

2016 新世代高通量生物醫學數據 之實驗設計，資料分析與結果記錄



LAB OF System Biology & Network Biology

中央研究院資訊科學研究所

@iis, Academia Sinica, TAIWAN

系統生物學與網路生物學實驗室



中央研究院
資訊科學研究所
Institute of Information Science
Academia Sinica



國家衛生研究院
National Health Research Institutes

林仲彥

Chung-Yen Lin

Oct 27, 2016

高通量生物學 (*High Throughput Biology*) 的時代來臨

新世代生化分析技術的進展，遍及在癌症醫學、臨床檢驗與生農醫藥的研究等各種生命科學領域，如全基因體序列、個人化基因差異、基因表現概況、蛋白質與代謝質體等，這些研究產生的資訊以 Big Data 的形式快速累積。

以基因體資料來說，隨著定序技術的快速演進，資料的快速成長，讓數據的傳送、儲存與計算，及多維度資料的整合與可視化等，已變成生物醫學研究人員無法閃避的數位障壁，必須仰賴與資訊科學家的合作，結合相關資訊技術、演算法的協助與新一代數據分析平台的開發，才能解決複雜的生命奧秘。



Bioinformatics in



中央研究院
資訊科學研究所
Institute of Information Science
Academia Sinica

• 資訊科學研究所生物資訊實驗研究群

Principal Investigators:

施純傑 Arthur Chun-Chieh Shih(Chair)

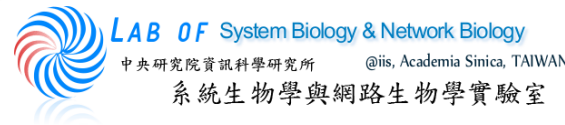
何建明 Jan-Ming Ho

宋定懿 Ting-Yi Sung

林仲彥 Chung-Yen Lin

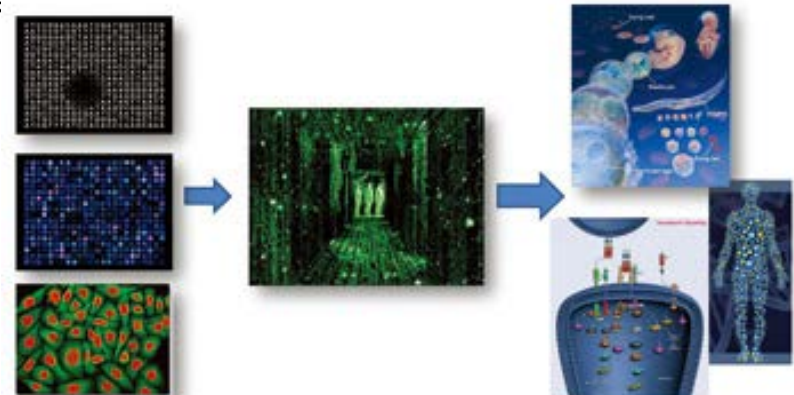
許聞廉 Wen-Lian Hsu

蔡懷寬 Huai-Kuang Tsai



• 我們的研究是以資訊技術為主，針對不同生物體學(omics) 上的生物醫農問題進行解析，大致分為:

- 利用新世代序列定序儀進行基因體和轉錄體分析
- 基因體/ 轉錄體重組演算法與程式開發
- 調控機制與網路
- 質譜儀分析的蛋白體學及代謝體學
- 蛋白質結構與功能預測
- 蛋白質交互作用網路分析
- 膜蛋白知識庫平台
- etc....





IT Innovations for Better Life

以創新資訊技術來增進生命品質



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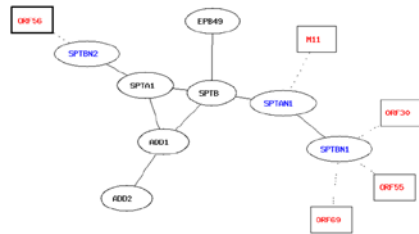
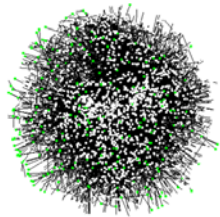
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系統生物學與網路生物學實驗室

研究成果(2014-2016)

① 以系統生物學策略分析病毒感染機制 (Virus-host interactomics/ transcriptomics: from network biology to bench research)

- 與UCLA腫瘤病毒研究室合作，分析流感、B/C型肝炎與乳突病毒等用藥前後病毒序列變異與抗藥性之關係，及與人類細胞之交互動態網路，還有鑑別出可供新藥物設計使用之高保守區域 (*PLoS Pathogens*, 2014, *Scientific Reports*, 2014, *mBio*, 2014)



UCLA

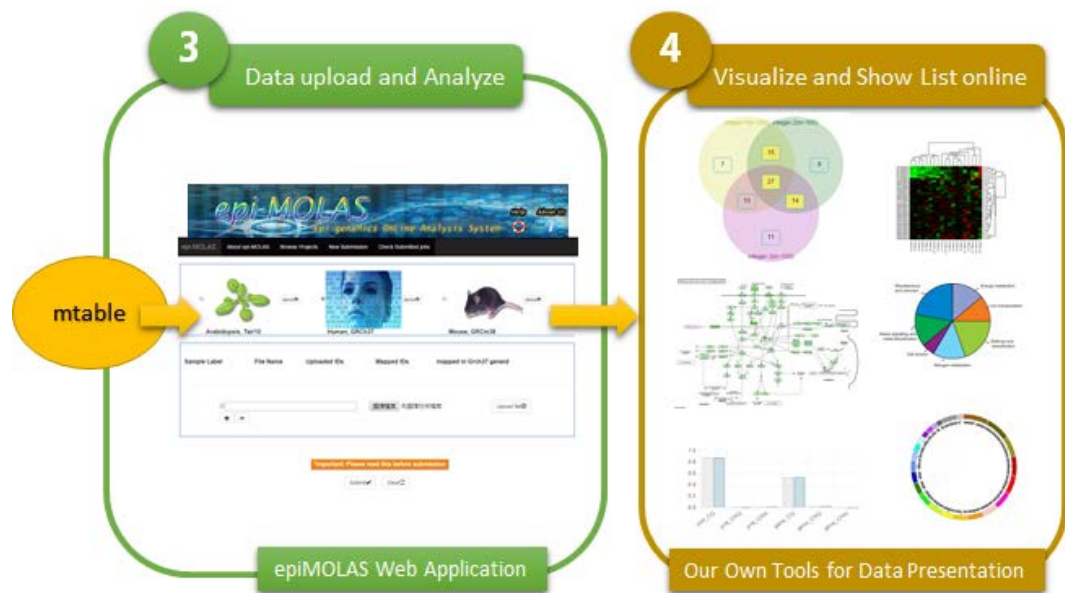
② 發展電子實驗記錄本(Developing Electronic Laboratory Notebook (ELN) for Research Community for Knowledge Management)

- 微軟公司贊助提供MS AZURE雲端平台兩年無償使用權 (2011-2013)
- 已研發各式平台之電子實驗室記錄本自動安裝程式，並有多國語系版本，live-DVD等，雲端平台等，支援手機等移動式裝置。



全基因體甲基化雲端分析平台

甲基化為調控基因表現的關鍵因子，也是同一套遺傳物質在不同發育階段下，其分化成不同組織的重要依據，是目前相當炙手可熱的研究主題，也是相關多維體醫藥研究的切入重點。然而，對於甲基化本身的分析及結果的呈現，目前並沒有合適的解決方案，於是本團隊與院內植微所的陳伯仰博士合作，協同開發了**第一個從原始定序數據開始，到結果圖像化呈現的完整分析平台**，將能大大減少傳統全基因體甲基化分析所需的時間，讓使用者能更專注在分析結果背後所代表的生物意義。本計畫將於未來結合基因表現之轉錄體資料與蛋白質交互作用網路，希望能更直接的呈現甲基化與基因調控之間的複雜關連，提昇多維基因體分析的精準度。



<http://symbiosis.iis.sinica.edu.tw/epimolas>

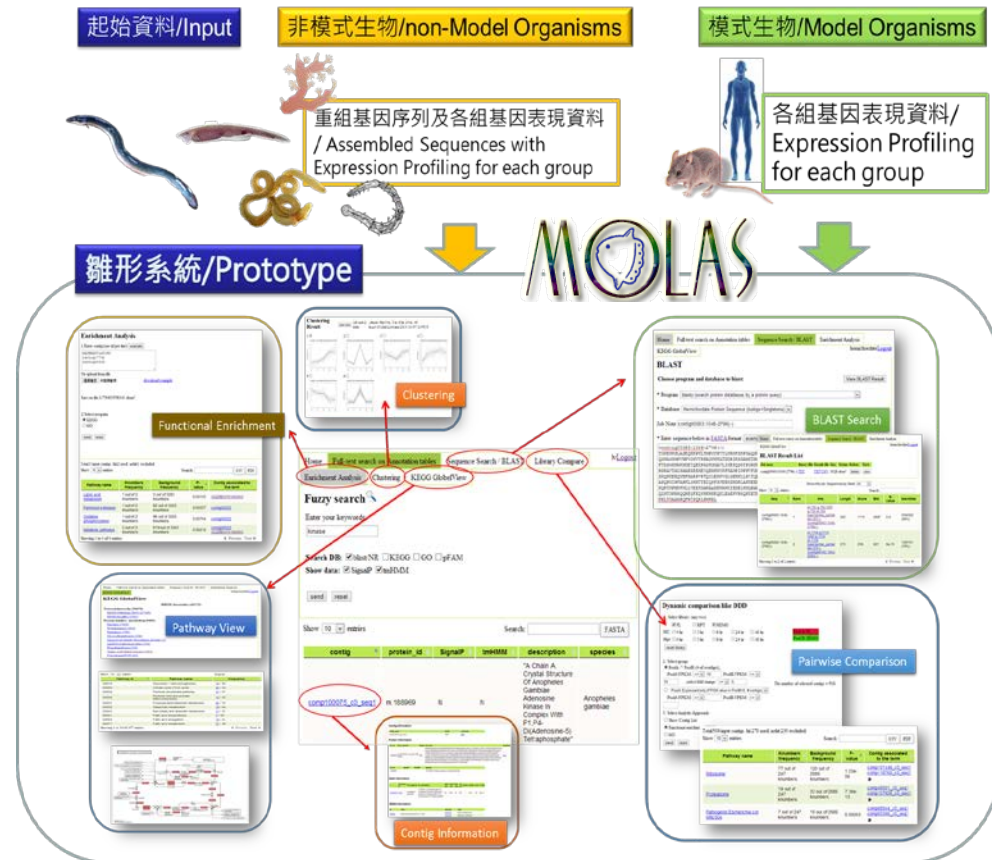
Publications: **BMC Genomics**. 2016 (to Appear).

Patent Application: **NA**

Technology Transfer: **NA**

Develop Platforms for Omics Studies

- MOLAS, Multi-Omics onLine Analysis System, a robust web application which can take gene expression data as inputs, map these expressed genes with build-in annotations for further analyses and unlock biological meaning of the complex data in an intuitive interface.
- MOLAS can be applied to identify those genes with specific expression profiling and tell the possible story inside.
- The Broad Institute in USA also developed similar system named as TrinotateWeb. But this system is hard to install and don't provide friendly interface and proper annotations to satisfy the requests for analysis.



MOLAS作為轉錄體解析與線上資料庫的快速建置平台

蠕蟲頭部再生機制研究



Name:
Password:

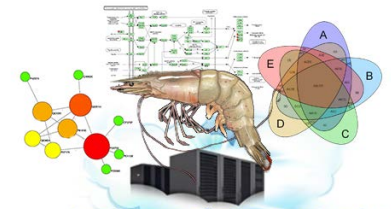
重組序列
Assembly



重組序列與其基因表現
Assembly + Expression



白蝦轉錄體與抗病機制之探討



LandScape of Transcriptomics
for Litopenaeus vannamei

Name:
Password:

Home Full-text search on Annotation tables Sequence Search / BLAST Library Compare [lvLogout](#)

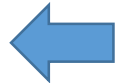
Enrichment Analysis Clustering KEGG GlobalView

Fuzzy search

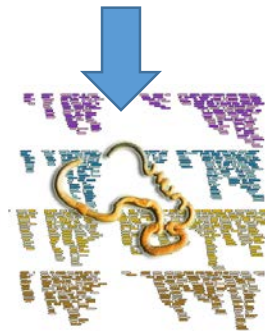
Enter your keywords:

Search DB: blast/NR KEGG GO pFAM
Show data: SignalP tmHMM

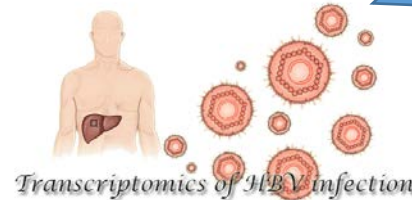
MOLAS



Name:
Password:



Name:
Password:



Name:
Password:



Name:
Password:

日本鰻幼體營養需求與優良種鰻之鑑別

半索動物發育機制研究

肝炎病毒致病機制之研究

早發型乳癌基因表現分析

技轉授權國內生物科技公司使用(非專屬授權)

<http://molass.iis.sinica.edu.tw>

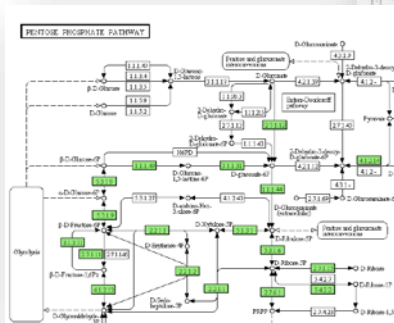
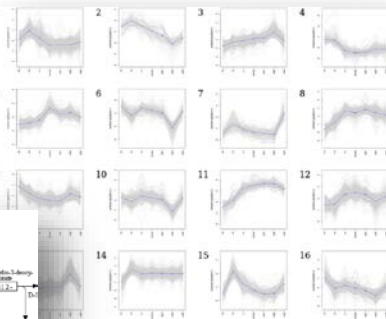
建構高經濟沉香木基因體資料庫

建構全球第一個沈香木的基因體資料庫，並透過光照類型的變化，以轉錄體的角度，來瞭解如何透過外界環境控制來影響香氣相關的二次代謝物的生成。本資料庫將能作為後續相關研究的基本基因底圖資料，提供全球沈香研究社群使用。



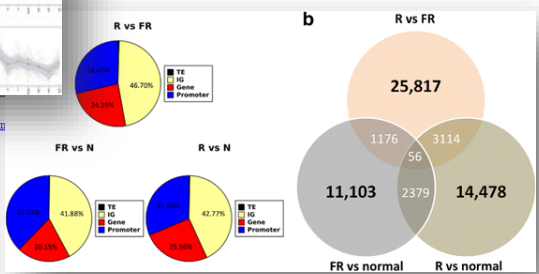
Agarwood is a resinous heartwood of agarwood producing tree species have perfumes, and especially Chinese herbs potentially have beneficial properties.

In this website, we try to present the transcriptome in keywords (Full text: those differential expressed genes and provide the global view on KEGG path



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economic value of these trees and extensive deforestation, many cultures, from religious ceremonies as incense, to medicinal compounds, but also in its non-volatile compounds, which are used in traditional medicine. Researchers can search the whole transcriptome in keywords. Using the functions of Library comparison and Clustering, and sent to perform analyses in deep. Meanwhile, we also provide the KEGG functional hierarchies.



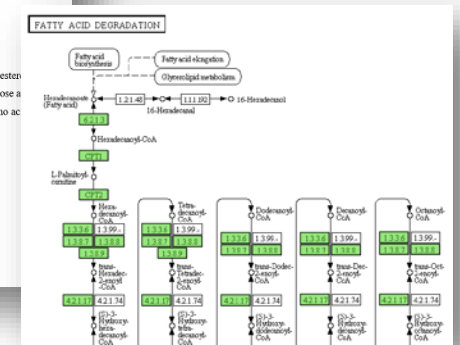
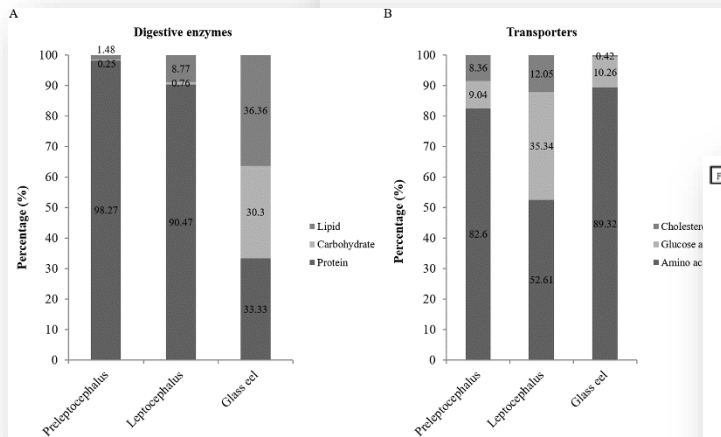
<http://molas.iis.sinica.edu.tw/agarwood>

Publications: **BMC Plant Biology**, v15 : 139
 Patent Application: **NA**
 Technology Transfer: **NA**

日本鰻鰻線發育早期之轉錄體資料庫

隨著鰻魚資源量的枯竭，鰻魚生活史各個階段的基礎生物學研究，將是鰻魚完全養殖成功與否的重要關鍵，攸關台灣鰻魚養殖產業的存續。本研究提供全球第一個日本鰻鰻線轉錄體的線上資料庫，並以次世代基因表現資料來說明鰻魚幼體階段，其可能的能量代謝模式，將對日後幼鰻飼料開發提供重要參考依據，提昇人工培育鰻線的存活率，將對未來鰻魚完全養殖的成功有所助益。

Japanese eel (*Anguilla japonica*) is a high economical aquacultural species. This single species has contributed to Taiwan aquaculture industry for several hundred millions US dollar value, sustains for more than 40 years but declined in recent years. One major reason of this decline is the amount of wild captured evers decreased dramatically during the past decades. Consequently, the price of evel goes up that makes great impacts on the industry. Possible causes of this decline include over-fishing on the wild stock population, habitat destruction, water pollution, and global climate change. Although we had a wealthy know-hows about eel farming, pond management, and distribution of live goods as well as manufactured food, the whole supply chain of is greatly rely on the captured evers in brackish water zone. (Figure, modified from



Publications: PLoS ONE, 10 (9): e0139105
 Patent Application: NA
 Technology Transfer: NA

<http://molas.iis.sinica.edu.tw/jpeel>

人類大腸癌與其他罕見癌症致病成因的探討



Access

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[nature.com](#) > [Journal home](#) > [Table of Contents](#)

Original Article

Modern Pathology, (22 July 2016) | doi:10.1038/modpathol.2016.137

Characterization of FN1-FGFR1 and novel FN1-FGF1 fusion genes in a large series of phosphaturic mesenchymal tumors

Jen-Chieh Lee, Sheng-Yao Su, Chun A. Changou, Rong-Sen Yang, Keh-Sung Tsai, Michael T Collins, Eric S Orvold, Chung-Yen Lin, Shu-Hwa Chen, Shyang-Rong Shih, Cheng-Han Lee, Yoshinao Oda, Steven D Billings, Chien-Feng Li, G Petur Nielsen, Eiichi Konishi, Fredrik Petersson, Thomas O Carpenter, Kesavan Sittampalam, Hsuan-Ying Huang and Andrew L Folpe

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SEARCH PUBMED FOR

- Jen-Chieh Lee
- Sheng-Yao Su

www.impactjournals.com/oncotarget/

Oncotarget, Vol. 7, No. 29

Research Paper

Over-expression of *AURKA*, *SKA3* and *DSN1* contributes to colorectal adenoma to carcinoma progression

Tzu-Po Chuang^{1,2,10}, Jaw-Yuan Wang^{3,4,5}, Shu-Wen Jao⁶, Chang-Chieh Wu⁶, Jiann-Hwa Chen⁷, Koung-Hung Hsiao⁸, Chung-Yen Lin⁹, Shu-Hwa Chen⁹, Sheng-Yao Su⁹, Ying-Ju Chen¹⁰, Yuan-Tsong Chen¹⁰, Deng-Chyang Wu^{11,12,13}, Ling-Hui Li¹⁰

¹Taiwan International Graduate Program in Molecular Medicine, National Yang-Ming University and Academia Sinica, Taipei, Taiwan

²Institute of Biochemistry and Molecular Biology, National Yang-Ming University, Taipei, Taiwan

³Division of Gastroenterology and General Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

⁴Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

⁵Center for Biomarkers and Biotech Drugs, Kaohsiung Medical University, Kaohsiung, Taiwan

⁶Department of Surgery, Division of Colon and Rectal Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

⁷Department of Internal Medicine, Tzu Chi General Hospital, Taipei Branch, Taipei, Taiwan

⁸Department of Colorectal Surgery, Tzu Chi General Hospital, Taipei Branch, Taipei, Taiwan

⁹Institute of Information Science, Academia Sinica, Taipei, Taiwan

¹⁰Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

¹¹Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

¹²Department of Internal Medicine, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan

¹³Center for Infectious Disease and Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan

Correspondence to: Ling-Hui Li, email: ll@ibms.sinica.edu.tw

Deng-Chyang Wu, email: dcchwu@yahoo.com

Keywords: colon cancer progression, malignant transformation, *AURKA*, *SKA3*, *DSN1*

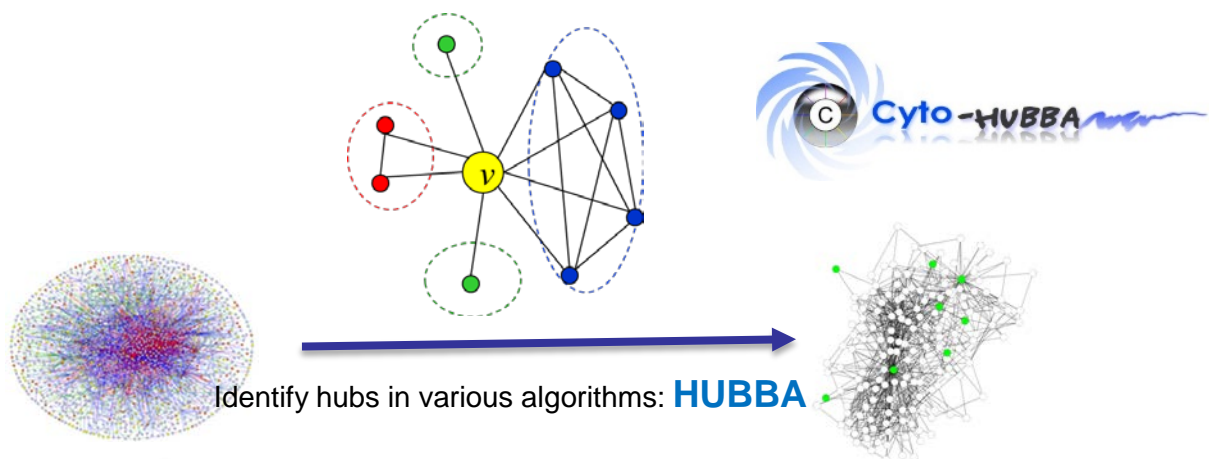
received: January 11, 2016

Accepted: May 28, 2016

Published: June 13, 2016

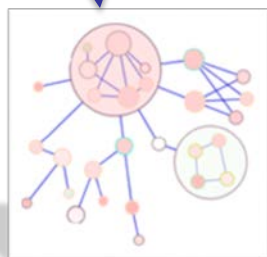
<http://molas.iis.sinica.edu.tw/>

Biological Network Analysis



Collaborated with
Prof. Ming-Ta Ko, IIS since 2008

Assemble protein complex: **Spotlight**



Hubba / Cytohubba: Discover what kind of network features are critical or essential for regulation and biological functions. For this goal, we have developed several new algorithms, published papers and wrapped them into web applications, like hubba and spotlight for biomedical research community. For running our works on most common platform for network analysis, cytoscape, we developed cytohubba as a plug-in in 3 our algorithms combined with other 10 popular topological methods. (BMC Bioinformatics, 2010, 2011, BMC Genomics, 2014)

Software Download ~8,800 times, Citations ~ 150 times

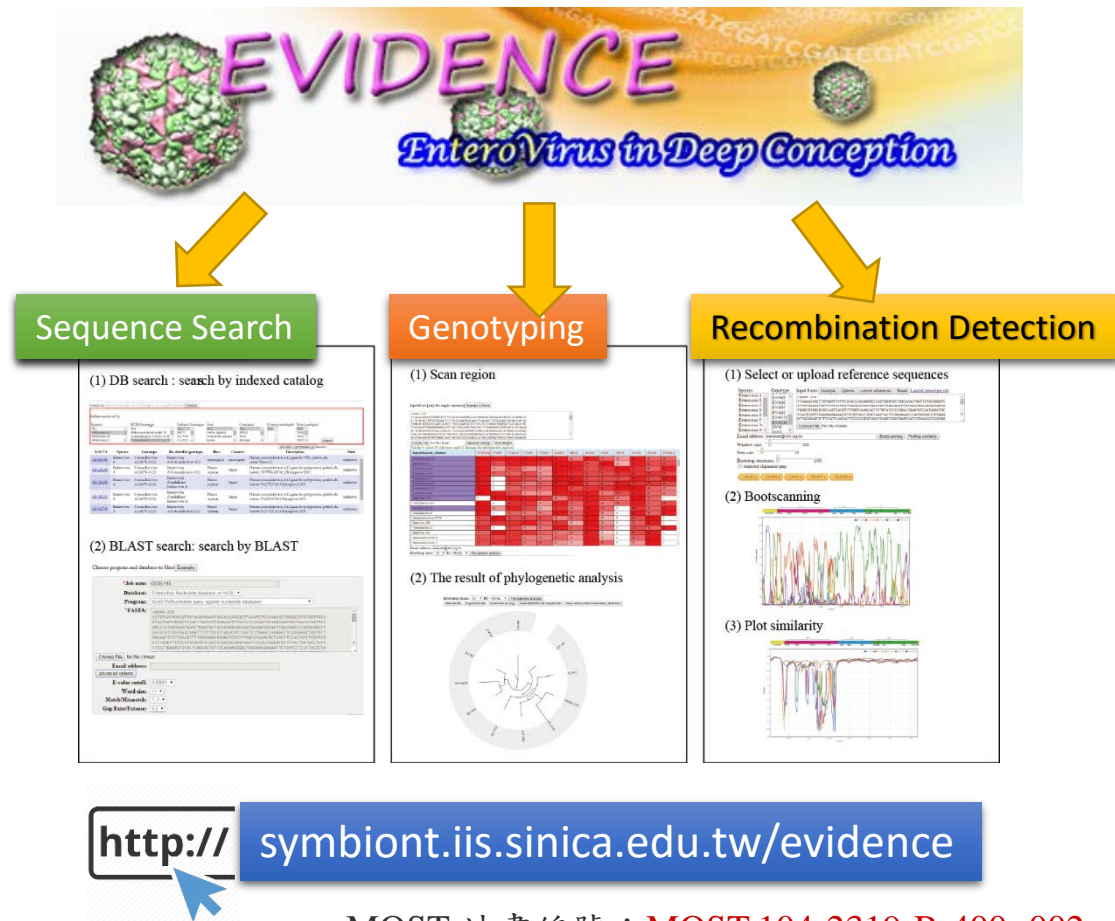
腸病毒自動分類系統與基因重組鑑別平台

本研究結合腸病毒過去數十年的血清學研究，與新一代的快速基因體定序所得之大量腸病毒全基因體之序列資料，建構了第一個腸病毒的自動分類系統與基因重組鑑別平台，可以透過臨床檢體的定序資料，以網路介面，進行線上的腸病毒類型鑑定，並觀察其基因片段是否與重症腸病毒相似，將提供臨床檢體的基因體快速分析流程，**以自行開發的演算法即時找出與重症相關的病毒品系與可能的基因重組狀況**，提供後續醫療的重要指標。本架構可運用於其他新興病毒之基因體研究。

Publications: **BMC Genomics**. 2015; 16(S12):S8.

Patent Application: **NA**

Technology Transfer: **NA**



MOST 計畫編號：MOST 104-2319-B-400 -002

NRPB 計畫編號：104

計畫主持人：林仲彥

Our Team Lead Two Genome Projects for Economic Important Organisms in Taiwan

➤ Giant Grouper

(タマカイ/龍膽石斑)

(*Epinephelus Lanceolatus*)

Over 7 billion NT dollars/ year



Supported by



創新轉譯農學研究計畫
Innovative Translational Agricultural Research Program

➤ Japanese Eel

日本鰻

(*Anguilla japonica*)

Over 10 billion NT dollars/ year



Supported by

科技部

Ministry of Science and Technology

Initiate Genome Projects for Economic Important Organisms in Taiwan

B : Knowledge of Biology

C : Bioinformatics/ IT



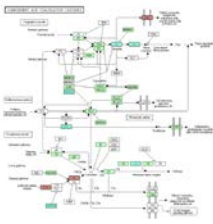
Supported by 

創新轉譯農學研究計畫
Innovative Translational Agricultural Research Program



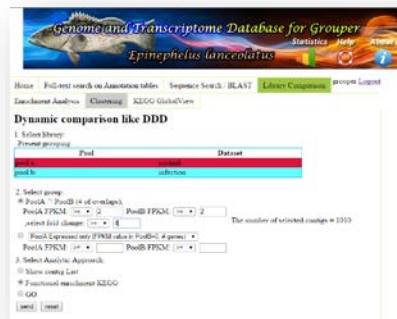
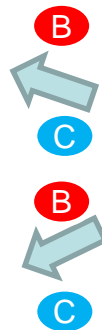
Physiological Regulation under Stress and infection

疾病防治



Genetic Breeding for Fries with disease resistance

分子育種



Construct Web database



Data integration and Annotation

Initiate Genome Projects for Economic Important Organisms in Taiwan

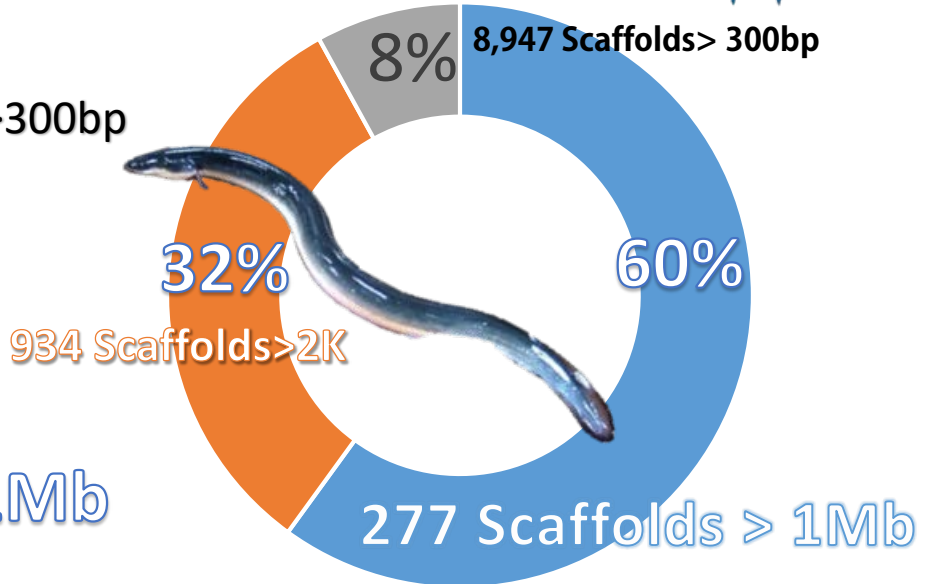
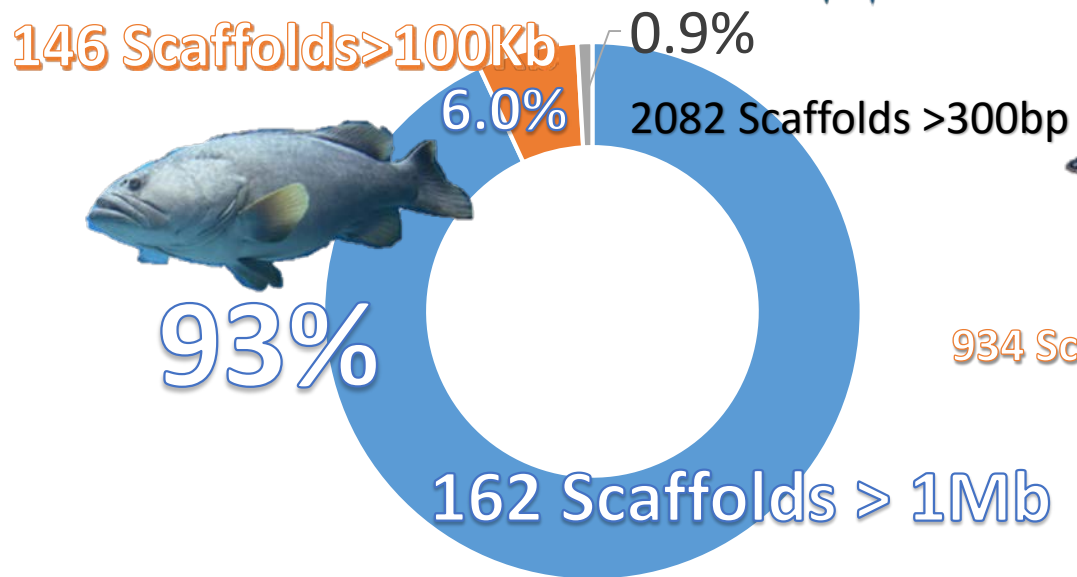
Grouper Genome Project

Most Complete genome for Grouper



Japanese Eel Genome Project

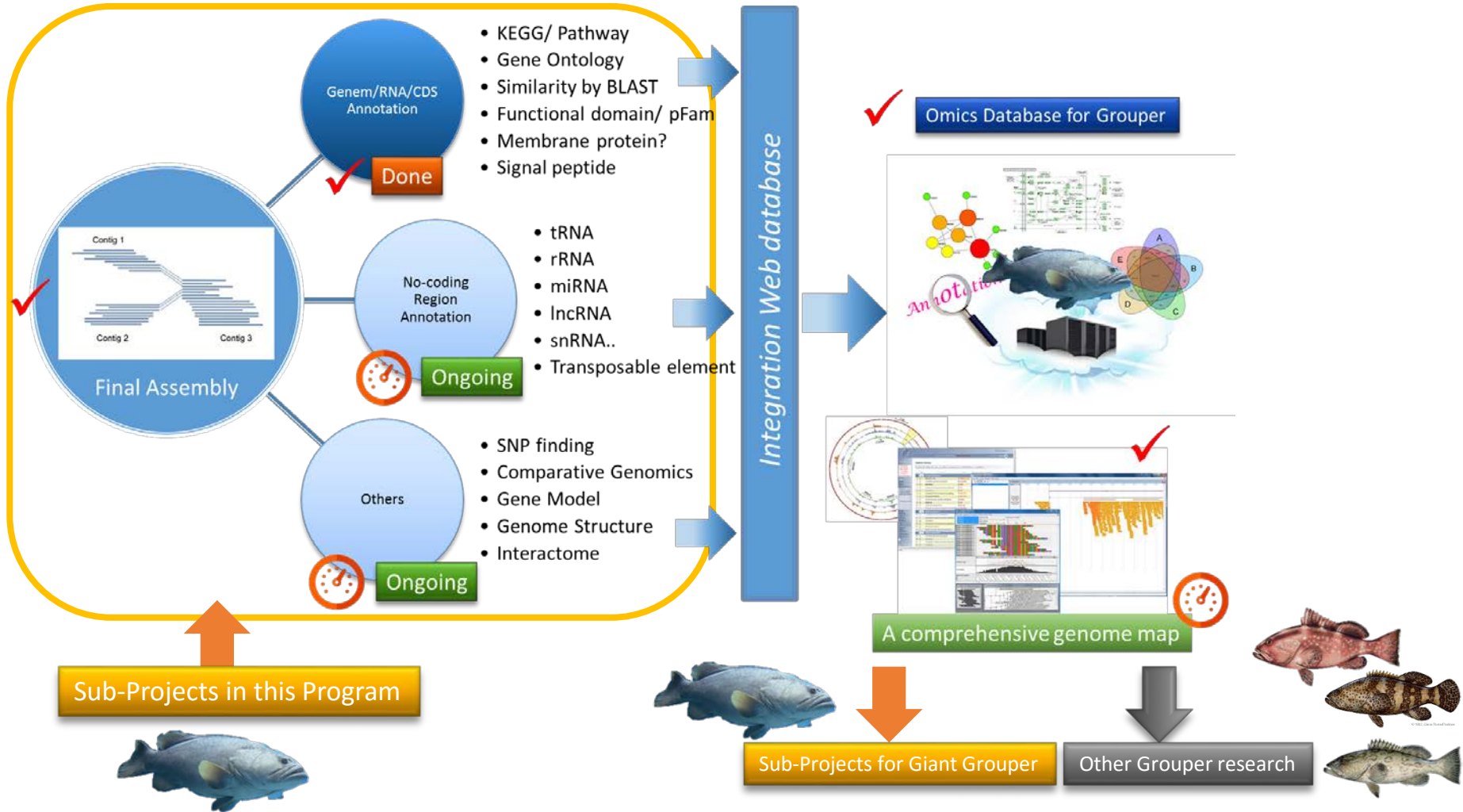
Most Complete genome for Japanese













Genome size: 1.06G
 N50: 5.1M base
 Coverage: 140x
308 Scaffolds for 99% Genome

Genome size: 1.20G
 N50: 1.4 M base
 Coverage: 150x
1,211 Scaffolds for 92% Genome

以龍膽石斑基因體為模版 來作為相近石斑之基因體與轉錄體研究平台



大型資料庫及資訊服務平台之 建立與營運

Web databases	Short Description & URL
	Database of Protein Interactome of <i>Helicobacter pylori</i> , <i>Bioinformatics</i> , 2005, http://dpi.nhri.org.tw/hp
	Database of Protein Interactome of <i>Drosophila melanogaster</i> , <i>BMC bioinformatics</i> , 2006, http://flydpi.nhri.org.tw
	Aftergenbank: Extraction of feature sequences from Genbank, http://aftergenbank.nhri.org.tw
	PAGE, Shrimp Genome Database, <i>Marine Biotechnology</i> , 2010, http://sysbio.iis.sinica.edu.tw/page
	Transcriptome of Coral with Symbiodinium, <i>Molecular Ecology</i> , 2014, http://ips.iis.sinica.edu.tw/coral/
	Transcriptome of Acorn worm, <i>Marine Genomics</i> , 2014, http://molas.iis.sinica.edu.tw/hemichordate/
	Genome and Transcriptome of Giant Grouper, http://molas.iis.sinica.edu.tw/grouper/
	Transcriptome of Japanese Eel, <i>PLoS ONE</i> , 2015, http://molas.iis.sinica.edu.tw/jpeel
	Genome and Transcriptome of Agarwood, <i>BMC Plant Science</i> , 2015, http://molas.iis.sinica.edu.tw/agarwood
	Multi-Omics onLine Analysis System (MOLAS), http://molas.iis.sinica.edu.tw

Web Applications/ Software	Short Description & URL
	Primer design Assistant (PDA), for PCR primer design, <i>NAR</i> 2003, http://dbb.nhri.org.tw/primer
	myBLAST: A BLAST Web Service and Standalone Program for Customized Databases and Result Analyzer with Parallel Computing, http://eln.iis.sinica.edu.tw/myblast
	POWER, phylogenetics web repeater, <i>NAR</i> , 2005, http://power.nhri.org.tw
	Spotlight, protein complex from biological networks, <i>Gene</i> , 2013, http://hub.iis.sinica.edu.tw/spotlight
	UPS, unique probe selector, for microarray and hybridization probe design, <i>BMC Genomics</i> , 2010, http://array.iis.sinica.edu.tw/ups
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	Hubba, Hub object analyzer for network biology, <i>NAR</i> 2008, http://hub.iis.sinica.edu.tw
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2016 新世代高通量生物醫學數據之 實驗設計，資料分析與結果記錄

9:40 - 10:50 黃智偉 先生 (Mr. Chi-Wei Huang)


電子實驗室記錄本/Elegance: Electronic Lab Notebook
on Cloud-- Digitize your experimental designs and
results into wisdom from Discovery to Publication

11:00 - 12:00 Shu-Hwa Chen Ph.D., 陳淑華 博士

次世代定序之線上基因概況與全基因體甲基化分析平台/
Multi-Omics onLine Analysis System (MOLAS) for
Expression Profiling and Whole genome Methylome



Thanks for your Attention

 **LAB OF System Biology & Network Biology**
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系統生物學與網路生物學實驗室