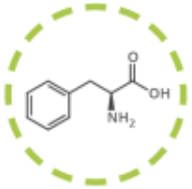

GLYCINE G
Gly
GGT, GGC, GGA, GGG

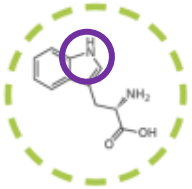

ISOLEUCINE I
Ile
ATT, ATC, ATA

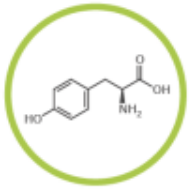

LEUCINE L
Leu
CTT, CTC, CTA, CTG, TTA, TTG

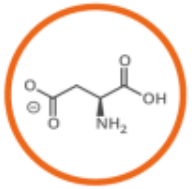

PROLINE P
Pro
CCT, CCC, CCA, CCG

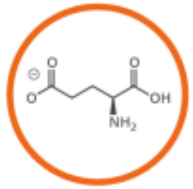

VALINE V
Val
GTT, GTC, GTA, GTG

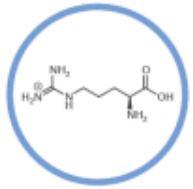

PHENYLALANINE F
Phe
TTT, TTC

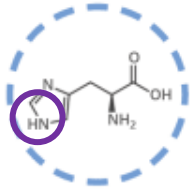

TRYPTOPHAN W
Trp
TGG

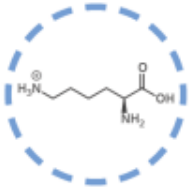

TYROSINE Y
Tyr
TAT, TAC

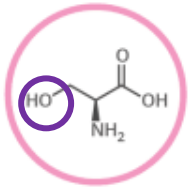

ASPARTIC ACID D
Asp
GAT, GAC

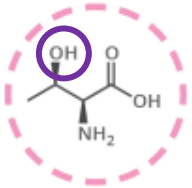

GLUTAMIC ACID E
Glu
GAA, GAG

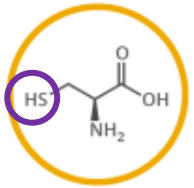

ARGININE R
Arg
CGT, CGC, CGA, CGG, AGA, AGG

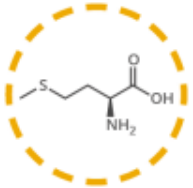

HISTIDINE H
His
CAT, CAC

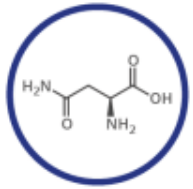

LYSINE K
Lys
AAA, AAG

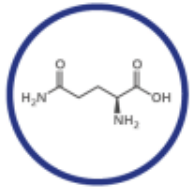

SERINE S
Ser
TCT, TCC, TCA, TCG, AGT, AGC


THREONINE T
Thr
ACT, ACC, ACA, ACG


CYSTEINE C
Cys
TGT, TGC


METHIONINE M
Met
ATG


ASPARAGINE N
Asn
AAT, AAC

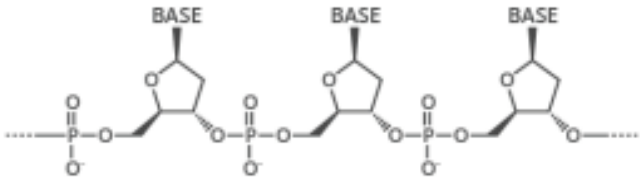

GLUTAMINE Q
Gln
CAA, CAG

Note: This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.

○ nucleophilic groups

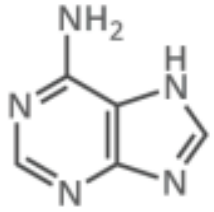
THE CHEMICAL STRUCTURE OF DNA

THE SUGAR PHOSPHATE 'BACKBONE'

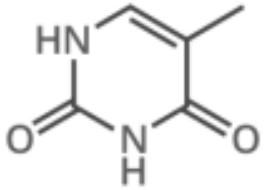


DNA is a polymer made up of units called nucleotides. The nucleotides are made of three different components: a sugar group, a phosphate group, and a base. There are four different bases: adenine, thymine, guanine and cytosine.

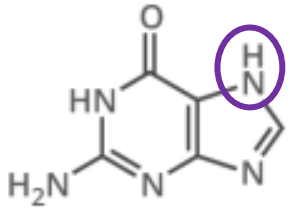
A ADENINE



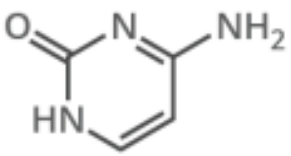
T THYMINE



G GUANINE

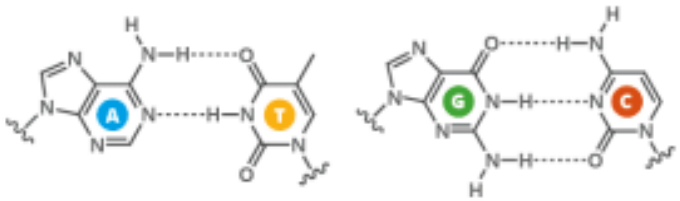


C CYTOSINE



WHAT HOLDS DNA STRANDS TOGETHER?

DNA strands are held together by hydrogen bonds between bases on adjacent strands. Adenine (A) always pairs with thymine (T), while guanine (G) always pairs with cytosine (C). Adenine pairs with uracil (U) in RNA.



FROM DNA TO PROTEINS

The bases on a single strand of DNA act as a code. The letters form three letter codons, which code for amino acids - the building blocks of proteins.

An enzyme, RNA polymerase, transcribes DNA into mRNA (messenger ribonucleic acid). It splits apart the two strands that form the double helix, then reads a strand and copies the sequence of nucleotides. The only difference between the RNA and the original DNA is that in the place of thymine (T), another base with a similar structure is used: uracil (U).

In multicellular organisms, the mRNA carries genetic code out of the cell nucleus, to the cytoplasm. Here, protein synthesis takes place. 'Translation' is the process of turning the mRNA's 'code' into proteins. Molecules called ribosomes carry out this process, building up proteins from the amino acids coded for.

THE CHEMICAL STRUCTURE OF DNA

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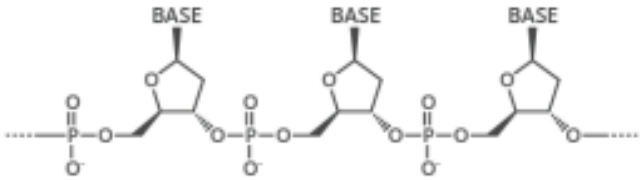

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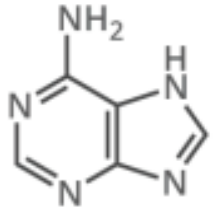
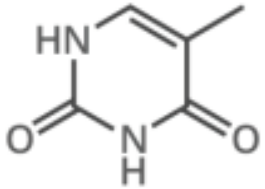


T THYMINE



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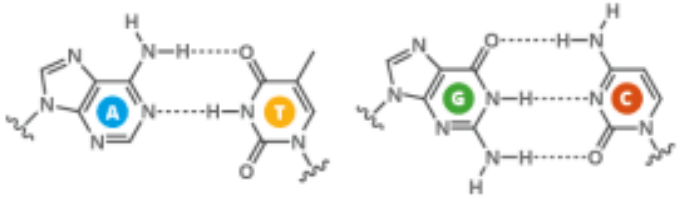

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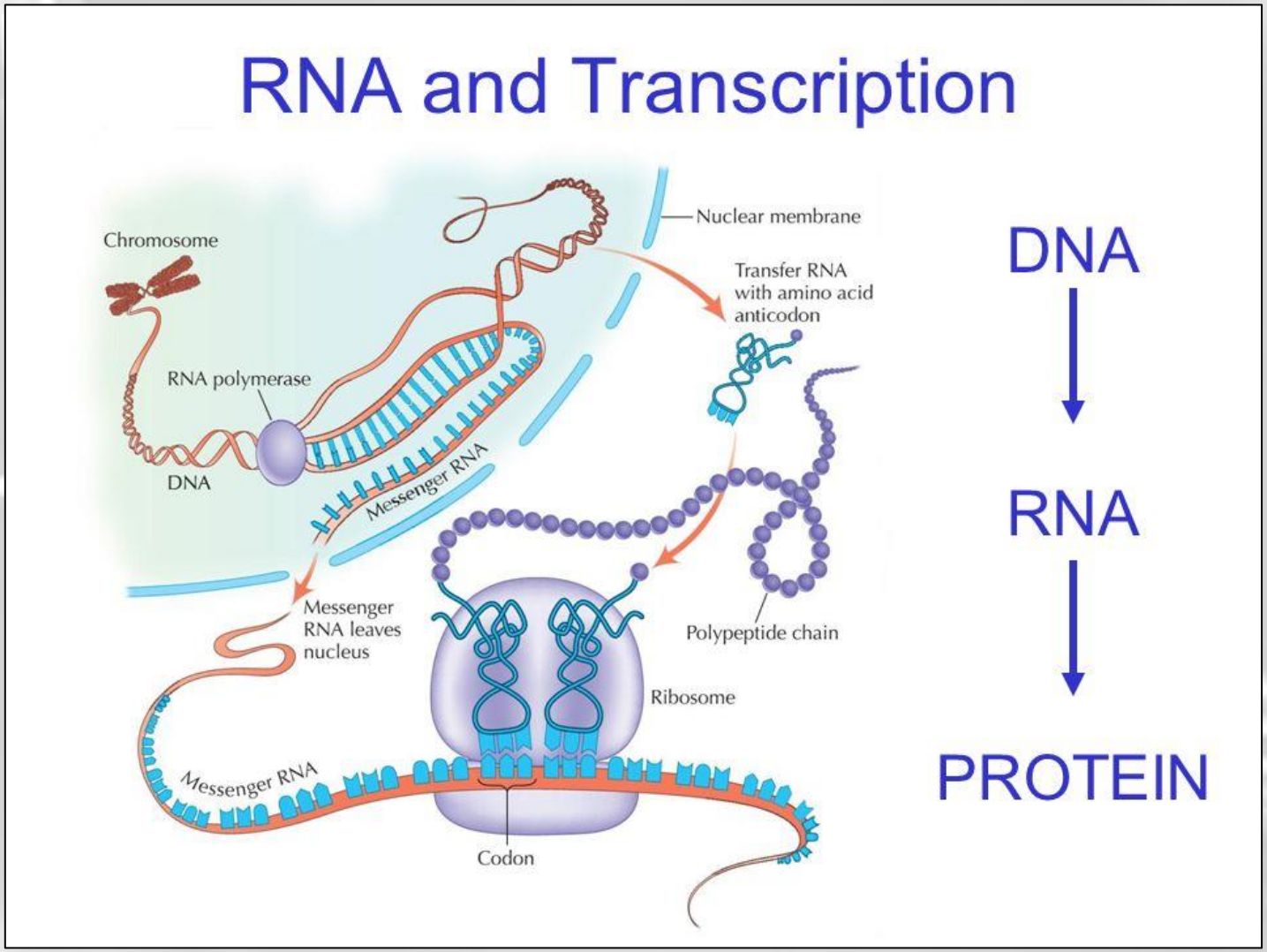
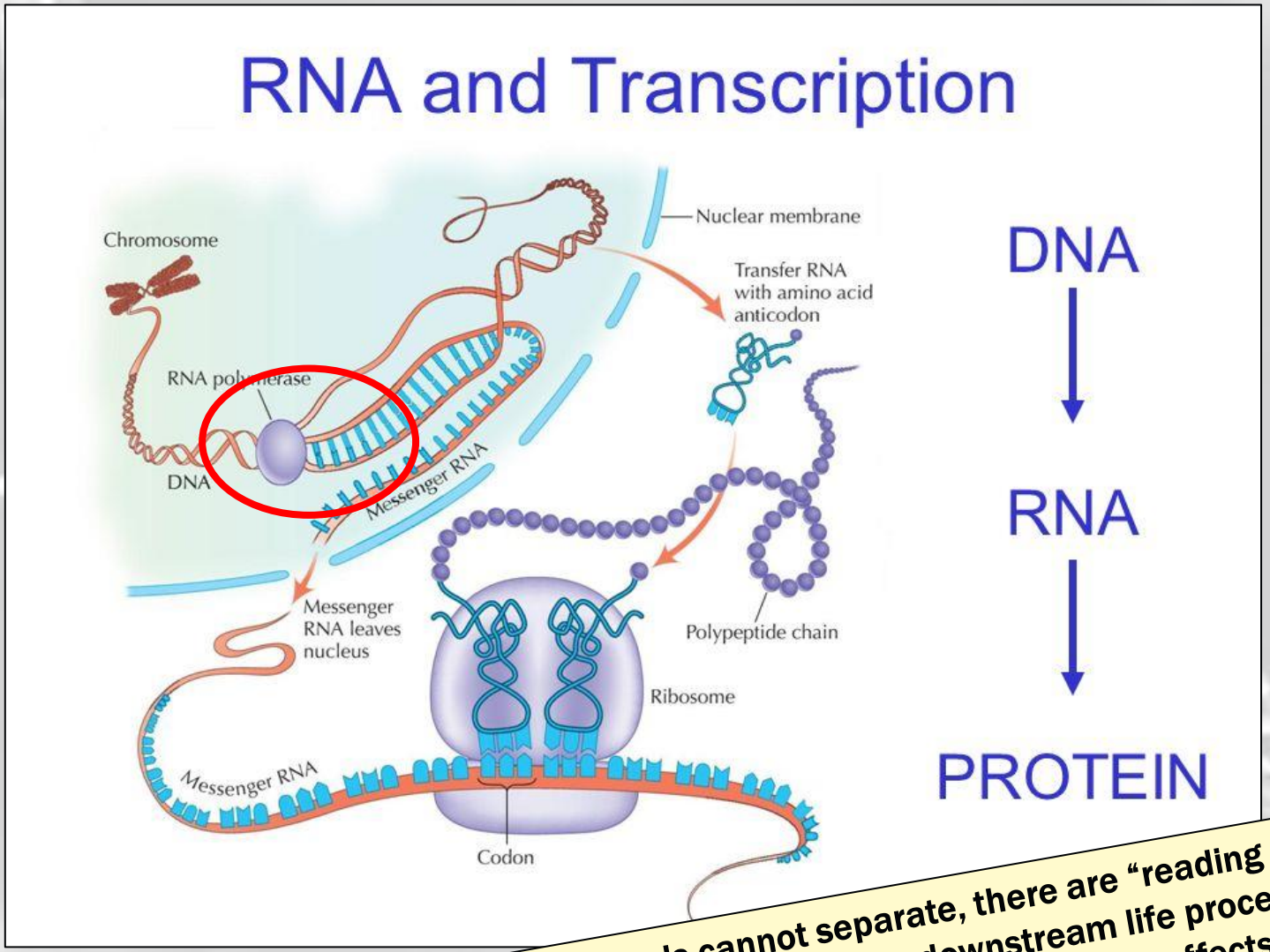
Thymine
G
C
Cytosine
Cytosine

DNA: The “Instructions”



DNA: The “Instructions”



If the DNA strands cannot separate, there are “reading errors”

- can generate impact on downstream life processes
- can lead to cell death and/or long term health effects of exposure

OPCW

DNA: The "Instructions"

RNA and Transcription

Placement of RSS bar code to read as UPC number

67386 911 51

DANGER: Contact Poison. Avoid contact with skin, mucous membranes, or eyes. Do not inhale the dust or vapor. In case of skin contact, wash with copious amounts of water for at least 15 minutes, followed by 2% sodium thiosulfate solution. See PRECAUTIONS and DOSAGE AND ADMINISTRATION in accompanying package insert. Store at controlled room temperature, 15-30°C (59-86°F). Protect from light and humidity.

NDC 67386-911-51 **1 Vial**

Trituration of
Mustargen®
(mechlorethamine HCl for injection)

℞ only

10 mg

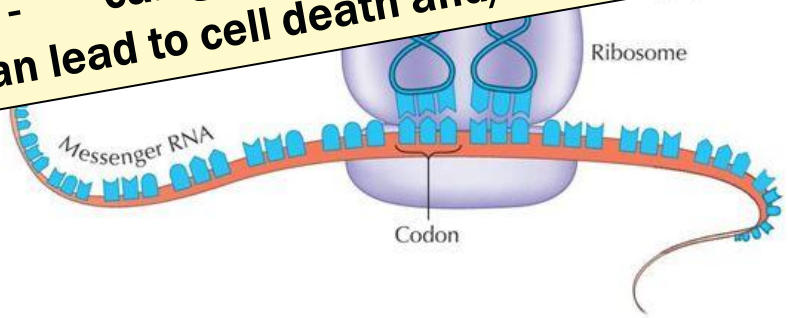
A Nitrogen Mustard – POISON
This vial contains 10 mg of mechlorethamine hydrochloride with sodium chloride q.s. 100 mg

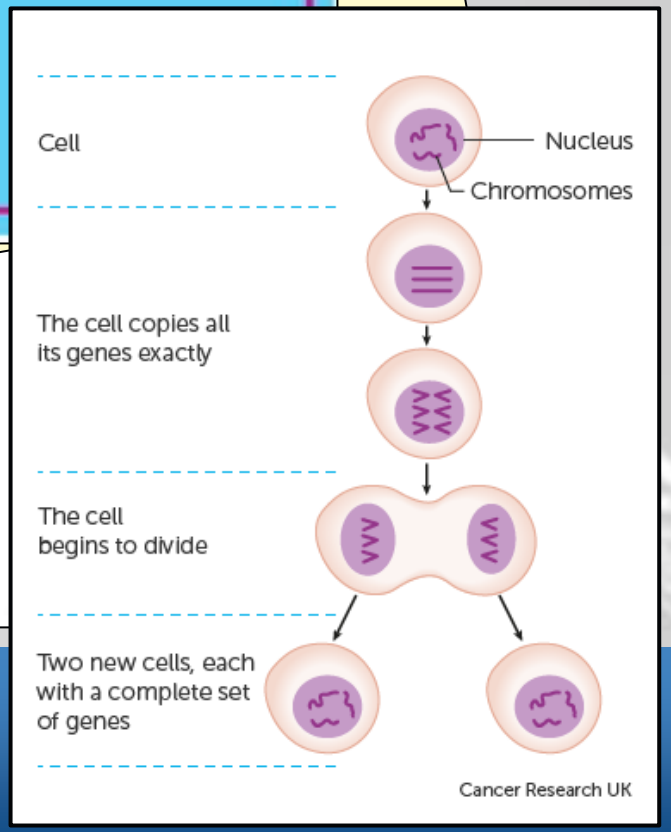
Lundbeck Inc.
Deerfield, IL 60015, U.S.A.

Lot:
Exp.:

780-03008-1

- can generate
- can lead to cell death and/or long





OPCW

Models, Diagrams and Plastic Parts Help Us to Visualize What Biochemistry Looks like…
What does it really look like?

Models, Diagrams and Plastic Parts Help Us to Visualize What Biochemistry Looks like…
What does it really look like?

Models, Diagrams and Plastic Parts Help Us to Visualize What Biochemistry Looks like…
What does it really look like?

Isopropyl alcohol:
rubbing alcohol and also a sarin precursor!

OPCW

DO YOU KNOW WHAT DNA LOOKS LIKE?

OPCW

#ScienceforDiplomats DNA Extraction Kit

Your kit contains:

- Strawberry in a plastic zipper bag
- 50 ml Falcon Tube
- Coffee filter
- A tube containing 20 of ml "DNA Extraction Solution"
- A vial containing 15 ml of 96% isopropyl alcohol
- Plastic pipette
- Eppendorf Tube (In case you'd like to take your DNA home with you!)

Plastic zipper bag containing strawberry

Falcon Tube

Coffee filter

DNA Extraction Solution

96% isopropyl alcohol

Pipette

Eppendorf Tube

DNA Extraction Solution:

Mix the following ingredients to prepare 1 litre of DNA Extraction solution (enough for 100 extractions)

- 100 ml of dish washing detergent
- 15 g of table salt
- 900 ml of water

DNA is like a set of "instructions"!

Here is your chance to see what the instructions for a strawberry look like!

Step 1

Start off by gently crushing the strawberry in the zipper bag. Push your fingers against the table surface to turn the strawberry into a pulp. This breaks open the cells.

Step 2

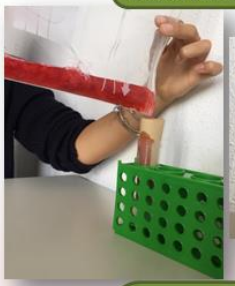
Pour the DNA extraction solution into the zipper bag containing the strawberry pulp. This breaks down the cell membranes and extracts the DNA into the solution. Gently swish the mixture around, try to minimize the amount of foam that forms.

Step 3

Use the coffee filter as a funnel in the 50 ml Falcon Tube. Fold the filter appropriately so that it is fully inserted into the tube.

Step 4

Slowly pour the content of the bag into the coffee filter funnel. Don't pour in too much solution at once to avoid overflow and spillage!

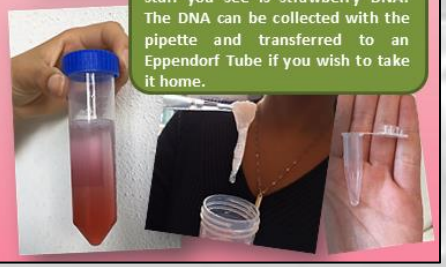


Step 5

Remove the coffee filter with the remaining strawberry cell debris. Pour 20 ml of 96% isopropyl alcohol into the 50 ml Falcon Tube. Observe what happens at the interface of the alcohol and strawberry DNA extract solution.

Step 6

The whitish, gooey, stringy, bubbly stuff you see is strawberry DNA! The DNA can be collected with the pipette and transferred to an Eppendorf Tube if you wish to take it home.



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International DNA Extraction Exercise

International DNA Extraction Exercise

OPCW

International DNA Extraction Exercise

OPCW

What Did We Learn Today?

- **The Scientific Basis of the Chemical Weapons Convention is "Biology"**
- **The Scientific Basis of "Biology" is "Chemistry"**
  - *functional groups of connected atoms (molecular structures) matter!*
- **Biological systems are made up of interacting components and chemical signals are an integral part of these processes**
  - Different classes of chemicals impact life processes through different mechanisms – understanding these mechanisms provides a basis for effective medical response
- **Models and analogies of how it all works are useful for understanding**
  - *However, the molecules of life are not rigid plastic parts!*
- **Science is fun!**

What Did We Learn Today?

- The Scientific Basis of the Chemical Weapons Convention is "Biology"
- The Scientific Basis of "Biology" is "Chemi
  - *functional groups of conn* *er!*
- Biol *and* chen
  - Di *t* me *r* eff
- Model *are useful for* unders
  - *However, the molecules of life are not rigid plastic parts!*
- Science is fun!

The purpose of the Chemical Weapons Convention is NOT to define scientific disciplines!

The purpose is to ban chemical weapons

The Convention draws upon a sound (and trans-disciplinary) scientific basis to set out its definitions

Scientific Advisory Board Update

ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

Working Together For a World Free of Chemical Weapons

Temporary Working Group on Investigative Science and Technology

Reporting to the Scientific Advisory Board (SAB), the Temporary Working Group (TWG) will in particular consider the following questions:

Question 1:
Which methods and capabilities used in the forensic sciences could usefully be developed and/or adopted for Chemical Weapons Convention-based investigations?

Question 2:
What are the best practices and analysis tools used in the forensic sciences for effectively cross-referencing, validating, and linking together information related to investigation sites, materials collected/analysed, and individuals interviewed?

Question 3:
What are the best practices for management of data collected in investigations, including compilation, curation, and analytics?

Question 4:
What are the best practices for the collection, handling, curation and storage, and annotation of evidence?

Question 5:
Which technologies and methodologies (whether established or new) allow point-of-care and non-destructive measurements at an investigation site to help guide evidence collection?

Question 6:
Which technologies and methodologies (whether established or new) can be used in the provenancing of chemical and/or material samples collected in an investigation?

Question 7:
Which methods are available (or are being developed) for the sampling and analysis of environmental and biomedical materials and can be used in the detection of toxic industrial chemicals relevant to the Chemical Weapons Convention?

Question 8:
Which technologies and methodologies (whether established or new) can be used in ensuring chain of custody and verifying authenticity (especially in regard to digital images and video recordings)?

Question 9:
Which technologies and methodologies (whether established or new) can be used to ensure the integrity of an investigation site?

Question 10:
Do collections of physical objects, samples, and other information for chemical weapons-related analysis exist and can they be made available to investigators for retrospective review? How might these collections be used to support investigations?

Question 11:
Are there stakeholders that the Technical Secretariat could usefully engage with to leverage their capabilities on investigative matters?

In addition, the TWG will provide advice on Technical Secretariat proposals for methodologies, procedures, technologies, and equipment for investigative purposes.

@opcw
@opcw_st
/opcwonline
/opcwonline
/company/opcw
/photos/opcw
/opcw

OPCW

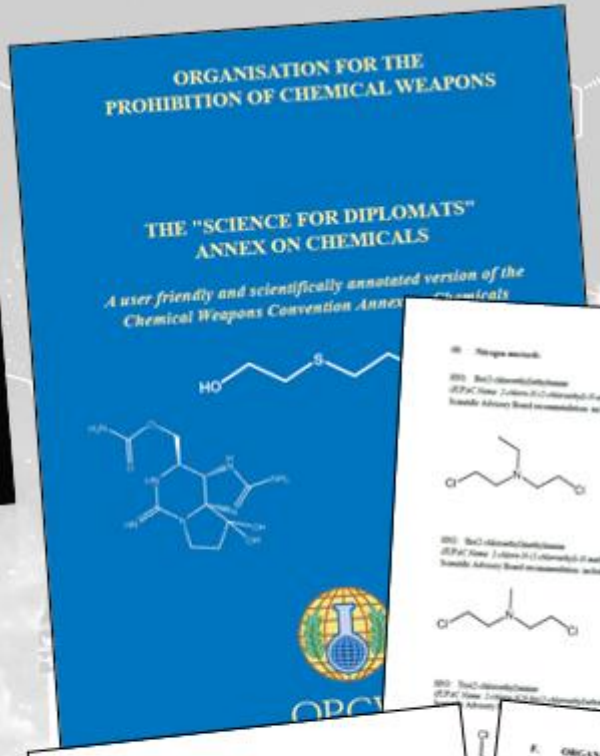
Scientific Advisory Board Update

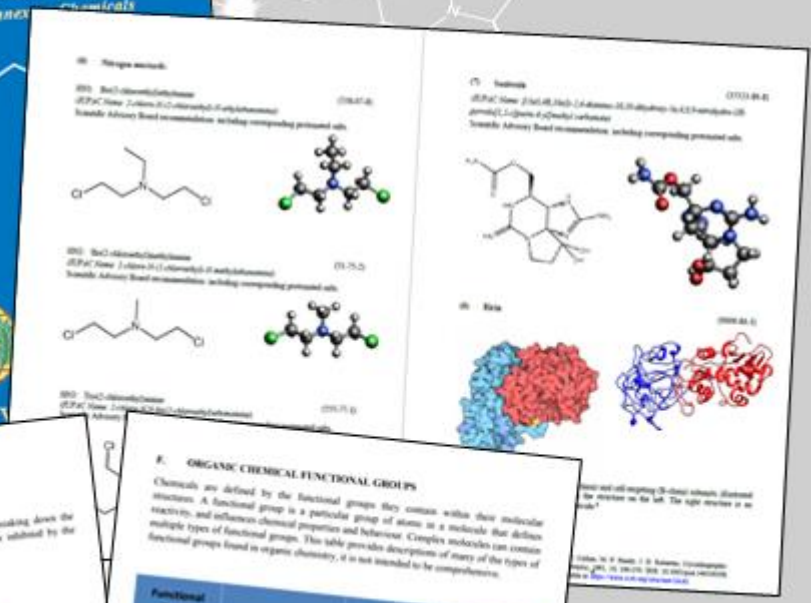
OPCW

Fourth TWG Meeting Held from 18-20 September Report is Forthcoming
The TWG will hold a final meeting to produce an end of Mandate report

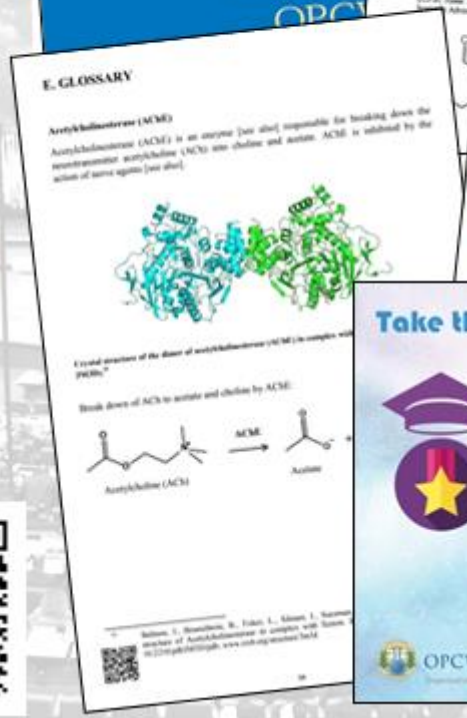
The “chemical mystery” returns for CSP-24


Science for Diplomats at EC-88
The Chemical Universe: Scheduled and Unscheduled
Tuesday, 10 July 2018
Ooms Room, OPCW
13:30 - 14:45
Light lunch served at 13:00


ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS
THE "SCIENCE FOR DIPLOMATS" ANNEX ON CHEMICALS
A user friendly and scientifically annotated version of the Chemical Weapons Convention Annex




SCIENCE FOR DIPLOMATS AT EC-90
Tuesday 12 March 2019
Ooms Room 13:30 - 14:45
Light Lunch Available at 13:00
The Expanding Chemical Universe: From C1 to C10 and beyond
A lunch time mission to boldly go where no delegation has gone before...


E. GLOSSARY
F. ORGANIC CHEMICAL FUNCTIONAL GROUPS


Take the Quiz!
Download the Quiz
Download the Answer Sheets
Download the Answer Key
Test your knowledge
of the Schedules of the Chemical Weapons Convention
with an Augmented Reality Schedules quiz!
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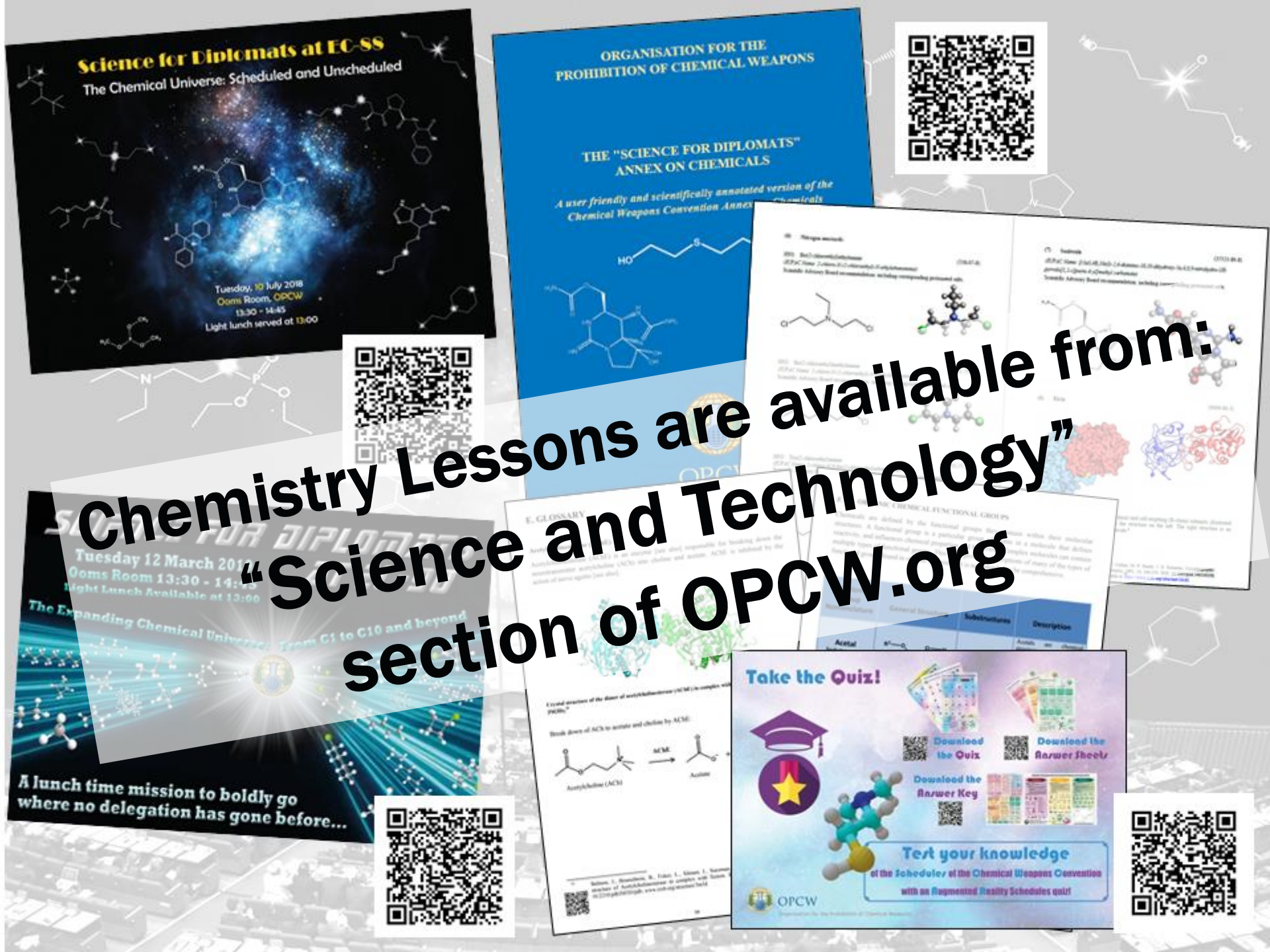
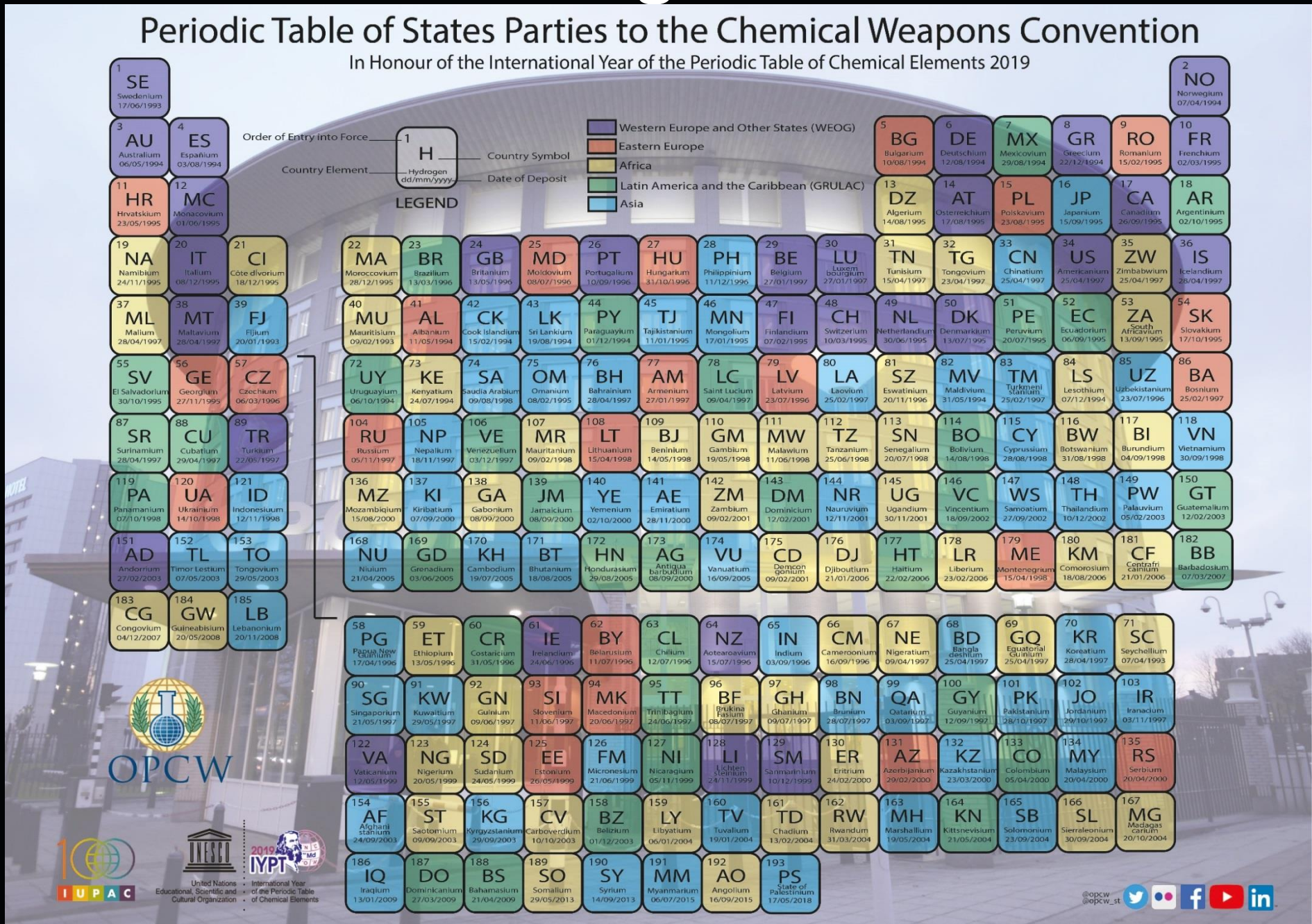


Chemistry Lessons are available from: "Science and Technology" section of OPCW.org

Thanks to All the Delegations Who Joined Us!



A Special Thank You for Today's Lunch!

Periodic Table of States Parties to the Chemical Weapons Convention

In Honour of the International Year of the Periodic Table of Chemical Elements 2019

Vielen Dank!

Order of Entry into Force — 1 H — Country Symbol
Country Element — Hydrogen — Date of Deposit (dd/mm/yyyy)

LEGEND

- Western Europe and Other States
- Eastern Europe
- Africa
- Latin America and the Caribbean
- Asia

1 SE Swedenium 17/06/1993
2 NO Norwegium 07/04/1994
3 AU Australium 06/05/1994
4 ES Españium 03/08/1994
10 FR Frenchium 02/03/1995
11 HR Hrvatskium 23/05/1995
12 MC Monacovium 01/06/1995
18 AR Argentinium 02/10/1995
19 NA Namibium 24/11/1995
20 IT Italium 08/12/1995
21 CI Côte d'Ivorium 18/12/1995
22 MA Moroccovium 28/12/1995
23 BR Brazilium 13/03/1996
24 GB Britannium 13/05/1996
25 MD Moldovium 08/07/1996
26 PT Portugalium 10/09/1996
27 HU Hungarium 31/10/1996
28 PH Philippinium 11/12/1996
29 BE Belgium 27/01/1997
36 IS Icelandium 28/04/1997
37 ML Malium 28/04/1997
38 MT Maltavium 28/04/1997
39 FJ Fijium 20/01/1993
40 MU Mauritisium 09/02/1993
41 AL Albanium 11/05/1994
42 CK Cook Islandium 15/02/1994
43 LK Sri Lankium 19/08/1994
44 PY Paraguayium 01/12/1994
45 TJ Tajikistanium 11/01/1995
46 MN Mongolium 17/01/1995
47 FI Finlandium 07/02/1995
54 SK Slovakium 17/10/1995
55 SV El Salvadorium 30/10/1995
56 GE Georgium 27/11/1995
57 CZ Czechium 06/03/1996
72 UY Uruguayium 06/10/1994
73 KE Kenyatium 24/07/1994
74 SA Saudia Arabium 09/08/1998
75 OM Omanium 08/02/1995
76 BH Bahrainium 28/04/1997
77 AM Armenium 27/01/1997
78 LC Saint Lucium 09/04/1997
79 LV Latvium 23/07/1996
86 BA Bosnium 25/02/1997
87 SR Surinamium 28/04/1997
88 CU Cubatium 29/04/1997
89 TR Turkium 22/05/1997
104 RU Russium 05/11/1997
105 NP Nepalium 18/11/1997
106 VE Venezuelium 03/12/1997
107 MR Mauritanium 09/02/1998
108 LT Lithuanium 15/04/1998
109 BJ Beninium 14/05/1998
110 GM Gambium 19/05/1998
111 MW Malawium 11/06/1998
118 VN Vietnamium 09/09/1998
119 PA Panamanium 07/10/1998
120 UA Ukrainium 14/10/1998
121 ID Indonesiuum 12/11/1998
136 MZ Mozambiqium 15/08/2000
137 KI Kiribatium 07/09/2000
138 GA Gabonium 08/09/2000
139 JM Jamaicium 08/09/2000
140 YE Yemenium 02/10/2000
141 AE Emiratium 28/11/2000
142 ZM Zambium 09/02/2001
143 DM Dominicanium 12/02/2001
151 AD Andorrium 27/02/2003
152 TL Timor Lestium 07/05/2003
153 TO Tongovium 29/05/2003
168 NU Niulium 21/04/2005
169 GD Grenadium 03/06/2005
170 KH Cambodium 19/07/2005
171 BT Bhutanium 18/08/2005
172 HN Hondurasium 29/08/2005
173 AG Antigua barbudium 08/09/2000
174 VU Vanuatium 16/09/2005
175 CD Democratic Republic of the Congonium 09/02/2006
176 NR Nauruium 23/02/2006
177 UG Ugandium 23/02/2006
178 VC Saint Vincium and the Grenadinium 23/02/2006
179 WS Samoium 23/02/2006
180 TT Trinidad and Tobagium 23/02/2006
181 LR Liberium 23/02/2006
182 ME Montenegrium 15/04/1998
183 KM Comorosium 18/08/2006
184 CF Central African Republicanium 21/01/2006
185 BB Barbadosium 07/03/2007
183 CG Congovium 04/12/2007
184 GW Guineabisium 20/05/2008
185 LB Lebanonium 20/11/2008
58 PG Papua New Guinium 17/04/1996
59 ET Ethiopium 13/05/1996
60 CR Costaricium 31/05/1996
61 IE Irelandium 24/06/1996
62 BY Belarusium 11/07/1996
63 CL Chilium 12/07/1996
64 NZ Aotearoavium 15/07/1996
65 IN Indium 03/09/1996
66 CM Cameroonium 16/09/1996
67 NE Nigeratium 09/04/1997
68 BD Bangladeshium 25/04/1997
69 GQ Equatorial Guinium 25/04/1997
70 KR Koreatium 28/04/1997
71 SC Seychellium 07/04/1993
90 SG Singaporium 21/05/1997
91 KW Kuwaitium 29/05/1997
92 GN Guinium 09/06/1997
93 SI Slovenium 11/06/1997
94 MK Macedonium 20/06/1997
95 TT Trinbagium 24/06/1997
96 BF Burkina Fasium 08/07/1997
97 GH Ghanium 09/07/1997
98 BN Brunium 28/07/1997
99 QA Qatarium 03/09/1997
100 GY Guyanium 12/09/1997
101 PK Pakistanium 28/10/1997
102 JO Jordanium 29/10/1997
103 IR Iranacium 03/11/1997
122 VA Vaticanium 12/05/1999
123 NG Nigerium 20/05/1999
124 SD Sudanium 24/05/1999
125 EE Estonium 26/05/1999
126 FM Micronesium 21/06/1999
127 NI Nicaragium 05/11/1999
128 LI Lichtensteinium 24/11/1999
129 SM Sanmarinium 10/12/1999
130 ER Eritrium 24/02/2000
131 AZ Azerbijanium 29/02/2000
132 KZ Kazakhstanium 23/03/2000
133 CO Colombium 05/04/2000
134 MY Malaysium 20/04/2000
135 RS Serbium 20/04/2000
154 AF Afghanistanium 24/09/2003
155 ST Saotomium 09/09/2003
156 KG Kyrgyzstanium 29/09/2003
157 CV Carboverdium 10/10/2003
158 BZ Belizium 01/12/2003
159 LY Libyatium 06/01/2004
160 TV Tuvalium 19/01/2004
161 TD Chadium 13/02/2004
162 RW Rwandum 31/03/2004
163 MH Marshallium 19/05/2004
164 KN Kittsnevisium 21/05/2004
165 SB Solomonium 23/09/2004
166 SL Sierraleonium 30/09/2004
167 MG Madagascarium 20/10/2004
186 IQ Iraqium 13/01/2009
187 DO Dominicanium 27/03/2009
188 BS Bahamasium 21/04/2009
189 SO Somalium 29/05/2013
190 SY Syrium 14/09/2013
191 MM Myanmarium 06/07/2015
192 AO Angolium 16/09/2015
193 PS State of Palestinium 17/05/2018

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IUPAC

UNESCO — United Nations Educational, Scientific and Cultural Organization

2019 IYPT — International Year of the Periodic Table of Chemical Elements

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منظمة حظر الأسلحة الكيميائية

禁止化学武器组织

Organisation for the Prohibition of Chemical Weapons

Organisation pour l'Interdiction des Armes Chimiques

Организация по запрещению химического оружия

Organización para la Prohibición de las Armas Químicas