



# The 8<sup>th</sup> Asia Partnership Conference of Pharmaceutical Associations

## Drug Discovery Alliances Session -Revitalization of Drug Discovery Using Natural Products by Open Innovation in Asia

### Taiwan Natural Products Resource Platform

**Yang-Chang Wu (吳永昌)**

Chair Professor

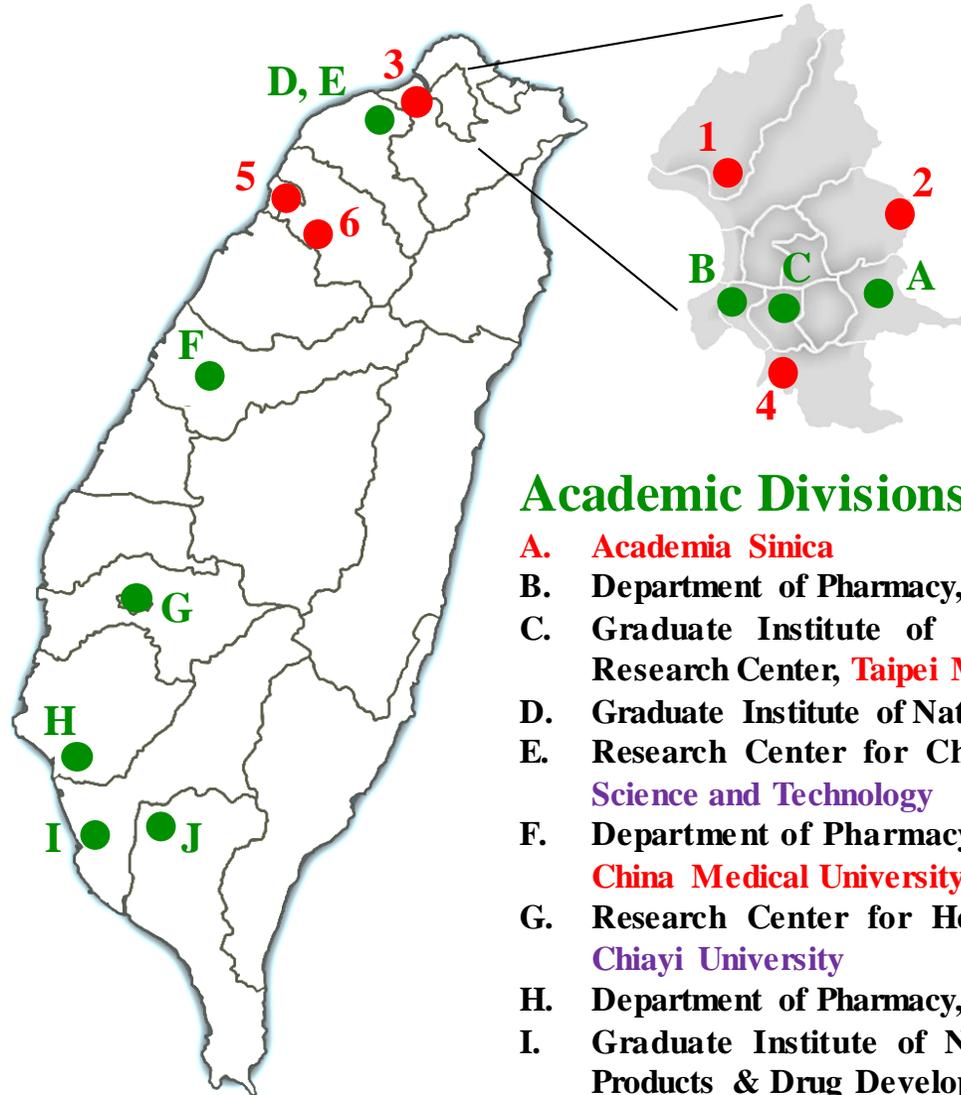
Graduate Institute of Natural Products

Kaohsiung Medical University

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# Terrestrial Natural Products Research in Taiwan



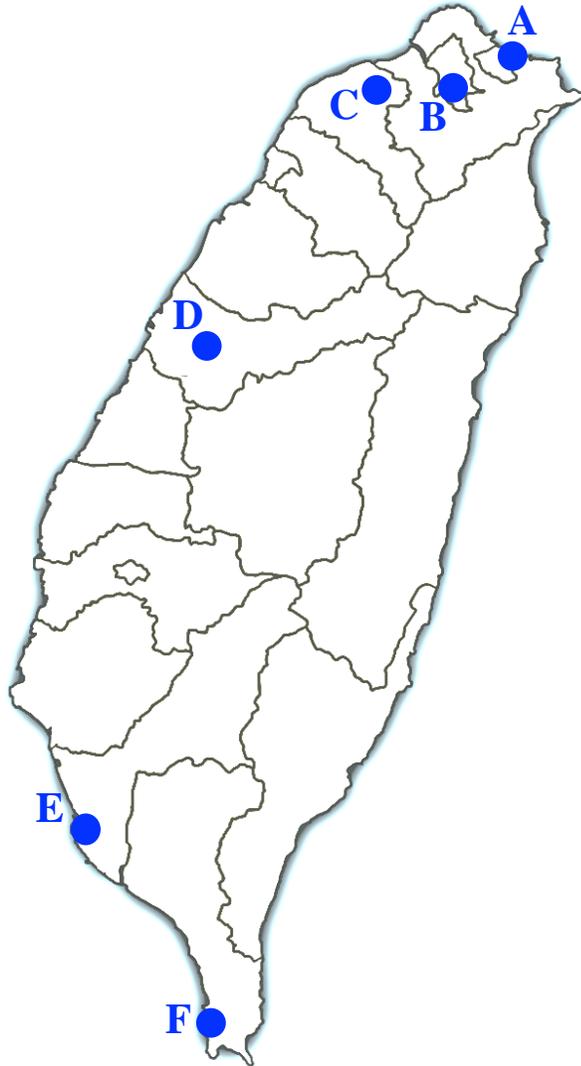
## Research Institutions

1. National Research Institute of Chinese Medicine
2. Development Center for Biotechnology
3. Medical and Pharmaceutical Industry Technology Development Center
4. Brion Research Institute of Taiwan
5. Food Industry Research & Development Institute
6. Industrial Technology Research Institute

## Academic Divisions

- A. Academia Sinica
- B. Department of Pharmacy, National Taiwan University
- C. Graduate Institute of Pharmacognosy and Traditional Herbal Medicine Research Center, Taipei Medical University
- D. Graduate Institute of Natural Products, Chang Gung University
- E. Research Center for Chinese Herbal Medicine, Chang Gung University of Science and Technology
- F. Department of Pharmacy and Research Center for Chinese Herbal Medicine, China Medical University
- G. Research Center for Herbal Medicine and Microbial Utilization, National Chiayi University
- H. Department of Pharmacy, Chia Nan University of Pharmacy and Science
- I. Graduate Institute of Natural Products and Research Center for Natural Products & Drug Development, Kaohsiung Medical University
- J. Department of Pharmacy and Service Center of Herbal Medicine and Bio-Health Industry, Ta Jen University

# Marine Natural Products Research in Taiwan



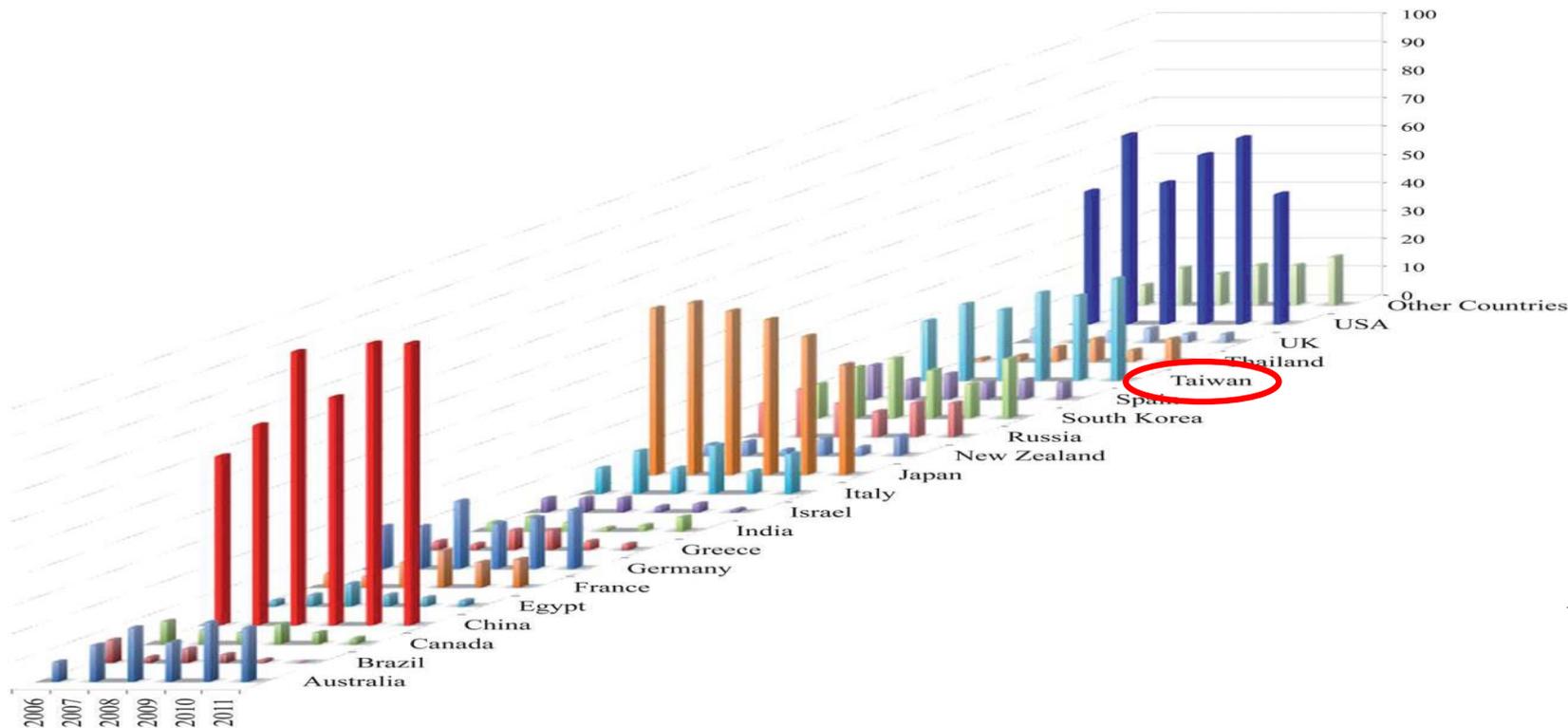
## Academic Divisions

- A. Department of Bioscience and Biotechnology, **National Taiwan Ocean University**
- B. Institute of Fisheries Science, **National Taiwan University**
- C. Research Center for Chinese Herbal Medicine, **Chang Gung University of Science and Technology**
- D. Department of Pharmacy and Research Center for Chinese Herbal Medicine, **China Medical University**
- E. Department of Marine Biotechnology and Resources, **National Sun Yat-Sen University**
- F. Graduate Institute of Marine Biology, **National Dong Hwa University / National Museum of Marine Biology and Aquarium**

# Highlight

Royal Society of Chemistry released a statistical analysis on Marine Natural products chemistry publications between 2006 and 2011:

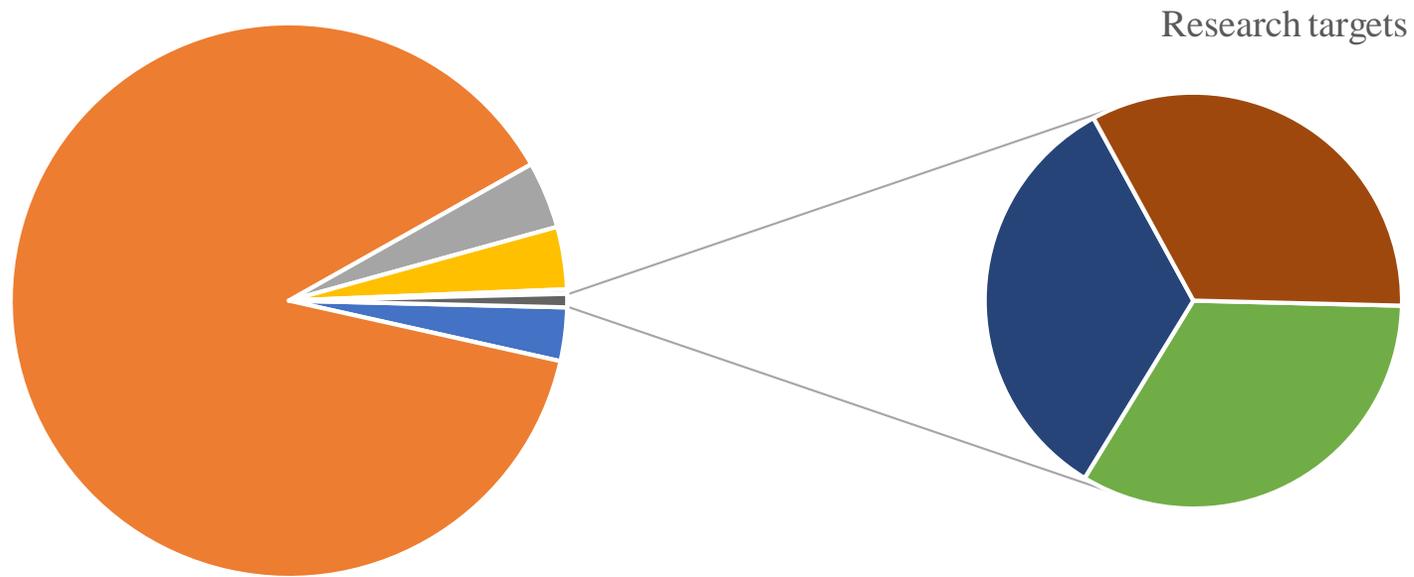
The total number of **research papers from Taiwan ranked fourth**, **average number of compounds reported per paper the first**, **number of citation the third** in the world.



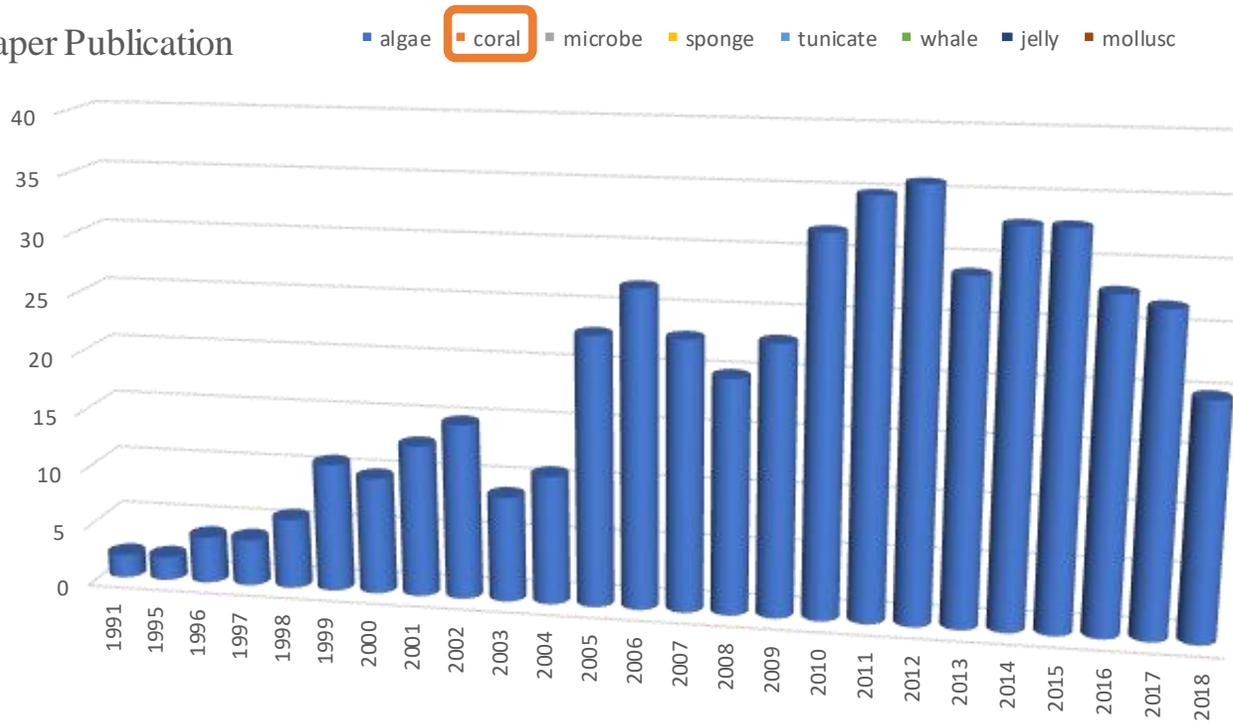
## Population

China:	1,350,000,000
USA:	310,000,000
JPN:	126,000,000
TWN:	23,000,000

*Nat. Prod. Rep.*, 2013, 30, 237

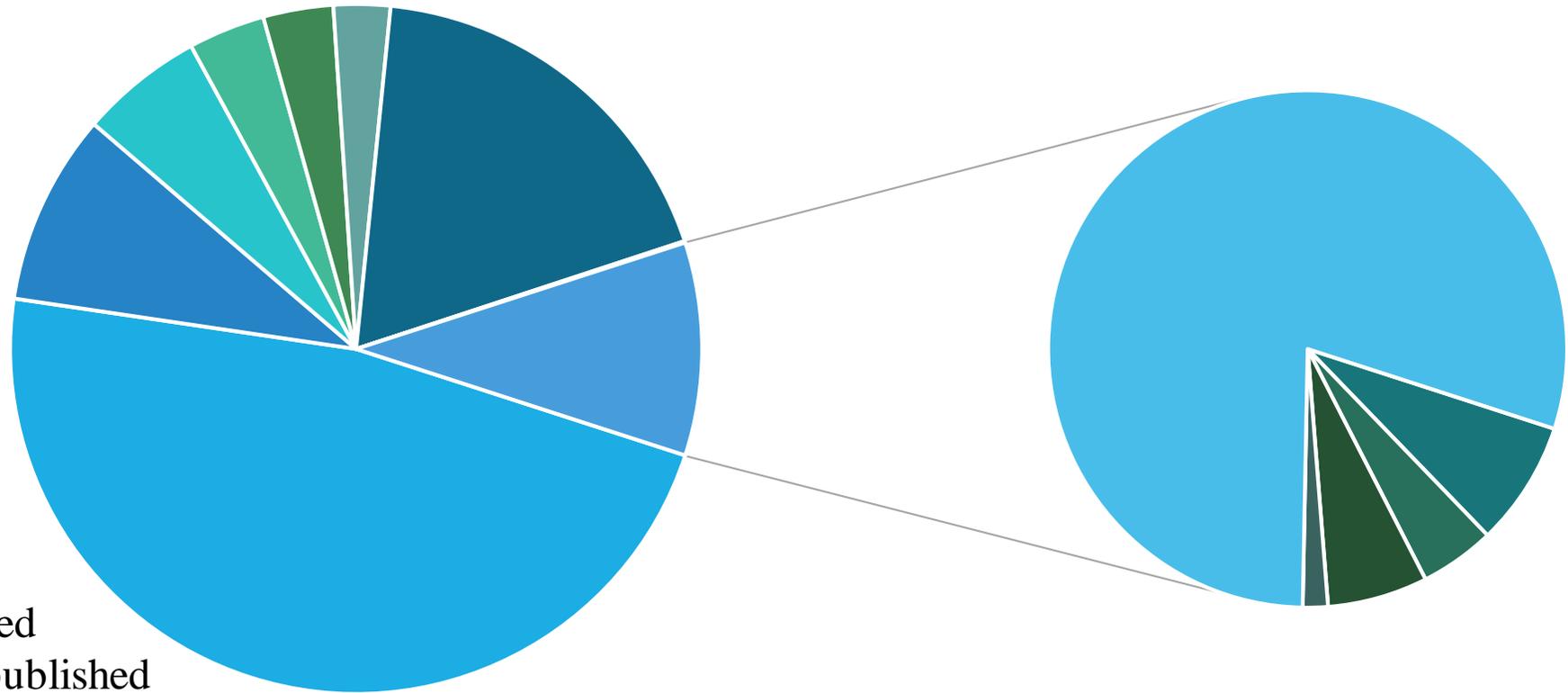


Paper Publication

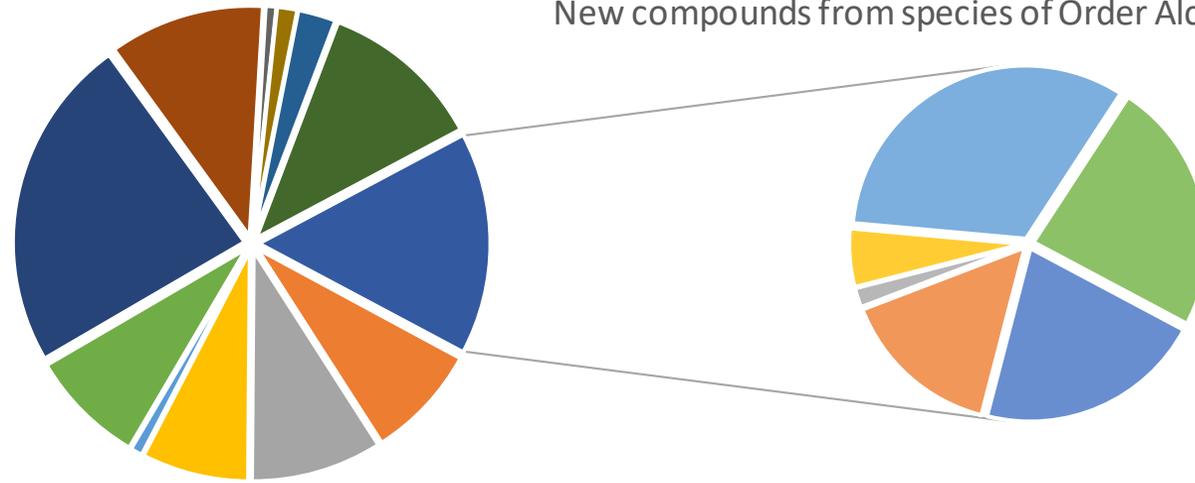


- > 500 papers publication
- Most are about the soft corals

13 Family  
99 species  
> 3000 compounds isolated  
1278 new compounds published



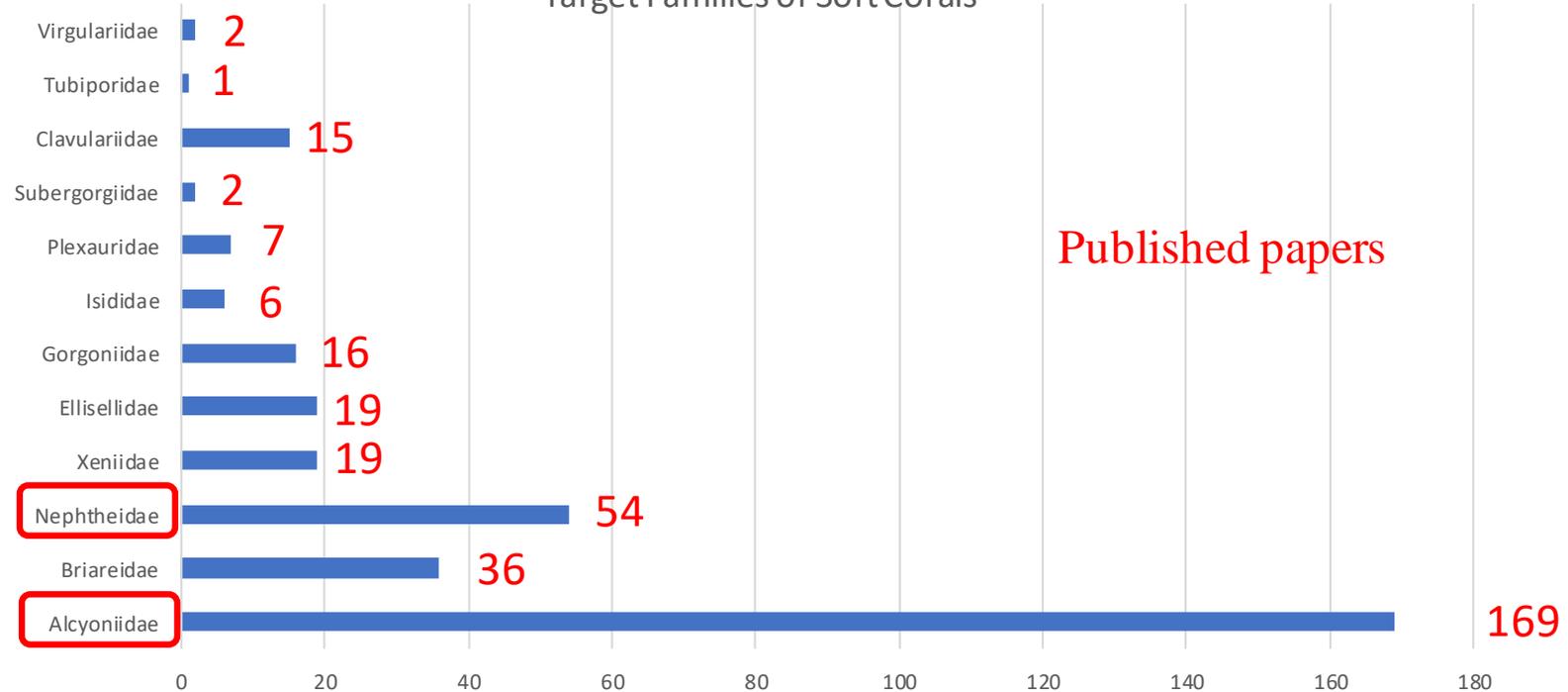
### New compounds from species of Order Alcyonacea

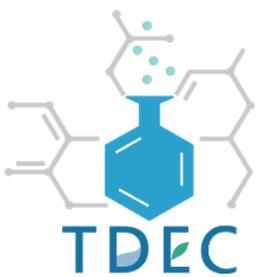


Studied Genera

海筆科  
 笙珊瑚科  
 羽珊瑚科  
 軟柳珊瑚科  
 網柳珊瑚科  
 竹珊瑚科  
 柳珊瑚科  
 鞭珊瑚科  
 傘軟珊瑚科  
 穗珊瑚科  
 皮軟珊瑚科  
 軟珊瑚科

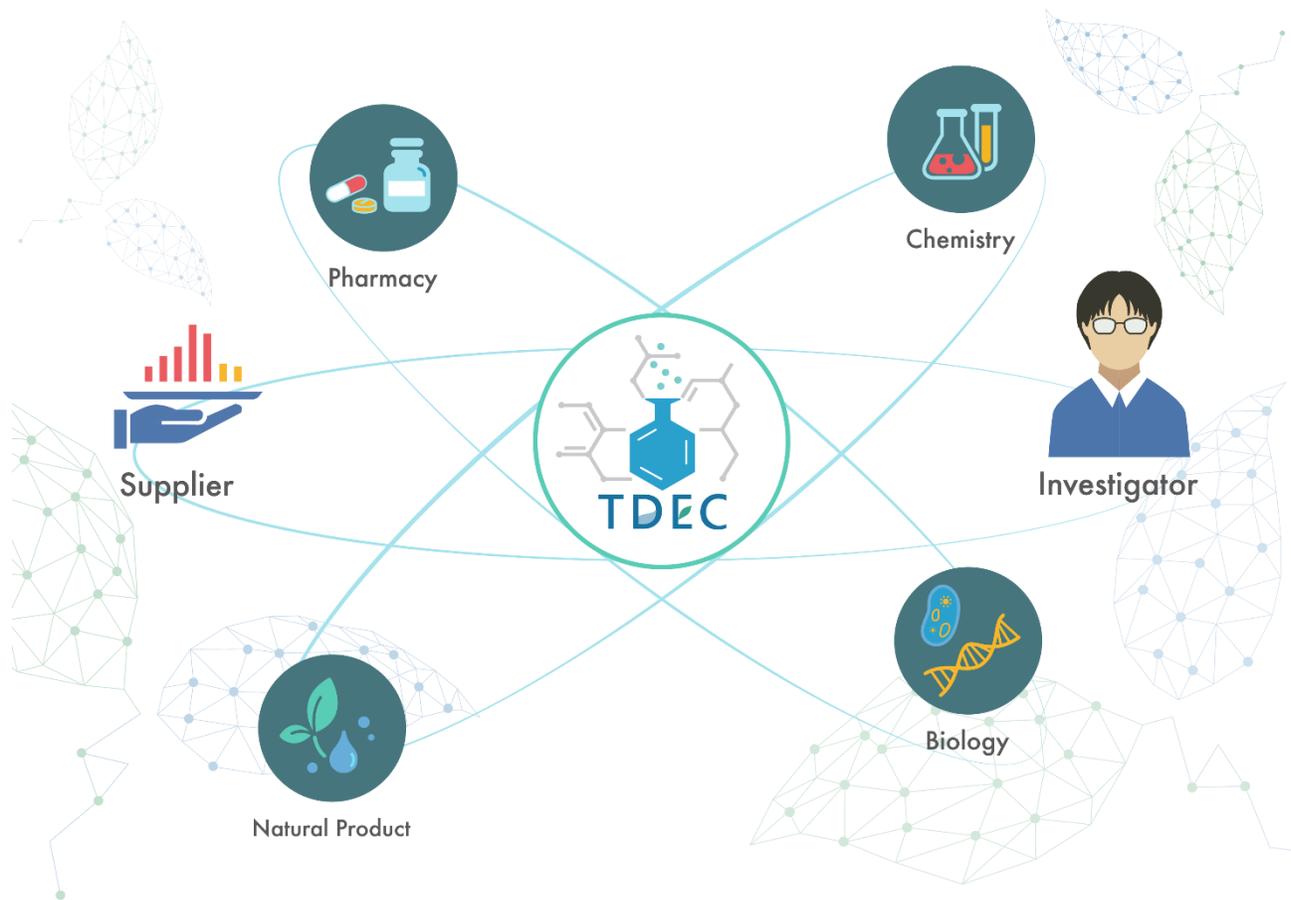
### Target Families of Soft Corals





# 台灣藥物樣品資料庫

Taiwan Database of Extracts and Compounds



**Welcome to TDEC And Join It!**

<https://tdec.kmu.edu.tw>

TDEC is a new concept for research information networking between natural products' suppliers and research investigators

**Compounds: 1,751** (2019.04.02 update)

# Taiwan Natural Products Library

- **Academia Sinica-**  
**Genomic Research Center (ca. 300,000 )**
- **National Research Institute of Chinese Medicine-**  
**Division of Chinese Medicinal Chemistry**
- **Development Center for Biotechnology-**  
**Institute of Chemical Pharmaceutical (ca. 3,000 )**
- **Industrial Technology Research Institute-**  
**Biomedical Technology Research Laboratories (ca. 130,000 )**
- **China Medical University-**  
**Research Center for Chinese Herbal Medicine**
- **Kaohsiung Medical University-**  
**Graduate Institute of Natural Products (ca. 1,750)**
- **Brion Research Institute of Taiwan**

# **Challenges** of Natural Resource

A young green plant with several leaves is growing out of a patch of cracked, dry earth. The background shows a cloudy sky with a warm, golden light, suggesting a sunset or sunrise. The overall scene conveys a sense of environmental stress and the struggle for survival in a dry, arid environment.

**Demand increasing**

**Unstable supply**

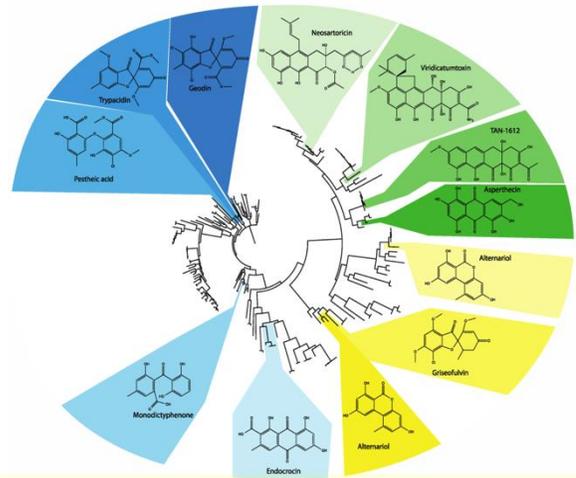
**Climate change**

**Plant disease**

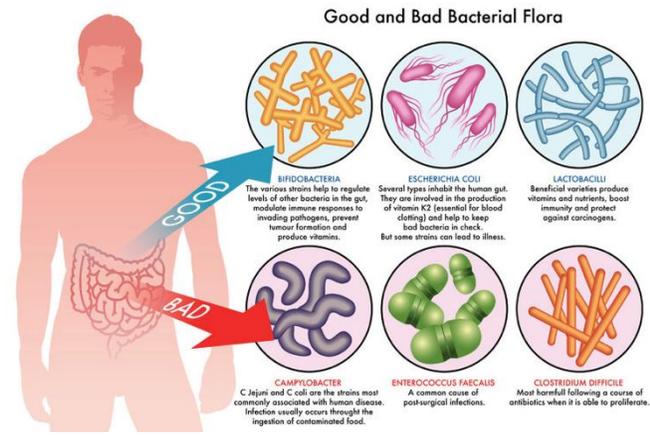
**Land competition**

# Microbial COMPOUND BANK

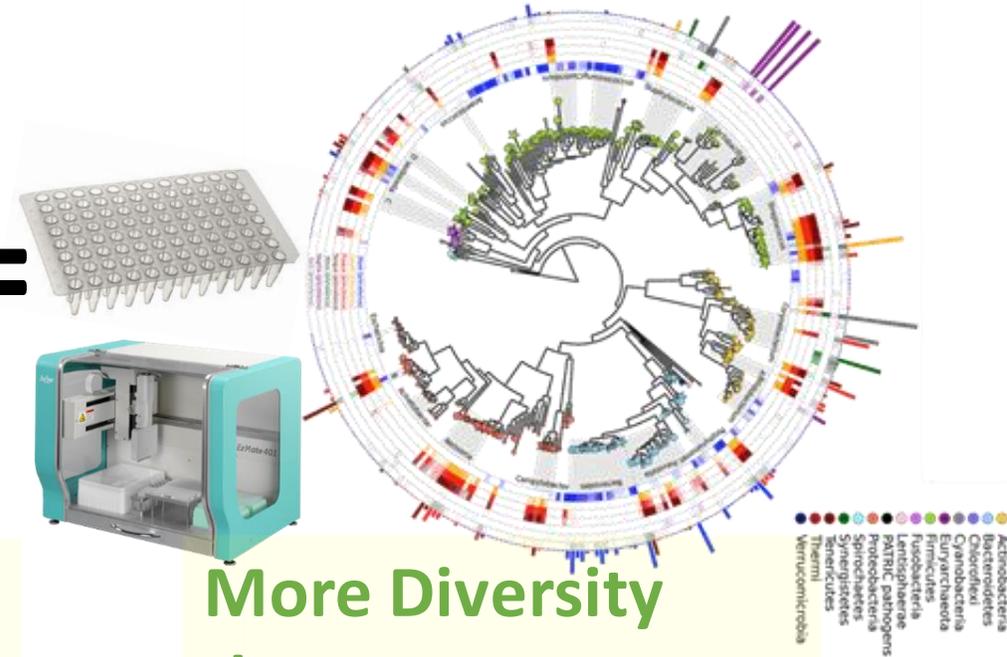
Microbial compounds producing is desperately in need.



X



=



**Biodiversity of Gene Library:**  
Evolutional pathways combinational natural enzymes of metabolic pathways to produce secondary metabolites

**Biodiversity of Probiotics Library:**  
Co-culturing probiotics combinational safety bacteria with functional secondary metabolites

**More Diversity than Nature:**  
Synthetic pathways are installed in functional probiotics library

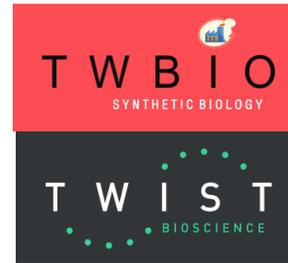
# Natural compounds biology platform



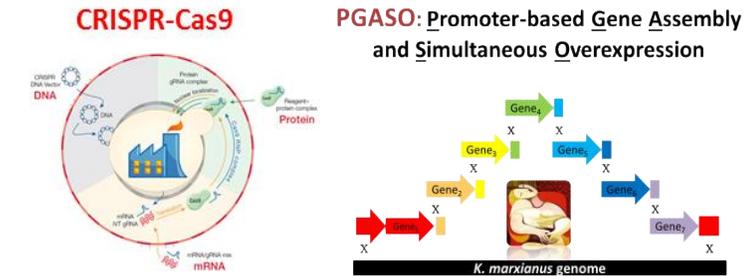
Natural products functional genomic data mining



Gene library synthesis & Building blocks constructing



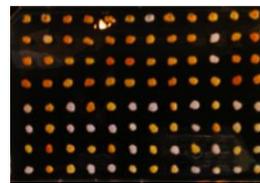
Host Engineering



Probiotics metagenomics & Strain isolation



Probiotics library collection & Functional screening



CRISPR-Cas9 (Delete GENES)  
PGASO (install Pathway)

Artificial pathway design & Automatic systems

The combination of probiotic library and artificial designer pathway will be functionally screened by automatic systems. After sequence validation, more diversity than natural compounds is possible and available for mass production.

More diversity than nature is possible & Mass production is available



# Probiotics biofactory



Traditional algae culturing

# 30 days



Natural Astaxanthin  
\$7,500/kg



Compare to traditional method

# 1/10 Turnover

# 1/20 Space

# 1/30 Water

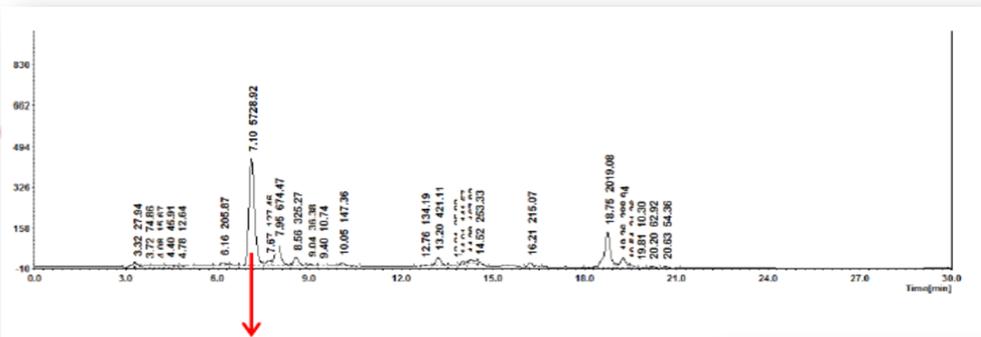
# 100% Function

# 3 days

# Purification & Identification



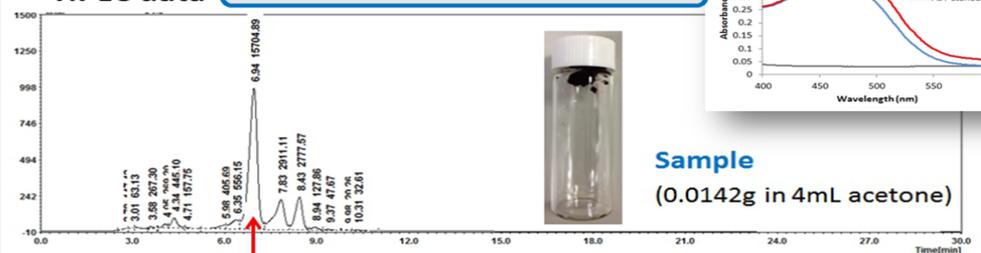
*CaroRED 2.0* is a high-quality of free form 3S, 3S' astaxanthin followed by other carotenoids such as canthaxanthin and  $\beta$ -carotene. It is extracted by supercritical carbon dioxide or ethanol extraction for application of hard capsules or tablet compression.



Astaxanthin: 24.2 mg/L

HPLC data

3S, 3'S astaxanthin 純化

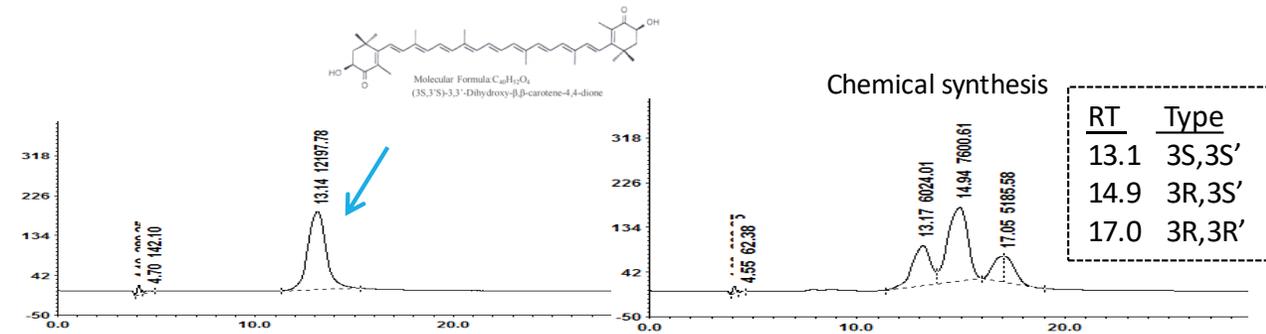
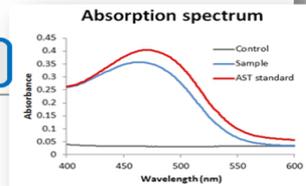


Astaxanthin 61.6%



Sample

(0.0142g in 4mL acetone)



3S, 3'S Astaxanthin has higher antioxidant activity than the 3R, 3'R and the 3R, 3'S stereoisomer. We can purify higher than 60% 3S, 3'S Astaxanthin.

# Purification & Identification



- Natural medicine pathway design
- Reliable compound editing
- Anti-microbial, Anti-cancer, Me better drug library
- Package and Purification



本頁標題：此次又增加生樟芝的幾張