NEW MEDICAL TREATMENTS AND THEIR DEPENDENCE ON BIODIVERSITY

Erik Ruuth

Lucía Acuña, Cecilia Miranda, Tania Alarcon, Evelin Aguchi, Emanuel Grassi.

A special thank to Cristian Desmarchelier

1. **<u>Instituto Misionero de Biodiversidad</u>**
2. Nature as a source of Health and Wellbeing
3. Why do natural products exist?
4. How are natural products used?
5. Pro's & Con's of natural products derivatives
6. Pharma Industry & Natural Products
7. Bioprospection and Perspectives
8. Impact of Climate changes and Biodiversity loss

- Presidenta del IMiBio
  Mgtr. Arq. L. B. Viviana Rovira

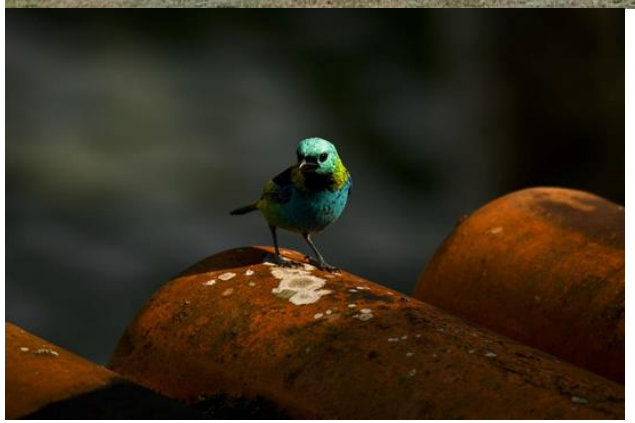
- Dir. Gral. Ejecutivo
  Dr. Emanuel M. Grassi

- Coordinador Científico
  Dr. Andrés Enrique Gustavo Ruuth

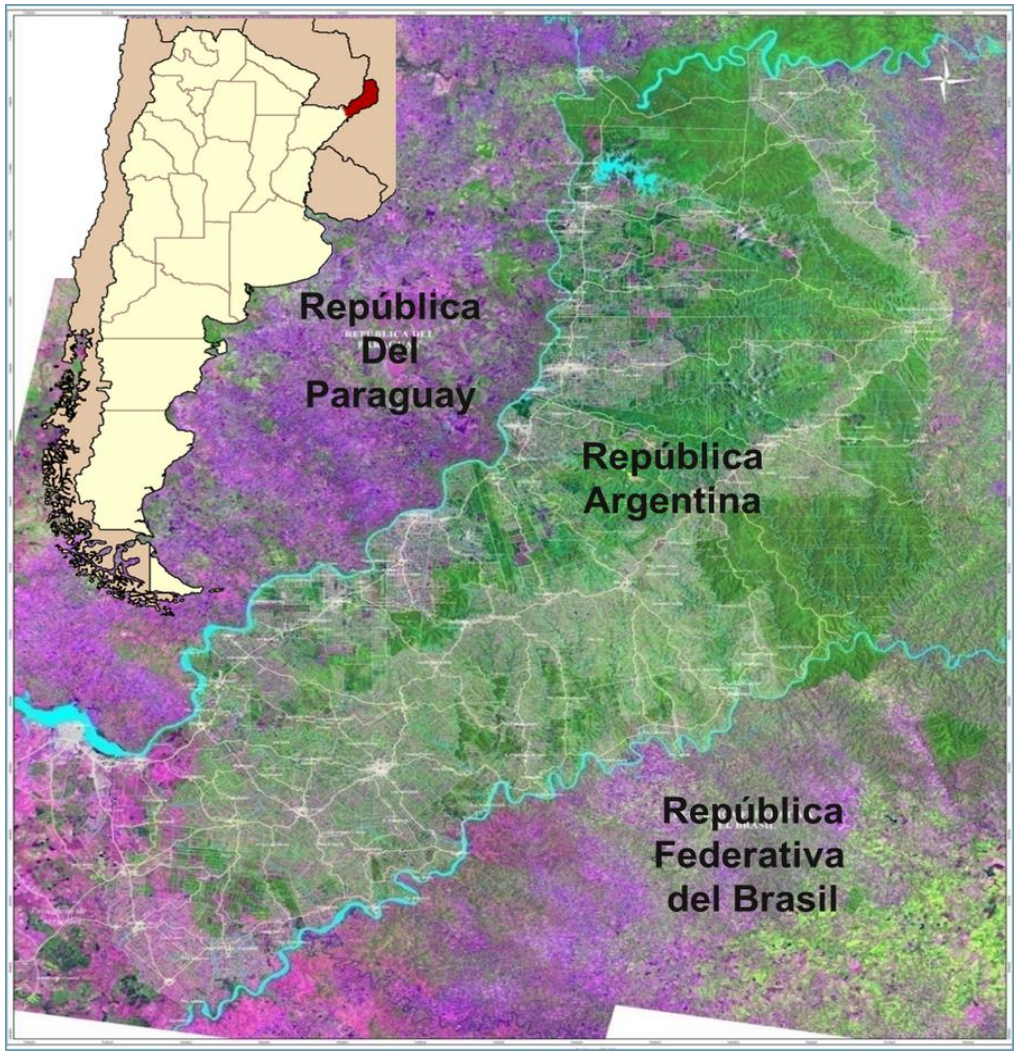
- Dir. Gral. de Admin. Financiera
  Cdor. Juan M. Roa

- Dir. Gral. de Asuntos Legales
  Abog. Silvana S. Cima

- Dir. Gral de S.I.G.
  Sr. Juan M. Solari



Misiones-Argentina - 52% of Argentina's Biodiversity



- Capital : Posadas
- Population: 1.280.960 Hab.
- Surface: 29.801 km^2
- 1% of continental Argentina
- +50% covered by native forest
- 2/3 of the forests are protected
- Argentina's Biodiversity Capital (2018)
- 91 % of International Frontiers
- 36 Border Crossings
- 25 million people transit yearly

Strategic Axles

Biodiversity and Science

Biodiversity and Health

Biodiversity and Society

Biodiversity and Management of the Genetic Resources

1. Instituto Misionero de Biodiversidad
2. **Nature as a source of Health and Wellbeing**
3. Why do natural products exist?
4. How are natural products used?
5. Pro's & Con's of natural products derivatives
6. Pharma Industry & Natural Products
7. Bioprospection and Perspectives
8. Impact of Climate changes and Biodiversity loss

Nature *per se* and Health / Wellbeing

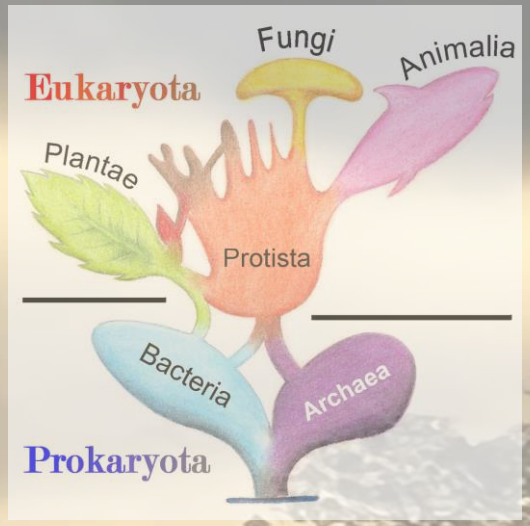
- Reconnecting with nature will Reduce anger, fear, and stress and increase pleasant feelings through Nature-Based Interventions (NBIs) - less intrusive and more cost-effective (doi: 10.7189/jogh.12.04099) (https://csh.umn.edu/)
- GOOD STUDIES are needed to ensure success of NBIs (doi: 10.7189/jogh.12.04099)
- A review summarised the outcome of 39/952
  - ✓ Positive outcomes on mental health, physical / physiological health, cognitive health. (doi: 10.7189/jogh.12.04099)

Nature *per se* and Health / Wellbeing

- Critical analysis (https://doi.org/10.1073/pnas.2304126120)
  - ✓ Most studies (>80%) were done in GLOBAL NORTH
  - ✓ Small studies (median 36 participants)
  - ✓ Mostly Observational studies
    - Interventional studies small and not standardised
  - ✓ Variable study design
  - ✓ Outcomes are not standardised
  - ✓ No guidance on how to go from research to NBI benefits and urban wellness planning (https://doi.org/10.1073/pnas.2304126120
  - ✓ **Urban planning** : Need of more data driven development when investing

1. Instituto Misionero de Biodiversidad
2. Nature as a source of Health and Wellbeing
3. **Why do natural products exist?**
4. How are natural products used?
5. Pro's & Con's of natural products derivatives
6. Pharma Industry & Natural Products
7. Bioprospection and Perspectives
8. Impact of Climate changes and Biodiversity loss

Why do natural products exist?



- NPs are the result of evolutionary processes & in all forms of life
- NPs can be divided into 2 types
  - ✓ **primary metabolites**, which are required for an organism to survive, and
  - ✓ **secondary metabolites**, which are not required for an organism to survive, but usually lend the organism some form of growth or survival advantage within its environment (
- S**econdary metabolites**: social signalling molecules (pheromones), chemoattractants, activation of symbiotic relationships, solubilization and transport of nutrients, and competitive weapons (repellents, venoms, toxins etc.) that are used against competitors, prey, and predators.
  - ✓ Gain advantage in the selection process by Chemical warfare
  - ✓ The function of many secondary metabolites is unknown.

https://wou.edu/chemistry/courses/online-chemistry-textbooks/ch105-consumer-chemistry/ch105-chapter-6-hydrocarbons/

What are they and what can we do with them?

- 4 chemical groups of NPs
  - ✓ ***alkaloids (***contain nitrogen), or
  - ✓ ***phenylpropanoids*** (from phenylalanine or tyrosine), or the
  - ✓ ***polyketides*** (from acetate and malonate), or
  - ✓ ***terpenoids***, (isoprene).
- **They target essential biological processes that are conserved across species, including humans**
  - ✓ Nervous system, immune response, or cellular functions, infections, inflammation, or cancer
- Therapeutic potential of NPs recognized by humans and identified by animals
  - ✓ Traditional medicines are based on plant extracts or other natural sources.
- Humans eventually developed pharmaceuticals out NPs

https://wou.edu/chemistry/courses/online-chemistry-textbooks/ch105-consumer-chemistry/ch105-chapter-6-hydrocarbons/

1. Instituto Misionero de Biodiversidad
2. Nature as a source of Health and Wellbeing
3. Why do natural products exist?
4. **How are natural products used?**
5. Pro's & Con's of natural products derivatives
6. Pharma Industry & Natural Products
7. Bioprospection and Perspectives
8. Impact of Climate changes and Biodiversity loss

How are natural products used?

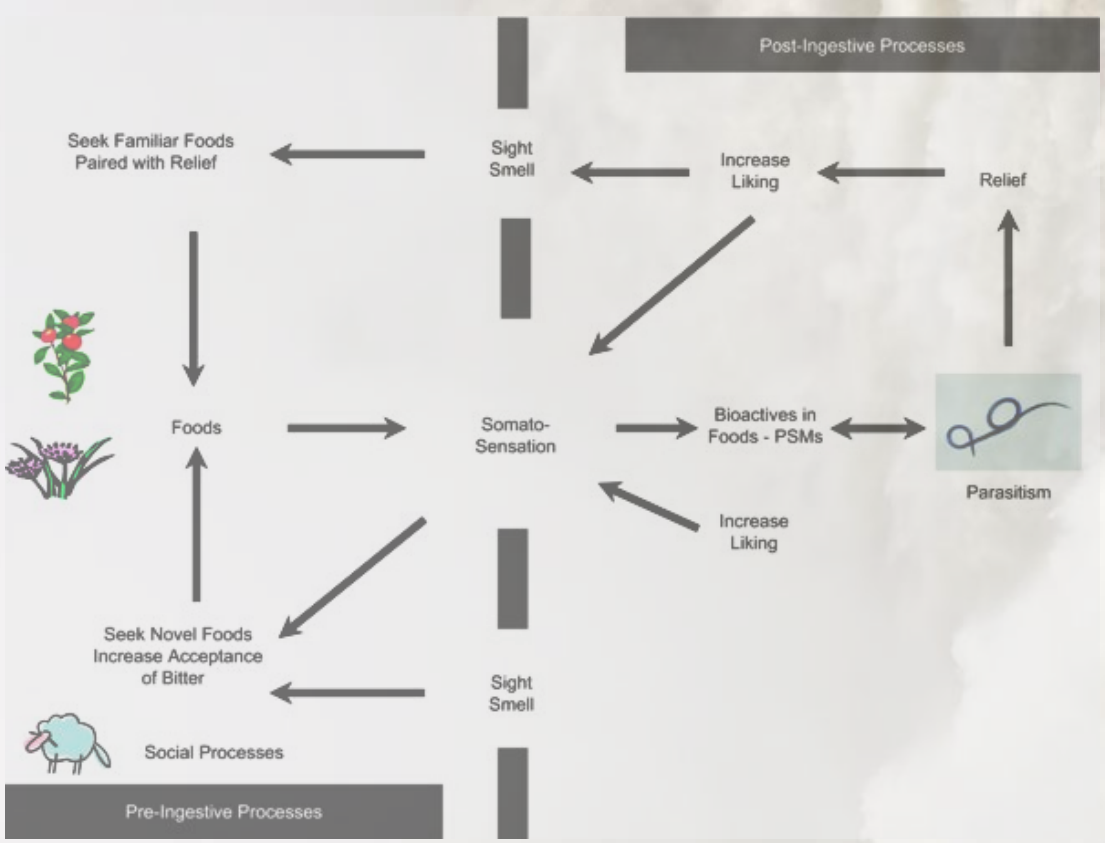
Animals self-medicate (zoopharmacognosy) for treatment of parasites

- **Cats** and **dogs:** vomiting
  - ✓ plant material to induce vomiting.
- **Birds**: feather parasites
  - ✓ "ant bathing"
- **Monkeys**: treat parasites
  - ✓ Chew leaves of pith (*Schistosoma*, *Plasmodium* and *Leishmania)*; stem juice of *Aframomum angustifolium (*anti-microbial activity); Leaves of the *Aspilia* plant (antinematode); sugar-based syrup to cover wounds
- **Brown Bears:**
  - ✓ *Carex* leaves for expulsion of parasites during hibernation; Paste of Osha roots ("bear root") and saliva and rub it through their fur to repel insects or soothe bites
- **Larvae**
  - ✓ *Grammia incorrupta* consume alkaloid-laden leaves that help fight off internal parasitic fly larvae. This phenomenon is said to be "the first clear demonstration of self-medication among insects".
- **Ants**
  - ✓ infected with *Beauveria bassiana*, a fungus, selectively consume harmful substances (reactive oxygen species, ROS) upon exposure to a fungal pathogen, yet avoid these in the absence of infection
- **Wild boars**
  - ✓ selectively dig up and eat the roots of pigweed which humans use as an antihelmintic.
- **Pigs**
  - ✓ Mexico eat pomegranate roots because of an alkaloid that is toxic to tapeworms.
- **Great bustards**
  - ✓ eat blister beetles of the genus *Meloe* maybe to decrease parasite load in the digestive system, cantharidin, the toxic compound in blister beetles, can kill a great bustard if too many beetles are ingested.

How are natural products used?

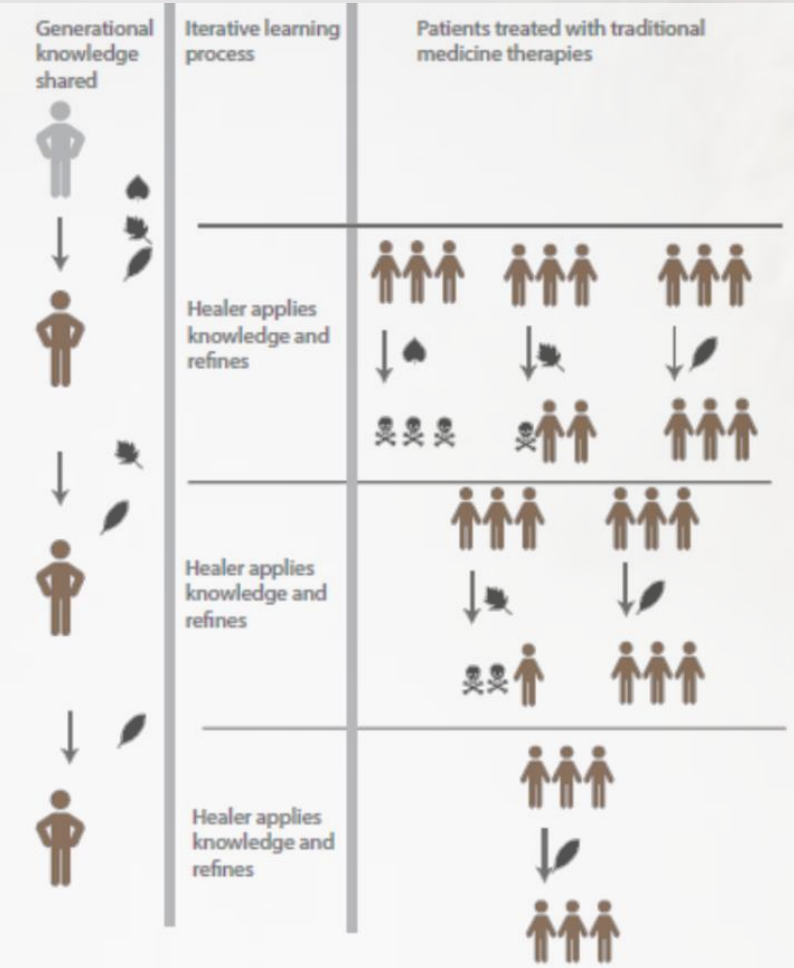
Animals self-medicate: zoopharmacognosy

- **African elephants** (*Loxodonta africana*) **<u>apparently self-medicate to induce labour by chewing on the leaves</u>** of a particular tree from the family Boraginaceae; Kenyan women brew a tea from this tree for the same purpose.



Proposed mechanism for liberation of gastrointestinal parasites and self-medication in **<u>ruminants</u>**

How are natural products used? Humans



The **intergenerational transfer** of traditional medicine knowledge is the foundation of the ethnopharmacological approach to bioprospecting natural products.

Ultimately, this **iterative process** results in a refined identification of the most effective natural product to treat a specific disorder.

The **collection of ethnopharmacological data requires working with individuals possessing the knowledge** of the use of the natural products as therapeutics.

Individuals with knowledge of the medicinal properties will often have cultivated specimens of the materials frequently used (A) and share standard documentation describing the activity and goals of the work with all participants involved in the activity (B). The individuals with the medical knowledge are enthusiastic in sharing their ethnopharmacological knowledge (C).

Capture d'écran 2024-09-04 à 10.42.42Capture d'écran 2024-09-04 à 10.42.42

Capture d'écran

How are natural products used?

Humans practice **T**raditional & **C**omplementary **M**edicine

- WHO advocates for the integration of traditional medicine practices into national health systems
  - ✓ WHO definition: The sum of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health and the prevention, diagnosis, improvement or treatment of physical and mental illness
- More than 50,000 biologically active plants (IUCN)
- Practice of T&CM is widely spread, used in170 countries
  - ✓ United States (42%); Australia (48%) France (49%) Canada (70%) Chile (71%), Colombia (40%) and up to **80%** in some African countries.
- Demand for T&CM is increasing
  - ✓ It represents **a more economical solution** to treatments and culturally acceptable
- Patients seek ownership of their health, a compassionate, and personalized treatment

https://www.who.int/news-room/questions-and-answers/item/traditional-medicine

IUCN, 2007, https:// www.iucn.org/theme/species/our-work/plants, accessed on 22 December 2017

1. Instituto Misionero de Biodiversidad
2. Nature as a source of Health and Wellbeing
3. Why do natural products exist?
4. How are natural products used?
5. **Pro's & Con's of natural products**
6. Pharma Industry & Natural Products
7. Bioprospection and Perspectives
8. Impact of Climate changes and Biodiversity loss

Herbal Medicines: Pro's & Con's

- Being "natural" doesn't necessarily mean they're safe to use.
- Complex Chemistry leads to Complex Interactions with registered medicines and other NPs: Poly-pharmacology
  - ✓ Disadvantage to define the MOA
  - ✓ Opportunity: mitigate Adverse event profiles
- Source of NPs: Variable - harvest in the wilds or large-scale cultivation
- Batch-to-batch variability high
  - ✓ Standardise batch profile
- Quality control parameters are needed: production, storage and further processing

DOI: 10.15406/ijcam.2018.11.00350

IUCN, 2007, https:// www.iucn.org/theme/species/our-work/plants, accessed on 22 December 2017

Herbal Medicines: Pro's & Con's

- All medicinal products should have the Same Standards of quality, clinical effectiveness and safety
- Lack of data is the major roadblock for acceptance of NPs by conventional medicine
  - ✓ **<u>Controlled clinical trials</u>** are needed to Establish Efficacy & AE profile
- Lack of regulatory framework and network
  - ✓ Increased interest to authorities (FDA, EMA, EFSA, TGA, Health Canada, etc.)
- Lack of appropriate GMP leads to poor contamination control (e.g. toxic metals, pesticides residues and microbes), adulteration and misidentification
- Traceability of raw materials – essential
  - ✓ Good Agricultural and Collection Practice (GACP) guidelines.

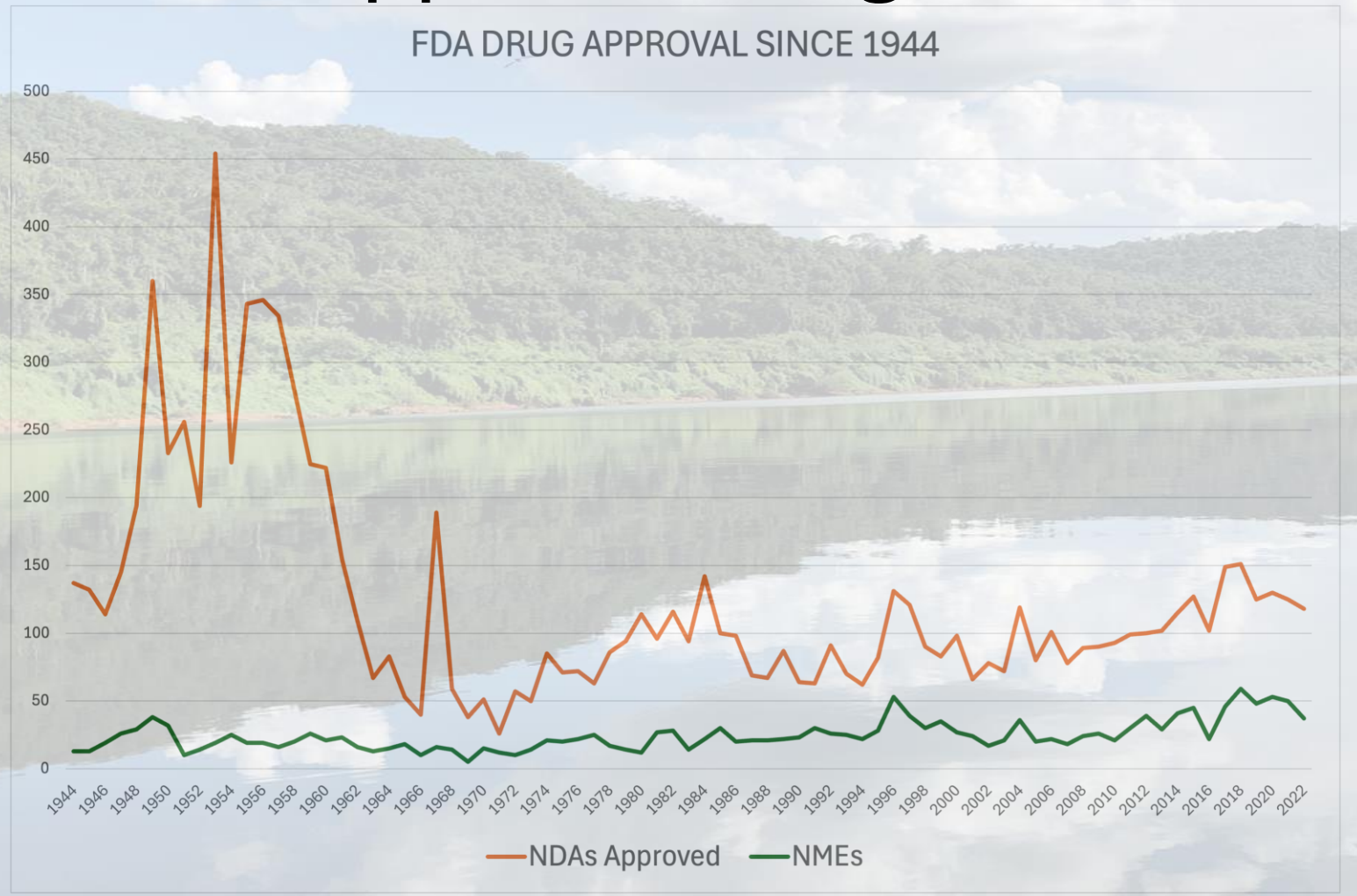
DOI: 10.15406/ijcam.2018.11.00350

1. Instituto Misionero de Biodiversidad
2. Nature as a source of Health and Wellbeing
3. Why do natural products exist?
4. How are natural products used?
5. Pro's & Con's of natural products derivatives
6. **Pharma Industry & Natural Products**
7. Bioprospection and Perspectives
8. Impact of Climate changes and Biodiversity loss

Pharma Industry & Natural Products

- Purification of natural products was the start of modern Pharma Industry
- Morphine was purified in 1805 (Friedrich Sertürner) and German **Merck** company started to commercialise in 1827
- **Bayer** patented Aspirin in 1899 and commercialized it; and aspirin is still a valuable drug
- Political Impact: Quinine, was purified in 1820 (Pelletier and Caventou). Its role in of malaria treatment was recognised and the Dutch government monopolised it for a century. Mid-20th century, **Janssen** commercialised quinine derivatives
- Other companies
  - ✓ **Takeda** sold Kampo Medicines (Traditional Japanese Herbal Medicines); **Parke Davies** sold adrenaline; **Sanofi** grew based on the selling of Artemisinin derivatives; **Hoechst** sold insulin, heparin, penicillin, cosrtisone, quinine, codeine; **Upjohn** sold « friable pills » of natural extracts

FDA Approved drugs over time



https://www.fda.gov/about-fda/histories-fda-regulated-products/summary-nda-approvals-receipts-1938-present#Notes

FDA Approved drugs over time and by type

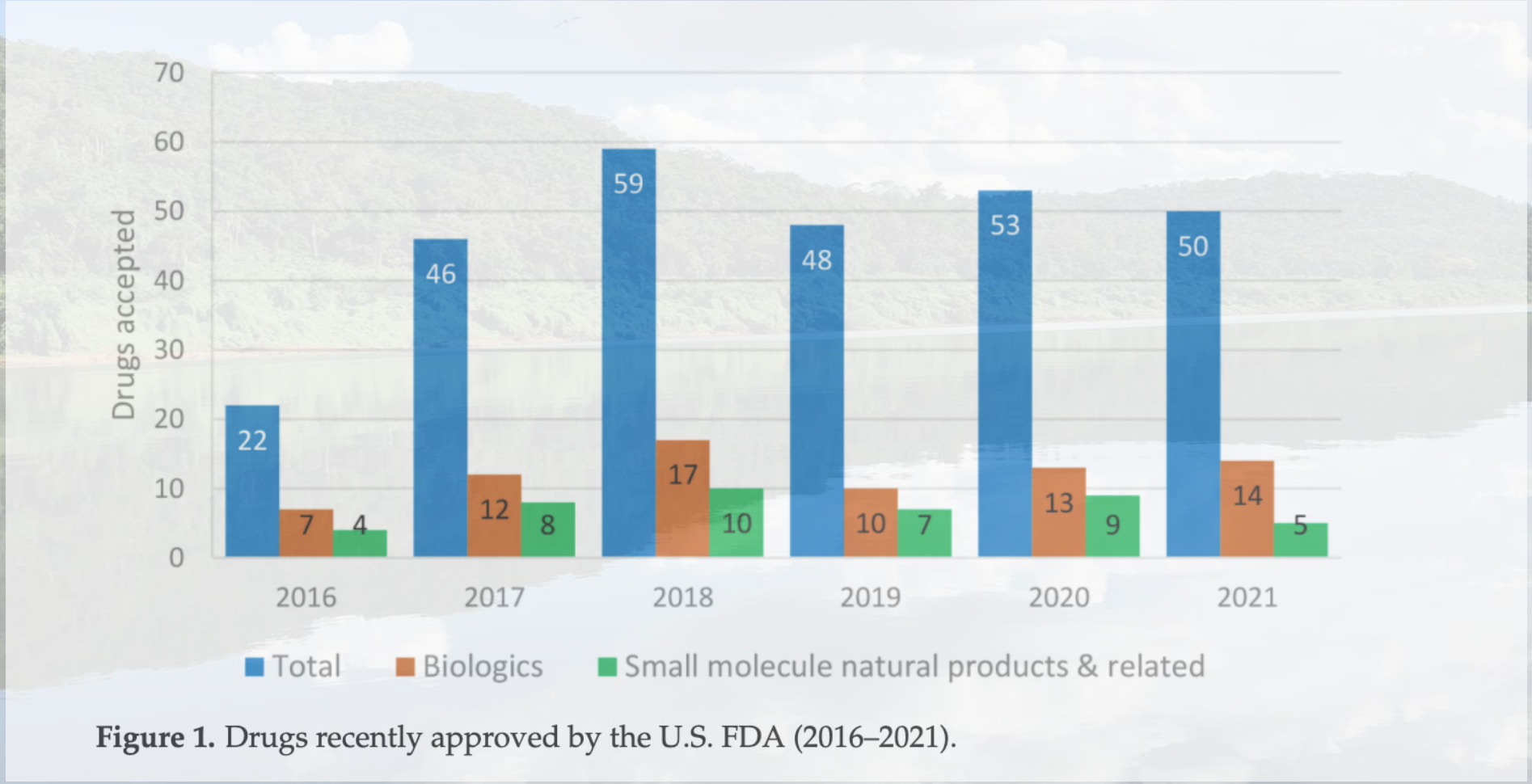


Figure 1. Drugs recently approved by the U.S. FDA (2016–2021).

Molecules 2022, 27, 8280. https://doi.org/10.3390/molecules27238280

Pharma Industry & Low NME discovery

- "Low hanging fruits" have been picked
- Higher Failure Rate in clinical development today than in the 1970s
  - ✓ Regulatory landscape is more complex: teratogens like thalidomide
- Response of Pharma: Increase the medicinal chemistry production
- Through advanced technological methods for identification of NMEs : HTS, combinatorial chemistry, CADD, SBDD, AI, ……
  - ✓ Gives a lot numbers to present

However

- **Low predictive validity of models** still give a high rate of failures
- Models are a Major roadblock for NME development

DOI:10.1371/journal.pone.0147215

Response to limits in the search for new drugs: Change models and Source

- Critically assess old models for their usefulness and predictivity
  - ✓ Discard exhausted models with low PV
  - ✓ Consider Garbage in = garbage out
- Create new models with high PV for screening and selection of drugs
- Look for new predictive models in nature by checking species of interest (**Krogh's Principle**)
  - ✓ Create new standards for models – See clinical trials
- Correct the Lack of methodological rigor
- Change source of NMEs to NATURE

(https://www.nature.com/articles/nature11556)

Pharma Industry Issues: High Margins & ROI

- Early purified NPs gave high growth rates to the Pharma business
- Pharma sector got used to high Operative profit margins of 20 – 30% & high ROIs since decades –Market expects such rentability
- R&D costs per novel drug increased nearly 100-fold between 1950 and 2010
- CONCLUSION: High profit margins & ROI concept constrains the NME development
  - ✓ Ex: Highly Antibiotics resistant bacteria (MDR, MRSA)

Animals that can serve as role models – Regenerative medicine

Spiny mouse (Acomys) & Axolotl salamander

- **Acomys** species
  - ✓ Scar-free healing in a wide-range of tissues beyond the skin
  - ✓ Skeletal muscle
  - ✓ Heart regeneration after oxygen-deprivation-induced cardiomyopathy
  - ✓ Acomys is a model for type 2 diabetes mellitus
- **Axolotl salamander** (Ambystoma mexicanum) Spinal cord injury can be fully repaired with functional reconnection of the rostral and caudal parts of the injured spinal cord

npj Regenerative Medicine (2021) 6:1 ; https://doi.org/10.1038/s41536-020-00111-1

Animals that can serve as role models - Cancer

- Long-lived animals have a more efficient anticancer defence
- Big animals have more efficient anticancer defences
- There is potential for improving anticancer therapies by introducing anticancer adaptations in humans that could result in increased cancer resistance.

Nat Rev Cancer . 2018 July ; 18(7): 433–441. doi:10.1038/s41568-018-0004-9

Animals that can serve as role models - Cancer

The naked mole rat

- Lives 32 years and NO cancer
- **2 early contact inhibition (ECI) mechansisms**
  - ✓ (activation of p16INK4A rather than p27) that increases cancer resistance.
  - ✓ The extracellular signal activating ECI is a unique high molecular mass hyaluronan (HMM-HA) secreted by naked mole rat cells
- **Four hits** for malignant transformation (humans 3 hits, mice 2 hits)
- 'Sense' the loss of either Tp53 or Rb1 tumor suppressors and trigger apoptosis or senescence

Nat Rev Cancer . 2018 July ; 18(7): 433–441. doi:10.1038/s41568-018-0004-9

Animals that can serve as role models – Cancer

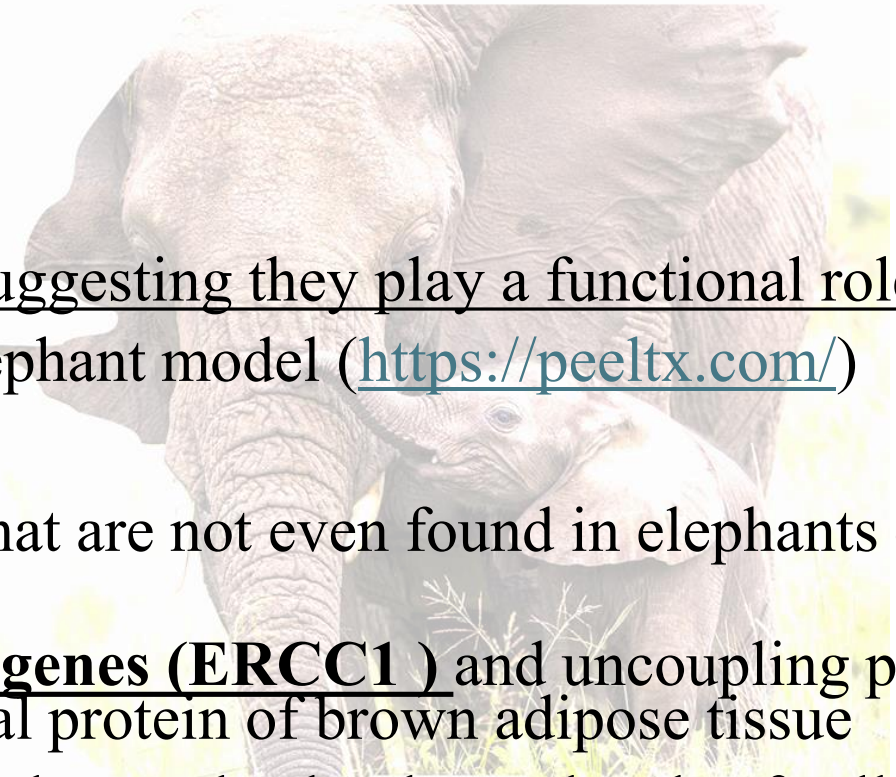
The Blind Mole Rats & Bats

- **Blind Mole Rats**
  - ✓ Live 21 years and resistant to cancer
  - ✓ **Cancer induction leads to necrosis**
  - ✓ **Increased expression of interferon β (IFNβ) mediates the necrosis**
- **Bats**
  - ✓ Long-lived & few cases of tumours
  - ✓ C**ounteract oxidative stress** - tumour resistance and pathogen control
  - ✓ **3/4 miRNA function as tumour suppressors** (miR-101-3p, miR-16-5p, miR-143-3p)
    - One down-regulated miRNA (miR-221-5p) may act as a tumorigenesis promoter
  - ✓ Reduced Growth Hormone and IGF signalling

Nat Rev Cancer . 2018 July ; 18(7): 433–441. doi:10.1038/s41568-018-0004-9

Animals that can serve as role models – Cancer

Elephants and Whales



ELEPHANTS: no cancer

- Increased induction of apoptosis
- **19 pseudogenes of the TP53**
- Positive selection for the TP53 copies - suggesting they play a functional role
- **PEEL**: biotech company based on the elephant model (https://peeltx.com/)

WHALES : no cancer

- Whales: **novel anticancer adaptations** that are not even found in elephants or humans.
- Positively selected **DNA excision repair genes (ERCC1)** and uncoupling protein 1 (UCP1), which encodes a mitochondrial protein of brown adipose tissue
- **Slower metabolism** of the largest mammals may lead to lower levels of cellular damage and mutations, and thus contribute to lower cancer incidence

Nat Rev Cancer . 2018 July ; 18(7): 433–441. doi:10.1038/s41568-018-0004-9

1. Instituto Misionero de Biodiversidad
2. Nature as a source of Health and Wellbeing
3. Why do natural products exist?
4. How are natural products used?
5. Pro's & Con's of natural products derivatives
6. Pharma Industry & Natural Products
7. **Bioprospection and Perspectives**
8. Impact of Climate changes and Biodiversity loss

How much drug is there left? Is it worth the effort?

- Current estimates of earths biodiversity
  - ✓ **Currently identified species 1,2 x 10^6 has resulted in 930 drugs with relation to nature**
  - ✓ Unknown species - conservative estimate of (8,7 – 1,2) x 10^6 = 7,5 x 10^6
  - ✓ Alternative Low estimate of biodiversity 82,4 x 10^6 (PLoS Biol 21(11): e3002388. https://doi.org/10.1371/journal.pbio.3002388)
  - ✓ Alternative High estimate of biodiversity 3,5 x 10^{12}
- **Estimates of drugs remaining to be discovered**
  - ✓ **CONSERVATIVE estimate: 7,5 x 930 ≈ 7 000 new drugs**
  - ✓ **LOW estimate: 82,4 x 930 ≈ 75 600 new drugs**
  - ✓ **HIGH estimate: 1 x 10^6 x 930 ≈ 0,9 x 10^9 new drugs**
- **There is a reservoir of potential new drugs in nature**

Bioprospection: How and For What?

- How?: **<u>Infrastructure!</u>** Focus on Sustainability, Cooperation and Business development
  - ✓ Sample acquirement
  - ✓ Knowledge banks
  - ✓ Sample storage: biobanks (and explore other ways)
  - ✓ Sample analytics: taxonomy, HT screening, chemistry, genomics, etc.
  - ✓ Data storage, Bioinformatics, and analysis: analysis of systems
  - ✓ Function search: predictive models
  - ✓ Regulatory framework
  - ✓ Industrial scaling up
  - ✓ Creative market generation
  - ✓ Business models: venture capital, long term investments, Angels

Sample Acquirement

Knowledge Banks: Examples

- Biodiversity Heritage Library (https://www.biodiversitylibrary.org/)
  - ✓ Smithsonian, Smithsonian Libraries and Archives, Natural History Building, 10th St. and Constitution Ave. NW, Washington DC, 20560
  - ✓ American Museum of Natural History (New York, New York), Field Museum of Natural History (Chicago, Illinois); Botany Libraries (Harvard University Herbaria) (Cambridge, Massachusetts); Ernst Mayr Library (Museum of Comparative Zoology) (Cambridge, Massachusetts); Marine Biological Laboratory of Woods Hole Oceanographic Institution (Woods Hole, Massachusetts); Missouri Botanical Garden (St. Louis, Missouri); Natural History Museum (London, England); The New York Botanical Garden (Bronx, New York); Royal Botanic Gardens, Kew (Richmond, United Kingdom); Smithsonian Institution (Washington D.C.); Academy of Natural Sciences (Philadelphia, Pennsylvania); California Academy of Sciences (San Francisco, California); Cornell University Library (Ithaca, New York); United States Geological Survey (Reston, Virginia); Library of Congress (Washington D.C.
- Biodiversity Heritage Library EU (https://pro.europeana.eu/project/bhl-europe)
  - ✓ Museum für Naturkunde (Berlin) (project leadership) ; Natural History Museum (London); National Museum (Prague); European Digital Library Foundation (Europeana); Angewandte Informationstechnik Forschungsgesellschaft AIT (Graz); Atos Origin Integration France (Paris) ; Freie Universität Berlin; Georg-August-Universität Göttingen (AnimalBase); Naturhistorisches Museum Wien; Oberösterreichische Landesmuseen (Linz); Museum and Institute of Zoology, Polish Academy of Sciences (Warszawa); Hungarian Natural History Museum (Budapest); University of Copenhagen; Naturalis (Leiden) ; National Botanic Garden of Belgium - Meise; Royal Museum for Central Africa (Tervuren) ; Royal Belgian Institute of Natural Sciences; Bibliothèque nationale de France (Paris) (Gallica) ; Museum national d'histoire naturelle (Paris) ; Spanish National Research Council (Madrid); Università degli Studi di Firenze; Royal Botanic Garden Edinburgh; Species 2000; John Wiley & SonsSmithsonian Institution (Washington); Missouri Botanical Garden (St. Louis); University of Helsinki; Humboldt-Universität zu Berlin
- Give all researchers in poor countries access to scientific journals!!!

Biodiversity Sample Storage - Biobanks

- Extractothèque (https://icsn.cnrs.fr/plateformes/extractotheque)
  - ✓ Institut de Chimie de Produits Naturelles, Université Paris – Saclay; 14K extracts from 6,5K superior plants •Oncology platform
- Naturebank (https://www.griffith.edu.au/institute-drug-discovery/unique-resources/naturebank)
  - ✓ Institute for Drug Discovery, Griffith University – Australia; 20K extracts + 112K fractions
- LNBio (https://lnbio.cnpem.br/)
  - ✓ Centro Nacional Pesquisa em Energia e Materiais ; 6K extracts; Platforms: oncology, cardiovascular, metabolic, infectious diseases
- Biobank at Fiocruz (https://www.frontiersin.org/journals/tropical-diseases/articles/10.3389/fitd.2024.1420326/full) (https://fiocruz.tghn.org/research-production/biological-collections/)
- Biobank at IMiBio (https://imibio.misiones.gob.ar/en/ampliar/investigaciones/biobanco)
- Biobank at the BAP project (https://imibio.misiones.gob.ar/en/ampliar/investigaciones/biobanco)
- Biobank: San Diego Zoo Wildlife Alliance safeguarding biodiversity and preserving hope (https://iucn.org/crossroads-blog/202309/biobanks-safeguarding-biodiversity-and-preserving-hope)
- Biobanks of Global Genome Biodiversity Network (https://www.ggbn.org/ggbn_portal/)
- Biodiversity Biobanks South Africa (**https://bbsa.org.za/**)

Sample Analytics: Genomics

- International Barcode of Life Consortium (https://ibol.org/)
- Earth BioGenome Project (EBP): Sequencing Life for the Future of Life (https://www.earthbiogenome.org/)
- Darwin Tree of Life Project (https://www.darwintreeoflife.org/)
- Genomics of the Brazilian Biodiversity Project (https://www.itv.org/en/genomics-of-the-brazilian-biodiversity-gbb/)
- Global Genome Initiative (GGI) (https://naturalhistory.si.edu/research/global-genome-initiative)
- Global Genome Biodiversity Network (https://www.ggbn.org/ggbn_portal/) Repositories & Biobanks

Sample Analytics: Genomics

- Assessment : Efforts should be increased by 2 orders magnitude (https://www.pnas.org/doi/epub/10.1073/pnas.2109019118)
  - ✓Variable quality,
  - ✓70% by 3 countries (US, China, Switzerland); 75% by Global North

https://doi.org/10.3897/arphapreprints.e103105
https://doi.org/10.3897/ab.e101876

Bioprospection: Biodiversity Access Platforms

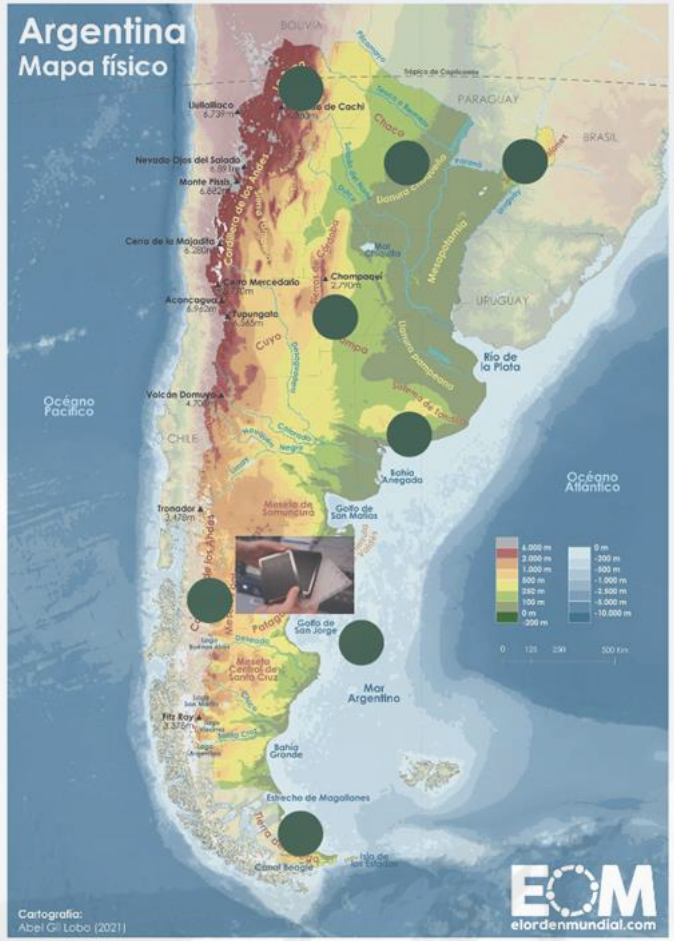
A branch of the bioeconomy focused on the **exploration of biodiversity** for small molecules, macromolecules, biochemical and genetic information that could be developed into **commercially valuable products** for the agricultural, food, cosmetics and pharmaceutical industries.

Partners

University of Patagonia •Chamber of Industry

•Ministry of Science & Technology

Argentina Network



Objetives:

Create a **Bank / Library of Extracts** representing the main marine an terrestrial ecosystems for screening in HTS platforms in search for novel active ingredients.

Create a **Network of Nodes** representing the biodiversity of the country.

Create an **interactive database** for fast access to information leading to collaborative screening activities.

Initial budget:

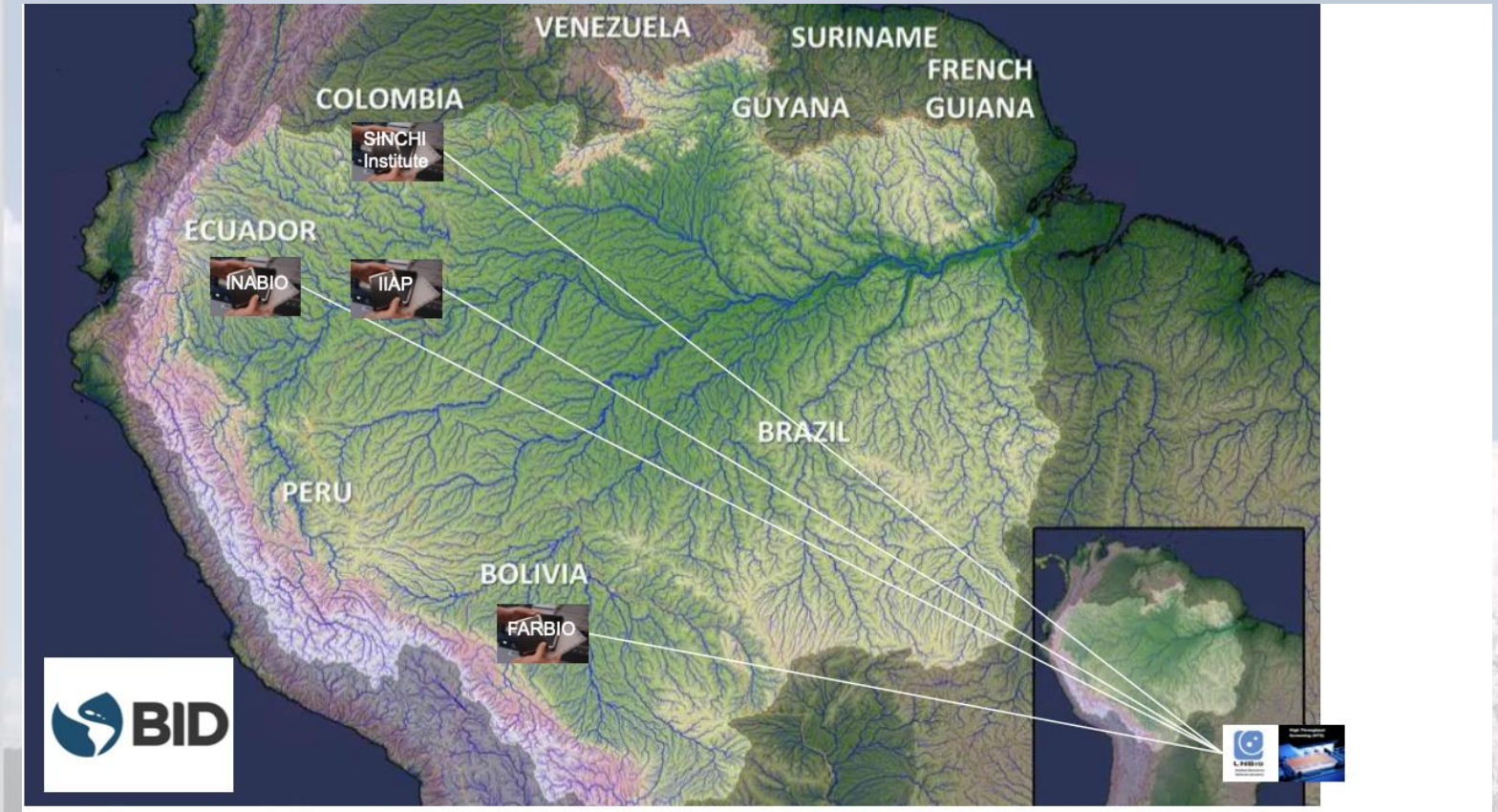
Aprox USD 100K from the Federal Government (equipment and operating expenses). Counterpart: Chamber of Industry of Puerto Madryn and University of Patagonia.

Team:

Drs Tamara Rubilar, Marisa Avaro and Augusto Crespi (UNPSJB, CONICET)

Cristian Desmarchelier

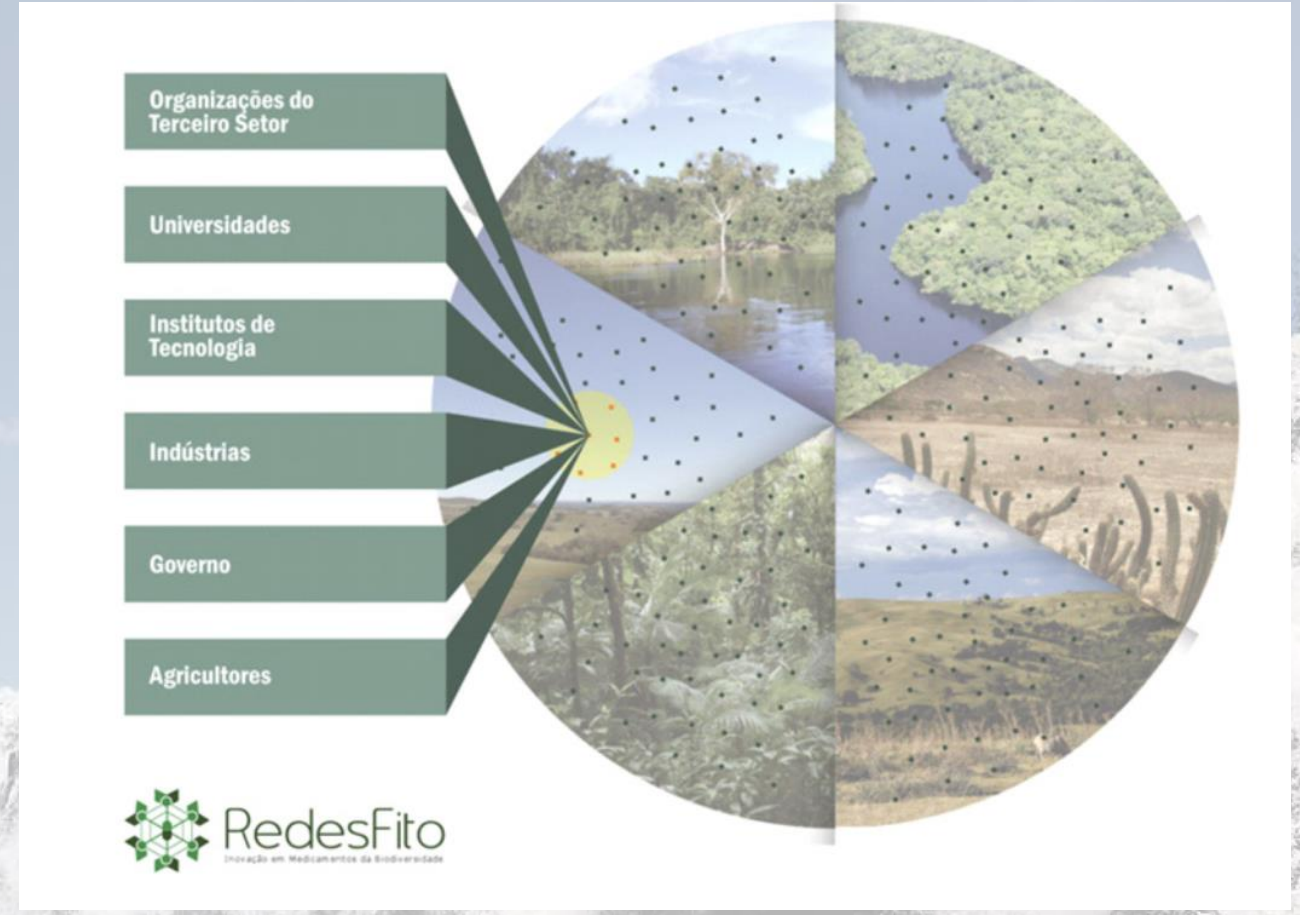
Western Amazonas and BID



Cristian Desmarchelier

- Feasibility analysis of introducing innovative models for bioprospecting in the Western Amazon Basin
- The Western Amazon is the richest part of the basin
- Unlike the Eastern (Brazilian) Amazon, a largely intact ecosystem

Brazil is the most biodiverse country and explores Biodiversity
Centro de Inovação em Biodiversidade e Saúde – RedesFito



https://redesfito.far.fiocruz.br/index.php/quem-somos/cibs

Brazil is the most biodiverse country and explores Biodiversity

- **Center for Innovation in Biodiversity and Drug Discovery** (CIBFar) (https://cibfar.ifsc.usp.br/homepage/)
  - ✓ Perform basic and applied science, as well as technological development in all the areas of biodiversity and drugs discovery on the basis of research that uses:
  - Chemistry of natural products
  - Synthetic organic chemistry
  - Molecular biology
  - Structural biology
  - Biochemist
  - Medicinal chemistry
  - Drugs design
  - Pharmacological assays
- Consortium of 5 well reknown and reputed institutes

1. Instituto Misionero de Biodiversidad
2. Nature as a source of Health and Wellbeing
3. Why do natural products exist?
4. How are natural products used?
5. Pro's & Con's of natural products derivatives
6. Pharma Industry & Natural Products
7. Bioprospection and Perspectives
8. **Impact of Climate changes and Biodiversity loss**

Impact of Climate changes and Biodiversity loss

RESEARCH | RESEARCH ARTICLE

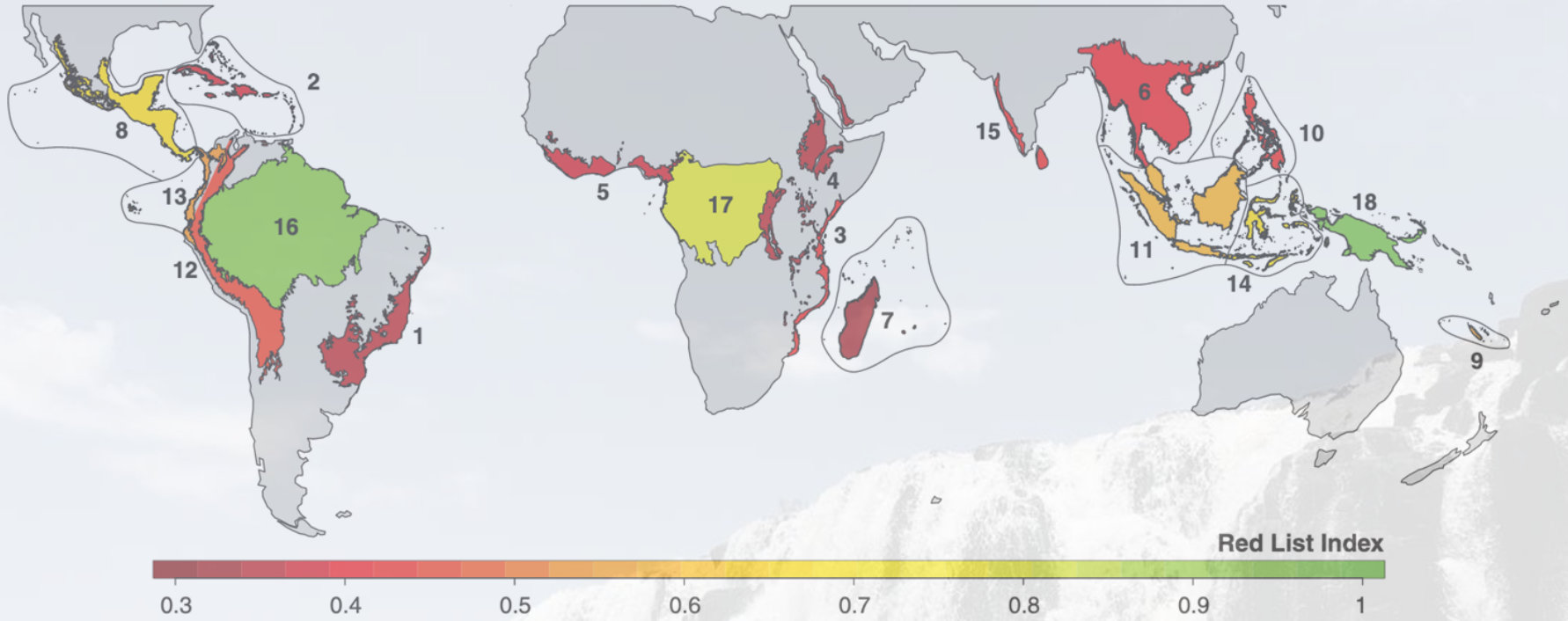


Fig. 4. Predicted RLI values for the 18 main tropical forest areas of the world. Predictions are based on the relationship between population size reductions and habitat loss, which could be obtained for all forests from forest cover maps and reports of their number of endemic species. Thus, these predictions are based solely on the population size reductions (i.e., IUCN criterion A2) of endemic species. The RLI ranges from zero (all species are classified as extinct) to one (no species are classified as threatened). The color scale ranges from lower, or worse, RLI values (dark red) to higher, or better, values (green). See supplementary materials and tables S6 and S7 for details and the full tropical forest names that correspond to the numbers in the map.

de Lima et al., Science 383, 219–225 (2024) 12 January 2024

Atlantic Forest: Evolution from 1940 to 2018

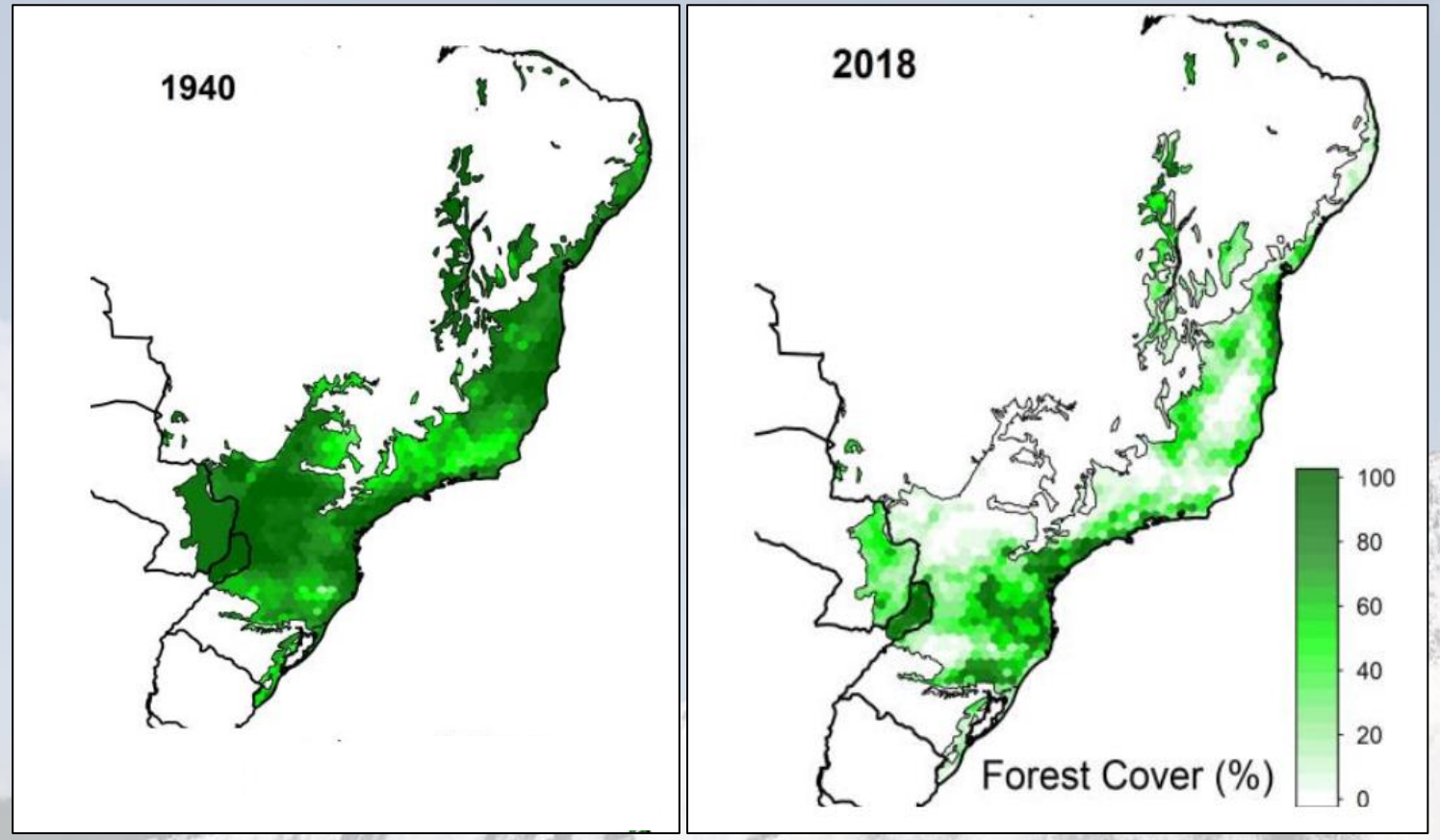


Fig. S1. The evolution of the percentage of forest cover per grid cell (0.5o of resolution) showing the deforestation patterns in the Atlantic Forest biodiversity hotspot. Forest cover was extracted from the ESA Land Cover series for the period between 1992 and 2018 and from historical reconstructions of land use for the period between 1940 and 1990 (see Methods for details). Average proportion of forest cover are: 1940= 79.8%; 1950= 75%; 1960= 68.2%; 1970= 58.9%; 1980= 47.4%; 1992= 29.6%; 2000= 29.1%; 2010= 29.5%; 2018= 29.7%. For all panels, bold lines are the limit of South-American countries and black lines are the limits of the Atlantic Forest. Maps projected using SIRGAS 2000 (EPSG:5641; Ellipsoid: GRS 1980).

de Lima et al., Science 383, 219–225 (2024) 12 January 2024. Supplemental Material.

Bioprospection: How and For What?

- How?: Bring collaboration to new levels of all parts. Develop creatively the red sections
  - ✓ Sample acquirement
  - ✓ Knowledge banks
  - ✓ Sample storage: biobanks (and explore other ways)
  - ✓ Sample analytics: taxonomy, HT screening, chemistry, genomics, etc.
  - ✓ Data storage, Bioinformatics, and analysis: analysis of systems
- **Improvement needed**
  - ✓ **Function search: predictive models**
  - ✓ **Regulatory framework**
  - ✓ **Industrial scaling up**
  - ✓ **Creative market generation**
  - ✓ **Business models: venture capital, long term investments, Angels**

Bioprospection: How and For What?

- For What?:
  - ✓ Improve people's livelihood
  - ✓ **Conservation of Biodiversity**
  - ✓ Improve knowledge about species
  - ✓ Conservation and restauration of nature
  - ✓ Improve health
  - ✓ Improve medicines
  - ✓ Promote One Health
  - ✓ Understand the systems of interactions in nature
  - ✓ **Create new markets based on new concepts of products**
  - ✓ **Think of new uses of biodiversity products**
- **Finally: provide a chance for survival**

Conclusions

If the goal is to save biodiversity and biomedicine for future generations, then:

- Cooperation and coordination of efforts should increase on all levels
- Overall efforts should be ramped up: public and private
- Global North and South should work together as equal partners
- Partnerships should be fair and just
- New Medicines: Look at nature for new predictive models to answer medical needs
- Consider a creative pharmacology that is guided by the observation and study of human physiological extremes
- Identify new uses and create markets for biodiversity products: think "out of the box "