"ปฐมบทจีโนมิกส์ประเทศไทย"

The Beginning of Genomics Thailand

การประชุมวิชาการครั้งที่ 1
สมาคมมนุษยพันธุศาสตร์แห่งประเทศไทย

E-Book

Presidential address

Vorasuk Shotelersuk

President, Thai Society of Human Genetics

First, I would like to thank all my faculty and colleagues for trusting me to be the first president of the Thai Society of Human Genetics. I intend to be determined and dedicated to laying the foundation of the Thai Society of Human Genetics to enable members to work thoroughly and efficiently according to society's mission, which in turn will benefit the Thai society.

The Genetics Society of Thailand, established in 1985, has a mission to study the genetics of all organisms covering humans, animals, plants, microorganisms, and others. Recently, the body of knowledge and technology in genetics and computers has rapidly advanced. For example, the first human reference genome was completed in 2003. In addition, sequencing technology has evolved into massive parallel sequencing or next-generation sequencing (NGS). Current technology can sequence all three billion bases of a human being within days with a cost in the realm of tens of thousands of baht. This technology evolution has moved genetics from pure science to medicine, and today many countries of the world have applied this knowledge of genetics into the public health system.

To discover new knowledge in human genetics and apply the knowledge and technology for health, medicine, and public health in Thailand rapidly and efficiently, a group of experts assembled and established "the Thai Society of Human Genetics" officially registered on December 27, 2019. The Thai Society of Human Genetics is an organization that brings together experts and interested individuals to create and use human genetics knowledge and technology to benefit humans.

Genetics are related to all stages of the human life cycle, spanning from the pre-marriage planning, prenatal and perinatal periods, infancy to old age. It is also involved in many aspects of life, both in creating good health based on evidence and illnesses. Genetic factors are related to diseases of all organs and systems. Genetics also involves ethical, legal and social issues such as pre-symptomatic disease testing, employment of those with genetic predisposition, development of abortion policy and non-discriminate use of human genetics information in health insurance. Therefore, those involved in human genetics include medical personnel, medical specialists, nurses, pharmacists, medical technologists, scientists, biologists, computer engineers, emerging science specialists such as genetic counsellors, bioinformaticians, variant scientists, as well as patients and families. Scholars in ethics, religion, law, society, economics and business from educational institutions and the civil servants from various departments in the Ministry of Public Health, Ministry of Higher Education, Science, Research and Innovation, and the whole of the Thai society, both at home and abroad will be involved.

The Thai Society of Human Genetics has a core mission of academic research, and applications of genetics in all areas related to human genetics for health, medicine, and public health. For genetics to benefit the wellbeing of people in society, it is imperative that experts clearly communicate the sciences to the people who are the ones using genetics technology services. When people have accurate information, positive attitudes, and proper recommendations, they can make the appropriate decisions that will ultimately benefit the country. Providers that use genetic technology in public and private sectors will provide services scientifically and ethically.

From the medical perspective, the body of knowledge and technology in human genetics has driven a paradigm shift in the use of clinical evidence. The era of evidence-based medicine, building the best clinical evidence from randomized placebo-controlled trials, provided us with information about the population average. Genomics has steered the evidence-based medicine era into the era of individualized medicine (personalized medicine), genomics medicine and precision medicine. The clinical practice of all medical specialties will be changed by genomics. Therefore, the first success indicator of our society is many members. We are open for specialists in other medical fields such as family physicians, preventive medicine, neurology, hematology, endocrinology, heart disease, pulmonary disease, gastroenterological disease, kidney and urinary tract disease, dermatology, immunology and ophthalmic disease, as well as healthcare professionals in other fields such as dentists, nurses, pharmacists, medical technicians, and anyone who see the values and are interested in participating in the activities of the Thai Society of Human Genetics. The second indicator is the number of activities that members of our society have been invited to participate in the community, academic and professional associations. This will result in a widespread and better understanding of human genetics.

In applying genetics for public health, the society's work will be closely aligned with the National Cooperative Plan for Genomics Thailand or "Genomics Thailand". One of the flagship projects is the whole genome sequencing of 50,000 Thais, including a group of single-gene diseases, rare diseases, undiagnosed diseases, cancer, non-communicable diseases, infectious disease, and pharmacogenomics. In addition to establishing the national genome database, it will also make definitive diagnoses that will significantly benefit the patients, their families, and society.

The Human Genetics Society also has a mission to promote the study of the impact of genetics knowledge and technology on ethics, law and social issues (Ethical, Legal and Social Issues; ELSI), seeing as genetics will play an important role in solving serious health and social problems such as the COVID-19 pandemic, for which molecular genetics will have an ever-increasing relevance for making diagnoses and discoveries of new knowledge for predicting disease severity.

Although the Thai Society of Human Genetics has only been recently established, it has a clear mission to provide great benefit to Thai society. Together with our knowledgeable members known for their capability, determination, dedication, selflessness, and devotion to the common good, I am certain that the Thai Society of Human Genetics will lay their foundations and grow quickly. It is a stage that will bring together and join spirit and forces to be the academic pillar for the benefit of society as a whole incessantly.

สาส์นจากนายกสมาคมมนุษยพันธุศาสตร์

ศาสตราจารย์นายแพทย์วรศักดิ์ โชติเลอศักดิ์

President, Thai Society of Human Genetics

ก่อนอื่นข้าพเจ้าต้องขอขอบพระคุณคณาจารย์และเพื่อนร่วมงานทุกท่านที่ไว้วางใจให้ข้าพเจ้าดำรงตำแหน่งนายกสมาคมมนุษยพันธุศาสตร์เป็นคนแรก ข้าพเจ้าตั้งปณิธานไว้ว่าจะมุ่งมั่น ตั้งใจ ทุ่มเทวางรากฐานของสมาคมฯ ให้แข็งแกร่งโดยไว เพื่อให้สมาชิกได้ทำงานตามพันธกิจของสมาคมฯ ได้อย่างเต็มที่และมีประสิทธิภาพอันจะยังประโยชน์ให้เกิดแก่ประเทศไทย

ประเทศไทยมีสมาคมพันธุศาสตร์แห่งประเทศไทยมาตั้งแต่ พ.ศ. 2528 โดยสมาคมพันธุศาสตร์แห่งประเทศไทยมีพันธกิจเกี่ยวกับพันธุศาสตร์ครอบคลุมสิ่งมีชีวิตทุกชนิด ทั้งมนุษย์ สัตว์ พืช จุลินทรีย์และอื่น ๆ ในระยะเวลาไม่นานมานี้ องค์ความรู้และเทคโนโลยีทางพันธุศาสตร์และคอมพิวเตอร์ก้าวหน้าขึ้นอย่างรวดเร็ว จีโนมอ้างอิงของมนุษย์ได้ทำแล้วเสร็จในช่วงปี พ.ศ. 2546 (ค.ศ. 2003) เทคโนโลยีการหาลำดับเบส (sequencing technology) พัฒนาจนเป็น massive parallel sequencing หรือ next generation sequencing (NGS) ซึ่งสามารถหาลำดับเบสทั้งสามพันล้านเบสของมนุษย์คนหนึ่งได้ในเวลาหลักวัน ด้วยค่าใช้จ่ายเพียงหลักหมื่นบาท วิวัฒนาการเทคโนโลยีแบบก้าวกระโดดนี้ทำให้พันธุศาสตร์ขยับจากการเป็นวิทยาศาสตร์บริสุทธิ์เข้าสู่การแพทย์และในปัจจุบันหลายประเทศในโลกได้นำองค์ความรู้ด้านพันธุศาสตร์นี้ประยุกต์เข้าสู่ระบบสาธารณสุขแล้ว

เพื่อให้การหาองค์ความรู้ใหม่ด้านมนุษยพันธุศาสตร์ และการประยุกต์ใช้ความรู้และเทคโนโลยีเพื่อสุขภาพ การแพทย์และการสาธารณสุขของประเทศไทยเป็นไปอย่างรวดเร็วและมีประสิทธิภาพ ผู้เชี่ยวชาญกลุ่มหนึ่งจึงได้รวมตัวกันก่อตั้ง “สมาคมมนุษยพันธุศาสตร์” ซึ่งได้รับการจดทะเบียนจัดตั้งสมาคมขึ้นอย่างเป็นทางการเมื่อวันที่ 27 ธันวาคม 2562 สมาคมมนุษยพันธุศาสตร์จะเป็นองค์กรที่รวบรวมผู้เชี่ยวชาญและผู้ที่สนใจเพื่อสร้างและใช้องค์ความรู้ตลอดจนเทคโนโลยีด้านมนุษยพันธุศาสตร์ให้เกิดประโยชน์กับมนุษย์มากที่สุด

เนื่องจากพันธุศาสตร์จะเกี่ยวพันกับทุกช่วงชีวิตของมนุษย์ ตั้งแต่ช่วงวางแผนแต่งงาน ช่วงก่อนและระหว่างตั้งครรภ์ ช่วงวัยทารกจนถึงวัยชรา และเกี่ยวข้องกับหลากหลายแง่มุมของชีวิต ทั้งด้านการสร้างสุขภาพที่ดี โดยอาศัยข้อมูลทางพันธุศาสตร์ที่มีหลักฐานทางวิชาการรองรับ ด้านความเจ็บป่วย ซึ่งปัจจัยทางพันธุกรรมมีความเกี่ยวข้องกับการเกิดโรคของทุกอวัยวะและทุกระบบ ด้านจริยธรรม กฎหมายและสังคม เช่น การตรวจโรคก่อนมีอาการ การจ้างงานผู้ที่มีการกลายพันธุ์ นโยบายการทำแท้ง และการทำประกันสุขภาพโดยไม่กีดกันด้วยข้อมูลพันธุกรรม ผู้ที่เกี่ยวข้องกับเทคโนโลยีด้านมนุษยพันธุศาสตร์ จึงมีทั้งบุคลากรทางการแพทย์ แพทย์ทุกสาขา (all physician) นักวิทยาศาสตร์ นักชีววิทยา วิศวกรคอมพิวเตอร์ ผู้เชี่ยวชาญในศาสตร์เกิดใหม่ เช่น นักให้คำปรึกษาแนะนำทางพันธุศาสตร์ (Genetic counsellors), Bioinformaticians, Variant scientists ตลอดจนผู้ป่วยและครอบครัว ผู้เชี่ยวชาญด้านจริยธรรม ศาสนา กฎหมาย สังคม เศรษฐศาสตร์และธุรกิจ

จากสถาบันการศึกษา หน่วยงานต่าง ๆ ในกระทรวงสาธารณสุข กระทรวงการอุดมศึกษา วิทยาศาสตร์ วิจัยและนวัตกรรม และทุกภาคส่วนของสังคม ทั้งในและต่างประเทศ

สมาคมมนุษยพันธุศาสตร์มีพันธกิจหลักด้านวิชาการ การศึกษา การวิจัยและการประยุกต์งานด้านพันธุศาสตร์ในทุกสาขาที่เกี่ยวข้องกับมนุษย์ เพื่อสุขภาพ การแพทย์และสาธารณสุข การที่พันธุศาสตร์จะเป็นประโยชน์เพื่อสุขภาพที่ดีของคนในสังคมโดยรวมได้ จำเป็นที่ผู้เชี่ยวชาญต้องสื่อสารองค์ความรู้ให้กับประชาชนผู้ใช้บริการทางด้านเทคโนโลยีด้านพันธุศาสตร์ เมื่อประชาชนได้รับข้อมูลข่าวสารจนเกิดความรู้และทัศนคติที่ดีพร้อมกับคำแนะนำที่ถูกต้อง ประชาชนจะสามารถตัดสินใจได้ดีและเป็นประโยชน์สูงสุดต่อประเทศ ผู้ให้บริการที่ใช้เทคโนโลยีทางพันธุศาสตร์จะดำเนินการตรวจวินิจฉัยหรือการพยากรณ์โรคได้ถูกหลักทางวิชาการ มีจรรยาบรรณทั้งในภาครัฐและภาคเอกชน

ในทางการแพทย์ องค์ความรู้และเทคโนโลยีด้านมนุษยพันธุศาสตร์ได้ผลักดันให้เกิดการปรับเปลี่ยนกระบวนทัศน์ในการใช้หลักฐานทางการแพทย์ เกิดการพัฒนาเปลี่ยนยุคจากการแพทย์ที่ใช้หลักฐานสำคัญที่สุดจาก randomized placebo-controlled trials ซึ่งจะได้ค่าเฉลี่ยของประชากร (population average) เข้าสู่ยุคการแพทย์เฉพาะบุคคล (personalized medicine) การแพทย์จีโนม (genomics medicine) และการแพทย์แม่นยำ (precision medicine) ซึ่งจะเปลี่ยนแปลงเวชปฏิบัติของแพทย์ทุกสาขา ดังนั้น ดัชนีชี้วัดความสำเร็จแรกของสมาคมฯ คือ จำนวนสมาชิกด้วยการเปิดกว้างสำหรับแพทย์และบุคลากรทางการแพทย์ทุกสาขา เช่น เวชศาสตร์ครอบครัว เวชศาสตร์ป้องกัน ประสาทวิทยา โลหิตวิทยา ตจวิทยา จักษุวิทยา โรคต่อมไร้ท่อ โรคหัวใจและหลอดเลือด อุรเวชช์ โรคระบบทางเดินอาหาร โรคไตและระบบทางเดินปัสสาวะ โรคภูมิคุ้มกัน ทันตแพทย์ พยาบาล เภสัชกร นักเทคนิคการแพทย์ และผู้มีความสามารถในด้านต่างๆ ที่เห็นคุณค่าและสนใจจะเข้าร่วมกับกิจกรรมของสมาคมมนุษยพันธุศาสตร์ เป้าประสงค์ที่สองคือ จำนวนกิจกรรมที่สมาชิกของสมาคมมนุษยพันธุศาสตร์ได้รับเชิญหรือมีส่วนร่วมในกิจกรรมของชุมชน สมาคมวิชาการและวิชาชีพอื่นๆ ซึ่งจะส่งผลให้เกิดความเข้าใจที่ดีที่เกี่ยวกับมนุษยพันธุศาสตร์ในวงกว้าง

ในส่วนของการประยุกต์งานด้านพันธุศาสตร์เพื่อการสาธารณสุขนั้น งานของสมาคมฯจะเกี่ยวข้องกับแผนปฏิบัติการบูรณาการจีโนมิกส์ประเทศไทย (Genomics Thailand) อย่างใกล้ชิด โดยมีโครงการเรือธงคือกดการถอดรหัสพันธุกรรมของคนไทย 50,000 คน ซึ่งจะมีทั้งกลุ่มโรคพันธุกรรมยีนเดียว โรคหายาก โรคที่ยังให้การวินิจฉัยไม่ได้ โรคมะเร็ง โรคเรื้อรังไม่ติดต่อ โรคติดเชื้อ และเภสัชพันธุศาสตร์ นอกจากจะได้ฐานข้อมูลจีโนมของคนไทยแล้ว ยังจะทำให้ได้การวินิจฉัยที่แน่ชัดอันจะเป็นประโยชน์อย่างยิ่งกับผู้ป่วย ครอบครัวและสังคมโดยรวม

สมาคมมนุษยพันธุศาสตร์ยังมีพันธกิจที่จะส่งเสริมการศึกษาผลกระทบของความรู้และเทคโนโลยีด้านพันธุศาสตร์ต่อจริยธรรม กฎหมายและสังคม (Ethical, Legal and Social Issues; ELSI) รวมทั้งศาสตร์นี้จะมีบทบาทสำคัญในการแก้ปัญหาทางสุขภาพและสังคมที่ส่งผลกระทบรุนแรง เช่น โรคระบาด COVID-19 โดยเทคโนโลยีทางอณูพันธุศาสตร์ถูกใช้เป็นหลักในการตรวจวินิจฉัยโรค รวมทั้งการหาองค์ความรู้ใหม่เพื่อการพยากรณ์ความรุนแรงของโรค

แม้ว่าสมาคมมนุษยพันธุศาสตร์จะเป็นสมาคมก่อตั้งใหม่ แต่ด้วยพันธกิจที่ชัดเจนมุ่งหวังจะดำเนินการให้เป็นประโยชน์อย่างยิ่งต่อสังคมไทย ประกอบกับสมาชิกเป็นผู้มีความรู้ ความสามารถ

มุ่งมั่น ทุ่มเท เสียสละและอุทิศตนเพื่อประโยชน์ส่วนรวม
ข้าพเจ้ามั่นใจว่าสมาคมมนุษยพันธุศาสตร์จะสามารถวางรากฐานและเติบโตได้อย่างรวดเร็ว
เป็นองค์กรที่จะทำให้สมาชิกมารู้จักและประสานพลังกันเพื่อเป็นที่พึ่งทางวิชาการและทำประโยชน์ให้เกิดแก่สังคมโดยรวมได้อย่างกว้างขวางสืบไป

Meeting program		
Day 1: 17th Feb 2022		
Time	Activity	Speakers
8.00-9.00	Registration	
9.00-9.30	Opening ceremony & opening remark	Dr Satit Pitutecha *Deputy Minister of Health, Thailand* Dr Nopporn Cheanklin *Executive Director, Health Systems Research Institute, Thailand*
9.30-10.00	First inaugural lecture (discourse to Professor Khunsupa Na-nakorn) How DNA ages: The discovery and implications of DNA protection and rejuvenation effects of DNA gaps	Professor Apiwat Mutirangura *Center of Excellence in Molecular Genetics of Cancer and Human Disease, Department of Anatomy, Faculty of Medicine, Chulalongkorn University*
10.00-10.30	First presidential address Human Genomics in Thailand: Past, Present & Future	Professor Vorasuk Shotelersuk *President, Thai Society of Human Genetics*
10.30-10.45	Break	
Plenary session (Moderator Dr Prasit Phowthongkum)		
10.45-11.10	Human genetics and genomics human resource training: Planning for Thailand and experiences in South East Asia	Professor Thanyachai Sura *President, Asia Pacific Society of Human Genetics* *President, Thai Medical Genetics and Genomics Association*
11.10-11.35	Cancer genetics and genomics: Where are we in the world stage?	Professor Manop Pithukpakorn *Faculty of Medicine Siriraj Hospital Mahidol University*
11.35-11.55	Cell and somatic gene therapy in the genomes editing era: Thalassemia and beyond	Professor Suradej Hongeng *Faculty of Medicine Ramathibodi Hospital Mahidol University*
Oral presentation: Clinical Genetics and Cancer Genetics (Moderator Dr Prasit Phowthongkum)		
11.55-12.05	O1A Orodental features associated with dentinogenesis imperfecta and osteogenesis imperfecta	Dr Narin Intarak *Faculty of Dentistry, Chulalongkorn University*
12.05-12.15	O1B Ano-Rectosigmoid cancer vs Proximal colon cancer: different mechanisms confirmed in the era of next-generation sequencing	Dr Phawin Koranantakul *Faculty of Medicine, Chulalongkorn University*
12.15-12.25	O1C Telemedicine in Cancer-genetic Clinic at King Chulalongkorn Memorial Hospital during the COVID-19 pandemic	Ms Chanchira Sriraksasin *Faculty of Medicine, Chulalongkorn University*
12.25-12.35	Break	
Luncheon Symposium		

12.35-13.00	Luncheon Symposium 1: Breaking the Interpretation Bottleneck; Evidence-Backed AI solutions for Genomic Analysis and Discovery at Scale	Michael Fietz, PhD FFSc (RCPA) *Senior Sales Specialist in Clinical Informatics Illumina*
13.00-13.25	Luncheon Symposium 2 Applications of PacBio Highly Accurate Long Read Sequencing in Rare and Inherited Diseases (PacBio)	Zuwei Qian *Director of Marketing (APAC), at Pacific Biosciences*
13.25-13.35	Break	
International session: Korean Genome Organization (Moderator Dr Surakameth Mahasirimongkol)		
13.35-13.55 (14.35-14.55 South Korean Time)	RORα enforces stability of the T-helper-17 cell effector program	Professor June-Yong Lee *Department of Microbiology and Immunology Yonsei University College of Medicine, South Korea*
13.55-14.15 (14.55-15.15 South Korean Time)	Regulation of histone methylation by PRC2 automethylation and RNA	Professor Chul-Hwan Lee *Department of Pharmacology, College of Medicine, Seoul National University, South Korea*
Oral presentation: Pharmacogenetics, Genetic technology & Applied Genetics (Moderator Assistant Professor Pajaree Chariyavilaskul)		
14.15-14.25	O2A Genetic variation profiling prediction of 51 pharmacogenes in a Thai population using whole-genome sequencing	Ms Natnicha Wankaew *Program in Bioinformatics and Computational Biology* *Graduate School, Chulalongkorn University*
14.25-14.35	O2B Revisit and proposal to expand to ethnic-specific secondary findings from the whole-exome sequencing of the Thai population	Ms Wanna Chetruengchai *Faculty of Medicine, Chulalongkorn University*
14.35-14.45	O2C Impact of G6PD deficiency and its Mutations on Diabetes Diagnosis by hemoglobin A1c in Thailand Cohort	Ms Punchalee Mungkalasut *Faculty of Medicine, Chulalongkorn University*
14.45-15.00	Break	
Parallel sessions start		

Room 1		Room 2	
15.00-16.30 (18 minutes each)	Genomics and Clinical Practice (Moderator Assistant Professor Thipwimol Tim-aroon)	15.00-16.30 (30 minutes each)	Genomics Sciences and Genomics Technology (Moderator Assistant Professor Pajaree Chariyavilaskul)
1. Genomics and adult patient care Dr Prasit Phowthongkum 2. Genomics and acute care settings: 89 cases and four-year experiences of rapid exome sequencing in severely ill children and adults with suspected monogenic conditions in Thailand Dr Wuttichart Kamolvisit 3. Genomics and dental health Associate Professor Thantrira Porntaveetus		1. Long read sequencing: 4th generation sequencing - end of decade epic of discovery Assistant Professor Patra Yeetong 2. Analysis of cancer stem cell-like population in patient-derived hepatocellular and cholangiocarcinoma organoids using single-cell RNA sequencing Associate Professor Nipan Israsena na Ayuthaya	

4. Primary Immune Disorder - Make them fight against germs again: Gene Therapy Professor Kanya Suphapeetiporn 5. Genomics and reproductive health Associate Professor Boonsri Chanrachakul	3. Mitochondrial manipulation technology: future of the future: from three parents' baby to somatic mitochondrial replacement therapy Associate Professor Sirisak Chanprasert University of Washington
Parallel sessions end	
End of Day 1 meeting	

Meeting program

Day 2: 18th Feb 2022			
Time	Activity	Speakers	
8.00-9.00	Registration	-	
Parallel sessions start			
Room 1		Room 2	
9.00-10.00 (20 minutes each)	Genomics education/ workforce preparation (Moderator Assistant Professor Thipwimol Tim-aroon)	9.00-10.00 (15 minutes each)	Bioinformatics/ data sciences/ AI (Moderator Assistant Professor Monnat Pongpanich)
1. Genetic knowledge gap in adult healthcare provider: challenge and solution Dr Prasit Phowthongkum 2. Genomics fellowship training experiences Professor Kanya Suphapeetiporn Professor Duangrudee Wattanasirichaigoon 3. Bioinformatics and genomics data scientist training in Thailand: Obstacles and opportunities Dr Chureerat Phokaew		1. Bioinformatics pipeline for long-read sequencing analysis: What is new? Assistant Professor Monnat Pongpanich 2. Bioinformatics for RNA sequencing analysis: xPore - A new bioinformatics tool for RNA modification identification Dr Naruemon Pratanwanich 3. Data management of Genomics Thailand Dr Sissades Tongsima 4. Data processing and variant prioritization standardization Dr Chumpol Ngamphiw	
10.00-11.00 (15 minutes each)	ELSI and policy (Moderator Dr Prasit Phowthongkum)	10.00-11.00 (20 minutes each)	Population genetics (Moderator Assistant Professor Bhoom Suktitipat)
1. Genomics Thailand: 2019-2021 Dr Surakameth Mahasirimongkol 2. Thailand National Essential Drug for Rare Diseases Working Group Professor Duangrudee Wattanasirichaigoon 3. Ethics and genome editing Professor Soraj Hongladarom 4. Ethical guidelines standard development for genomics research Dr Prasit Phowthongkum		1. Polygenic risk scores in diverse populations: the importance of inclusivity Dr Jakris Eu-ahsunthornwattana 2. Population genetics: return nationality to Thais (Sirinthorn Project) Associate Professor Kornkiat Vongpaisarnsin 3. Population and Thai ancestry Associate Professor Jatupol Kampuansai	
Parallel sessions end			
11.00-11.30	Break		
Oral presentation: Basic Science & Translational Genetics (Moderator Assistant Professor Pajaree Chariyavilaskul)			
11.30-11.40	O3A From cat to human heart	Dr Chupong Ittiwut *Faculty of Medicine, Chulalongkorn University*	
11.40-11.50	O3B KCNQ2 Function	Ms Suphalak Chokvithaya *Faculty of Dentistry, Chulalongkorn University*	
11.50-12.10	Break		
Luncheon Symposium			
12.10-12.40	Luncheon Symposium 3 Population Genomics in Mobile Internet Era (BGI)	Mr Chen Gang	

12.40-13.10	Luncheon Symposium 4: Improving the Practice of Healthcare using Predictive Genomics Today	David Hanna *Director, Sales and Business Development* *Microarray Genotyping* *Thermo Fisher Scientific*
13.10-13.20	Break	
Plenary Session (Moderator Dr Prasit Phowthongkum)		
13.20-13.50	Panoramic not only for pandemic	Professor Thiravat Hemachudha
13.50-14.20	COVID-19 in Thailand	Department of Medical Science, Ministry of Public Health, Thailand
14.20-14.30	Break	
International session: Genomic in the UK (Moderator Dr Surakameth Mahasirimongkol)		
14.30-15.10 (8.30-9.10 GMT)	Genetics human resource development program in the UK	Dr Michelle Bishop *Associate Director* *Learning and Training at Wellcome Connecting Science, the Wellcome Genome Campus, UK*
Award presentation		
15.10-16.00	Award Closing ceremony	
End of the conference		

First inaugural lecture (discourse to Professor Khunsupa Na-nakorn)

How DNA ages: The discovery and implications of DNA protection and rejuvenation effects of DNA gaps

Apiwat Mutirangura

Center of Excellence in Molecular Genetics of Cancer and Human Disease, Department of Anatomy, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand

Epigenetic loss causing DNA damage accumulation in the elderly is a master key initiating and driving the ageing process. Since 2008, my research team has discovered and studied the DNA protection role of a poorly recognized epigenetic mark, which are naturally occurring DNA gaps. Our current research identified an exon of a gene that acts as molecular scissors producing the gaps. Transfection of the molecular scissors produced new DNA gaps. These gaps protected DNA from damage and ultimately rejuvenated senescent cells and ageing rats. We found significant levels of naturally occurring DNA gaps in all kinds of eukaryotic cells in replicating and non-replicating cells. The DNA gaps were found retained in the hypermethylated genome and nonacetylated heterochromatin. The DNA gap levels were decreased in the mutants that lacked chromatin-condensing proteins, such as high-mobility group box proteins and Sir2. Chronological ageing in yeast reduced the number of DNA gaps, and the DNA gap reduction sheared DNA and diminished cell viability. Therefore, the naturally occurring DNA gaps are more common in youth and play epigenetic roles in preventing DNA damage. We named the gaps because of their role as youth-associated genome-stabilizing DNA gaps or Youth-DNA-GAPs. The molecular scissors ultimately reversed all ageing features in the two ageing rat models to be similar to those of young organisms. The plasmid increased DNA gaps, improved liver and brain function, reduced liver fibrosis, visceral fat, and aging and DNA damage associated proteins. This discovery has immense implications in medicine to cure age and DNA damage-associated diseases.

First presidential address

Human Genomics in Thailand: Past, Present & Future

Vorasuk Shotelersuk

President, Thai Society of Human Genetics

In the past: Genomics is for academicians and researchers

While "genetics", the study of heredity, dates back to Gregor Mendel in the mid1800s, the term "genomics" was first coined in 1986 by a scientist, Dr Tom Roderick. Genomics, the study of the entirety of an organism's genes (3 billion nucleotides of 20,000 genes in humans), became possible only due to technical advances in DNA sequencing and computer sciences.[1]

At present: Genomics has been applied to medicine and public health

Since all cells are designed and controlled by genes, (almost) all diseases have a genetic contribution, and the practical and affordable technology to do the human genome has become available, it is unsurprising that genomics is taking a central role in diagnosis. Genomics has steered the evidence-based (population average) medicine era into the era of individualized medicine (personalized medicine), genomics medicine and precision medicine. As appropriately categorized in Genomics Thailand, a national initiative to do 50,000 genome sequencing for Thai people, the first groups of disciplines to take advantage of genomics are genetic diseases, cancer, non-communicable diseases, infectious diseases and pharmacogenomics.[2,3] Thai genomicists continue to contribute new knowledge to the world literature by identifying new human disease genes.[4]

In the future: Genomics involves everyone at any point in the life cycle

Scientists in every era have thought that "their time" is exceptional (e.g. the times of restriction endonuclease, PCR, and Sanger sequencing). We think that, too, due to the availability of massively parallel sequencing. Nonetheless, the future certainly promises even more exciting molecular technologies and health applications. It is not a question of if but when genomics will play a central role in medical treatments and every step of human lives, from preconception (selection of preferred traits) to organ replacement (genetically modified pig heart xenotransplantation) and rejuvenation.

'Genomics literacy is essential for all of us.'

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Plenary session 1

Human genetics and genomics human resource training: Planning for Thailand and experiences in South East Asia

Thanyachai Sura

President, Asia Pacific Society of Human Genetics
President, Thai Medical Genetics and Genomics Association

Plenary session 2

Cancer Genetics and Genomics: Where are we in the world stage?

Manop Pithukpakorn

Faculty of Medicine Siriraj Hospital
Mahidol University

Beginning in 1990, the human genome project has brought significant discoveries in medical genetics and application of genetic knowledge in common diseases. It has transformed the traditional medical concept that genetics involve only in extremely rare inherited diseases, to the new concept that genetic factor significantly contributes in the mechanism and progression of most diseases, as well as the response and side effects of the treatment. This concept integrates into a fundamental principle of precision medicine. Cancer is the best example to demonstrate the benefit of genomics and precision medicine. It has been universally accepted that cancer is a genetic disorder that results in abnormal cell growth and the invasiveness and spreading potential to other parts of the body. Better understanding in cancer genetics and genomics leads to new types of cancer diagnostic tests and several novel drugs which are designed to target specific genetic abnormalities in cancer.

The unprecedented throughput, speed and cost of next generation sequencing (NGS) enables researchers to investigate genetic contribution of cancer and implement this technology to the real-world medical practice. From the beginning of The Cancer Genome Atlas (TCGA) program in 2006, We currently see widespread use of NGS to discover genetic alterations in each patient, to identify potential treatment target, and to predict response of medical treatment. In clinical practice, oncologists could select the best and most appropriate treatment for each patient, based on the patient's genetic data. Cancer genome testing becomes a standard tool in cancer diagnosis and treatment. For example, lung cancer patients with genetic alterations could get significant benefit from novel targeted therapies that specifically act on certain molecular pathway. In Thailand, testing for specific alterations in EGFR gene is reimbursable and anti-EGFR targeted therapy becomes standard treatment for lung cancer patients with identified EGFR mutations. This novel approach improves cancer treatment efficacy, patient outcome, quality of life, reduce healthcare cost and overall social and economic burden. With several actionable mutations with available targeted therapies emerging, more extensive cancer genome testing such as comprehensive genomic profile (CGP) would soon be a common diagnostic test for all cancer patients. Genomics Thailand would play significant role to facilitate the adoption and accessibility of CGP in cancer diagnosis and treatment plan in the near future.

Plenary session 3

Cell and somatic gene therapy in the genomes editing era: Thalassemia and beyond

Suradej Hongeng

Faculty of Medicine Ramathibodi Hospital
Mahidol University

Plenary session 4

Panoramic not only for pandemic

Thiravat Hemachudha

Thai Red Cross-Emerging Infectious Diseases-Health Science Centre
Faculty of Medicine, Chulalongkorn University

On behalf of the Pattani project Team: Sira Sriswasdi, PhD, Phatthamon Virojanapirom, PhD, Chanida Ruchisrisarod, MSc, Chatchai Nopvichai, PhD, Thirawat Supharatpariyakorn,M.Eng.(Biochemical Engineering), Nathwut Thongkhong, MD, Wiput Phoolcharoen, MD

Success in delineating mechanisms or driver gene(s) not only requires whole or partial gene sequencing but also needs to integrate input parameters among various areas such as clinical/routine and successive biomedical-immunological search in combination with deep machine learning or artificial intelligence tools. Such integration as pan- or multi-OMICS has been proven successful in identifying driver genes in the critical form of Covid-19 and defining vascular dysregulation as an early role in Alzheimer's disease. In addition, this multi-OMICS can also identify genes responsible for cannabis addiction and subsequent development of schizophrenia.

We have translated from these lessons the transmission dynamics of Covid-19 in Pattani province in Ampur Yarang and Thung Yang Daeng. By employing measurements of antibody (in 2020-1), T cell memory and cytokine responses (in 2021) from blood specimens and MALDI-ToF from saliva samples (in 2021), the silent transmission was clearly evident over time from 2020 to 2021 from infected individuals to household and community members (where in 2020 this population remained naïve by lacking infective evidence). T cell memory tended to wane early within half a year, whereas the antibody disappeared even earlier. Artificial intelligence segregates the population into 6 clusters reflecting status relating to covid-19 infection and spread(transmission). Biomarkers for susceptibility or resistance to infection and disease are to be further elucidated.

Plenary session 5

COVID-19 in Thailand

Department of Medical Science
Ministry of Public Health, Thailand

International session 1: Korean Genome Organization

RORα enforces stability of the T-helper-17 cell effector program

June-Yong Lee

Department of Microbiology and Immunology
Yonsei University College of Medicine, South Korea

T helper 17 (Th17) cells regulate mucosal barrier defences and promote multiple autoinflammatory diseases. Th17 cells have also been implicated as having important functions in regulating tumour growth. However, there is disagreement about whether they promote (as suggested for colorectal cancers) or retard it (as suggested by our preliminary data), which may be due to differences in tumour microenvironments. Although the pathogenic activity of these cells is dependent on signals emanating from the innate immune system, such as IL-23 and serum amyloid A (SAA) proteins, the transcriptional programs that sustain Th17 cells *in vivo* remain obscure. Our recent work indicates that RORα governs optimal Th17 responses in peripheral tissues. Thus, the absence of RORα in T cells led to significant reductions in both RORγt expression and effector function amongst Th17 cells, due to the need for cooperative RORα and RORγt binding to a newly-identified Rorc enhancer element that is essential for Th17 lineage maintenance *in vivo*. Altogether, these data point to a non-redundant role of RORα in Th17 lineage maintenance via reinforcement of the RORγt transcriptional program.

International session 2: Korean Genome Organization

Regulation of histone methylation by PRC2 automethylation and RNA

Chul-Hwan Lee

Department of Pharmacology, College of Medicine
Seoul National University, South Korea

Polycomb Repressive Complex 2 (PRC2) is a histone methyltransferase (HMT) that catalyzes mono-, di-, tri-methylation of lysine 27 on histone H3 (H3K27me1, -me2, me3), essential for maintaining developmental gene silencing in metazoans. PRC2 core complex comprises EED, SUZ12, and two mutually exclusive and interchangeable catalytic subunits, EZH1 and EZH2. The HMT activity of PRC2 can be modulated by many different factors, including RNA and automethylation. Here, we identify the lysine residues at which EZH1/EZH2 are automethylated, with EZH2-K510 and EZH2-K514 being the major such sites in vivo. Automethylated EZH2/PRC2 exhibits a higher level of histone methyltransferase activity and is required for attaining proper cellular levels of H3K27me3. While occurring independently of PRC2 recruitment to chromatin, automethylation promotes PRC2 accessibility to the histone H3 tail. The role of RNA in PRC2 recruitment and its activity has been studied; however, its precise mechanism is poorly understood. While RNA seems critical for PRC2 to associate with chromatin stably, RNA inhibits the catalytic activity of PRC2. How PRC2 releases from RNA and methylate H3K27 is yet known. Recent studies have identified several RNA binding sites within PRC2 core subunits, and one of the major sites is located at EZH2 automethylation sites. These findings suggest that EZH2 automethylation could negatively regulate RNA binding to access histone H3 tail.

International session 3: Genomic UK

Genomics human resource development program in the UK

Michelle Bishop

Associate Director, Learning and Training at Wellcome Connecting Science, the Wellcome Genome Campus, UK
https://www.genomicseducation.hee.nhs.uk/

The talk will cover:

1. Overview of the genomics profession in the UK and how it is used.
2. Development of the healthcare workforce that deliver genomics services, concentrating on genetic counsellors and their training programme.
3. Health Education England (HEE) Genomics Education Programme resources to support the education of both the specialist (genomics) and generalist (e.g. family physicians) health workforce.
4. Showcase what HEE Genomics Education Programme does to develop the genetics/genomics professions.

Genomics and adult patient care

Prasit Phowthongkum

Division of Medical Genetics and Genomics
Department of Medicine, Faculty of Medicine
Chulalongkorn University

Genetics and genomics have long been considered pediatric specialities and recently get more interested in reproductive medicine and prenatal care settings. In contrast, genetics and genomics are less known for significant health problems among adult healthcare providers. Comprehensive genomic testing such as exome-sequencing and genome-sequencing is currently widely applied in pediatric settings, including critical illness patients, as the yield and utility are well established significantly improved than traditional methods. We argue that with a careful patient selection, exome-sequencing in adult patients suspected of monogenic disorders can reach a high yield comparable to the pediatric population in our patient cohort.

Genomics and acute care setting:
89 cases and four-year experiences of rapid exome sequencing in severely ill children and adults with suspected monogenic conditions in Thailand

Wuttichart Kamolvisit

Center of Excellence for Medical Genomics,
Medical Genomics Cluster, Department of Pediatrics,
Faculty of Medicine, Chulalongkorn University
Excellence Center for Genomics and Precision Medicine
King Chulalongkorn Memorial Hospital, The Thai Red Cross Society,
Thailand

Wuttichart Kamolvisit[1,2,*] , Prasit Phowthongkum[2,3] , Ponghatai Boonsimma[1,2] , Chalurmpon Srichomthong[1,2,] Chupong Ittiwut[1,2] , Chureerat Phokaew[1,2] , Rungnapa Ittiwut[1,2] , Aayalida Buasong[1,2] , Adjima Assawapitaksakul[1,2] , Wanna Chetruengchai[1,2], Kanya Suphapeetiporn[1,2] , Vorasuk Shotelersuk[1,2]

[1]Center of Excellence for Medical Genomics, Medical Genomics Cluster, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[2]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, Bangkok, Thailand
[3]Division of Medical Genetics and Genomics, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

A rapid diagnostic test can facilitate the critical decision, leading to precision management in intensive care units (ICUs) settings. Monogenic conditions cause more than 10% of all diseases in newborns admitted to ICUs. As the immediate improvement in turnaround time and cost-effectiveness, rapid next-generation sequencing (rNGS), such as rapid exome sequencing (rES), can be an effective diagnostic tool for critically ill children and adults. While these technologies have been performed and evaluated primarily on children living in developed countries, using rES in different ethnicities and health care systems may impact diagnostic yield and optimal algorithms.

This session will share our four-year experience with rES in 89 patients from 11 public hospitals across Thailand. We will first describe the framework used to collect phenotype information, analyze the exome data, and return the result to the primary physician. Then we will utilize case-based learning to explore real-life problems and the possible idea to improve the rES workflow. Finally, we will discuss the ethical and policy challenges we confront.

Learning Objectives:

1. Assess utilization of rES in the critical care setting
2. Describe the rES workflow from collecting patient phenotype to returning genotype results to the primary physician
3. Explore the case-based problem and discuss strategies to engage in a multi-disciplinary team to optimize algorism for individual case
4. Discuss about the ethical and policy challenges of rES in Thailand

Genomics and dental health

Thantrira Porntaveetus

Genomics and Precision Dentistry Research Unit
Department of Physiology
Faculty of Dentistry, Chulalongkorn University

Precision medicine is an emerging approach for disease management that is individually tailored based on a person's genetic background, lifestyle, and environment. With an advance in next-generation sequencing technology and bioinformatics, health care has been transformed into a precision one. The world, including Thailand, is entering a whole ageing society. One of the most common health problems leading to the decline of the general well-being of the elderly is deteriorating oral health, including alveolar bone destruction, dental infection, tooth loss, and oral cancer. Orodental hard tissues and skeleton share similar ultrastructure, function, and molecular pathways during development. Connective tissue disorders cause anomalies in ectodermal organ, connective tissues, bone, and teeth. To date, several connective tissue and orodental disorders still cannot be prevented and entirely treated, leaving the patients with deformities. Prevention and precise management of genetic disorders require a better understanding of the etiology and pathomechanism of the diseases. An efficient way to elucidate them is to study monogenic syndromes with clear-cut phenotypes such as skeletal dysplasias and ectodermal dysplasias. Our team, Genomics and Precision Dentistry Research Unit and Medical Genomic Cluster, provides genetic diagnosis and medical and dental care for the patients with genetic disorders and carries out clinical research focusing on phenotypic and ultrastructural characterization, pathogenic variant identification with several next-generation sequencing techniques, and investigations of cellular and molecular mechanisms of orodental and connective tissue disorders using multi-omics, genetic manipulation, and animal models. We aim to gain valuable insights into disease etiology and pathomechanism and explore precise management of the disorders.

Primary Immune Disorder - Make them fight against germs again: Gene Therapy

Kanya Suphapeetiporn

Department of Pediatrics
Faculty of Medicine, Chulalongkorn University

Several genetic diseases, including primary immunodeficiency disorders, have been cured by bone marrow transplantation. However, donor availability constrains its usage. Recent technologies have made human induced pluripotent stem (iPS) cells a foreseeable and realistic source to release this limitation. In addition, induced pluripotent stem cell (iPSC) technology, combined with advancement in genome editing technology such as CRISPR-CAS, provides unprecedented opportunities for modelling human diseases. For example, it can be applied when animal models cannot fully recapitulate human diseases due to interspecies differences. Furthermore, for rare genetic diseases that patients' tissues are difficult to obtain, it can produce unlimited cell types for investigating various aspects of disease mechanism and serve as a platform to test novel therapies.

Primary immunodeficiency disorders, also known as inborn errors of immunity, are a group of more than 400 potentially serious disorders caused by defects in genes responsible for different components of the immune system. Recent advances in gene-based therapies and bone marrow transplantation have made treatments possible in otherwise fatal diseases. In the last decade, miss-match or even haploidentical bone marrow transplantation results have improved, allowing more treatment options for patients without matched bone marrow. Nevertheless, autologous cells could benefit patients with a high risk of developing complications. Gene editing in iPSCs or adult hematopoietic stem cells could prove to be viable alternatives. While more research is required to generate long-term engraftable hematopoietic stem cells from iPSCs, the iPSC approach allows the generation of homogenous populations of selected, mutation-free cells for transplantation. With the rapid improvement of gene targeting tools, direct genome engineering in adult hematopoietic stem cells could be archived with high efficacy and safety for clinical translation in the near future.

Genomics and reproductive health

Boonsri Chanrachakul

BPH (Hospital Administration)
MD, PhD, MSc (Medical Genetics)
Maternal Fetal Medicine
Samitivej Sukhumvit Hospital, Bangkok, Thailand

Genetic disorders and congenital abnormalities account for 3-5% of all live births. Genetic diseases are also responsible for 20% of newborn mortality and 10-30% of pediatric hospital admission. These disorders can pass abnormal genes or genetic risk to the future generations. Previously, it took 15 years to perform human genome sequencing, costing billions of dollars. With advanced technology, the next generation sequencing (NGS) can process much faster with lower cost. Carrier screening has been used to identify individual or couple at risk of having a child with an autosomal recessive or X-linked genetic disorders. Our center has provided preconception carrier screening since 2017. A total of 169 individuals have been tested for carrier status (2017-December 2021). Sixty-nine percent of them carries at least one genetic condition. Thalassemia is the most common finding (1 in 4), followed by GJB2-related DFNB1 non-syndromic hearing loss and deafness (1 in 6). Eight percent of the couples had the same genetic disorders. Inborn errors of metabolism genetic disorders are one of the common findings. According to these results, all newborns delivered at our center have been tested for expanded newborn screening since January 2021.

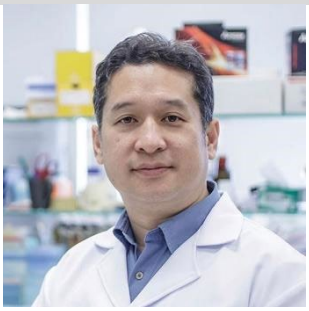
Long read sequencing: 4th generation sequencing - end of decade epic of discovery

Patra Yeetong

Division of Human Genetics, Department of Botany, Faculty of Science, Chulalongkorn University

Benign Adult Familial Myoclonic Epilepsy (BAFME) is an autosomal dominant disorder characterized by adult-onset cortical tremor or action myoclonus predominantly in the upper limbs and generalized seizures. We studied a Thai family with a type of epilepsy, benign adult familial myoclonic epilepsy type 4 (BAFME4), and localized its gene to chromosome 3q26.32-q28. Then, we used single-molecule real-time sequencing and found expansions of TTTTA and insertions of TTTCA repeats in intron 1 of YEATS2 in one affected family member. Of all the available members in the family—comprising 13 affected and eight unaffected—repeat-primed PCR and long-range PCR revealed the cosegregation of the TTTCA repeat insertions with the TTTTA repeat expansions and the disease status. For 1,116 Thai control subjects, none harbour the TTTCA repeats, while four had the TTTTA repeat expansions. Therefore, our findings suggest that BAFME4 is caused by the pentanucleotide TTTCA repeat insertion and TTTTA repeat expansion in intron 1 of the YEATS2 gene. This will provide a further understanding of the molecular basis of the disease, which is caused by the same molecular pathology as with other BAFMEs.

Analysis of cancer stem cell-like population in patient-derived hepatocellular and cholangiocarcinoma organoids using single-cell RNA sequencing

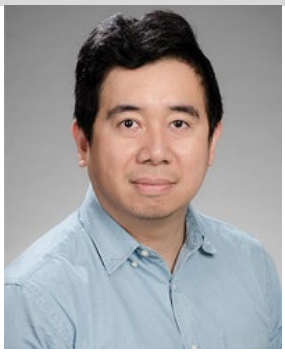


Nipan Israsena na Ayuthaya

Center of Excellence for stem cell and cell therapy
Department of Pharmacology
Faculty of Medicine, Chulalongkorn University

Primary liver cancers, including hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA), are an important cause of cancer-related deaths in Thailand and worldwide due to the ineffectiveness of currently available treatments. The recently developed organoid technology, which allows a long-term culture of patient-derived liver cancer cells in 3D while maintaining morphology, expression pattern, and the genetic heterogeneity of the original tumors, is a powerful research tool for discovering biomarkers and therapeutic drugs for various cancers. We successfully established and characterized 30 primary liver cancer organoids (13 HCC and 17 CCA) from Thai patients. Transcriptomics and single-cell analysis reveal heterogeneity within each patient-derived cancer organoid and demonstrate a strong correlation between metabolic genes, molecules involved in the immune check point pathway and cancer stem cell-associated markers in a subpopulation of both HCC and CCA. Liver cancer organoid drug screening with a selected compound library including repurposing drugs yielded promising candidates. Our results could lead to the development of new therapeutic strategies for HCC and CCA.

Mitochondrial manipulation technology: future of the future
From three parents' baby to somatic mitochondrial replacement therapy



Sirisak Chanprasert

Division of Medical Genetics
University of Washington, USA.

Genomics education/ workforce preparation

Genetic knowledge gap in adult healthcare provider: challenge and solution

Prasit Phowthongkum

Division of Medical Genetics and Genomics
Department of Medicine, Faculty of Medicine
Chulalongkorn University

Adult health care providers have Inadequate basic knowledge and skills to apply Genetics and Genomics in their daily patient care. Although the application of Genetics and Genomics is well established in some medical specialties such as oncology, general oncologists do not think they have enough understanding or confidence to use genetics knowledge or tests for their patients care. Poor genomic literacy among adult healthcare providers is a global phenomenon, not an exception. The attitudes of a non-genetic specialist towards this highly sophisticated specialty is also an important challenge. Many genetic specialists consider genetics a minor field involved with rare conditions that they rarely encounter in their practice. To name a few relatively common genetic conditions in adult patients: Hypertrophic cardiomyopathy, Familial Hypercholesterolemia, Hereditary Breast and Ovarian Cancer Syndrome, Lynch syndrome, Thalassemia, Glucose$_6$Phosphate dehydrogenase deficiency, Charcot Marie Tooth together affected more than ten per cent of Thai adults. Undergraduate Preclinical and clinical curriculum development medical selective genetics rotation for postgraduate trainees are some attempts to facilitate the usage of genomics. Recently, trying to fill some gaps, the one-year medical genetics fellowship training is one of the methods offered to internal medicine graduates.

Genomics fellowship training experiences

Kanya Suphapeetiporn

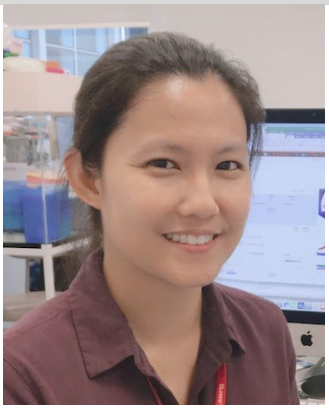
Department of Pediatrics, Faculty of Medicine
Chulalongkorn University

Duangrudee Wattanasirichaigoon

Medical Genetics Division
Faculty of Medicine Ramathibodi Hospital
Mahidol University

Genomics education/ workforce preparation

Bioinformatics and genomics data scientist training in Thailand: Obstacles and opportunities



Chureerat Phokaew

Center of Excellence for Medical Genomics
Medical Genomics Cluster, Department of Pediatrics
Faculty of Medicine, Chulalongkorn University

Excellence Center for Genomics and Precision Medicine
King Chulalongkorn Memorial Hospital
The Thai Red Cross Society, Thailand

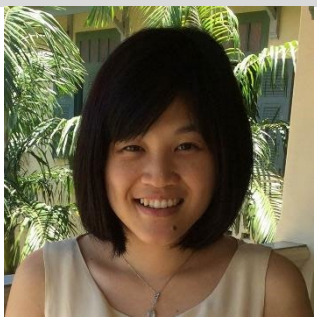
Research Affairs, Faculty of Medicine, Chulalongkorn University

In Thailand, genomics terms have become widely recognized from several private medical genome services and a public genomics service like the Genomic Thailand project. Whether we are ready or not, we are dealing with the rapid growth of the genomics data and the requirement of bioinformatics jobs primarily related to genomics data analysis. Bioinformatics has become an essential skill set for life science jobs, no doubt. However, several bioinformatics workshops from several specialists lunch out to improve expertise and confidence in data analysis and interpretation over the last decade in Thailand. Nevertheless, we still witnessed a continuing shortage of this specific expertise. From our experience, we witness a huge demand and interest in short courses and the bioinformatics class of life science degree programs. Inadequate bioinformatics teaching in life science education programs leading a controversy between theory and practice. These suggest a bioinformatics training is urgently needed at all educational levels and professional roles. The sustainable solutions will be added to the bioinformatics, command line, programming, and data science education of current and future generations of life scientists. We might transform the current education degrees or generate new programs for a new specific career path such as variant interpretation, genomics data scientist, and data scientist in the upcoming future of Thailand.

Bioinformatics pipeline for long-read sequencing analysis: What is new?

Monnat Pongpanich

Department of Mathematics and Computer Science, Faculty of Science, Chulalongkorn University



Long-read single-molecule DNA sequencing technologies revolutionize genomics research. It overcomes many limitations of short-read sequencing data. Long read data improves the sensitivity for detecting structural variation (SV) since it spans SV breakpoint. It can also span repeat elements or repetitive regions, allowing tandem repeat expansion detection. It solves the problem of distinguishing sequence between functional gene and its pseudogenes; thus, it enables characterizing these genes such as CYP2D6, a major drug-metabolizing gene. In addition, it allows mapping a highly polymorphic region such as the human leukocyte antigen (HLA) region. With HiFi sequencing, 99.9% accuracy has been achieved at around nine passes. However, Pacbio long read data is different from short-read sequencing technologies in many aspects, including the read length, GC-skewing, error types and error abundance. Therefore, current short read tools might not be applicable to analyze long-read data. Analysis pipelines for long-read require adapting current short-read or dedicated tools. Here, I will present a pipeline for detecting single nucleotide variants (SNVs), SV, tandem repeat expansion for tandem repeat disorders, typing HLA, calling star alleles for pharmacogenes.

Bioinformatics for RNA sequencing analysis: xPore - A new bioinformatics tool for RNA modification identification

Naruemon Pratanwanich

Department of Mathematics and Computer Science, Faculty of Science, Chulalongkorn University

RNA modifications such as N6-methyladenosine (m6A) have been found to contribute to molecular functions of RNAs and have been implicated in the developmental process, cell-fate determination, and cancer. The emerging roles of RNA modifications in human cancer suggest that uncovering the importance of epitranscriptomics will provide powerful implications in precision oncology. However, the identification of differences in RNA modifications has been challenging. I will present our computational method, **xPore**, to identify differential RNA modifications from direct RNA sequencing data. Based solely on the raw current intensity profiles, we extend a standard two-component Gaussian mixture model to accommodate multi-sample comparisons. For each site, the model learns two distributions, the signal properties shared across samples while allowing the probability associated with each distribution to be inferred specifically for each sample. Having incorporated prior knowledge into the model, we can determine the signal distributions of the modified kmers and quantitatively estimate the modification rates accordingly. xPore was evaluated on transcriptome-wide m6A profiling data with and without replicates for prioritising differentially modified sites. In addition, the application of xPore on direct RNA-Sequencing data from 6 human cell lines revealed the landscape of RNA modifications, i.e. differentially modified sites across all cell lines with cell type-specific modification rates. With xPore, I will demonstrate that RNA modifications can be quantitatively identified from direct RNA-sequencing data with high accuracy, opening many new opportunities for large scale applications in precision medicine.

Bioinformatics/ Data sciences/ AI

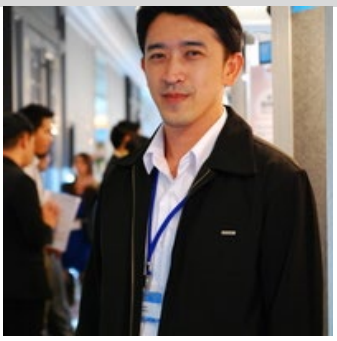
Data management of Genomics Thailand

Sissades Tongsima

National Biobank of Thailand (NBT),
National Science and Technology Development Agency (NSTDA),
Thailand

Genomics Thailand (GeTH) aims to apply insights into the molecular basis of disease to improve Thailand healthcare services. Such insights are obtained from analyses of large numbers and the size of human genome data. The country requires an extensive computational genomic infrastructure to successfully launch genomic medicine services to conduct the nationwide population genomics project. NSTDA partakes in Genomics Thailand and entrusts researchers from the National Biobank of Thailand (NBT) to create the underlying genomic computational environment that enables standard genome data processing and offers the most comprehensive reference genetic variation database for Thais. In addition to supporting the high-performance computing hardware and the Thai reference genetic variation database, NBT produces various software for tracking DNA samples and managing the corresponding sequencing data produced by whole genome sequencing (WGS) of 50000 Thai volunteers (50KGeTH), including E-enrollment software, phenotype collection tool, and the 50KGeTH specimen management system. Variants from each WGS data will be extracted via the GATK best practices' variant calling protocol and predicted molecular effects that may influence patients' clinical phenotypes. To complete the computational ecosystem, NBT creates bioinformatic tools to help prioritize and visualize the genomic landscape for five disease groups: rare/undiagnosed diseases, cancer, non-communicable disease, pharmacogenomics and infectious disease.

Data processing and variant prioritization standardization



Chumpol Ngamphiw

National Biobank of Thailand (NBT),
National Science and Technology Development Agency (NSTDA),
Thailand

Successful large-scale whole-genome sequencing project demands high standard/quality protocols that minimize potential errors lurking at every stage of the project. Genomics Thailand launched the nation largest human population genomics that recruits 50,000 Thai volunteers for whole-genome sequencing. To do this, we adopted “best practices” protocols from Genomics England, the earliest forerunner to conduct population genomics. Particularly, once sequencing is done, the raw sequencing reads (FASTQ format) will go through sequencing quality evaluation by NSTDA. GATK4 best practices protocol will be deployed to identify sequencing variation, while structural variation detection will be handled separately using bioinformatic tools to process reads aligned to human RefSeq. Global Alliance also recommends these procedures for variant calling for Genomics and Health (GA4GH), an international organization founded to standardize genomic data processing and sharing. To assist variant scientists/physicians in interpreting the potential pathogenic variants that might explain the underlying etiology, we construct a web-based platform called variant annotation and prioritization platforms (VAPP) that offer users various filtering utilities to prioritize etiologic variants candidates. The variant mentioned above calling protocol and genomic data processing utilities shall become the country computational genomic enabling platform that fosters and drives the implementation of genomic medicine and future genomics-driven businesses.

Genomics Thailand: 2019-2021

Surakameth Mahasirimongkol

Division of Genomic Medicine and Innovation Support
Department of Medical Sciences
Ministry of Public Health, Thailand

Genomics Thailand is the initiative to increase the competitiveness of Thailand economy, beginning in 2017 from the coalition of three ministries, the Ministry of Public Health, Ministry of Education and Ministry of Sciences and Technology. The cabinet approved the Genomics Thailand national cooperative plan on 26th March 2019, a critical milestone of genomics in Thailand. This plan came from the shared vision of the political leaders and scientific community. With estimated funding of around 20 million USD per year until 2024, this plan is one of Thailand's largest medical sciences research plans.

In the past two years, the national DNA extraction center, the whole genome sequencing center, and the national genome data center were established at various organisations. Around 5,000 DNA samples had already been enrolled by January 2022. We expect the first 10,000 whole-genome sequences to be generated and interpreted in 2022. The clinical genetic services were expanded based on the rare disease clinical service network, the hereditary breast and ovarian cancer screening program, and pharmacogenetics tests included in the national health benefit package under the national health security office. The regulation of genomic medicine is established in October 2021, and the standard of NGS analysis will be made available by mid-2022. The first four-month genetic counselling course was initiated in January 2022, and the two-month training for medical technologists has been going on for two years since 2020.

With the first 50,000 WGS data, Genomics Thailand aims to develop a standardized actionable clinical genomic information system that enables genomic medicine from primary health care to tertiary health centers. We plan for the second phase of Genomics Thailand, where health and economic benefit will be fully recognized by integrating genetic information into primary health care.

Thailand National Essential Drug for Rare Diseases Working Group

Duangrudee Wattanasirichaigoon

Medical Genetics Division
Faculty of Medicine Ramathibodi Hospital
Mahidol University

Ethics and genome editing

Soraj Hongladarom

Department of Philosophy
Faculty of Arts, Chulalongkorn University

Ethical guidelines standard development for genomics research

Prasit Phowthongkum

Division of Medical Genetics and Genomics
Department of Medicine, Faculty of Medicine
Chulalongkorn University

Genomics technology made an unprecedented speed of biology discovery which is likely to affect medicine and healthcare. However, due to the nature of the field: massive data generation and manipulation, largely unknown short to long term effects on human health and the results that can affect family and non-family members such as ethnic groups create unique ethical problems previously un-encountered justify particular guidelines for its own field's concerns. In collaboration with the National Research Council, Thai Societies of Human Genetics developed the first draft of ethical standards for human genomic research. The recent Privacy Data Act has had a significant effect on our guideline development and the future draft of the Human Research Act.

Polygenic risk scores in diverse populations: The importance of inclusivity

Jakris Eu-ahsunthornwattana

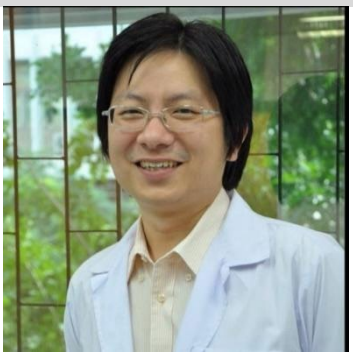
Department of Community Medicine
Faculty of Medicine Ramathibodi Hospital
Mahidol University

Polygenic risk scores (PRS) utilize a combination of genetic variants to predict complex traits of interest. There have been significant improvements in the methodologies used in constructing PRS and their predictive utility in recent years, which led to increasing interest and utilization and even commercialization. However, one crucial remaining issue limiting their utility is the heterogeneity of the population and transportability across the populations. This talk will discuss the causes of this, including the source data, allele distribution, linkage disequilibrium pattern and heterogeneity of the environmental factors, and the impact and implications of this issue when a PRS is applied in diverse populations.

Population genetics: Return nationality to Thais (Sirinthorn Project)

Kornkiat Vongpaisarnsin

Department of Forensic Medicine
Chulalongkorn University



เนื่องด้วยเทคโนโลยีทางพันธุศาสตร์ที่เจริญก้าวหน้า ทำให้ความรู้ทางพันธุศาสตร์มนุษย์และการแพทย์มีความก้าวหน้าในหลากหลายมิติทั้งในด้านการค้นหาสาเหตุของโรค ความเข้าใจกระบวนการของการเกิดโรครวมถึงการรักษาในระดับเซลล์ หรือในระดับสารพันธุกรรม ฯลฯ ในบริบทของนิติพันธุศาสตร์ (Forensic Genetics) การนำข้อมูลทางพันธุศาสตร์จากเทคโนโลยีการตรวจลำดับสารพันธุกรรมรุ่นใหม่ (Next generation sequencing, NGS) ได้ถูกนำมาประยุกต์ใช้เพื่อการแก้ปัญหาทางนิติวิทยาศาสตร์ในหลากหลายปัญหาที่ยังไม่ได้รับการแก้ไขในอดีตด้วยข้อจำกัดของวิทยาศาสตร์และเทคโนโลยี

ปัจจุบันนี้ความรู้ทางนิติพันธุศาสตร์สามารถนำมาประยุกต์ใช้สำหรับการตรวจพิสูจน์เอกลักษณ์บุคคล, การหาความสัมพันธ์ทางเครือญาติ, การทำนายความสัมพันธ์ของชาติพันธุ์ หรือการสืบค้นบนฐานข้อมูลสารพันธุกรรมประชากรเพื่อหาผู้กระทำความผิดในคดีต่าง ๆ เป็นต้น ปัญหาหนึ่งที่อาจส่งผลต่อหลากหลายหน่วยงานของรัฐและประเทศ คือปัญหาของการพิสูจน์บุคคลไร้รัฐ หรือบุคคลที่ยังไม่มีการระบุสัญชาติ ซึ่งนับเป็นปัญหาที่ส่งผลกระทบต่อระบบรัฐในด้านต่าง ๆ เช่น การเข้าถึงสิทธิในการรักษาพยาบาล หรือการเข้าถึงสิทธิพื้นฐานในการศึกษา เป็นต้น การแก้ปัญหาบุคคลไร้รัฐฯ จะต้องอาศัยความร่วมมือของกระทรวงและหน่วยงานต่าง ๆ เช่น มหาดไทย ยุติธรรมฯ และมหาวิทยาลัย เพื่อนำกระบวนการทางนิติวิทยาศาสตร์และความรู้ด้านนิติพันธุศาสตร์เข้ามาแก้ไขปัญหาของการระบุความสัมพันธ์ระหว่างบุคคลที่มีสัญชาติแล้วกับบุคคลไร้รัฐฯ

Population and Thai ancestry

Jatupol Kampuansai

Department of Biology, Faculty of Science,
Chiang Mai University

Wibhu Kutanan[1], Jatupol Kampuansai[2], Metawee Srikummool[3]
[1]Department of Biology, Faculty of Science, Khon Kaen University
[2]Department of Biology, Faculty of Science, Chiang Mai University (email: Jatupol.k@cmu.ac.th)
[3]Department of Biochemistry, Faculty of Medical Science, Naresuan University

The geography of Thailand that situates in the center of Mainland Southeast Asia with a diverse landscape coupled with a prolonged human occupation history promote an extensive ethnolinguistic diversity in Thailand with a population size of ~68.6 million people speaking 68 different recognized languages belonging to five linguistic families: Tai-Kadai, Austroasiatic, Sino-Tibetan, Austronesian, and Hmong-Mien. The archaeological and linguistic evidence suggests a complex population structure and history of the ethnolinguistic groups of Thailand. In addition, one of the most important questions for scholars interested in Thai prehistory is who the predecessors of the present-day Thai people were. Two main hypotheses, indigenous and immigrant, have been proposed and this is where genetics can provide more insights. Thanks to the advent of next generation sequencing technologies, it has become feasible to generate large amounts of sequence data for entire populations. Here, we provide several new insights into the genetic prehistory of total 70 Thai ethnolinguistic groups based on sequencing of complete mtDNA genomes, partial Y chromosome sequences of ~2.3 mB and genome-wide data using the Affymetrix Axiom Genome-Wide Human Origins array. Our major findings are: contrasting patterns of paternal vs. maternal genetic variation, more ancient lineages and heterogeneity of the Austroasiatic-speaking groups; genetic differences among the four major groups according to geographic region (North, Northeast, Central and South); and Indian admixture in central and southern Thais.

Keywords: ethnolinguistic groups, genome-wide, mitochondrial genomes, Y chromosome

Amelogenesis imperfecta: tooth characteristics and genetic variants in Thai families

Kanokwan Sriwattanapong[1*], Anucharte Srijunbarl[2], Sermporn Thaweesapphithak[1], Thantrira Porntaveetus[1,3]

[1]Genomics and Precision Dentistry Research Unit, Medical Genomics Cluster, Department of Physiology, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand
[2]Dental Materials R&D Center, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand
[3]Master of Science Program in Geriatric Dentistry and Special Patients Care (International Program), Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand

Introduction: The mutation in *FAM83H* gene is one of the causes of autosomal dominant hypocalcified amelogenesis imperfecta (AI), affecting enamel formation. (MIM 130900)
Objective: To investigate genetic alteration and tooth characteristic of Thai families affected with AI.
Methods: Exome and Sanger sequencing were employed to detect genetic variants. Tooth color, roughness, mineral density, hardness, mineral content, and ultrastructure of AI teeth obtained from affected individuals were examined and compared with the control teeth obtained from healthy individuals.
Results: Three patients and affected family members were identified with the nonsense variant, c. 1387C>T, p.Gln463*, in *FAM83H*. The color of AI teeth ranged from white-yellowish to brown-black. Tooth surface was porous and irregular. The AI teeth showed reduced mineral density, hardness, and main inorganic contents, calcium and phosphorus, compared to those in the controls. Short enamel rods with wide interrod areas and abnormal enamel-dentin junction were observed in AI teeth.
Conclusions: The *FAM83H* – AI teeth showed abnormalities in color, surface roughness, mineral density and content, and hardness.

Key Reference: Nowwarote, N., Theerapanon, T., Osathanon, T., Pavasant, P., Porntaveetus, T., & Shotelersuk, V. (2018). Amelogenesis imperfecta: A novel *FAM83H* mutation and characteristics of periodontal ligament cells. Oral Diseases, 24(8), 1522-1531.

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Contact information: Kanokwan Sriwattanapong, PhD. E-mail: kanokwan.sr@chula.ac.th
Genomics and Precision Dentistry Research Unit, Department of Physiology, Faculty of Dentistry, Chulalongkorn University, Bangkok 10330, Thailand
Tel: 662-218-8695; Fax: 662-218-8691

Orodental features associated with dentinogenesis imperfecta and osteogenesis imperfecta

Narin Intarak[1*], Thanakorn Theerapanon[1], Lawan Boonprakong[2], Thantrira Porntaveetus[1,3]
*Corresponding author

[1]Genomics and Precision Dentistry Research Unit, Medical Genomics Cluster, Department of Physiology, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand.
[2]Oral Biology Research Center, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand.
[3]Master of Science Program in Geriatric Dentistry and Special Patients Care (International Program), Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand.

Introduction: Dentinogenesis imperfecta (DGI) is one main features of osteogenesis imperfecta (OI). The patient affected with DGI-OI have brown and brittle teeth. To date, there is a lack of understanding of the DGO-OI teeth ultrastructure and properties.
Objectives: To determine genetic variant causing DGI-OI and investigate the microscopic characteristics and physical and mechanical properties of the teeth affected with DGI-OI compared with those of the normal teeth.
Methods: Exome and Sanger sequencing were performed to identify genetic variants. Three DGI-OI teeth obtained from 3 unrelated patients were examined in comparison with 9 control teeth from age-matched healthy individuals. The colorimetry, micro-computerized tomography, Knoop microhardness, energy dispersive X-ray spectroscopy, scanning electron microscopy, and histology were employed.
Results: The patients were identified with the heterozygous missense variants in the *COL1A2* gene. The c.1531G>T, c.2027G>T, and c.3106G>C variants were detected in patient-1, -2, and -3 respectively. All DGI-OI teeth significantly reduced microhardness in the dentin. Enamel microhardness was significantly reduced in patient-2. Elevated carbon levels were found in the teeth of patient-1 and patient-3. Numerous ectopic calcified masses, sparse and obstructed dentinal tubules, dentin holes, and collagen disorientation were observed in all DGI-OI teeth.
Conclusion: The patients affected with DGI and OI had altered tooth structure and properties comprising weak dentin, abnormal carbon composition, and abnormal dentin ultrastructure. This study expands the understanding of the phenotypic spectrum of dentinogenesis imperfecta associated with osteogenesis imerfecta.

Acknowledgements: NI is supported by the Ratchadapisek Somphot Fund for Postdoctoral Fellowship, Chulalongkorn University. This research is supported by the Health Systems Research Institute (64-124), Thailand Research Fund (MRG6280001), the 90th Anniversary of Chulalongkorn University Fund, Ratchadapiseksompotch Endowment Fund, Chulalongkorn University (RCU_H_64_002_32, 764002-HE01).

Keywords: Dentinogenesis imperfecta, osteogenesis imperfecta and COL1A2

Genetic variation profiling prediction of 51 pharmacogenes in a Thai population using whole-genome sequencing

Natnicha Wankaew[1*], Pajaree Chariyavilaskul[2,3], Monpat Chamnanphon[3,] Adjima Assawapitaksakul[4], Wanna Chetruengchai [4], Monnat Pongpanich[5], Vorasuk Shotelersuk[4]

[1]Program in Bioinformatics and Computational Biology, Graduate School, Chulalongkorn University, Bangkok, Thailand
[2]Clinical pharmacokinetics and pharmacogenomics research unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3]Department of Pathology, Faculty of Medicine, Srinakharinwirot University, Nakornnayok, Thailand
[4]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand
[5]Department of Mathematics and Computer Science, Faculty of Science, Chulalongkorn University, Bangkok, Thailand

Background: Genetic variations contribute to differences in drug responses in individuals and they differ among populations. Variation in pharmacogenes had been explored in many populations, but Asians have been understudied. In Thailand, only one study investigated star allele frequencies in 25 pharmacogenes of 291 Thais with Brugada syndrome. Even in the same geographical regions, there were contrasting findings between studies. To determine more comprehensive list of pharmacogenes, this study will examine 51 genes (26 additional genes from the previous study) in 171 individuals from a general Thai population.
Objectives: We aim to identify a star allele profile of 51 pharmacogenes on 171 individuals from a general Thai population. In addition, we want to compare pharmacogenes variants frequencies among the Thai population and other ethnicities and detect some potentially novel pharmacogenes variants that might be specific to the Thai population.
Methods: 171 unrelated Thai genomes from all regions of Thailand were used to predict the star allele profile of 51 pharmacogenes by using Stagazer® **.**
Results: We identified twenty predicted pathogenic variants which have not previously been reported. Every individual had ≥3 genes with a non-normal phenotype. Our report indicated that 40 of 51 pharmacogenes had ≥1 individual with non-normal phenotype, and there are 13 genes had ≥25% of individuals with non-normal phenotypes.
Conclusions: Pharmacogenetic landscape in Thai provide guidance for genotyping policy in Thailand and Southeast Asian countries, moving the nation a step closer to personalized medicine.

Acknowledgements: This work was supported by Chulalongkorn University Graduate Scholarship to Commemorate the 72nd Anniversary of His Majesty King Bhumibol Adulyadej. Ratchadapiseksompotch Fund, Chulalongkorn University (764002-HE01), TSRI Fund (CU_FRB64001_01_30_10), Thailand Research Fund (DPG6180001), and Health Systems Research Institute.

Keywords: individual drug response, pharmacogenes, star allele, variants frequencies, whole-genome sequencing

Long-read amplicon sequencing of the *CYP21A2* in 48 Thai patients with steroid 21-hydroxylase deficiency

Nithiphut Tantirukdham[1,2,*], Taninee Sahakitrungruang[3], Ratikorn Chaisiwamongkol[3], Monnat Pongpanich[4,5], Chalurmpon Srichomthong[6,7], Adjima Assawapitaksakul[6,7], Aayalida Buasong[6,7], Siraprapa Tongkobpetch[6,7], Patra Yeetong[8] and Vorasuk Shotelersuk[6,7]

[1]Genetics Program, Division of Human Genetics, Department of Botany, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand
[2]Molecular and Genomics Research Laboratory, Centre of Learning and Research in Celebration of HRH Princess Chulabhorn's 60th Birthday Anniversary, Chulabhorn Royal Academy, Bangkok 10210, Thailand
[3]Division of Pediatric Endocrinology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330 Thailand
[4]Department of Mathematics and Computer Science, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand
[5]Omics Sciences and Bioinformatics Center, Faculty of Science, Chulalongkorn University, Bangkok, 10330, Thailand
[6]Center of Excellence for Medical Genomics, Medical Genomics Cluster, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand
[7]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok 10330, Thailand
[8]Division of Human Genetics, Department of Botany, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand
*Presenter

Introduction: Congenital adrenal hyperplasia (CAH) is most commonly caused by 21-hydroxylase deficiency (21-OHD), an autosomal recessive disorder resulting from biallelic pathogenic variants (PVs) in *CYP21A2*. With a highly homologous pseudogene and various types of single nucleotide and complex structural variants, the identification of PVs in *CYP21A2* has been challenging.
Objectives: To leverage long-read next-generation sequencing combined with locus-specific PCR to detect PVs in *CYP21A2* and to determine its diagnostic yield in patients with 21-OHD.
Methods: 48 Thai patients with 21-OHD comprising 38 sporadic cases and five pairs of siblings were enrolled. Two previously described locus-specific PCR methods were performed. Amplicons were subject to long-read sequencing.
Results: All 96 PVs in *CYP21A2* in the 48 patients were successfully identified. The combined techniques were able to detect 26 structural variants (27%; 26/96) in 22 patients, with 18 having monoallelic and 4 having biallelic structural variants. The remaining PVs were pseudogene-derived mutations (63%; 60/96), entire gene deletions (2%; 2/96), missense variants (3%; 3/96), a splice-site variant (2%; 2/96), a frameshift variant (1%; 1/96), a nonsense variant (1%; 1/96) and a rearrangement (1%; 1/96). Notably, a splice-site variant, IVS7+1G>T, which was identified in a pair of siblings, has not previously been reported.
Conclusions: Our approach exploiting locus-specific PCR and long-read DNA sequencing has a 100% diagnostic yield for our cohort of 48 patients with 21-OHD.

Acknowledgements: We would like to thank the patients and their families for participating in this study. This work was supported by Ratchadapiseksompotch Fund, Chulalongkorn University (764002-HE01), TSRI Fund (CU_FRB640001_01_30_10), Thailand Research Fund (DPG6180001), and Health Systems Research Institute (64-132).

Keywords: Congenital adrenal hyperplasia, 21-hydroxylase deficiency, Locus-specific polymerase chain reaction, Long-read amplicon sequencing

Whole exome sequencing and functional studies of a *STAT6* variant in a family of familial hemiplegic migraine

Chupong Ittiwut[1□], Rungnapa Ittiwut[2, 3□*], Ponghatai Bunsimma[2, 3], Aurauma Chutinet[4], Nijasri Charnnarong[4], Kanya Suphapeetiporn[2, 3], Vorasuk Shotelersuk[2, 3]

[1]Central Laboratory, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
[2]Center of Excellence for Medical Genetics, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand.
[3]Excellence Center for Medical Genetics, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, 10330, Thailand.
[4]Chulalongkorn Stroke Center, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, 10330, Thailand.
□Both authors contributed equally to this work

Introduction: Familial hemiplegic migraine (FHM) is a monogenic disorder. So far, the identified variants in 3 genes, *CACNA1A, ATP1A2* and *SCN1A* contributes to less than half of the patients. **Objective:** To study the functional effect of *STAT6* variant identified in FHM patients. A novel candidate gene of FHM **Methods:** A family of FHM was collected, and exome sequencing was performed, followed by PCR-RFLP and segregation analysis. STAT6 is the transcription factor of many downstream genes. One of those is the COX genes involved in prostaglandin production related to the pathophysiologic change in Migraine. Therefore, prostaglandin conversion related *to COX1 and COX2 promoters were chosen to test* promoter luciferase activity. In addition, Immunoblotting for a protein of interest was done to detect the active function form of the proteins.
Results: The patient and her affected son identified a missense c.1606C>T (p.R536W) in the *STAT6* gene. This variant was identified in 4/249796 gnomAD alleles and not found in our in-house Thai exome database. The prediction score from SIFT and PolyPhen2 were damaging. Luciferase activity of the *COX1* and *COX2* promoter did not show a significant difference between *STAT6* wild-type and the variant. Western blot from transfected 293FT cells showed that the p.R536W STAT6 was still active (Phosphorylated-STAT6), at the same level as the wild-type STAT6.
Conclusions: In this study, we identified the *STAT6* c.1606C>T (p.R536W) variant in a family with FHG. However, there was no difference in regulation activity and protein active form between STAT6 wildtype and variant.

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Keywords: STAT6, familial hemiplegic migraine, migraine

Ano-Rectosigmoid cancer vs Proximal colon cancer: different mechanisms confirmed in the era of next-generation sequencing

Phawin Kor-anantakul[1,3,*], Prasit Phowthongkum[2,3]

[1]Center of Excellence for Medical Genomics, Medical Genomics Cluster, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
[2]Division of Medical Genetics and Genomics, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
[3]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand.

Introduction: Colorectal cancer is the fourth common cancer in Thailand. Diagnosis of hereditary cancer syndrome, which presents with colorectal cancer, drastically changes management. Microsatellite instability, the hallmark of Lynch syndrome-associated colorectal cancer, is usually identified in cancer from the proximal sites rather than ano-rectosigmoid area.
Objectives: Compared the incidence of Lynch syndrome (LS) in ano-rectosigmoid cancer vs proximal colon cancer.
Methods: This retrospective observational study reviewed the medical records of the patients who were referred to the genetic cancer clinic at King Chulalongkorn Memorial Hospital for genetic evaluation and counselling regarding the hereditary nature of cancers. Patients who underwent multiple gene panel testing with commercially available next-generation sequencing were included for further review. *MLH1, MSH2, MSH6, PMS2,* and *EPCAM* are the minimal sets of genes tested. APC-associated Familial adenomatous polyposis was excluded.
Results: Medical records of 59 patients from June 2018 to December 2021 were reviewed. Twenty-nine patients with rectosigmoid cancer had positive gene panel results for Lynch syndrome for only 2 cases (6.8%). On the other side, thirty patients with colon cancer had positive gene panel results for LS for 9 cases (30.0%).
Discussion: Almost five-fold higher incidence of Lynch syndrome among patients presenting with proximal colon cancer vs ano-rectosigmoid colon suggestive and confirm the long-known of observation of different mechanisms of the cancer of different sites. However, the factors that govern these differences have never been explored. Microbiomes spatial differences might contribute to the contrast incidence of Lynch syndrome of proximal and distal sides.
Conclusion: Lynch syndrome is more identified in patients with proximal colon cancer.

The authors declare no financially conflicts of interest.

Keywords: ano-rectosigmoid; gene panel; next-generation sequencing; cancer; hereditary cancer syndrome

Novel Mutation in *SOST* Causing Autosomal Dominant Craniodiaphyseal Dysplasia in Thai Twins

Thammakamon Akkaratham[1,2,*] , Kanya Suphapeetiporn[1,2], Wuttichart Kamolvisit[1,2]

[1]Center of Excellence for Medical Genomics, Medical Genomics Cluster, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[2]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand,

Introduction: Craniodiaphyseal dysplasia (CDD) (OMIM 122860) is an autosomal dominant progressive bone overgrowth disorder due to increased bone formation caused by pathogenic variants in *SOST*. The incidence of this disease is extremely rare, with only 2 case reports for CDD (Bieganski et al. 2007 and Kim et al. 2011).
Objectives: To report 15 years old twin males with CDD, who had facial distortion and severe increased intracranial pressure and to review phenotypic spectrums of CDD.
Methods: We extracted DNA from peripheral blood leukocytes of twin boys and the mother. Peripheral blood leukocyte DNA from twin A was undergone whole-exome sequencing (WES). In addition, DNA from his presumed fraternal twin B and mother was undergone PCR-Sanger sequencing to obtain segregation data. Unfortunately, the father's sample was unable to be obtained as he passed away a long time ago from an irrelevant issue.
Results: We detected a heterozygous c.67G>C (p.Gly23Arg) in *SOST* from WES analysis of twin A. PCR-Sanger sequencing data from twin B showed the same heterozygous missense variant as seen in twin A but not in their mother. The variant is considered likely pathogenic according to ACMG/AMP standard guidelines (PM1, PM2, PP1 and PP4). Furthermore, while short stature was frequently reported in CDD, both of our patients have normal height.
Conclusions: We reported adolescent twin patients with a novel likely pathogenic variant in *SOST*, a gene known to cause CDD. Our findings expand both mutational spectrums of *SOST* and phenotypic spectrums of CDD.

Acknowledgments: This study was supported by the Health Systems Research Institute and Thailand Research Fund (DPG618000).

Keywords: Craniodiaphyseal dysplasia, *SOST*, Whole-exome sequencing, Thai, Twins

Patient-Reported Phenotyping: The power of social media in rare disease diagnosis and Potential Use of Off-target Exome analyses for Mitochondrial DNA Analysis and concerns

Chupong Ittiwut and Prasit Phowthongkum

Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, Bangkok, Thailand

Introduction: Whole exome sequencing (WES) analyses effectively identify pathogenic variants in nuclear genes; however, the mitochondrial genome is generally considered off-target. There has been shown to possibly increase the diagnostic yield of pathogenic mtDNA variants identification by WES re-analysis and troubleshooting in pre-and post-annotation processes. This prompted us to reanalyze and look for the genetic defect in mtDNA in a female with a self-reported phenotype in her personal social media space (Instagram) suggestive of mitochondrial disorders with stroke-like episodes. Unfortunately, the laboratory did not receive full clinical pictures from referring physicians, which hindered variant prioritization.
Objectives: To evaluate abilities and limitations to identify candidate mtDNA variants by WES analysis in a case without mutation in the nuclear genes and to demonstrate the power of social media in obtaining a clinical diagnosis for rare disease patients.
Methods: WES analysis was performed. No nuclear genome variants potentially explain the patient's symptoms were identified. All mtDNA variants were manually predicted for variability and pathogenicity by HmtVar (https://www.hmtvar.uniba.it/query). Exomiser® variant prioritization is used as another orthologous method. Variant interpretations were performed to determine whether they were contributable to the disease.
Results: Thirty-five candidate mtDNA variants were captured at good quality. These include the chrM-11387-T-C (hg19) in the *MT-ND4* gene that was primarily classified as likely pathogenic m.11387T>C (p.Y210H); however, it was later re-classified as a synonymous m.11386T>C (p.L209=). This suggesting of different or incomplete information of mitochondrial sequence reference database.
Discussion: We previously identified a common recurrent mitochondrial variant for Mitochondrial Encephalomyopathy, Lactic Acidosis with Stroke like Episodes (MELAS), commonly called A3243G using WES with the Sureselect® (Agilent) captured kit. In contrast, the NextSeq® (Illumina) will not capture mitochondrial sequence and considers this an off-target area. However, the sensitivity and specificity of mtDNA variant detection using our current pipeline cannot be established due to small sample numbers. This article suggested a potential utility of WES data to identify or discover mtDNA variants. Although, using this off-target sequence must be cautiously performed due to the inherent nature of the mitochondrial disorders and the incomplete/inconsistent reference data. Another message for molecular diagnostic laboratories is obtaining clinical data from as many sources as possible to aid the diagnosis. In this case, social media might play a potential source of useful information.
Conclusions: Interpretation of pathogenic mtDNA variants in the off-target WES analysis should be made with caution. Reliable coverages, read depths, captured method-dependent, reference sequences, and analysis pipelines should be concerned. In addition, social media can help laboratories obtain useful clinical information aids in the clinical diagnosis of rare diseases.

Acknowledgements: Authors thank the patients and their families for participation in this study.

Keywords: mtDNA exome Off-target

Cancer Genetic Service at King Chulalongkorn Memorial hospital

Chanchira Sriraksasin and Prasit Phowthongkum

Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

Introduction: In 2020, more than 190,000 new cancer cases in Thailand were diagnosed with cancer. Increased awareness of hereditary cancer and the development of targeted cancer therapies have increased requests for genetic counselling services. Cancer genetic services have been established in KCMH since 2017. We described the prevalence of pathogenic germline variants in patients with cancer using cancer panel genetic testing at our clinic. Unfortunately, few patients who could not afford the test underwent research exome sequencing.
Methods A retrospective review of patients seen at the genetic cancer clinic at KCMH between July 2018 and December 2021. Genetic testing was offered to individuals with personal or family history suggestive of genetic cancer susceptibility conditions.
Results: A total of 414 patients were included. Pathogenic/Likely pathogenic germline variants were identified in 88 patients (21.25%). We identified moderate and high penetrance cancer susceptibility genes in breast and ovarian cancer syndrome (*BRCA1, BRCA2, PALB2, RAD51C*), Lynch syndrome, Familial adenomatous polyposis, Juvenile Polyposis Syndrome, Hereditary diffuse gastric cancer syndrome, Li-Fraumeni Syndrome, PTEN-Hamartoma Tumor Syndrome, Tuberous Sclerosis Complex, Birt-Hogg-Dubé Syndrome, Neurofibromatosis type I, Neurofibromatosis type II, Hereditary Leiomyomatosis and Renal Cell Cancer, von-Hippel Lindau syndrome. One very interesting patient diagnosed with co-occurrence of von-Hippel Lindau Syndrome and neurofibromatosis type I carries three likely pathogenic variants in cancer-predisposing genes (*VHL, NF1* and *BRCA1*). All patients will undergo pre-test counselling by a clinical geneticist and/or genetic counsellor. The counselling personnel confirmed the results to provide the most accurate interpretation and risk analysis with the family and personal history contexts. Patients were properly referred for obtaining cancer-specific surveillance or prophylactic surgery, such as 12 patients bilateral salpingo-oophorectomy for *BRCA1/2* patients during this analysis. Targeted therapy, i.e. PARP inhibitors, were initiated in several *BRCA1/2* patients. Aggressive gastric cancer surveillance, bridging for more definitive total gastrectomy for *CDH1* asymptomatic carrier with a positive family history of members who died from aggressive diffuse gastric cancer. During the pandemic era of COVID-19, we experimentally provided the service using telemedicine, and we presented this data in another abstract for this conference.
Conclusions Since we established the genetic cancer service at King Chulalongkorn Memorial Hospital, we have included several hundred patients considered high risk of cancer genetic susceptibility. With the advent of affordable genetic testing and proper genetic counseling, we improved the standard of care for cancer patients. However, lack of awareness from other specialists, including oncologists, lack of genetic health care professionals (geneticists and genetic counsellors) who are specialized or have interests in cancer genetics, lack of specific guidelines of management of newer or moderate penetrance cancer genes are among some factors identified as the challenges for sustainable cancer genetic service.

Keywords: Cancer Genetics, Genetic counselling, Cancer Multigene testing, Next-generation sequencing

The Influence of Arylacetamide deacetylase Genetic Polymorphisms on Rifapentine Plasma Concentration in Thai Patients with Latent Tuberculosis Infection

Weeraya Phaisal[1,2,3,*], Monpat Chamnanphon[4], Sasiwimol Ubolyam[5,6], Anchalee Avihingsanon[5,6], and Pajaree Chariyavilaskul[2,3]

[1]Interdisciplinary Program of Biomedical Sciences, Graduate School, Chulalongkorn University, Bangkok, Thailand,
[2]Clinical Pharmacokinetics and Pharmacogenomics Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand,
[3]Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[4]Department of Pathology, Faculty of Medicine, Srinakharinwirot University, Nakornnayok, Thailand
[5] HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), Thai Red Cross AIDS Research Centre, Bangkok, Thailand.
[6]Tuberculosis Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

Introduction: Genetic variations in drug-metabolizing enzymes affect the pharmacokinetics of antituberculosis drugs. AADAC are essential enzymes responsible for the deacetylation of rifapentine to biologically active 25-desacetyl rifapentine.
Objectives: To determine genotype frequencies of *AADAC* genetic polymorphisms and correlate their genotype with plasma rifapentine concentrations.
Methods: A total of 226 patients were included in the study. The blood sample was collected to investigate *the AADAC (rs1803155) genotype* using MassARRAY technology. Rifapentine pharmacokinetics parameters were determined at week-4 post-treatment using a high-performance liquid chromatography technique.
Results: The frequency of *AADAC* genotype was GG = 47 (20.8%), GA= 108 (47.8%), and AA= 71 (31.4%). The AADAC was not significantly affected all pharmacokinetic parameters of rifapentine. However, the AADAC genotypes presented that patients with GG genotypes were 2-fold lower C_{max} and $AUC_{0\text{-}24hr}$ of rifapentine, and 2-fold higher CL and CL_R of rifapentine than patients who were AA and GA genotypes.
Conclusions: Rifapentine exposure varied with *AADAC* rs1803155 genotype. The G allele might be likely to lower rifapentine exposure. Further study of the effect of pharmacogenomics on drug exposure should be conducted in large subjects.

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Keywords: arylacetamide deacetylase, genetic polymorphisms, rifapentine, tuberculosis

Telemedicine in Cancer-genetic Clinic at King Chulalongkorn Memorial Hospital during the COVID-19 Pandemic

Chanchira Sriraksasin and Prasit Phowthongkum

Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

Introduction: The COVID-19 pandemic has impacted many healthcare systems worldwide. Healthcare services for non-COVID-19 patients were disrupted. Appointments were cancelled or postponed affected time-sensitive health issues, especially cancer patients. Genetics services traditionally considered non-essential services have been mostly deferred; however, genetic evaluation and testing are now an integral part of cancer care service because of their potential to inform surgical decisions, chemotherapy, and targeted treatments. Various telehealth models have been used in cancer genetics in recent years. We explored the usage of telehealth cancer genetics service offered during the peak of the pandemic era of COVID-19 at the tertiary University-based hospital: King Chulalongkorn Memorial Hospital (KCMH).
Methods This is a cross-sectional descriptive study of patients who visited the Cancer genetic clinic at KCMH in April 2020. The genetic counsellor reminded the appointment via telephone. If patients could not come in due to travel restrictions or infectious contact risks, we offered the telemedicine option by Line Video Call. Patients would give verbal consent before starting teleconsultation on the appointment day. Patients were asked to preinstall Line Mobile Application. We logged in Line Desktop-Mode for our service via the video call function. Using the Modified Likert Scale, we developed the questionnaires that include demographics data, technical requirements, pretest and posttest anxiety, and knowledge level.
Results During the study period, we saw 27 patients: 37.03% in-person and 62.97% via teleconsultation. Three patients turned down telemedicine visits: due to technical problems (2 patients), and 1 deferred the visit and wanted to come in person later with no obvious reason. Patients who chose the telegenetic counselling service are slightly younger, higher educated, earned higher income, and own more sophisticated mobile phones. They were also more anxious at baseline and more knowledgeable regarding cancer genetics. Unsurprisingly, the patients who chose the tele-genetic counselling lived dispersedly throughout the country, whereas all patients who visited the clinic in person resided in Bangkok Metropolitan Area and nearby. Gender might play a role in selecting the service as men preferred teleservice (possible technical savvier). The tele service patients were more likely to install the program by themselves and patients turned down the service due to technical problems (Internet speed or cannot use it at all). New patients were biasedly chose to have in-person (both patients and genetic counsellor biases) visits. The knowledge score was increased, and the anxiety level was decreased at the same degree between the tele genetic counselled patients and the in-person patients. New patients who later decided to have genetic tests were significantly delayed in telegenetic counselled patients for twelve months.
Conclusions. The teleservice utilization was proposed to overcome the limitation of geographical/physical distance with the patients and clinical center. The service might increase the accessibility of the patients. However, this does not alleviate the socio-economic and educational background problems. Some patients had difficulty using the online service due to technical matters. Careful selection and offering the patients suitable for teleservice such as follow-up visits might benefit the patients. The effectiveness in reducing anxiety and knowledge improvement seems to be equivalent between video, and face-to-face consultation proved the concept of no increase harmful with the non-in-person counselling as we long feared.

Revisit and proposal to expand to ethnic-specific secondary findings from the whole-exome sequencing of the Thai population

Wanna Chetruengchai[1,2*], Vorasuk Shotelersuk[1], Prasit Phowthongkum[1]

[1]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, 10330, Thailand
[2]Interdisciplinary Program of Biomedical Sciences, Graduate School, Chulalongkorn University, Bangkok, 10330, Thailand

Introduction: The authors (WC, VS) previously reported the secondary findings (SF) of Thai whole exome-sequencing (ES). Clinical consideration provoked the un-answered questions regarding the pathogenicity or the penetrance of the genes recurrently found in the cohort. Furthermore, thalassemia/hemoglobinopathy syndromes and X-linked glucose-6-phosphate dehydrogenase (G-6-PD) deficiency are the two most prevalent genetic disorders globally and are highly concentrated in Thailand and Southeast Asia. Although α-thalassemia syndromes, primarily due to partial or whole gene deletion, were not reliably detected with WES, the inclusion of β –Thalassemia, with small nucleotide changes, is readily diagnosed with WES. The prevalence of symptomatic G6PD female carriers is poorly studied, but the detection of male G6PD from WES should be considered diagnostic. The practical recommendation to avoid offensive drugs can be given to these patients.
Objective: To reanalyze three recurrent pathogenic variants in our cohorts. To determine the frequency and spectrum of pathogenic (P) or likely pathogenic (LP) variants in ß-Thalassemia, non-deletional α-Thalassemia, and G6PD using WES in the Thai population in the same cohort. Also, the SF using ACMG recommendation of reporting SF version 3 in adult Thai patients seeking other primary genetic diagnoses with WES.
Method: Narrative critical reanalysis of three recurrent variants in previous Thai cohorts: *PTEN, TGFBR2,* and *MYBPC3.* Exomes of the unrelated Thai 1599 healthy patient's parental individuals were reanalyzed for pathogenic variants in *G6P, HBB, HBA1,* and *HBA2*. Exomes of the unrelated Thai adult patients are analyzed for secondary findings and extended to newly proposed genes *(G6P, HBB, HBA1, and HBA2).*
Results: *TGFBR2* (rs34833812) and *MYBPC3* (rs573916965)are the two most prevalent recurrent variants in our previous analysis. Another recurrent variant is in *PTEN.* The conflicting interpretations submitted in ClinVar raised some concerns about their pathogenicity. For *PTEN* and *TGFBR2*, the penetrance is traditionally considered very high, while the prevalence of the diseases is rare. Whether the penetrance of these two specific variants is not as high as other variants that could only be discovered in this population-level cohort or the prevalence of these rare disorders are not uncommon as we believed. However, excluding these three variants, the prevalence of the actionable SF is still as high as 9.0%. Of the 1559 exomes, we identified 2 P/LP variants in the homozygous state of 11 individuals (0.7%) responsible for α-Thalassemia. The most prevalent variant in this phenotypic category is *HBA2*:c.427T>C in Hb Constant Spring, representing 0.6% of our cohort. The 0.1% responsible for Hb Paksé c.429A>T. The homozygous variants of these two variants produced the asymptomatic or mild disease. For G6PD deficiency, we identified 10 P/LP variants in the homo/hemizygous state of 71 individuals (4.55%). The prevalence rate was 4.1% in males and 0.45% in females. c.961G>A (p.Val321Met; rs137852327) found in 34 individuals (2.18%) is the most common one. Adding these two syndromes, nearly 15% of Thai healthy individuals might have secondary findings from exome analysis. From the separate analysis of our lab, we identified the SF in the ACMF SF3.0 in 14.6% of adult patients suspected of monogenic disorders submitted samples for WES. The most common PV was found in *SCN5A*. However, with the standard variant classification by ACMG/AMP, this variant should be classified as a variant of uncertain significance or the risk variant rather than a causative variant. Our adult patients cohort identified one homozygous Hb E and 3 G6PD deficiency males. Again, after excluding the *SCN5A* variant, the prevalence of actionable findings in Thai adults is 8.13% (3.30-12.96). If Hemoglobinopathy and G6PD deficiency are included as suggested, the prevalence would be as high as 11.38% (5.77-16.99).

Conclusion: Revisit the SF variants in our previous cohort has been performed. Although the recurrent variants in this cohort might not fulfil clinically significant PV, the background findings are still considered as high as close to 1 in 10 people. Adding the thalassemia syndromes and G6PD deficiency into the analysis, more than 1 in 6 people could benefit from WES SF analysis. This data is similar to the adult diagnostic exome sequencing patients.

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Keywords: Exome sequencing, G6PD, Thalassemia.

Impact of G6PD deficiency and its Mutations on Diabetes Diagnosis by hemoglobin A1c in Thailand Cohort

Punchalee Mungkalasut[1*] and Chalisa Louicharoen Cheepsunthorn[2]

[1]Biomedical Sciences Program, Graduate School, Chulalongkorn University, Bangkok, Thailand.
[2]Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

Introduction: Glucose 6-phosphate dehydrogenase (G6PD) deficiency is the most prevalent inherited enzymopathies. It leads to hemolytic anemia, spontaneously or provoked by oxidative stress. Reduced life spans of erythrocytes could affect the level of glycated hemoglobin (HbA1c) and the diagnosis and monitoring of diabetes mellitus type 2 (DMT2). The association between HbA1c levels and G6PD deficiency has not yet been elucidated.
Objectives: To investigate the impact of G6PD deficiency and its frequent mutations in Thai population, including *G6PD*^{Viangchan} (G871A) and *G6PD*^{Mahidol} (G487A), on HbA1c levels.
Methods: A total of 632 blood samples excluded from thalassemia cases were analyzed for G6PD activity using an automated UV-based enzymatic assay (Mindray, PRC). Fasting plasma glucose (FPG) data from annual checkups was collected. The HbA1c levels were determined by enzymatic assay (Abbott Laboratories, USA). The *G6PD* mutations in all samples were genotyped using TaqMan SNP genotyping assay and PCR-RFLP.
Results: HbA1c levels were positively correlated with G6PD activity (p<0.01; r=0.238). Notably, the FBG/HbA1c ratio in *G6PD*^{Viangchan} was moderately reversely correlated with G6PD activity (p<0.05; r=-0.428). Additionally, individuals with *G6PD*^{Viangchan} (4.88±0.38 mg%, n=83) and *G6PD*^{Mahidol} (4.77±0.40 mg%, n=23) had statistically significantly lower HbA1c levels than those with wild type *G6PD* (5.22±0.37 mg%, n=526; p<0.01).
Conclusions: This is the first study to show an association between G6PD phenotype and HbA1c levels. *G6PD* pathogenic variant, especially *G6PD*^{Viangchan,} is associated with a decrease in HbA1c level. Our results highlight the impact of G6PD deficiency on using HbA1c in monitoring and diagnosing DMT2.

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Keywords: G6PD deficiency, *G6PD* Viangchan, DM, HbA1c, Thailand

Driving Genetics Discovery, Association and Screening with the Asian Screening Array (ASA)

Punna Kunhapan, Nusara Satproedprai, Tassamonwan Chaiyasung, Chutchanok Tammakai, Nuanjun Wichukchinda, and Surakameth Mahasirimongkul

Division of Genomic Medicine and Innovation Support, Department of Medical Sciences

The Centre for Medical Genetics has developed a Thai Human Genetics Database in the Genomics Thailand Project. The database currently includes genetic data from more than 13,000 Thai people. DNA samples from these people were genotyped using the Infinium Asian Screening Array (ASA) version 1.0. This microarray genotyping platform measures genotypes at 659,184 Single Nucleotide Polymorphisms (SNPs), including many Asian-specific SNPs. Samples in the database come from various sources – including studies of tuberculosis, systemic lupus erythematosus, periodontitis, and pharmacogenetics studies – and include healthy controls. The database has enabled the discovery of new genetic associations for many diseases and traits. It has also facilitated studies of gene-environment interaction, including infectious disease studies. The data will become a valuable tool to support the work of clinicians, scientists, public health policy planners and ethnographic researchers.

Corresponding author E-mail: surakameth.m@dmsc.mail.go.th

Keyword: Single Nucleotide Polymorphisms: SNPs, Microarray genotyping

A *de novo* hemizygous synonymous variant with splicing aberration of X-linked lymphoproliferative syndrome type 1

Kansinee Jeungsathapatchai[1,*] ,Yanapong Chaisithikarnkha[2], Rungnapa Ittiwut[2,] Chupong Ittiwut[3] and Kanya Suphapeetiporn[2,]

[1]Medical Sciences Program, Faculty of Medicine, Chulalongkorn University, Bangkok, 10330, Thailand.
[2]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, 10330, Thailand.
[3]Central Laboratory, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Introduction: X-linked lymphoproliferative syndrome type 1 (XLP1) is a primary immune deficiency disorder susceptible to Epstein–Barr virus (EBV) infection associated lymphoproliferative disorder.. It is caused by pathogenic variants in *SH2D1A* encoding a protein that plays an important role in stimulating B and T cells. *XIAP* pathogenic variants cause X-linked LP2, which is unable to be differential diagnosis solely by clinical characteristics.
Objectives: To identify a pathogenic variant in a thirteen-year-old male patient suspected of XLP with a diagnosis of EBV hemophagocytosis and to characterize its functional effect.
Methods: Genomic DNA was isolated from peripheral blood leukocytes. The DNA sample was prepared as an Illumina sequencing library and in the exome capture step. The captured libraries were sequenced using Illumina HiSeq 4000. Trio-WES analysis was performed. The identified variant was verified by PCR-Sanger sequencing and demonstrated the splicing aberration effect by RT PCR from total RNA using specific primers to *SH2D1A.*
Results: A *de novo* hemizygous synonymous NM_002351.5:c.117C>T (21 bp 5' upstream of the first intron) variant in *SH2D1A*, previously reported as c.416C>T, p.Gly39Gly (cDNA mutation = c.118_139del, p.Val40Ilefs*34) was identified. This mutation was found to create an aberrantly spliced product wherein the last 22 bases of exon 1 in patients with X-linked lymphoproliferative disease was deleted, as demonstrated in previous studies.
Conclusions: A previously reported hemizygous synonymous variant in the *SH2D1A* gene known to be related to an XLP1 was identified in our patient. Splicing aberration effect of synonymous variant should be ruled out before discarded.

Acknowledgements: We would like to thank the patient and family for participation in this study.

Keywords: X-linked lymphoproliferative syndrome type 1, *SH2D1A*, hemizygous synonymous variant

From cat to human hearts

Rungnapa Ittiwut, Chupong Ittiwut, and Prasit Phowthongkum

Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, Bangkok, Thailand

Background: Genetic testing for personalized medicine is important not only for humans but feline pals. Many inherited diseases have been investigated to date. Hypertrophic cardiomyopathy (HCM) identified about one-third of young Maine Coon cats, the most famous natural breed cats in North America. It recently gained more popularity among Thai cat lovers, in which heterozygous or homozygous mutations in the MYBPC3 gene corresponded. Cats can serve as a naturally occurring animal model for genetic diseases with closed phylogenetically and physiologically that appeared in the most prevalent variant in Main Coon cats is also a pathogenic variant in human hypertrophic cardiomyopathy
Objectives: To introduce genetic testing for *MYBPC3*-related HCM to Maine Coon cats in a hot spot mutation.
Methods: PCR amplification and sequencing of exons 2 and 23 were performed on genomic DNA samples isolated from peripheral leukocytes of an unaffected Maine Coon kitten and a two-year-old queen Maine Coon cat who suffered from saddle thrombosis as a result of HCM.
Results: The affected cat carries apparent homozygous variants c.94G>C (p.Ala31Pro: A31P), whereas the unaffected kitten does not bear any variants tested, includes Maine Coon specific variant (A31P), a polymorphism: c.220G>A (p.Ala74Thr), or Rag Doll specific variant: c.2460C>T (p.Arg820Trp) of the *MYBPC3*. The affected cat was deceased. The unaffected kitten is still healthy and was screened negative for hypertrophic cardiomyopathy at six months old echocardiography. He will be followed up every year for the chance of developing HCM in case of non-A31P-feline HCM exists. Three other Maine Coon cats are awaiting screening with this simple hot spot targeted testing to determine their future.
Conclusions: This is potentially to establish the first feline genetic testing for early detection of HCM in Maine Coon cats. Commonly, this testing is recommended for breeding farms to reduce the chance of genetic perpetuation. Here, we reported for the first time in the country to expand genomics and precision medicine approach to our beloved feline friends

Tooth Missing in a Thai Patient Associated with a Novel De Novo Variant in the *EDAR* Gene

Sermporn Thaweesapphithak, Thantrira Porntaveetus

Genomics and Precision Dentistry Research Unit, Department of Physiology, Chulalongkorn University, Bangkok, Thailand

Introductions: The EDA/EDAR/EDARADD pathway plays an important role in embryonic development. Specifically, it is critical for forming ectodermal organs, including the skin, hair, nails, teeth, salivary glands, and sweat glands. Alterations in the EDA/EDAR/EDARADD signalling result in tooth agenesis that can be nonsyndromic or syndromic associated with ectodermal dysplasias (ED).
Objectives: To identify the genetic variant causing multiple missing teeth in a Thai patient.
Methods: A Thai girl with oligodontia and her parents were recruited. Clinical and radiographic examinations were performed. Genomic DNA was collected from peripheral blood. Genetic variants were identified by exome sequencing. The identified variant was confirmed by Sanger sequencing and investigated using bioinformatics tools.
Results: The patient presented with a missing six permanent teeth. Oral examinations showed that she had a low salivary flow rate. The patient's hairs, nails, and sweating rate were within the normal limit. Exome and Sanger sequencing identified that the patient harboured a novel *de novo* heterozygous frameshift insertion, c.1087-_1088insGA, (p.Thr363ArgfsTer10), in the *EDAR* gene (NM_022336.4). The variant was not found in the 1000 Genomes Project, Genome Aggregation Database, our in-house database of 2,166 Thai exomes, and has never been reported. The variant was predicted to result in a truncated protein. The parents were nonconsanguineous and did not have a tooth missing. The c.1087_1088insGA was not detected in the parents.
Conclusions: Here, we report the patient with mild ectodermal dysplasias affecting the teeth and salivary flow, associated with the novel *de novo* heterozygous variant in *EDAR*. The study expands the genotypic spectrum of *EDAR*.

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Keywords: missing teeth, next-generation sequencing, ectodermal organs.

Novel Germline Variants Identified in Thai Patients with Familial Adenomatous Polyposis Syndrome: A Retrospective Study

Atchara Tunteeratum, MD, Kanin Sriudomporn, MD, Manisa Boosabaratana, BSc, Pollawat Khemthong, BSc, Thanyachai Sura, MD

Division of Medical Genetics, Department of Internal Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background: Colorectal cancer is the second most common malignancy in Thai patients. Familial adenomatous polyposis (FAP) syndrome is the second most common hereditary colorectal cancer. This study aimed to determine the type of mutations found in *APC* gene among Thai FAP patients and to evaluate the clinical correlation of each *APC* genotype.
Methods: We included blood samples from patients with a history of colorectal cancer who underwent either APC hotspot sequencing or whole APC gene sequencing in Ramathibodi Genetic Clinic between December 1st, 1998 to December 31st, 2021 and their family members.
Results: There were 22 germline *APC* variants identified in 24 non- familial individuals, consisting of 6 deletion variants, 4 duplication variants, 8 nonsense variants, 3 missense variants and 1 splice site variant. In 16 mutations identified via whole gene sequencing, 10 variants were found in exon 15 (62.5%). Other variants were identified in exon 1, exon 5, exon 10, exon 14 and intron 2. Three mutations were novel. Eighteen carriers of disease-causing variants had undergone colonoscopy, and colonic polyps were found in all cases.
Conclusion: We identified 3 novel variants in the *APC* gene of patients with FAP (c.3207delG, c.3663dupT, and c.3440A>G). The c.3927_3931delAAAGA variant is considerably the hotspot *APC* germline mutation in this study (12.5%).

Keywords: Colorectal cancer, Familial Adenomatous Polyposis, APC