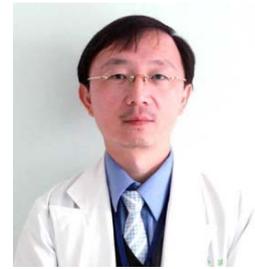


Chia-Ming Chang 張家銘 (IS1)



CURRICULUM VITAE

Chia-Ming Chang

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A. Education and Positions

- Assistant professor, Department of Medicine, School of Medicine, National Yang Ming University (2016)
- Ph.D., Institute of Oral Biology, National Yang Ming University (2016)
- Research fellow, Institute for Systems Biology, U.S.A. (2013)
- Attending, Division of Genetics and Prenatal Diagnosis, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taiwan (2007)
- Director of Cytogenetic Laboratory, Taipei Veterans General Hospital, Taiwan (2007)
- Fellow, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taiwan (2004)
- Resident, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taiwan (1999)

B. Research interesting

- Next generation sequencing (NGS)- and artificial intelligence (AI)-based personalized medicine

The majority of contemporary human health problems arises from complex diseases such as cancer or schizophrenia. The development of a complex disease usually involves multiple genetic aberrations. One major goal of personalized medicine is to recognize or predict complex diseases in order to prevent or treat them early and effectively. We have developed a method that can measure the joint effect of multiple variants on complex diseases by converting nearly 10 million of genome-wide SNPs to a functionome consisted of 5197 Gene Ontology-defined functions. With the

dimensionality problem solved, a machine learning algorithm, a form of Artificial Intelligence (AI), could then be trained to recognize, classify and predict disease susceptibility for complex diseases. In the future, we plan to complete the development of our AI model and to improve it on, especially, multi-class classification. More important, we aim to discover the deleterious cellular functions, as well as the involving genes/proteins, in disease susceptibility for various complex diseases. Our research will offer a big step toward realizing the goals of personalized medicine on complex diseases.

C. Professional Qualities

- Genomic medicine
- Personalized medicine
- Precision medicine
- Bioinformatics
- NGS analytics
- Programming with R language
- AI and machine learning
- Prenatal diagnosis
- Obstetrics and gynecology

An integrative analytics pipeline for clinical genome sequencing

Genome sequencing is a powerful tool to detect the genetic aberrations of congenital malformations because of its ability of examining all the genetic variations in human genome in a short time with a relatively low cost. However, processing the large amount of sequencing data produced by genome sequencing is a tricky task. Whole genome sequencing or exome sequencing will produce large amount of information containing approximately ten million variants or hundreds of thousands genetic variants, respectively. Correct annotation and precisely recognizing the exact genetic variants response for the congenital malformations from the data is the critical step for its clinical genome sequencing.

Currently, there is no agreed analytics pipeline for clinical genome sequencing. Based on our knowledge of genome medicine, experience of genome counseling and technique of data science, we have developed a bioinformatic pipeline to deal with clinical genome sequencing data. The pipeline is designed to meet the requirements of precise detection, comprehension, automation, integration, and scalability. In addition to generate legible results, it can also establish a native database, organize the analyzed data for further applications such as data mining or AI-based analytics.

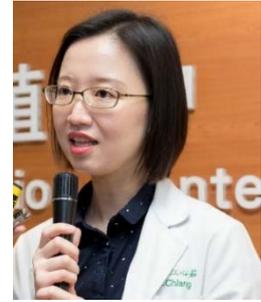
The principles and strategies are to find out all possible pathogenic variants as possible, annotate these variants using the latest genetic database, assess their sequencing qualities, and filter the genetic aberrations based on their evidence. Finally, these candidate pathogenic variants are selected by their correlation between the patient's clinical findings and laboratory tests.

Using this analytics system, we have analyzed more than 60 genome sequencing cases (whole genome or exome sequencing), including congenital malformations, cancers, and normal healthy persons. Among 29 congenital malformations, 86% (24/29) showed positive findings, including confirmed (9/29), associated (10/29) or suspected (6) genetic aberrations, the detection rate is 65.5% (confirmed and associated). For the 14% (4/29) undiagnosed cases, we will still follow up and re-analyze using the updated database every 6 months. The limitation of this system is false positive. But the false positive findings can be filtered out by clinical findings and laboratory tests.

In conclusion, with appropriate bioinformatic techniques and strategies, genome sequencing shows potential capability and is a recommended tool to detect the genetic variants for cases with congenital malformations.

Keywords: clinical genome sequencing, bioinformatic pipeline, congenital malformation

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CURRICULUM VITAE

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A. Education

1. Medical degree in China Medical University, School of Chinese Medicine, Taichung city, Taiwan
2. Attending physician in Division of Infertility, Department of Gynecology, Kaohsiung Chang Gung Memorial Hospital, Taiwan
3. PhD candidate in Chang Gung University, Graduate Institute of Clinical Medical Sciences, Tao-Yuan, Taiwan

B. Employment Record (current)

1. Assistant Professor, Kaohsiung Chang Gung Memorial Hospital, Taiwan
2. Chief Physician of Assisted Reproductive Center, Kaohsiung Chang Gung Memorial Hospital, Taiwan

C. Honor and Awards (current)

1. 2019 Invited speaker, JSE-TES Exchange Session in TES (Taiwan Endometriosis Society, Taipei, Taiwan).
2. 2018 Oral Presentation* in ESHRE (European Society of Human Reproduction and Embryology, Barcelona, Spain). *One of the only two oral presenters from Taiwan.
3. 2018 Oral presentation in JSOG, Congress Award (The 70th. Annual Congress of Japan Society of Obstetrics and Gynecology, Sendai, Japan).
4. 2017 Oral presentation in JSOG, Congress Encouragement Award (The 69th. Annual Congress of Japan Society of Obstetrics and Gynecology, Hiroshima, Japan).

Chronic hepatitis C infection ties to an increased risk of recurrent miscarriage regardless of anti-viral treatment

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Background: Both chronic hepatitis C virus (HCV) infection which is prevalent in Asia and spontaneous abortion closely links to systemic inflammation. Nevertheless, the impact of HCV infection or responding antiviral treatment on the risk of miscarriage remains uncertain. Hence, we intended to investigate the rate of miscarriage in fertile women with chronic HCV infection.

Methods: We conducted a nationwide population-based cohort study between 1997 and 2013. A total of 3,540 HCV-infected women aged 16-35 years were included. Control group (N=14,160) were selected by 1:4 matching on age, income and urbanization. Besides, sub-cohort analysis for rate of miscarriage was performed according to HCV-treatment group (N=653) and non-treatment group (N=653).

Results: HCV women had significant higher miscarriage rate as compared with non-HCV counterparts (26.5% vs 22.2%; $p < 0.0001$). The mean age of first miscarriage was 30.3 ± 4.8 and 31.2 ± 4.9 years in the HCV and non-HCV group, respectively ($p < 0.0001$). After adjustment, HCV group had an overall 1.33-fold increased risk of miscarriage (95% CI 1.25-1.41; $p < 0.0001$). Furthermore, the risk of miscarriage was even higher for those HCV women receiving complete antiviral therapy (IRR 2.05; 95% CI 1.46-2.89; $p < 0.0001$). Subanalysis showed the HCV-associated miscarriage risk increased with the times of abortion ($p = 0.0031$), but did not differ between HCV-treatment and non-treatment subgroups ($p = 0.5428$).

Conclusion: No matter what/how antiviral therapy was administered, female chronic HCV carriers had substantially high risk of recurrent miscarriage in the fertile age. The finding implies that early conception on the diagnosis of HCV or prior to anti-HCV treatment is suggested to increase rate of live birth.

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CURRICULUM VITAE

Yu-Fang Huang, M.D.

CURRENT POSITION

1. Associate Professor, member of Gynecologic Service,
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A. Education

1993-2000 M.D., College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.

B. PROFESSIONAL POSITION

- 2015- Associate Professor of Ministry of Education in Obstetrics and Gynecology, Taiwan
- 2013- Board-certified gynecologic oncologist, Taiwan Association of Gynecologic Oncologists (TAGO)
- 2009-2015 Assistant Professor of Ministry of Education in Obstetrics and Gynecology, Taiwan
- 2004- Member, Section of Gynecologic Service, Department of Obstetrics and Gynecology, National Cheng Kung University Hospital, Taiwan
- 2005-2009 Study physician, Center of Excellence for Clinical Trial and Research in Oncology Specialty
- 2005-2009 Member, Evidence-Based Medicine Center, National Cheng Kung University Hospital, Taiwan
- 2006-2009 Rewarded Doctor for Clinical Trials, Department of Health, Executive Yuan, Taiwan

C. LICENSURE

National Board of Medical Examiners Diplomat, Taiwan, 2000

National Board in Obstetrics and Gynecology, Taiwan, 2004

Taiwan Association of Gynecologic Oncologist, Taiwan, 2013

D. ACTIVITIES AND SERVICE

1. Member of a gynecologic oncology laboratory
2. Member of gynecologic oncology surgery
3. Patient care for gynecologic diseases
4. Member of pelvic floor reconstruction and anti-incontinence surgery
5. Member of robotic-assisted gynecological surgery
6. Mentor of gynecologic ultrasound
7. Mentor of evidence-based medicine

E. HONORS & AWARDS

1. The 8th place in Award Presentation (Basic & Translation). 2017 22th Taiwan Joint Cancer Conference, Taipei, Taiwan
2. The 1st place in Xu Qiantian Anti-cancer Research Excellent Paper Award. The 58th Annual Congress of Taiwan Association of Obstetrics and Gynecology, Tainan, Taiwan
3. The 8th place in Award presentation (Clinical). 2019 24th Taiwan Joint Cancer Conference, Taipei, Taiwan

***In vitro* and *in vivo* investigations of prognosis-associated proteins in malignant ascites of ovarian cancer**

Investigators are dedicated to exploring the biomarkers which characterizes disease progression or drug resistance in epithelial ovarian cancer (EOC). The development of alternative therapeutic methods target the upregulated genes or proteins mostly discovered from cancer cells or cancer microenvironment. For instance, I will be demonstrated *in vitro* and *in vivo* investigations of a prognostic factor, vitamin D binding protein (DBP), identified from malignant ascites in EOC. We analyzed ascites, serum, and tissue samples of patients with newly diagnosed EOC to determine the prognostic effects of DBP. We verified DBP function using orthotopic animal models and DBP regulation in ovarian cancer cell lines. Moreover, we provide the evidence that in the presence of vitamin D receptor (VDR), DBP regulated VDR and thus provoked cell aggressiveness via activation of the insulin-like growth factor-1/ insulin-like growth factor binding protein-2/Akt axis, and induced suppression of vitamin D-responsive genes. A nuclear factor-kappa B p65 binding site in the VDR promoter was recognized as a key determinant of DBP-dependent VDR promoter activation. We highlight the importance of DBP in ovarian tumor progression and the potential application of DBP as a therapeutic target for EOC.