Alphanosos

" Develop 21st century's safe, superiorly efficient and natural drugs and bio-actives with 1/tenth of resources and risks of traditional approaches "

Rapid discovery plan to stop COVID-19 outbreak NOW

We are reinventing plant-based antimicrobial control, well-being and medicine through our R&D based on proprietary Artificial Intelligence.

Our patent-pending discoveries are incorporated into commercial products and generate our first revenues.

Tomorrow, we will use them for providing health preservation products personalized on the basis of somatic and microbiota genetic profiles and AI

Alphanosos

Rapid discovery plan to stop COVID-19 outbreak

R&D / Clinical trial/ Validation phase of Alphanosos AI based compound discovery

Discovery of and patent application (with positive EPO search report) on anti-bacterial plant mix family with 750 active mixes exemplified.

Active on WHO critical and high priority organisms, mycobacteria

Animal model validation of activity (dog pyoderma, mouse systemic)

2 Licensing deals for cosmetic use in place (COSMOS certified APIs)

Discovery of plant mix family active on cancer cell lines in collaboration with Swiss EPFL (patent in preparation)

Validation of 2019-nCoV cure through correspondence by NIAID/NIH **"..very impressive**!....."

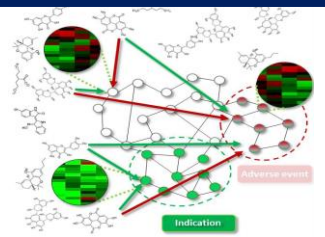
NB: same would be applicable to any other microorganism where an in vitro assay is available

Collection of botanicals for screening

Collect collection of plants (samples already available at Alphanosos) for screening and early production of active Water Extracts of Complex Mixes of Edible Plants.

Plants selected for availability, documented innocuity and acceptable costs.

Drug Discovery



Rapid and proven AI guided experimental discovery platform. Results after 5-15 experimental iterations.

Mode of action is massively parallel system perturbation towards which normal eukaryotic cells are far more robust than impaired (cancer/infected) cells and microorganisms

Drug Production

Treatments will be based on readily available botanical edibles (obtainable in metric-tons at pharmaceutical of food supplement grade), and can be mass produced immediately

Rapid Deployment

The treatments, have a regulatory status of food/food supplement before medical claim and can go directly to patients.

Sustainable Commercialization

Decentralized production, adaptation to locally produced / ethnic botanicals

SPENT TO DATE : € 2,400,000	FUNDING NEEDED: € 500,000 (Alphanosos + virology partner)	FUNDING NEEDED: € 500,000		FUNDING NEEDED: € 500,000
2015- Present	Finalized by end of March 2020 (if started 2nd week of March)	April 2020	Mai 2020	By end July 2020

Key enabling reasons for Alphanosos' paradigm shifting approach to emergency control of epidemics/pandemics

The actives are non-fractionated (crude water extracts) of synergistic mixes from botanical edibles which are ***stricto sensu*** **still edibles** before medical claims

⇒ In its guidelines to botanical drugs, the FDA is opening the possibility for such actives to enter immediately phase II

⇒ They are nearly certainly safe (as safe as trying a new recipe in a restaurant) by common sense and theory

⇒ To be compared to any NCE which is nearly certainly toxic at discovery stage (and often even after)

Key enabling reasons for Alphanosos' paradigm shifting approach to emergency control of epidemics/pandemics

The actives can be mass produced immediately, that means ***stricto sensu*** **next day after discovery**

⇒ Deployment can be rapid, and really still have an impact in the current coronavirus crisis

⇒ For an NCE, industrial Seveso class scale-up requires months and complex technical validation because of risk of chemical impurities

Key enabling reasons for Alphanosos' paradigm shifting approach to emergency control of epidemics/pandemics

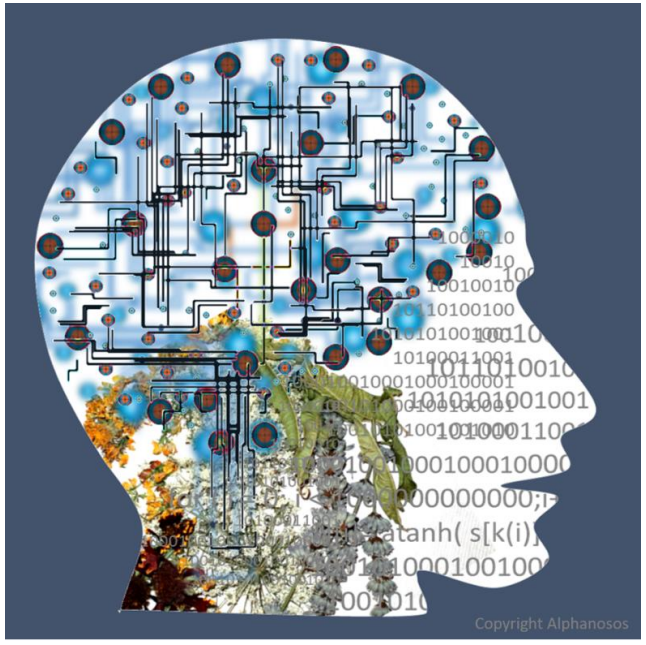
The mixes can be tailored to the virus of concern in a matter of 5-15 experimental discovery iterations, that means ***stricto sensu*** in a matter of 2 weeks in "7/7" collaboration with a lab mastering coronavirus cultivation

⇒ Mode of action means little sensitivity to virus mutations, and if the virus mutates, few additional discovery iterations will be necessary

⇒ Existing anti-cancer discoveries could already have activity

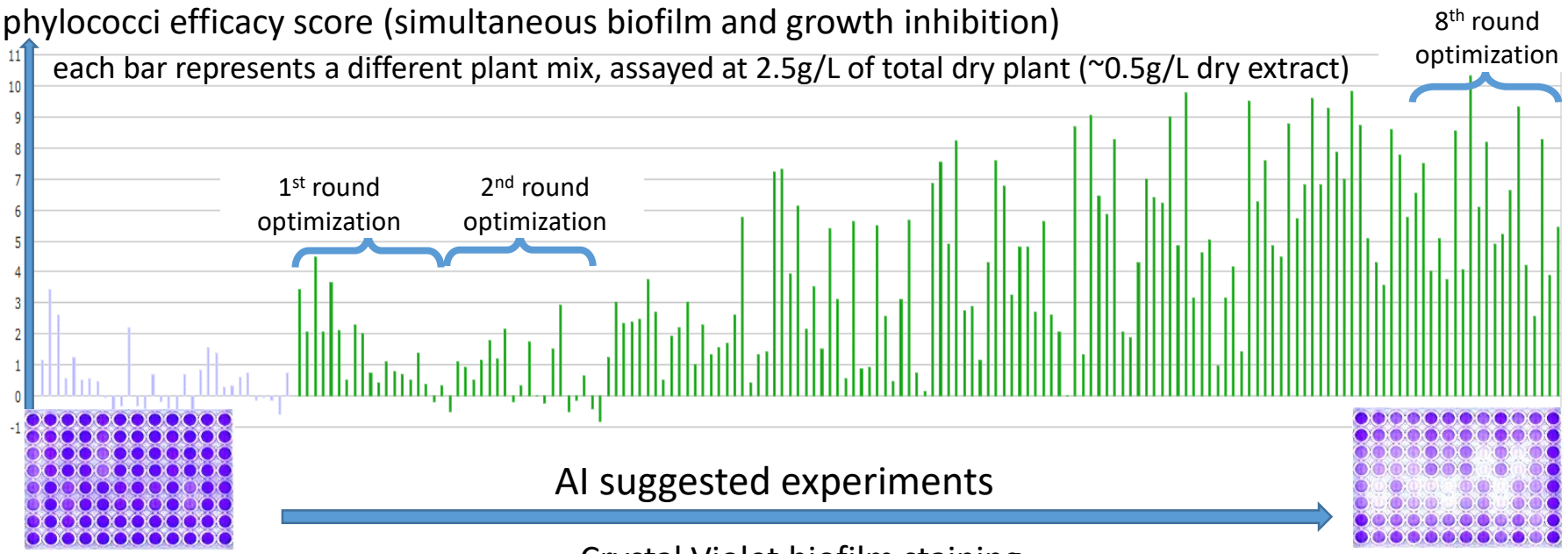
⇒ In comparison, for a vaccine,

- The delay before preventive(/curative?) product is a matter of months
- success/efficacy is not guaranteed *a priori*
- after a mutation in the virus, it becomes generally meaningless



Alphanosos' AI based compound discovery methodology applied to antimicrobials

NB: Real data presented



Round 0: evaluate 40 out of ~10^{31} possible mixes

8th round optimization (in total, ~600 mix evaluated)

Results:

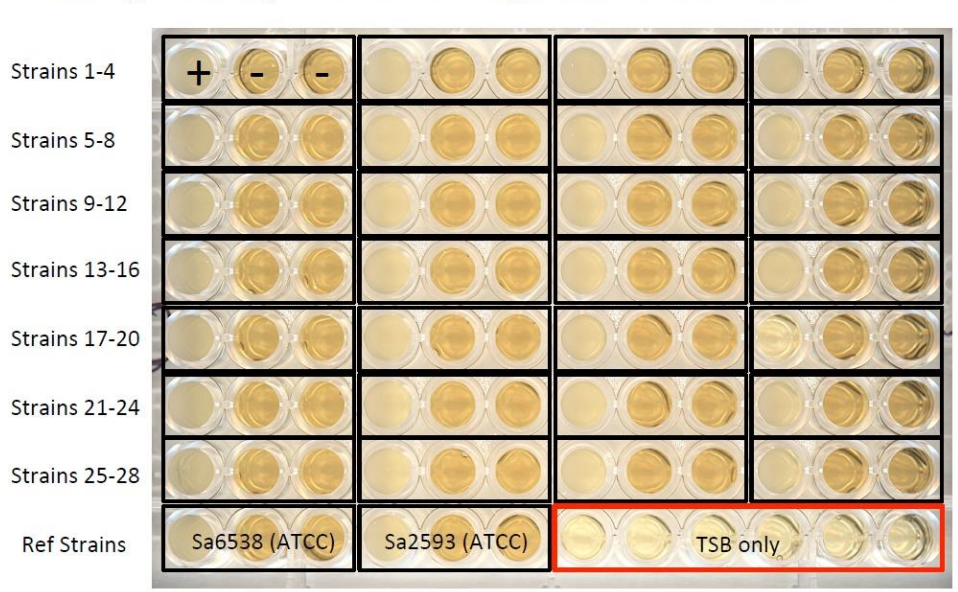
- Patent pending family of narrow and broad spectrum mixes (3 to 20 plants) with typical MIC ranging 0.02% – 0.4% (w/v)
- Animal model results: topical and systemic by oral administration

Alphanosos Our Anti-staphylococci discoveries:

For *Staphylococci* (including MRSA) : **MIC90 = 500µg/mL**
MIC100 = 0.2% (w/v)

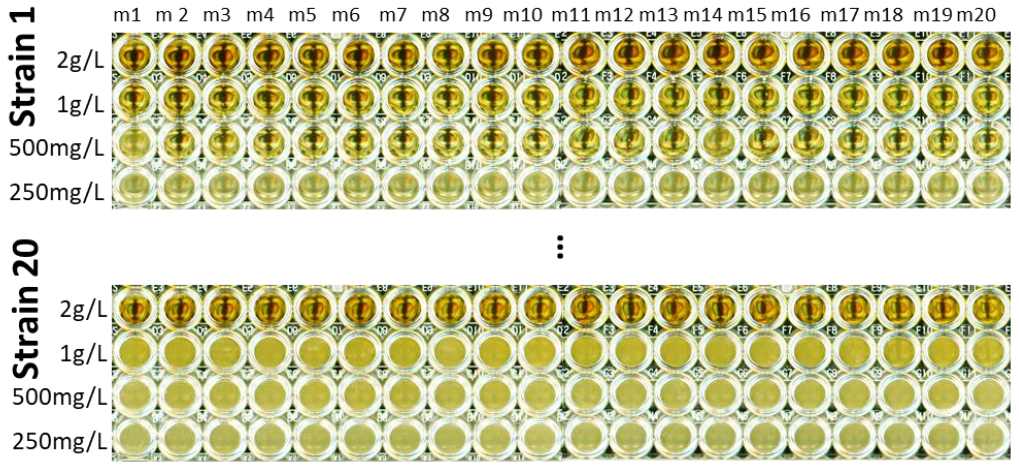
NB: composed of plants' "water soluble totum"

Killing activity of W16P576 against planktonic cells
(also preventing biofilm formation)



Experiment by Prof Ensoli's group IFO, Rome, Italy, on clinical strains from severe dermatitis patients (including multiple resistant, MRSA)

Reproducibility of 20 different W16P576 preparations (m1 to m20) with each of 16 plants in a preparation chosen among 3 different batches for each plant (producer, year, conventional or organic…)



Tested on 20 clinical *S. pseudintermedius*, 10 from dog skin infections and 10 from dog ear infections (including multiple resistant, MRSP)

Peer reviewed publications in preparation

Preliminary *in vivo* data of antimicrobial WECMEPs

No sign of *per os* toxicity but evidence of *per os* efficacy

Study performed by an independent CRO

1 **Absence of toxicity in OF1 mice** following a 2 times a day **oral treatment** for 12 days with 1.5mg/g, 0.5mg/g and 0.15mg/g plant extract : *mortality, weighing, signs of suffering*

NB: as envisaged/predicted by theory

2 **Proof of principle of systemic action *in vivo* despite passage through digestive system:**

Lethal intraperitoneal infection murine model
on 2 groups of 10 OF1 mice, using *S. aureus* Newman at $1.7x10^7$ cfu/mice

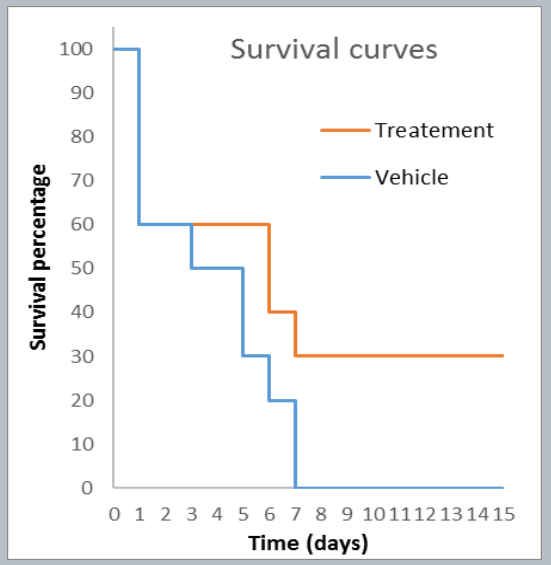
Treatment with WECMEP W16P576:

⇒ ***per os***, oral gavage

⇒ **1 dose/day**:10 µl/g plant extract at 20g/L (200mg/kg)

⇒ dose = (typical) 6 mg extract from **15 mg total herbs / mouse** (weight adjusted at 0.5mg/g [mix/mouse])

⇒ **Human equivalent could be a "soda can" at 60g/L extract**
NB: extract mix is an "aromatic preparation" (EU regulations) before drug claim



30% survival at 15 days with treatment,
0% survival with vehicle

To be seen as proof of principle for systemic effect by ingestion

Alphanosos Extended spectrum of action of top 5 active WECMEPs (as of july 2019)

in vitro status: Demonstrated / Preliminary

WHO priority pathogens list for R&D of new antibiotics

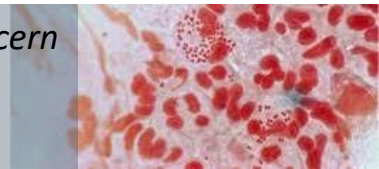
Priority 1: CRITICAL

- ***Acinetobacter baumannii*, carbapenem-resistant**
- ***Pseudomonas aeruginosa*, carbapenem-resistant**
- *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

Priority 2: HIGH

- ***Enterococcus faecium*, vancomycin-resistant**
- ***Staphylococcus aureus*, methicillin-resistant, vancomycin-resistant**
- ND — *Helicobacter pylori*, clarithromycin-resistant
- ND — *Campylobacter* spp., fluoroquinolone-resistant
- *Salmonellae*, fluoroquinolone-resistant
- ***Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant**

Gonorrhea is a re-emerging disease (78 million new cases per year) that is of great concern to the WHO, particularly due to antibiotic resistance. This disease is not specific to emerging countries. Indeed, it is the second cause of infectious disease in the USA.



Alphanosos — Extended spectrum of action of top 5 active WECMEPs (as of july 2019)

in vitro status: Demonstrated / Preliminary

Mycobacteria

- ***Mycobacterium smegmatis*** (representative organism) — Demonstrated
- *Mycobacterium bovis* — ND
- *Mycobacterium tuberculosis* (attenuated) — Preliminary

WHO: Resistance to tuberculosis drugs is a formidable obstacle to fighting a disease that causes around 10 million people to fall ill, and 1.6 million to die, every year. In 2017, around 600 000 cases of tuberculosis were resistant to rifampicin – the most effective first-line drug – and 82% of these people had multidrug-resistant tuberculosis.

Miscellaneous

- ***Propionibacterium acnes*** — Demonstrated
- ***Klebsiella pneumonae*** — Demonstrated
- *Listeria monocytogenes* — Preliminary
- ***Borrelia burgdorferi*** — Preliminary
- *Streptococcus uberis* (bovine mastitis) — Demonstrated
- *Streptococcus mutans* — Preliminary
- *Streptococcus pneumoniae* — *In progress*
- *Candida albicans* (***C. albicans / S. aureus mixed biofilms***) — Demonstrated
- *Vibrio parahaemolyticus* — Preliminary
- *Vibrio vulnificus* — Demonstrated
- *Vibrio alginolyticus* — Preliminary
- *Vibrio harveyi* — Preliminary

Potential preventive/curative “soda” against cholera
WHO:” each year there are 1.3 million to 4.0 million cases of cholera, and 21 000 to 143 000 deaths worldwide due to cholera

First set of anti-tumor-cell candidate synergistic botanical extract mixes

Discovered using Alphanosos' AI methodology and collaboration with EPFL, Switzerland

Results obtained after 8 rounds of optimizatrion

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
BIOMOLECULAR SCREENING FACILITY
Dr Gerardo Turcatti

- Seeding of cancer cells
- Addition of Alnosos mixes
- Digital holographic microscopy reading
  - Direct acquisition of 4 pictures/well
  - Phase contrast pictures reconstruction
  - Extraction of confluence and OPD values
- Presto Blue reading
- Data formatting

Frozen transportation

x 8-20 cycles

Cloud data exchange

Alphanosos

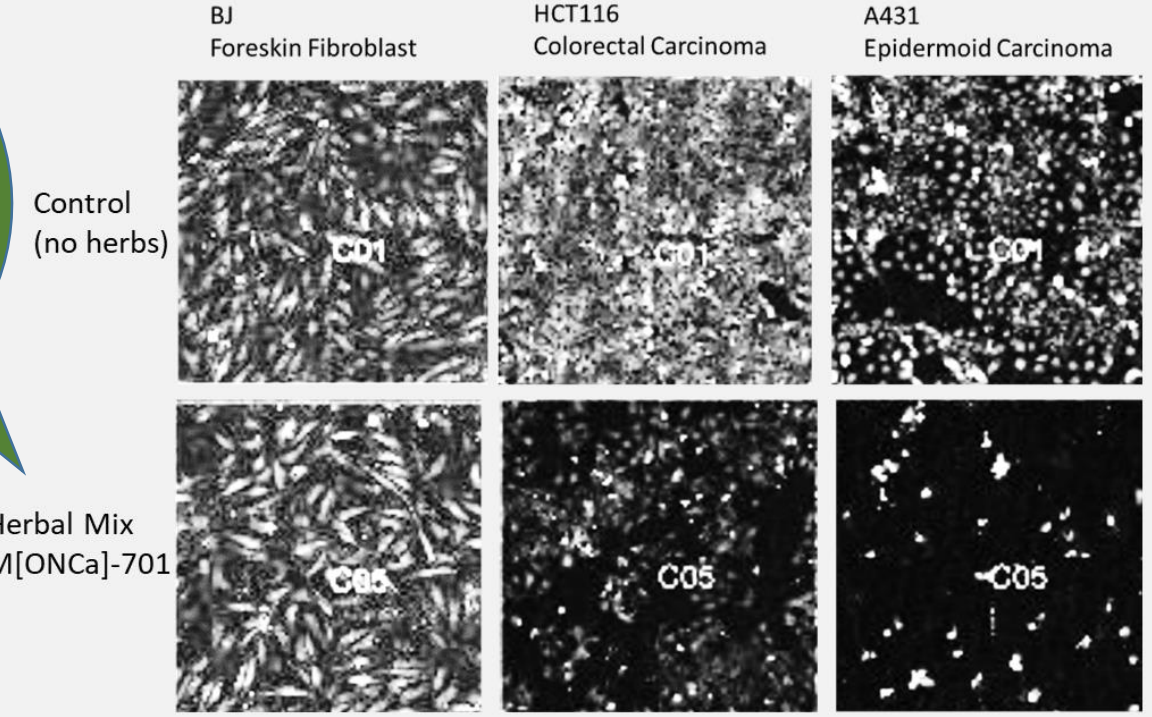
NB: IP on mixes belongs 100% to Alphanosos

- Preparation of a new set of mixes
- **Artificial Intelligence**
  - ⇒ Transformation of quantitative data into neuronal signals
  - ⇒ Learning phase (improvement of the "artificial brain")
  - ⇒ Generation of the composition of a new set of mixes (interrogation of the "artificial brain")

Kills specifically the cancer cells, no toxicity for the normal cells

Phase contrast images (reconstructed from OPD images) of the effect of a selected mix of 20 plants obtained after 6 rounds of optimization

Nominal (approx.) concentrations in test is 700mg/L total dry extract made from 1,7g/L total (dried) plants, thus 85mg/L of each dried plant



NB: visually percieved activity is confirmed by dead/live assay data (Presto Blue)

Mode of action makes it a POC for cells infected by viruses

How to use edibles for creating superiorly efficient and safe “system drugs”

The technological challenge

The edible plant paradox

- safe despite being a mix of hundreds of actives
- mixes of edibles safe too, and recognized so by the authorities
- activity against bacteria
- potential anti-cancer actives

[Link to theory preprint (BioRxiv)]

Mode of action is massively parallel system perturbation towards which normal eukaryotic cells are far more robust than impaired (cancer/infected) cells and microorganisms

Massively Parallel Phyto-Pharmacology, naturally safe!

Water **E**xtracts of **C**omplex **M**ixes of **E**dible **P**lants

Alphanosos’ WECMEPs

NB: Synergistic mixes => patentable actives

BUT

from a library of 300-1000+ edibles,

there are $10^{10\text{-}40+}$ possible mixes of 5-20 edibles

Traditional Brute force discovery is not an option!

Alphanosos’ AI specialized algorithms enable this revolution

Alphanosos

Targeted dietary imbalance

An untapped mode of action

Edibles are safe… unless dietary imbalance is maintained over prolonged period!

[Link to theory preprint (BioRxiv)]

What is "prolonged period"?

Depends on organism system's dynamics

What is "dietary imbalance" ?

System biology notion of robustness

Imbalance in microorganisms (and cancer cells) is much more easy to achieve than in human organisms

Organism	Diatery time	Generation time	System's Robustness
Humans/pets/farm animals	24h	10-20 years	Very High
Microorganism acute infections	Minutes	0'5-1 hour	Much less than human cells
Microorganism silent/slow infections	Hours?	Day(s)	Much less than human cells
Tumor cells	Hours?	"Months" (to metastasis)	Less than non-mutated cells

New approach to antimicrobials and anticancer:

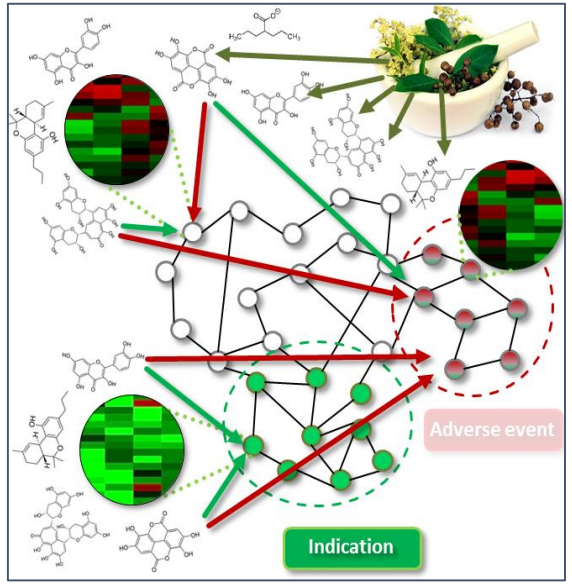
Targeted dietary imbalance

- Will make selected microorganism/tumors extinct before human health is impaired
- Will promote desirable microorganisms
- **"EUBIOTICS"** *(combining prebiotic and antibiotic activities)*

Alphanosos' solution:

Massively Parallel Phyto-Pharmacology from edibles: From « miraculous bullet » to « magic* shotgun »

** « Any sufficiently advanced technology is indistinguishable from magic » Arthur C. Clarke*



Alphanosos

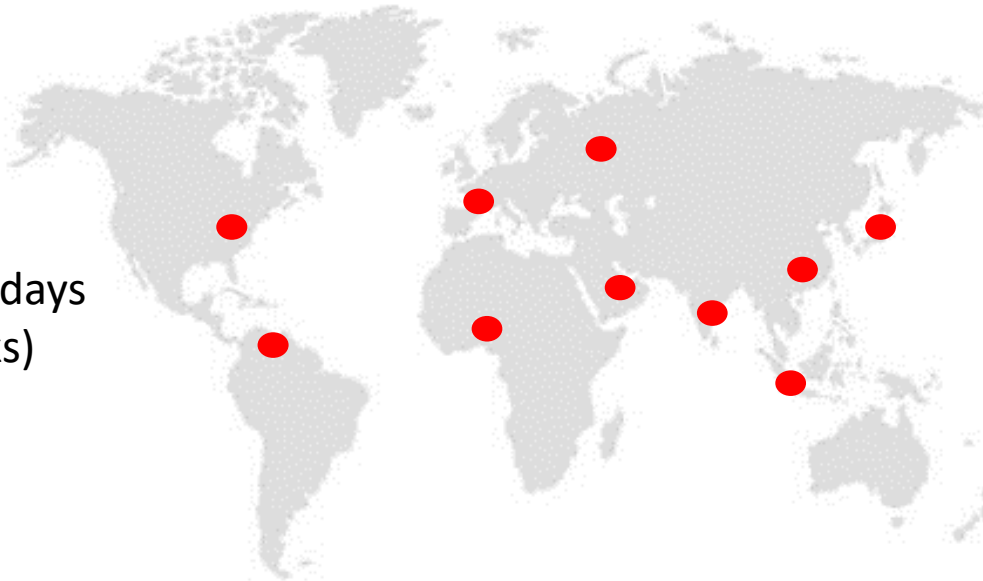
Beyond COVID-19

Capitalize on COVID-19 experience

To be extended seasonal flu and to any other viral crisis: Ebola, Lassa, …
Also for bacterial epidemics, e.g., tuberculosis, cholera, …

Rapid international epidemic control intervention force:
Countermeasures to naturally emerging and terrorist biothreats

- Assemble collections of botanical from and in different parts of the world:
  ⇒ ensure acceptability from different populations
- Exercise periodically
- For rapid discovery response to emergence of novel pathogen
- For rapid deployment with WHO logistics of discovered WECMEP
- From de novo (fast growing organisms): Bacteria in 24-36 hours, Virus in 10 days
- Accumulate pre-validated WECMEP collection (e.g., 1000 doses frozen stocks)
  ⇒ maximize chances of immediate response
- Predictive genomics: AI to relate DNA/RNA sequence to treatment



Yearly Budget (tentative):

- *600-900'000€ per emergency center*
- *1.5~2'000'000 for genomics based AI*