臺灣兒科醫學會第二三二屆學術演講會時間表

民國106年11月18日(星期六)

第一講堂

08:30 ~ 10:00 **第一單元：感染學**
(1~9題)

10:00 ~ 10:10 **休息**

10:10 ~ 10:50 **第二單元：腎臟學**
(10~13題)

10:50 ~ 11:00 **休息**

11:00 ~ 11:30 **第三單元：小兒成長與發育**
(14~16題)

12:00 ~ 13:00 **附加研討會**
主持人：李宏昌教授
主　題：羅伊氏乳酸桿菌在兒童功能性腹痛的應用
演講者：Dr. Iva Hojsak

第二講堂

08:30 ~ 10:30 **第七單元：腸胃學、營養學**
(37~48題)

10:30 ~ 10:40 **休息**

10:40 ~ 11:40 **第八單元：血液、腫瘤學**
(49~54題)

12:00 ~ 13:00 **附加研討會**
主持人：戴任恭部長、刁茂盟主任
主　題：談兒童急性胃腸炎診斷治療建議
演講者：劉明發醫師、楊俊仁理事長

第一會議室

08:30 ~ 10:30 **第十單元：新生兒學**
(71~82題)

10:30 ~ 10:40 **休息**

10:40 ~ 12:00 **第十一單元：醫學人文、教育及其他**
(83~90題)

第一講堂

13:10 ~ 14:20 **第四單元：肺臟學**
(17~23題)

14:20 ~ 14:30 **休息**

14:30 ~ 15:30 **第五單元：重症學**
(24~29題)

15:30 ~ 15:40 **休息**

15:40 ~ 16:50 **第六單元：神經精神醫學**
(30~36題)

第二講堂

13:10 ~ 14:30 **第九單元：過敏免疫風濕病學**
(55~62題)

14:30 ~ 14:40 **休息**

14:40 ~ 16:00 **第九單元：過敏免疫風濕病學**
(63~70題)

第一會議室

13:10 ~ 15:00 **第十二單元：心臟血管學**
(91~101題)

15:00 ~ 15:10 **休息**

15:10 ~ 16:30 **第十三單元：內分泌學/ 醫學遺傳學、新陳代謝學**
(102~109題)

民國106年11月19日(星期日)

第一講堂

09:00 ~ 12:00 **教育演講**
主　題：基層兒科診所經營研討會
主持人：陳武元醫師、林應然醫師
演講者：曾崇芳醫師、林釗尚醫師、蔡梓鑫醫師、劉茂彬醫師、曾曉鐘醫師

12:00 ~ 13:30 **附加研討會**
主持人：戴任恭部長、劉清泉教授
主　題：全人類輪狀病毒疫苗與流感疫苗的新進展
演講者：黃立民教授、黃玉成教授

第二講堂

09:00 ~ 11:00 **特別演講**
主　題：兒童發展的精準醫學
主持人：陳錫洲醫師、楊瑞成醫師
演講者：遲景上醫師、趙文崇主任、廖淑芬醫師、鐘育志醫師

12:00 ~ 13:30 **附加研討會**
主持人：劉清泉教授、陳彥旭醫師、盧柏樑醫師
主　題：台灣登革病毒感染及危險因子探討
演講者：何宗憲醫師、張科醫師、齊嘉鈺醫師

第一講堂

13:30 ~ 14:00 **頒獎**

14:00 ~ 14:10 **休息**

14:10 ~ 16:50 **醫學的科學、倫理與法律講座**
主持人：林秦延教授、李秉穎醫師
主　題：亞太地區執行世界衛生組織兒童權利公約的策略：兒童感染症防治的議題與策略
演講者：Prof. Usa Thisyakorn、Prof. Lulu Bravo、Dr. Nobuhiko Okabe、劉定萍主任

地址：高雄醫學大學附設中和紀念醫院啓川大樓六樓(高雄市三民區自由一路100號)

第八單元：血液、腫瘤學

日期：民國106年11月18日(星期六)
時間：10:40~11:40
地點：第二講堂

主持人：江東和、巫康熙

10:40~10:47 49. 探討薑黃素是否透過誘發急性骨髓性白血病細胞分化而緩解阿糖胞苷誘發之多重抗藥表型
曾羽辛[1]、林佩瑾[1,2,3]
高雄醫學大學附設醫院小兒部[1]、小兒部血液腫瘤科[2]；高雄醫學大學醫學院醫學系小兒科[3]

10:47~10:54 50. 治療單純中樞神經復發的兒童白血病：不加做中樞神經放射治療的可能性
羅亞婷、章人欽、邱世欣、林佩瑾、蘇秀蘭、廖優美
高雄醫學大學附設中和紀念醫院小兒血液腫瘤科

10:54~11:01 51. 急性淋巴性白血病病人於引導期化學治療時發生嗜中性球低下發燒有關的危險因子
歐宗顥、沈靜芬、鄭兆能、陳建旭
國立成功大學醫學院附設醫院小兒部

11:01~11:08 52. 癌末病童不實施心肺復甦術醫療照護之探討
江東和[1]、陳世翔[1]、溫玉娟[2]、余婷娟[2]、李銘櫻[2]、楊兆平[1]
林口長庚紀念醫院兒童醫學中心兒童血液腫瘤科[1]、護理部[2]

11:08~11:15 53. 兒童神經內分泌腫瘤的診斷與治療：單一機構之經驗
陳世翔[1]、楊兆平[1]、陳仁熙[2]、賴勁堯[3]、薛純[4]、江東和[1]、洪悠紀[1]、張從彥[1]
林口長庚紀念醫院兒童血液腫瘤科[1]、血液腫瘤科[2]、小兒外科[3]、病理科[4]

11:15~11:22 54. 兒童血友病之表現：中國醫藥大學兒童醫院報告
翁德甫、巫康熙、彭慶添
中國醫藥大學兒童醫院

11:22~11:40 討論

were harvested and centrifuged, and the supernatants were collected for performing ELISA for quantifying IL-8 concentrations in triplicate (human IL-8 ELISA development kit PreproTech EC, determined at 405 nm on a SpectraMax reader, and calculated using the standard curves plotted from serially diluted standard solutions in MS Office Excel 2007).

Results: First, the polyacrylamide gel in silver staining showed absence of the O-antigen in the complex of LPS purified from *S*. Typhimurium Δ*wzxE*. Second, the IL-8 secretion was significantly decreased in the Caco-2 cells infected with *S*. Typhimurium Δ*wzxE* compared with those cells infected with S. Typhimurium wild-type SL1344 (117.8 ± 35.3 pg/ml vs. 159.9 ± 26.7 pg/ml, $p < 0.05$). Third, the IL-8 secretion levels were significantly attenuated in the HT-29 cells infected with *S*. Typhimurium Δ*wzxE* compared with those cells infected with S. Typhimurium wild-type SL1344 (36.2 ± 7.5 pg/ml vs. 276.4 ± 64.1 pg/ml, $p < 0.05$). In addition, the IL-8 secretion was also significantly decreased in the HT-29 cells treated with the purified LPS from *S*. Typhimurium Δ*wzxE* compared with those cells treated with LPS from *S*. Typhimurium wild-type SL1344 (23.8 ± 1.9 pg/ml vs. 141.5 ± 34.8 pg/ml, $p < 0.05$).

Conclusions: The *wzxE* gene is required for biosynthesis of O-antigen in lipopolysaccharide of *S*. Typhimurium. The *wzxE* gene of *S*. Typhimurium is also responsible for induction of IL-8 secretion from human intestinal epithelial cells after bacterial infection. Our study provides a novel evidence in the role of *wzxE*in pathogenicity of *S*. Typhimurium in human intestinal epithelium.

48 Genomic and Gut Microbiota Significances of Two Biliary Atresia Infants with Distinct Outcome

膽道閉鎖的基因變異、腸道菌叢差異性和臨床預後之關聯探討

Hsin-Yeh Lin, Shih-Yen Chen, Chi-Neu Tsai, Wen-Shan Chiang, Hsun-Ching Chao, Ming-Wei Lai, Chien-Chang Chen, Cheng-Hsun Chiu, Jin-Yao Lai
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林欣曄、陳世彥、蔡七女、江文山、趙舜卿、賴明瑋、陳建彰、邱政洵、賴勁堯
林口長庚紀念醫院兒童內科部

Background: The impact of gut microbiota and genomic correlation on infantile biliary atresia is of limited study. Our study analyzed the genetic and gut microbiota differences of two biliary atresia infants with distinct disease outcome.

Methods: Two biliary atresia (BA) infants received Kasai's operation before 60 day-old of age. The infant with good outcome (BA-G) had jaundice resolved gradually within one month while the other infant with poor outcome (BA-P) has progressive liver cirrhosis and finally underwent liver transplantation when 6-month-old. Their fecal samples were collected at two time points with interval of 1 month. Universal primers for the 16S variable regions V1–3 and V3–5 were used for polymerase chain reaction (PCR) amplification. Sequences were aligned and microbiota composition was characterized compared to the Human Microbiome Project (HMP) database. The genome of these two BA patients were analyzed via Affymetrix SNP6.0 to disclose fragment aberration exists.

Results: A significantly decreased Shannon diversity index (entropy score) of the intestinal microbiota in patient with poor outcome (BA-P1, 1.8; BA-P2, 1.6) compared to the patient with good outcome (BA-G1, 3.0; BA-G2, 3.5) and healthy infant (3.2). Greater richness in phylum level of Bacteroidetes in patient with poor outcome, Proteobacteria in patient with good outcome, and Firmicutes in healthy infant were disclosed. Other than decreasing in microbial diversity, the patient with poor outcome had abundance (80%) in species of Enterobacter, Bacteroides and Clostridium which is different from that of patient with good outcome, who showed abundance (near 90%) of Escherichia, Enterobacter and unclassified Enterobacteriaceae. Further analysis demonstrated an overall significant higher richness in Bacteroides ($P < 0.01$) in patient with poor outcome and Escherichia in patient with good outcome ($P = 0.03$). In healthy infant, the species of Firmicutes phylum including Clostridium sensu stricto, Veillonella, and Streptococcus composed the predominant taxa. A significantly increased species composition of Bifidobacterium breve ($P = 0.0159$) was found in the later phase of good-outcome patient compared to its early phase. Genomic analysis showed the poor outcome patient with a deletion in chromosome 7q36.3 including a gene VIPR2 (receptor of VIP), which is essential for bile acid production and regulation.

Conclusions: The microbiota community was significantly different in biliary atresia infants with distinct outcome. Poor disease outcome is correlated with genetic deletion, bile acid dysregulation and subsequent gut dysbiosis. The results will facilitate further studies of the interaction between the genomic medicine, gut microbiome, and hepatobiliary disease in children and infancy.

49 To Investigate Whether Curcumin Relieves Ara-C-induced Multidrug Resistance Phenotype by Inducing Differentiation of Acute Myeloid Leukemia Cells

探討薑黃素是否透過誘發急性骨髓性白血病細胞分化而緩解阿糖胞苷誘發之多重抗藥表型

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高雄醫學大學附設醫院小兒部[1]、小兒部血液腫瘤科[2]；高雄醫學大學醫學院醫學系小兒科[3]

Background: Acute myeloid leukemia (AML) accounts for 15-20% of pediatric leukemia, which is characterized by the accumulation of acquired genetic changes in vivo, blocking the normal differentiation process of hematopoietic progenitor cells, inducing proliferation and multidrug resistance phenotype of tumor cells. Great progress has been made in

the treatment for AML by better understanding of leukemogenesis development of novel anticancer agents and application of individual pharmacogenetic background. However, the emergence of multidrug resistance phenotype is still an important factor leading to cancer treatment failure. Cytarabine (Ara-C) is a key component of AML chemotherapy. Small dose use of Ara-C can promote hematopoietic progenitor cell differentiation. However, long-term or high-dose use can cause neurotoxicity and induce multidrug resistance phenotype. Preserving cell differentiation abilities and preventing drug toxicities and multidrug resistance phenotype will create new opportunities for Ara-C chemotherapy in AML. Many studies are devoted to the study of dietary phytochemicals in cancer prevention and therapy. Curcumin is a yellow spice and phenolic compound from plant turmeric. Curcumin can reverse drug resistance in cancer and increase the sensitivity of leukemia cells to Ara-C. This study investigated whether curcumin could promote the differentiation of hematopoietic progenitor cells by PI3K, NF-B, MAPK or STAT signaling pathway, and eliminate the multidrug resistance phenotype induced by Are-C

Methods: The Ara-C resistant cell lines, termed R-Ara-C HL60, was established by continuously exposed to increasing concentrations of Ara-C up to 1000 nM. XTT assay was used to measure the cytotoxic effect of AraC alone or in combination with curcumin on HL-60 and R-Ara-C HL60 cells. Flow cytometry was used to detect the expression of differentiation markers of granulocyte and monocyte. Western blot analysis was used to detect whether PI3K/AKT, NF- kB, MAPK/ERK and STAT signaling were regulated by AraC or curcumin.

Results: Ara-C induced CD11b, the differentiation marker of granulocyte and monocyte, expression in HL60 and R-Ara-C HL60 cells. Curcumin is the same as Ara-C inducing CD11b expression in above both cell lines.

Conclusions: The current medical treatment is still unable to solve the problem of multidrug resistance phenotype in chemotherapy treatment of acute myeloid leukemia. If Curcumin can reverse the multidrug resistance (MDR) phenotype and increase the sensitivity of leukemia cells to Ara-C, it will bring new dawns in the treatment of leukemia.

50 Treating Isolated Central Nervous System Relapse Childhood Acute Lymphoblastic Leukemia without Cranial Irradiation

治療單純中樞神經復發的兒童白血病：不加做中樞神經放射治療的可能性

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Background: For decades, intensive systemic chemotherapy combined with intensive intrathecal chemotherapy and delayed cranial irradiation have stand as the golden standard of treatment for pediatric patients with isolated central nervous system relapse acute lymphoblastic leukemia. Nevertheless, survivors of childhood ALL are at risk for treatment induced neurocognitive dysfunction. Cranial radiotherapy, especially, causes a significant debilitating cognitive decline in children. Here, we report the case of a patient with isolated CNS relapse (CR1 less than 18 months) of pediatric acute lymphoblastic leukemia fortuitously treated without irradiation.

Methods: A 5 years old girl with the diagnosis of precursor B-ALL was initially treated according to the TPOG – ALL-2002 SR-B protocol. Unfortunately, isolated central nervous system was noted when she received routine CNS preventive intrathecal chemotherapy during the early continuation phase. Bone marrow revealed a complete remission status and MRD technology was not available at our hospital at that time. Intensive intrathecal chemotherapy combined with systemic chemotherapy (myriad of TPOG-2002-VHR and POG9061) were administered. Fortuitously, CNS radiotherapy was not performed.

Results: Currently, this patient is seventeen years old and remains disease free for more than 10 years.

Conclusions: To the best of our knowledge, this report represents the first case of isolated central nervous system relapse pediatric acute lymphoblastic leukemia that treated without irradiation after the literature review. Despite recent progress, a complete understanding of how the central nervous system microenvironment interacts with pediatric acute lymphoblastic leukemia cells still elusive. Our case will be additive evidence for possibility of favorable clinical outcomes of pediatric isolated central nervous system relapsed pediatric acute lymphoblastic leukemia treated without irradiation. Since central nervous system is the second common site of relapse in children with acute lymphoblastic leukemia. Large-scaled, prospective studies are still needed that will focus on the feasibility and effects of chemotherapy without irradiation to a selected subgroup of patients

51 Risk Factors for Febrile Neutropenia in Acute Lymphoblastic Leukemia Patients during Induction Chemotherapy

急性淋巴性白血病病人於引導期化學治療時發生嗜中性球低下發燒有關的危險因子

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Background: Febrile neutropenia is a serious and potentially life-threatening complication in patients with hematological malignancy. Prolonged neutropenia is the major risk for opportunistic infection, especially invasive fungal infection. The aim of this study is to analyze the factors associated with febrile neutropenia and invasive fungal infection at a medical center in southern Taiwan.

Methods: All patients age under 33 years with the diagnosis of acute lymphoblastic leukemia (ALL), receiving TPOG-ALL-2013 induction protocol from Jan. 2013 to Jun.

2017 at National Cheng Kung University Hospital were enrolled. Clinical characteristics and laboratory findings were retrieved retrospectively from medical records. Neutropenia was defined as absolute neutrophil counts less than 500/uL. Persistent febrile neutropenia was defined as fever associated with neutropenia status lasting over 72 hours. The definition of invasive fungal infection follows consensus of European Organization for Research and Treatment of Cancer/Invasive fungal infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG).

Results: Totally 61 patients were enrolled with age ranged from 1 to 33 years. 24 patients (39.9%) experienced febrile neutropenia and more than half of them (14, 58.3%) received fluconazole as empiric anti-fungal therapy. ANC count at nadir was significantly lower among patients with febrile neutropenia (ANC: 45±70/uL) compared to those without fever (ANC: 103±113/uL, p =0.028). But, risk group (p =0.07), doses of epirubicin (p =0.703) and intensive therapy at day 22 (p = 0.28) were not statistically associated with febrile neutropenia. Patients with persistent febrile neutropenia had significantly higher WBC count at diagnosis (WBC: 77185±89167/uL vs. 27070±52782/uL, p = 0.011) and worsen neutropenic condition (ANC: 30±51/uL vs. 95±108/uL, p = 0.034) than those without. Invasive fungal infection was observed in 5 (35.7%) patients, including Candida spp. in 2 cases, yeast-like in 1 case, and Aspergillus spp. in 2 cases.

Conclusions: The severity of neutropenia is signficantly correlated with febrile neutropenia and invasive fungal infection. Early intervention, including granulocyte stimulation factor injection, or prophylactic antifungal therapy can not be overlooked in patients with prolonged and profound neutropenia.

52 "Do Not Resuscitate" Orders among Children with Cancer at the End of Life

癌末病童不實施心肺復甦術醫療照護之探討

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江東和[1]、陳世翔[1]、溫玉娟[2]、余婷娟[2]、李銘櫻[2]、楊兆平[1]
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Background: There were many reports about the "do not resuscitate" (DNR) order while practicing in the critical care units and conducting hospice affairs but limited in the pediatric oncology issues. This study investigated the possible flaws in the execution of the DNR order among patients who received oncological care in a tertiary institution.

Methods: A retrospective review of patients treated between 2007 and 2016 in a tertiary referral pediatric oncology unit in Taiwan. The course of 225 patients who died between 2007 and 2016 was reviewed. The following data were collected: age at death, gender, disease and its status, place of death and survival. There were 127 males and 98 females with a median age of 10.0 years (range 0.4-23.4 months). 83 patients had leukemias, and 142 had malignancies other than leukemia. The t-test and the $\chi 2$ test were applied as appropriate.

Results: The study found that 46.2% of patient deaths occurred in the pediatric oncology ward; 51.6% of patient deaths occurred in the intensive care unit, and 2.2% of patients died in their home or at another hospital. The median interval from signing a DNR order to death was 2 days (range, 0-88 days). Other findings included the following: 95 of 225 (42.2%) patients died after attempted cardiopulmonary resuscitation and 130 (57.8%) died with a DNR order in effect, and the median age at death was 10.0 and 10.1 years, respectively. DNR orders, all of which were signed by surrogates, were more likely to be accepted by patients with slowly deteriorating disease and longer overall survival.

Conclusions: From the study of patient deaths in this tertiary-care children's hospital, it was concluded that an explicit DNR order is now the rule rather than the exception, with more DNR orders being written for patients over 10 years old who were hospitalized for cancer care.

53 Diagnosis and Treatment Outcome of Pediatric Neuroendocrine Tumors: a Single Center Experience

兒童神經內分泌腫瘤的診斷與治療：單一機構之經驗

Shih-Hsiang Chen[1], Chao-Ping Yang[1], Jen-Si Chen[2], Jin-Yao Lai[3], Chuen Hsueh[4], Tang-Her Jaing[1], Iou-Jih Hung[1], Tsung-Yen Chang[1]
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Background: Neuroendocrine tumors (NETs), often referred to as carcinoid tumors, are increasingly recognized in the adult population. But they are relatively rare within the pediatric population. We aim to report the diagnosis and treatment outcome of pediatric NETs in a single center.

Methods: Patients aged 18 years or younger with newly diagnosed NETs between January 2012 and December 2016 were identified from Linkou Chang Gung Cancer Center registry. The clinical features, laboratory data, and treatment outcomes were reviewed.

Results: A total 4 children with newly diagnosed NETs were reported with a median age of 11.5 years (12.1, 13.7, 6.7, and 10.8 years, respectively). There were 3 boys and 1 girl. Two patients had functional NETs. One presented with duodenal ulcers and a hepatic tumor. Grade 2 gastrinoma with Zollinger-Ellison syndrome was diagnosed. He was treated with H2 blockers, proton pump inhibitors, long-acting octreotide and everoilmus. He died of tumor progression 5 months later. The other one presented with Cushing syndrome and a pancreatic tumor with several hepatic tumors. Grade 1 pancreatic ACTH-producing NET

was diagnosed. He was treated with chemotherapy (dacarbazine) and long-acting octreotide, followed by Whipple operation for tumor debulking. Radiofrequency ablation of hepatic tumors and eerolimus were applied postoperatively. He was alive without progression at the last follow-up. Two NETs were not functional. One had a history of T-cell acute lymphoblastic leukemia post unrelated hematopoietic stem cell transplantation. Grade 1 gastric NET was diagnosed 7.5 months after transplantation. She received subtotal gastrectomy without chemotherapy. She had concomitant graft-versus-host disease which was difficult to control by enhanced immunosuppression. Unfortunately, she died of multiorgan failure related to pulmonary infectious complication. The other one presented with a huge abdominal tumor with several hepatic tumors. Grade 3 NET, probably arising from pancreas, was diagnosed. He was undergoing cisplatin-based chemotherapy at last followed-up.

Conclusions: Pediatric NETs are rare, and the optimal treatment of NETs in children is unknown based on our institutional experience spanning over 5 years . Pediatric oncologists need to collaborate with adult oncologists to provide the most complete cancer care possible for these patients.

54 Complications of Hemophilia in Children: Report of Children's Hospital of China Medical University

兒童血友病之表現：中國醫藥大學兒童醫院報告

Te-Fu Weng, Kang-Hsi Wu, Ching-Tien Peng
Division of Pediatric Hematology & Oncology, Children's Hospital of China Medical University, Taichung, 40447, Taiwan
翁德甫、巫康熙、彭慶添
中國醫藥大學兒童醫院

Background: To describe the prevalence, presentation and complications in children ≤12 years with hemophilia.

Methods: We used a standardized collection tool to obtain consented data on eligible babies aged ≤12 years with hemophilia enrolled in the Children's Hospital of China Medical University.

Results: Of 30 children, 83% (25/30) had hemophilia A, 17%(5/30) had hemophilia B, 20% (6/30) patients were diagnosed within one month of birth. Diagnosis was prompted by positive family history 60% (18/30), bleeding 40%(12/30); 70% (21/30) bled during the first two years. The most common events were bleeding (soft tissue, oral bleeding, tarry stool) and head injury. There were 4/30 episodes of intracranial hemorrhage (ICH): 2 spontaneous and 2 intra-ventricle hemorrhage of prematurity. 2 patients had acute appendicitis and received appendectomy. Only 4 patients had central venous access devices, including 2 patients for prophylaxis and treatment of ICH, other 2 patients for ITI. Inhibitors occurred in 5/30 (17%) children, 3 patients are high responder and 2 patients are transient inhibitors. All patients received recombinant factor replacement.

Conclusions: Bleeding events in hemophilic children were common. Minor head trauma, soft tissue and oropharyngeal bleeding were the leading indications for treatment. However, incidence rate (13%) of spontaneous ICH is significantly high in our patients. The further study of national hemophilia registry was recommended.

55 Genome-wide DNA Methylation Analysis Identifies the Crucial Role of β-catenin (CTNNB1) in the Pathogenesis of Kawasaki Disease

甲基化晶片分析出β-catenin於川崎症重要的致病機轉

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Background: Kawasaki disease (KD) is the most frequent cause of cardiac illness in children under five years old. While KD's etiology is largely unknown, genome-wide studies in recent years have indicated that epigenetic factors may play a vital role in its pathogenesis.

Methods: We enrolled 24 KD patients and 24 non-KD controls to access their DNA methylation status using HumanMethylation450 BeadChips. Results were confirmed using pyrosequencing at CpG methylation sites according to the array data. Furthermore, another 34 KD patients and 62 control subjects were enrolled for expression validation. Functional study was performed using knockdown target gene expression in endothelial cells.

Results: Of the 3193 CpG methylation regions with a methylation difference ≥ 20% between KD and controls, 3096 CpG loci revealed hypomehtylation, with only 3% (97 CpG loci) being hypermethylated. Pathway buildup by sub-network analysis identified 11 networked genes among hypermethylated regions, including four transcription factors nuclear factor of activated T-cells 1 (NFATC1), v-ets avian erythroblastosis virus E26 oncogene homolog 1 (ETS1), runt related transcription factor 3 (RUNX3), retinoic acid receptor gamma (RARG), and the activator β-catenin (CTNNB1). Ten of these network-selected genes demonstrated a considerable mRNA decrease in KD patients. Furthermore, β-catenin knockdown in endothelial cells with venous (HUVEC) or arterial (HCAEC) origins drastically increased expression of CD40 and CD40L.

Conclusions: This study is the first to identify network-based susceptible genes of hypermethylated CpG loci, their expression levels, and the functional impact of β-catenin which could be involved in both the cause and development of KD.