分類	第 168 次聯合學術研討會(107 年會)
中文標題	利用基因剔入小鼠模式探討 Asx11 突變之生物學意義及其在白血病發生之角色
Title	The distinct biological implications of Asxl1 mutation and its roles in leukemogenesis revealed by a knock-in mouse model
性質	原著(original article)
內容	Acute leukemia
報告方式	壁報論文
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Abstract	Purpose Additional sex combs-like 1 (ASXL1) is frequently mutated in myeloid malignancies. Recent studies showed that hematopoietic-specific deletion of Asxl1 or overexpression of mutant ASXL1 resulted in myelodysplasia-like disease in mice. However, actual effects of a “physiological” dose of mutant ASXL1 remain unexplored. Methods We established a knock-in mouse model bearing the most frequent Asxl1 mutation and studied its pathophysiological effects on mouse hematopoietic system. Results Heterozygotes (Asxl1tm/+) marrow cells had higher in vitro proliferation capacities as shown by more colonies in cobblestone-area forming assays and by serial re-plating assays. On the other hand, donor hematopoietic cells from Asxl1tm/+ mice declined faster in recipients during transplantation assays, suggesting compromised long-term in vivo repopulation abilities. There were no obvious blood diseases in mutant mice throughout their life span, indicating Asxl1 mutation alone was not sufficient for leukemogenesis. However, this mutation facilitated engraftment of bone marrow cell overexpressing MN1. Analyses of global gene expression profiles of ASXL1-mutated versus wild-type human leukemia cells as well as heterozygote versus wild-type mouse marrow precursor cells, with or without MN1 overexpression, highlighted the association of in vivo Asxl1 mutation to the expression of hypoxia, multipotent progenitors, hematopoietic stem cells, KRAS and MEK gene sets. ChIP-Seq analysis revealed global patterns of Asxl1 mutation-modulated H3K27 tri-methylation in hematopoietic precursors. Conclusions We proposed the first Asxl1 mutation knock-in mouse model and showed mutated Asxl1 lowered the threshold of MN1-driven engraftment and exhibited distinct biological functions on physiological and malignant hematopoiesis, although it was insufficient to lead to blood malignancies.
關鍵字	Asxl1、MN1、造血幹細胞、異體骨髓增殖
Keyword	Asxl1; MN1; hematopoietic stem cell; engraftment
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片檔案，經部份修改後轉成 PDF 檔格式，掛於血液病學會網站上供該會會員瀏覽下載。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	WT1 突變影響帶有 CEBPA double mutation 急性骨髓性白血病病人之預後
Title	Concomitant WT1 mutations predict poor prognosis in acute myeloid leukemia patients with double mutant CEBPA
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告
作者	田豐銘，侯信安，唐季祿，郭遠燁，陳建源，蔡承宏，姚明，李啟誠，林建廷，黃聖懿，柯博升，徐思淳，吳尚儒，蔡偉，周文堅，田蕙芬
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Abstract	Acute myeloid leukemia (AML) with CEBPA double mutations (CEBPAdm) is characterized by favorable clinical outcome. However, a substantial portion of CEBPAdm patients still relapses and dies of disease progression. In this study, we aimed to investigate the prognostic impact of concomitant gene mutations and to refine the risk assessment in CEBPAdm patients. We focused on the 69 (9.1%) CEBPAdm patients identified in a cohort of 756 de novo AML patients. 72.5% of CEBPAdm patients had additional genetic alterations at diagnosis. GATA2 mutation was the most frequent co-occurring genetic alteration (33.8%), followed by FLT3-ITD (14.5%), NRAS (14.5%), TET2 (13.2%), and WT1 mutations (11.8%). Patients harboring concomitant WT1 mutations had a trend of lower complete remission (CR) rate and a higher relapse rate (80% vs. 34%, P=0.047) than those with wild-type WT1. Co-occurring WT1 mutations predicted shorter overall survival and disease-free survival (median, 14 months vs. not reached (NR), P=0.021; 7.8 months vs. NR, P=0.008) (Figure 1). Integration of WT1 mutations could further divide the European Leukemia Net favorable-risk patients into three subgroups (Figure 2). All WT1-mutated patients who obtained CR relapsed if not transplanted, and long-term survivors were only witnessed in those who received allogeneic hematopoietic stem cell transplantation (allo-HSCT). In conclusion, concomitant WT1 mutations predict poor survival in CEBPAdm patients, and upfront allo-HSCT may be indicated in these patients for long-term disease control.
關鍵字	急性骨髓性白血病，基因突變，CEBPA, WT1, 預後
Keyword	acute myeloid leukemia, genetic alterations, CEBPA, WT1, prognosis
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片檔案，經部份修改後轉成 PDF 檔格式，掛於血液病學會網站上供該會會員瀏覽下載。
	*本篇有附圖(參見附件)

分類	第 168 次聯合學術研討會(107 年會)
中文標題	長鏈非編碼核醣核酸 KIAA0125 的高表達量在急性骨髓性白血病是一個獨立的不良預後因子
Title	Higher expression of long non-coding RNA KIAA0125 is associated with characteristic clinical and biological features and is an independent poor prognostic factor in acute myeloid leukemia
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告
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Abstract	Purpose: Long non-coding RNAs (lncRNAs) are non-protein coding RNAs longer than 200 nucleotides. Recently, a number of lncRNAs have been shown to play important roles in cancer biology. lncRNA KIAA0125 is one of the 11 genes in an expression signature significantly associated with prognosis in cytogenetically normal acute myeloid leukemia (AML) patients shown in our previous report. Independent studies have reported KIAA0125 as an important marker for unfavorable prognosis. In this study we aimed to investigate its clinical relevance in AML. Material & Methods: We performed global RNA arrays for bone marrow samples from 347 newly diagnosed de novo AML patients in the National Taiwan University Hospital, who had adequate cryopreserved cells and detailed demographic, clinical, and genetic data for analysis. The KIAA0125 expression level extracted from the array data was analyzed for its clinical relevance. We also validated our findings by analyzing the public databases of AML. Results: The 347 patients were divided into two groups based on the median level of KIAA0125 expression. Higher KIAA0125 expression was inversely associated with favorable-risk karyotypes including t(8;21) and t(15;17). Patients with M1 by the French-American-British classification more frequently had higher KIAA0125 expression ($p<0.001$), while those with M3 (acute promyelocytic leukemia) had significantly lower levels of KIAA0125 expression ($p<0.001$). To investigate the association of gene mutations with KIAA0125 expression in AML, we analyzed mutations in 17 AML-associated genes. We found that patients with higher KIAA0125 expression had significantly higher incidence of FLT3-ITD, and mutations of RUNX1, and DNMT3A, compared to those with lower expression. Among the 227 patients receiving standard chemotherapy, those with higher KIAA0125 expression had a lower complete remission rate ($p<0.001$), and shorter overall survival ($p=0.001$) than those with lower expression after a median follow-up of 57.0 months. The prognostic significance could be validated in another two independent cohorts, TCGA and GSE12417. In multivariate analyses, higher expression of KIAA0125 remained to be an unfavorable prognostic factor for OS

	independent of age, white blood cell counts, karyotype, FLT3-ITD, CEBPA double-mutations, MLL-PTD, RUNX1, WT1, and TP53 mutations (p=0.011). We further used Ingenuity Pathway Analysis (Qiagen) to profile the differentially expressed mRNAs between patients with higher and lower KIAA0125 expression, and constructed a gene regulation network involving HOX gene family. The Gene Set Enrichment Analysis further confirmed the KIAA0125 was associated with leukemia stem cell (LSC) signatures. Conclusions: Higher expression of KIAA0125 in AML patients was correlated with mutations of RUNX1, DNMT3A, and FLT3-ITD but negatively associated with favorable-risk karyotypes. Higher expression of KIAA0125 was an independent unfavorable prognostic factor, probably due to its relationship with LSC signatures. The results of the pathway analysis may pave the way for further basic studies. Further larger studies are warranted to confirm our findings.
關鍵字	急性骨髓性白血病，白血病幹細胞，長鏈非編碼核醣核酸, KIAA0125，風險分層，預後
Keyword	Acute myeloid leukemia, Leukemic stem cell, Long non-coding RNA, KIAA0125, Risk-stratification, Prognosis
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。
	*本篇有附圖(參見附件)

分類	第 168 次聯合學術研討會(107 年會)
中文標題	急性骨髓性白血病之分子演化動態分析：臨床應用和預後影響
Title	The Clinical Implication and Prognostic Impact of Dynamic Molecular Evolution in Acute Myeloid Leukemia
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告
作者	陳睿哲 1、蔡承宏 1,2,3、唐季祿 1,2、郭遠燁 4、林建嶔 1,5,6、曾美瑄 1、姚明 1、李啟誠 1,2、黃聖懿 1、柯博升 1、徐思淳 1,5、林建廷 1,2、吳尚儒 1、陳建源 1、蔡偉 1、周文堅 1,5、侯信安 1、田蕙芬 1
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Abstract	Purpose Although the majority of acute myeloid leukemia (AML) patients achieve complete remission (CR) after induction chemotherapy, about half of them relapse with a dismal prognosis. Serial assessment of the dynamic molecular aberrations during follow-ups can help clarify the mechanisms of leukemia progression. The advance and progress in the next generation sequencing provide us a good chance to comprehensively analyze gene mutations longitudinally. Materials & Methods We used TruSight myeloid panel (Illumina, USA), focusing on 54 genes related to myeloid neoplasms, to investigate the gene mutations of the bone marrow mononuclear cells from 154 adult de novo AML patients who obtained CR but relapsed. Complete serial cytogenetic data were available in 92 (59.7%) patients. Results At diagnosis, 98% patients had at least one genetic alteration including 44.7% patients had both cytogenetic and gene aberrations, 48.0% patients had only gene mutations and 5.3% patients had only cytogenetic abnormalities. The most prevalent gene mutations at diagnosis were NRAS mutations, followed by FLT3-ITD, and NPM1 mutations. At relapse, 77.3% patients had genetic evolution, including 12.0% with cytogenetic evolution, 37.0% with molecular gene evolution, and 28.3% with both cytogenetic and molecular gene evolution. Comparing the gene mutations between diagnosis and relapse, IDH1, SRSF2, STAG2, SMC3, NPM1, ASXL1, and TP53 mutations remained stable during disease evolution; in contrast, NRAS, SF3B1, FLT3, and KRAS mutations were unstable. Sixty-seven (43.5%) patients had CR samples at 30 15 days after the first induction chemotherapy. Among them, 23 (34.3%) patients had persistent leukemia associated gene mutations at CR; these patients had a significant poorer overall survival (OS) than those without detectable gene mutations at CR (median 19.5 vs. 25.1 months, P=0.019). One hundred and fifty-four patients were separated into two groups according to clonal genetic evolution patterns: Group 1 of patients had stable mutations (n=57) or gain of novel mutations (n=32) at relapse (type 1 of evolution); Group 2 had clonal sweeping, such as loss of previously harbored mutations (n=43) or mixed gain and loss of mutations (n=22), at disease progression (type 2). Type 2 evolution was positively associated with inv(16), NRAS, and CEBPA mutations but negatively associated with FLT3-ITD at diagnosis. In univariate analysis, type 2 evolution pattern predicted a longer OS than type 1 (median 25.1 vs. 19.5 months, P= 0.034). In multivariate Cox proportional hazards regression analysis, type 2 pattern was still an independent good prognostic factor (P=0.026). Conclusions The majority of de novo AML patients had genetic evolutions at relapse, including cytogenetic, molecular genetic evolutions, or both. Persistence of leukemia associated gene mutations at CR was associated with a significant poorer OS. Genetic evolution patterns were heterogeneous in AML and type 2 clonal evolution was associated with distinct genetic alterations and better outcomes than type 1.
關鍵字	急性骨髓性白血病、白血病相關基因突變、細胞株演化、次世代定序
Keyword	Acute myeloid leukemia, leukemia associated gene mutation, clonal evolution, next generation sequencing
著作權授權同意書	

分類	第 168 次聯合學術研討會(107 年會)
中文標題	PiRNA 在急性骨髓性白血病的表現與預後意義：一套三個 PiRNA 組成的整合性預後評估系統在預測急性骨髓性白血病預後之應用
Title	Expression and Prognostication of PIWI-interacting RNAs (piRNAs) in Acute Myeloid Leukemia (AML): A 3-piRNA Scoring System Predicts Prognosis in AML Patients
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告
作者	尤達權 1，蔡承宏 1,2,3，郭遠燁 4，曾美瑄 1，姚明 1，李啟誠 1,2，黃聖懿 1，柯博升 1，徐思淳 1,5，林建廷 1,2，吳尚儒 1， 陳建源 1，蔡偉 1，唐季祿 1,2，侯信安 1，周文堅 1,5，田蕙芬 1
Author	Ta-Chuan Yu 1, Cheng-Hong Tsai 1,2,3, Yuan-Yeh Kuo 4, Mei-Hsuan Tseng 1, Ming Yao 1, Chi-Cheng Li 1,2, Shang-Yi Huang 1, Bor-Sheng Ko 1, Szu-Chun Hsu 1,5 Chien-Ting Lin 1,2, Shang-Ju Wu 1, Chien-Yuan Chen 1, Woei Tsai 1, Jih-Luh Tang 1,2, Hsin-An Hou 1, Wen-Chien Chou 1,5, Hwei-Fang Tien 1
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Abstract	**Introduction & Purpose** PIWI-interacting RNAs (piRNAs) are a group of 24-31 nucleotide-length RNAs that play important roles in gene silencing, epigenetic regulations and germ stem-cell maintenance. The piRNAs were found dysregulated in various kinds of tumor tissues. However, their roles in tumorigenesis are largely unknown. Recently, it was found that piRNAs expressions could predict prognosis in Hodgkin lymphoma, but the biologic and prognostic relevance of piRNAs in AML remain unclear. The aim of this study was to establish a concise scoring system based on piRNA expression and to elucidate its clinical implications. **Materials & Methods** The global gene expression profiles, including 2,041 piRNA probes, of 176 adult patients with *de novo* non-M3 AML who received standard chemotherapy were analyzed using the Affymetrix Human Transcriptome Array 2.0 chips. We randomly divided patients into the training cohort (n=88) and validation cohort (n=88). We used the multivariate Cox proportional hazards regression analysis to build the piRNA risk score system and explored its clinico-biological significances. This piRNA risk score system was further verified in the validation cohort. **Results** We identified three piRNAs, which were significantly associated with disease free survival (DFS). A robust risk scoring system composed of the sum of the piRNAs was constructed. The piRNA risk score = [TC15000168.hg.1] + [TC15000551.hg.1] + [TC15001906.hg.1]. The median of risk scores was used as the cut-off to divide patients into lower- and higher-score groups. The clinical parameters including hemoglobin, white blood cell, and platelet counts

	at diagnosis and the distribution of cytogenetic changes were similar between the two groups. Patients with higher scores had significantly less *CEBPA*$^{\text{double-mutation}}$ (P=0.044). The higher-score group had a lower complete remission rate (61.4% vs. 84.1%, P=0.030), higher relapse rate (77.8% vs. 48.6%, P=0.022), shorter DFS (median 9.0 vs. 78.3 months, P=0.002) and overall survival (OS) (median 17.6 months vs. not reached, P<0.001) compared with the lower-score group. In multivariate analysis, the independent poor prognostic factors for both OS and DFS included age more than 50 years, white blood cell counts at diagnosis more than 50,000 /μL, unfavorable-risk cytogenetics, *RUNX1* mutations, and higher piRNA risk scores, while *CEBPA*$^{\text{double-mutations}}$, *IDH2*, and *NRAS* mutations were independent favorable prognostic factors regarding OS. The higher piRNA risk score remained to be an independent poor prognostic factor for OS and DFS (both P<0.001) within the validation cohort. We utilized Ingenuity Pathway Analysis to analyze the potential underlying pathway associated with higher piRNA risk score and constructed a network centered by *ERK* and *HOX* family genes. **Conclusion** This piRNA risk score system is a robust and easy to use risk-stratification tool. The piRNA scores were associated with distinct molecular alterations and independently correlated with clinical outcomes. Further prospective studies are warranted to validate our findings.
關鍵字	piRNA，急性骨髓性白血病，預後，基因突變
Keyword	piRNA, acute myeloid leukemia, prognosis, gene mutation
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	前瞻性觀察性研究：在嗜中性球低下使用先發治療期間，其半乳甘露聚醣數值的變化
Title	A Prospective Observational Study: Changes of Serum Galactomannan Level during the Neutropenia Period under Preemptive Antifungal Treatment
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告
作者	王元欽，張鴻
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Abstract	Background Patients with neutropenia are at risk of invasive fungal disease (IFD). As definitive diagnosis of IFD is difficult, patients are usually treated

	empirically. Emerging diagnostic tools, such as galactomannan (GM) has significantly improved the convenience and accuracy of IFD diagnostic accuracy. Routine surveillance and preemptive antifungal treatment have been reported with variable success. The aim of this study is to evaluate the incidence of IFD and feasibility of preemptive antifungal treatment in patients with hematologic malignancies. Designs and Methods Patients with hematologic malignancies receiving chemotherapy and experiencing severe neutropenia (i.e. absolute neutrophil count <500/μL), were prospectively enrolled in this study. During the neutropenia period, blood samples were collected biweekly for detection of serum GM for consideration of preemptive antifungal treatment. Results During the study period from April 2014 until October 2017, 81 patients were included and 155 chemotherapy sessions were administered. All patients experienced severe neutropenia. In total, only 3 patients were found with elevated serum GM, which was equivalent to an incidence of 3.7% for patients and 1.9% for chemotherapy sessions on average. All three patients were treated in a preemptive manner and all recovered well from their IFD's. We found serum GM remained abnormal for months even with effective treatment. Conclusion The incidence of invasive aspergillosis is low and preemptive antifungal treatment is effective in our experience. Prolonged elevation of serum GM did not suggest an inferior outcome.
關鍵字	半乳甘露聚醣，嗜中性球低下，先發治療
Keyword	Galactomannan, neutropenia, preemptive antifungal
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	異常選擇性剪接對非 M3 急性骨髓性白血病人在臨床和生物學上的影響
Title	The clinical and biological implications of aberrant alternative splicing in patients with non-M3 acute myeloid leukemia
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告

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Abstract	Background Aberrant alternative splicing (AS) is important in the pathogenesis of cancer development. However, studies on the significance of AS in acute myeloid leukemia (AML) are still limited. In this study, we analyzed the clinical and biological implications of aberrant AS in AML. Materials and Methods A total of 171 newly diagnosed non-M3 AML patients, who received standard induction chemotherapy and had complete clinical and genetic information were enrolled. Twenty healthy marrow donors were included as controls. RNAs extracted from mononuclear cells in the bone marrow (BM) were hybridized on the microarrays of Affymetrix Human Transcriptome Array 2.0, which contained >6 million distinct probes covering coding, non-coding transcripts, and exon-exon junctions among 67539 genes. The splicing index (SI) of a probe in a gene was derived from the ratio between AML patients and normal controls in terms of the probe intensity divided by the gene expression level, i.e., SI = [(intensity of probe A in gene A) / (gene A expression level)] -AML patient / [(intensity of probe A in gene A) / (gene A expression level)] -normal control. SI had to be less than -2 or more than 2 to be denoted as an aberrant AS event. A gene with at least one aberrant AS event would be called an aberrant AS gene. SI values were log2 transformed and analyzed for the association with overall survival (OS) by the univariate Cox proportional hazards model. The aberrant AS events were then merged into a Least Absolute Shrinkage and Selection Operator (LASSO) regression for constructing a scoring system applied to predict OS and relapse-free survival (RFS). Results Univariate Cox analysis identified 95 OS-associated aberrant AS events (P<0.01; n=171) in 69 coding and 6 non-coding genes. A simple scoring system incorporating 9 aberrant AS events was developed by LASSO regression model, composed of aberrant AS events in APP, CD93, CT45A3, CUX2, PIK3R3, RORA, SCRN1, and ZSCAN31, and a non-coding transcript. A high score was predictive of inferior OS (Figure 1A; P<0.001; median survival, 18.0 vs. 108.1 months) and RFS (Figure 1B; P=0.005; median survival, 10.2 vs. 88.8 months). A higher score predicted lower complete remission and higher relapse rates ((P=0.01, and 0.006, respectively, Table 1). Higher score was closely associated with FLT-3-ITD, but not mutations in spliceosome (P=0.589, Table 2) and other genes. There was no relationship between aberrant AS score and age, hemogram, cytogenetics, or FAB classification. Multivariate analyses revealed a higher aberrant AS score as an independent unfavorable prognostic factor for OS and RFS (both P< 0.001) (Table 3). Conclusion

	We present the clinical and prognostic impact of an aberrant Alternative Splicing scoring system in de novo, non-M3 AML patients. Large prospective cohorts are needed to confirm our observations.
關鍵字	核糖核酸陣列、選擇性剪接、急性骨髓性白血病、最小絕對壓縮挑選機制迴歸分析
Keyword	RNA microarray, alternative splicing, Acute myeloid leukemia, Least Absolute Shrinkage and Selection Operator (LASSO) regression
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。
	*本篇有附圖(參見附件)

分類	第 168 次聯合學術研討會(107 年會)
中文標題	以卷積神經網絡辨識急性骨髓性白血病、急性淋巴性白血病和多發性骨髓瘤
Title	Classifying Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, and Multiple Myeloma by Convolutional Neural Networks in Taiwan
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告
作者	劉嘉仁、劉耀中、黃昱中、余坤興
Author	Chia-Jen Liu, Yao-Chung Liu, Yu-Chung Huang, and Kun-Hsing Yu
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Affiliations	Division of Hematology, Department of Medicine, Taipei Veterans General Hospital School of Medicine, National Yang-Ming University Medical Oncology, Dana-Farber Cancer Institute Department of Biomedical Informatics, Harvard Medical School
Abstract	Background Acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) and multiple myeloma (MM) are prevalent hematological malignancies worldwide. The estimated new cases of AML, ALL, and MM were 19,950, 6,590, and 30,330 in the U.S. in 2016, respectively (Siegel RL et al. 2016 CA Cancer J Clin). Bone marrow aspiration and biopsy are essential for the diagnosis in most cases. However, these examinations require a thorough evaluation of the histopathology slides by hematopathologists. Convolutional neural network (CNN) is the state-of-the-art technology of image recognition, and has been shown to successfully distinguish chest X-ray films of tuberculosis, fundus photography of diabetic retinopathy, and skin lesions (Lakhani et al. 2017 Radiology; Gulshan et al. 2016 JAMA; Esteva et al. 2017 Nature). However, the utility of CNN in classifying hematological histopathology is not established. In this study, we developed classification methods to diagnose AML, ALL, and MM using the whole slide scan images of bone marrow aspiration smears. Materials/Methods We collected the images of patients with newly diagnosed AML, ALL and MM at Taipei Veterans General Hospital between November 2009 and September 2017.

	The final cohort consisted of 261 AML, 102 ALL, and 210 MM cases. The median age at diagnosis was 62 (range 1–96) years; 58.3% of patients were male, and 41.7% were female. The cohort was split into a training set (80%) and a testing set (20%). Three ImageNet-based CNN architectures (AlexNet, GoogLeNet, and VGGNet) were used as the baseline models. Stochastic gradient descent was employed to refine the weights in the CNNs using the training set. The finalized model was tested on the held-out test set. Prediction accuracy and the area under the receiver operating characteristic curves (AUCs) were analyzed to evaluate the performance of the algorithms. All CNN models were trained using Caffe version 1.0.0, and statistical analysis was performed with R version 3.3.2. Results CNN successfully classified AML, ALL, MM with high accuracy. The accuracy of the models based on the AlexNet, GoogLeNet, and VGGNet architectures were 0.952, 0.905, and 0.921, respectively. The classification accuracy of distinguishing AML from MM is 0.995–1.000. Categorizing ALL as MM is the most common misclassification by CNN (4.2–5.4%). CNN could also predict genomic features in AML images in our cohort. Conclusion CNNs successfully classified the histopathology images of AML, ALL and MM from the bone marrow aspiration of 573 newly diagnosed patients in Taipei VGH. These images were taken in different settings by different groups, which ensure the generalizability of our trained models. These results demonstrated the utility of convolutional neural networks in classifying hematology histopathology images. The classification performance can be enhanced with a larger training set. Our developed methods are generalizable to other hematological malignancies or other cancers.
關鍵字	急性淋巴性白血病、急性骨髓性白血病、卷積神經網絡、深度學習、多發性骨髓瘤
Keyword	Acute lymphoblastic leukemia; Acute myeloid leukemia; Convolutional neural network; Deep learning; Multiple myeloma
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	以深度測序監測帶有費城染色體陽性之急性淋巴性白血病其 BCR-ABL1 激酶區突變點消長及在臨床上的應用
Title	Clinical relevance of monitoring BCR-ABL1 kinase mutations in patients with Philadelphia-positive acute lymphoblastic leukemia by deep sequencing
性質	原著(original article)
內容	Acute leukemia
報告方式	口頭報告
作者	黃盈蓉 1, 郭明宗 1,2, 洪玉馨 1, 滕傑林 3, 王博南 1, 張鴻 1, 高小雯 1,2, 湯崇志 1,2, 馬銘君 4, 李欣學 5, 譚傳德 6, 邱世欣 7,林棟樑 1, 裴松南 4, 林東輝 1, 張家瑋 8, 陳丘鎮 1, 施麗雲 1,2,*
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單位	1 林口長庚紀念醫院血液腫瘤科，2 林口長庚大學，3 台中榮民總醫院血液腫瘤科，4 高雄長庚紀念醫院血液腫瘤科 5 成大醫院血液腫瘤科，6 和信醫院血液

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Abstract	Background and Purpose: Tyrosine kinase inhibitors (TKIs) improve outcomes of patients with Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL). However, resistance to treatment with tyrosine kinase inhibitors is frequent and most often associated with the development of point mutations in the BCR-ABL1 kinase domain (KD). We aimed to analyze ABL1 KD mutations in Ph+ ALL patients with TKIs-poor responders and try to early detection of mutations by deep sequencing to facilitate early switch to appropriate therapy. Patients and Methods: We retrospectively analyzed 33 Ph+ ALL (P190: n = 32; P210: n = 1) BM samples, 31 with relapsed (BCR-ABL1 ≦ 0.6 log reduction, equivalent to > 20% lymphoblasts) and 2 refractory (BCR-ABL1 persistently < 1 log reduction) following TKI therapy. BCR-ABL1 transcript levels were measured by RQ-PCR with TaqMan assay. A total of 103 samples were analyzed from the time of refractory/relapse (R/R) backwards to the time of diagnosis by next generation sequencing (NGS). The cut-off value of positive for mutation was 3%. Results: Fourteen KD mutations were first detected in 40.6% (13/32) of P190 BCR-ABL1 patients in the R/R samples with single mutant in 8 cases and multiple mutants in 5 cases. Longitudinal analysis back to the time of diagnosis identified 20 mutants during TKIs therapy. T315I, an imatinib/dasatinib/nilotinib resistant mutation, was the most common mutation detected (46.2%). The time frame with disease status and T315I levels are shown in figure 1. Appearance of T315I clone was detected between 4 and 17 months after start of TKI therapy, it could be traced back to a level as low as 4% in a patient with hematologic remission when BCR-ABL1 level was 1.8 log reduction and followed by frank BM relapse 2 months later with a mutation level increasing to 63.6% (Pt no. 6). F317L was the second most common mutation (23.1%) and rapidly emerged in one patient treated with dasatinib throughout (0% to 100% in 3 months). Other mutant patterns were complex but dynamic landscape could be well followed by NGS. E450G level continuously increased in one patient, it could be detected (6.9%) 5 months earlier before molecular relapse with BCR-ABL1 level of 2.1 log reduction when BM was still in hematologic remission. In another patient treated with imatinib throughout, carrying E355G (59.2%), E255K (20.8%), E453K (7.7%), L248V (4.5%), and M244V (3.7%) at BM relapse, three mutations were further increased (E355G: 78%, E255K: 34%, L248V: 23.5%) 10 days later when the other two mutations disappeared. Conclusions: Our study showed that deep sequencing by NGS could earlier detect very low burden resistance mutations, like T315I, and early predict treatment failure, which in turn can guide early clinical intervention.
關鍵字	費城染色體陽性之急性淋巴性白血病, BCR-ABL1 激酶區突變, T315I, 次世代定序
Keyword	Philadelphia-positive acute lymphoblastic leukemia, BCR-ABL1 kinase mutations, T315I, next generation sequencing
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	CDK4/6 抑制劑(LEE011, ribociclib)以及此藥物與化學治療藥物併用之抗小鼠淋巴血癌效果
Title	Anticancer activity of CDK4/6 inhibitor (LEE011, ribociclib) and its combinations with chemotherapy drugs on mouse lymphocytic leukemia cells.
性質	原著(original article)
內容	Acute leukemia
報告方式	壁報論文
作者	潘思妤, 陳巧倫, 戴宗玄, 楊名琦, 陳輿碩, 林柏每, 楊文祺, 林勝豐, 蘇裕傑
Author	Sih-Yu Pan, Chiao-Lun Chen, Tzong-Shyuan Tai, Ming-Chi Yang,Yu-Shuo Chen, Po-Mei Lin, Wen-Chi Yang, Sheng-Fung Lin, Yu-Chieh Su
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Abstract	Background The cyclin D-cyclin-dependent kinase (CDK) 4/6-inhibitor of CDK4-Rb pathway regulates cellular proliferation by controlling the G1 to S cell cycle checkpoint. The loss of regulation of the cyclin D-CDK4/6-INK4-Rb pathway is frequently observed in some hematological malignancies like lymphoma and leukemia. Thus, the development of selective CDK4/6 inhibitors may be a novel therapeutic approach for patients with leukemia. LEE011 (ribociclib) is a potent CDK4/6 inhibitor. In some recent studies, it showed active in T-ALL and the combination therapy with corticosteroids and/or mTOR inhibitors warrants further investigation. Here, we investigated the therapeutic efficacy of LEE011 in lymphocytic leukemia cell line (L1210). Methods Cytotoxicity effect of LEE011 in L1210 cells was assessed after 24 and 48 h by using cell viability assays, clonogenic survival assays, and cell cycle analyses. Cell cycle analysis by flow cytometry and PI3K/CDK4 related signal transduction pathway and the relative regulatory molecules were examined by western blotting to detect protein expression. Combination LEE011 with hydroxyurea and cyclophosphamide will also be used to treat the L1210 cells to show if there are synergic effect for anticancer effects. Results: LEE011 does not significantly inhibit L1210 cell proliferation even with the dose up to 5 uM. But further analysis with flow cytometry revealed G1 arrest of L1210 cells after treatment of LEE011 with very low dose. Besides, the treatment with LEE011 in leukemia cells would down-regulate the levels pRB without the change of mTORC1 downstream effectors, including S6K1, 4EBP1,eIF4E were not changed. The combination effects of Lee011 and chemotherapy agents will also be presented. Conclusions: These data indicate that single use of LEE011 may not be a good therapeutic option for lymphocytic leukemia. But combined with chemotherapeutic agent, it may enhance the antitumor activity of lymphocytic leukemia both in vitro
關鍵字	CDK4/6 抑制劑, 淋巴血癌
Keyword	CDK4/6 inhibitor, lymphocytic leukemia

著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	周邊造血幹細胞和骨髓造血幹細胞移植於嚴重再生不良性貧血-台北榮總經驗分享
Title	Peripheral Stem Cell Transplantation Versus Bone Marrow Transplantation in Severe Aplastic Anemia - Experience of Taipei Veterans General Hospital
性質	原著(original article)
內容	Anemia and other RBC disorders
報告方式	口頭報告
作者	柯博伸，劉嘉仁，洪英中，劉耀中，葉秋梅，余垣斌，蕭樑材，邱宗傑，劉俊煌，高志平
Author	Po-Shen Ko, Chia-Jen Liu, Ying-Chung Hong, Yao-Chung Liu, Chiu-Mei Yeh, Yuan-Bin Yu, Liang-Tsai Hsiao, Tzeon-Jye Chiou, Jin-Hwang Liu, Jyh-Pyng Gau
單位	1)臺北榮民總醫院內科部血液科 2)國立陽明大學醫學院
Affiliations	1)Division of Hematology and Oncology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan 2)School of Medicine, National Yang-Ming University, Taipei, Taiwan
Abstract	Background Definitive therapies for aplastic anemia (AA) include hematopoietic stem cell transplantation (HSCT) and immunosuppressive therapy (IST). The incidences of AA vary in different areas of the world, reportedly being three to five times higher in Asia than in North America and Europe. For patients aged > 40 without HLA-MSD, IST with horse anti-thymocyte globulin (h-ATG) and cyclosporine are the first choice but h-ATG is not available in some Asian countries, including Taiwan. Peripheral blood stem cell transplantation (PBSCT) has increased in recent years, but bone marrow (BM) was the preferable graft source for SAA recipients in previous studies. There are insufficient data to support the use of PBSCT. We conducted a cohort study to report the outcomes of patients with SAA who underwent allogeneic HSCT. Methods SAA patients receiving allogeneic HSCT were consecutively enrolled since 1985. All patients were followed up until death, and the date of latest follow-up, or April 31, 2016. The maximum follow-up period was 31 years. Patients receiving cord blood stem cell transplant were excluded. Rather than the standard conditioning regimen: cyclophosphamide 200mg/kg (CY-200) and ATG, we used CY-200 and total body irradiation (TBI) (range 200–1,200 cGy). Rabbit ATG (r-ATG) was added additionally in the conditioning regimen for 59 (39.6%) patients at physicians' discretion. The primary endpoint was mortality. The survival probability was estimated using the Kaplan–Meier method. The risk factors for mortality were calculated using a Cox proportional hazards model, and hazard ratios (HRs) and the 95% confidence intervals (CIs) were calculated. We used a multivariate Cox proportional hazards model to identify risk factors for mortality while adjusting for possible independent confounding factors. All risk factors with $p < 0.1$ in the univariate model were entered into the multivariate analysis. Conclusion

	In the lack of h-ATG, we adopted CY 200-TBI as the conditioning regimen rather than the standard CY 200-ATG and reported OS of 76.0% in 149 SAA patients receiving allogeneic HSCT in Taiwan. Infection is still the major mortality cause and should be monitored cautiously. Despite TBI as a concern for developing malignancies, only one patient in our cohort died of PTLD. We have identified the age at transplantation of ≥ 30, conditioning regimen with TBI > 300 cGy, and transplant year < 2000 were independent predictors of death, indicating the outcomes improved chronologically. The comparison between PBSC and BMSC remained an unresolved issue so far. Herein, PBSCT is not a risk factor for death versus BMT in our cohort.
關鍵字	嚴重再生不良性貧血，造血幹細報移植
Keyword	Severe aplastic anemia, hematopoietic stem cell transplantation
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	以人工智慧發展於分析流式細胞儀資料中偵測移植前微量殘餘疾病之技術，用於預測急性骨髓性白血病病患接受異體造血幹細胞移植後之預後
Title	An Artificial Intelligence Approach of Detecting Pre-transplant Minimal Residual Disease with Flow Cytometry Data to Predict Outcomes in Acute Myeloid Leukemia Patients Receiving Allogeneic Hematopoietic Stem Cell Transplantation.
性質	原著(original article)
內容	Hematopoietic stem cell transplantation including stem cell biology
報告方式	口頭報告
作者	Bor-Sheng Ko1, Chi-Cheng Li2, , Yu-Fen Wang2, Jeng-Lin Li3, Pei-Fang Weng2 , Hsin-An Hou1, Xiu-Wen Liao2 , Chien-Ting Lin2 , Jia-Hou Liu2 , Hwei-Fang Tien1 ,Chi-Chun Lee3, Jih-Luh Tang1,2
Author	柯博升 1，李啟誠 2，王毓棻 2，李政霖 3，翁佩芳 2，侯信安 1，廖秀文 2，林建廷 2，劉家豪 2，田蕙芬 1，李祈均 3，唐季祿 1,2
單位	1. 國立台灣大學醫學院附設醫院內科部血液科 2. 國立台灣大學台成幹細胞治療中心 3. 國立清華大學電機工程學系
Affiliations	1. Division of Hematology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan 2. Tai-Cheng Stem Cell Therapy Center, National Taiwan University Hospital, Taipei, Taiwan 3. Department of Electrical Engineering, National Tsing Hua University, Hsinchu, Taiwan
Abstract	Purpose In this study, we aimed to develop automated Flow cytometry (FC) data interpretation algorithm using artificial intelligence (AI) technology in supporting physicians to conduct rapid and reliable MRD detection for AML patients outside manual FC data gating. Materials and Methods Retrospective FC data of AML or MDS from 2009 to 2017 for MRD detection at the National Taiwan University Hospital were used. Totally 4350 data samples (3090 from FASCalibur and 1260 from FASCantoII-Senior) were included. The whole dataset was randomly divided to the Training set and the Validation set, taking 80%

	and 20% samples respectively. The final concordance with manual interpretation was estimated on the blinded Validation set. The numerical values of the 6 fluorescent channels of each tube (100,000 cells with FSC, SSC, FITC, PE, PerCP, APC) were considered as raw feature attributes. The data was first statistically-modelled with a sub-dictionary approach in learning a multivariate Gaussian mixture model. Then a probabilistic derivation based on Fisher scoring was exploited to compute the L2-normalized fixed-dimensional input representations. The raw feature attributes were then encoded into a Fisher representational vector. Lastly, vectors of each tube were concatenated as the final high-dimensional input to the supervised machine learning classifier, i.e., a support vector machine with linear kernel. For outcome predicting analysis, we included 94 AML patients with available pre-allo-HSCT FC data. Their clinical parameters, progression-free survival (PFS) and overall survival (OS) after allo-HSCT are recorded. Results For the Calibur Training set, the concordance rate of AI algorithm with manual analysis in differentiating AML vs. normal, MDS vs. normal, and abnormal vs normal was as high as 91.8%, 94.0%, and 90.8%, respectively. Similar rates were noted for the CantoII-Senior Training set: 88.0%, 85.5%, and 84.4%. The final concordance rates for the overall Validation set was 87.9%, 87.9% and 85.1%, respectively. The algorithm developed from only single tube (CD13, CD16, CD45, FSC and SSC) can achieve almost identical concordance rates as to that from all 12 tubes. The AI system is 100 times faster than the trained professionals in interpreting one FC data (7 secs vs 15-30 mins). For 94 AML patients with available pre-HSCT FC data, 38 were classified to have residual disease detected by AI system and 56 were normal. Those with normal FC had significantly longer post-HSCT OS compared to those with abnormal FC (NR vs 6.5 months, $p<0.001$), and also PFS (NR vs 4.5 months, $p<0.0001$). Multi-variate analysis further confirmed the prognostic significance. Conclusions This study demonstrated that AI could be an efficient and reliable diagnostic and prognosis prediction tool for AML. In the future, we like to incorporate other test results simultaneously measured for those patients as our next phase of advancing the AI system.
關鍵字	人工智慧，流式細胞儀資料，微量殘餘疾病，急性骨髓性白血病，異體造血幹細胞移植
Keyword	Artificial intelligence, Flow cytometry, Minimal residual disease, Acute myeloid leukemia, Allogeneic hematopoietic stem cell transplantation.
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	來自嚴重再生不良性貧血病童的骨髓間質幹細胞有較高的細胞凋亡與較強的 PBMC 抑制
Title	Increased apoptosis and PBMC suppression in bone marrow mesenchymal stem cells from children with severe aplastic anemia
性質	原著(original article)

內容	Hematopoietic stem cell transplantation including stem cell biology
報告方式	口頭報告
作者	趙玉華，楊順發，彭慶添，巫康熙
Author	Yu-Hua Chao, Shun-Fa Yang, Ching-Tien Peng, Kang-Hsi Wu
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Affiliations	Department of Pediatrics, Chung Shan Medical University Hospital, Taichung, Taiwan; Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan; Division of Pediatric Hematology-Oncology, Children's Hospital, China Medical University, Taichung, Taiwan
Abstract	The immune mediated pathogenesis is considered an important factor of severe aplastic anemia (SAA), but mechanisms underlying which remain to be elucidated. Mesenchymal stem cells (MSCs) are essential to the establishment of the specialized microenvironment in the bone marrow, and MSC insufficiency could predispose to the development of SAA. In the present study, bone marrow MSCs from five children with SAA and five controls were compared. We found that SAA MSCs were characterized by a high percentage of cells in the abnormal sub-G1 phase of the cell cycle, suggesting an increased rate of apoptosis in SAA MSCs. Compared with control MSCs, peripheral blood mononuclear cell (PBMC) proliferation was significantly decreased when PBMCs co-cultured with SAA MSCs ($P = 0.009$). There were aberrant cytokine profiles secreted by SAA MSCs, with higher concentrations of IL-6, IFN-γ, TNF-α, and IL-1β in the conditioned medium. Using PBMC proliferation assay, we demonstrated additional immunosuppressive effects of SAA MSCs ($P = 0.016$) and their conditioned medium ($P = 0.016$). Our data showed increased apoptosis and PBMC suppression of SAA MSCs, and the alterations of MSCs may contribute to abnormally functional microenvironment in the SAA bone marrow.
關鍵字	細胞凋亡與較強，免疫抑制，間質幹細胞，嚴重再生不良性貧血
Keyword	apoptosis, immunosuppression, mesenchymal stem cells, severe aplastic anemia
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	HLA 半相合移植治療復發與頑固型何杰金氏淋巴癌單一中心經驗報告
Title	Haploidentical Hematopoietic Stem Cell Transplantation for the Treatment of Relapsed and Refractory Hodgkin's Lymphoma
性質	原著(original article)
內容	Hematopoietic stem cell transplantation including stem cell biology
報告方式	口頭報告
作者	梁世昕，林精湛，葉士芃，白禮源
Author	Ching-Chan Lin, Su-Peng Yeh, Li-Yuan Bai

單位	中國醫藥大學附設醫院血液腫瘤科
Affiliations	Division of Hematology and Oncology, Department of Medicine, China Medical University Hospital
Abstract	The prognosis of relapsed and refractory Hodgkin's lymphoma (HL), is poor, especially those who had relapsed disease after autologous hematopoietic stem cell transplantation (HSCT). Recently, haploidentical HSCT shows promising outcome for this group of patients. Here we report 4 cases of relapsed and refractory Hodgkin's lymphoma treated with haploidentical HSCT at China Medical University Hospital. 3 of these had prior autologous HSCT. Another 1 had refractory disease to salvage chemotherapy as well as Nivolumab. 3 patients received salvage Brentuximab Vedotin and achieved complete remission (1 patient) or good partial remission (2 patients) before haploidentical HSCT. All the 4 patients received TBI 200cGy and Fludarabine/Cyclophosphamide as conditioning and post-transplant Cyclophosphamide (PTCy) plus low dose ATG/CSA/short course MMF as GVHD prophylaxis. All the 4 patients had complete donor chimerism and PET negative complete remission after haploidentical HSCT. None had acute GVHD. 2 patients had limited stage chronic GVHD. With follow-up 8 months to 40 months, all the patients remained in PET negative complete remission. Haploidentical HSCT using PTCy strategy with RIC conditioning is an effective and safe treatment for relapsed and refractory Hodgkin's lymphoma.
關鍵字	半相合移植，何杰金氏淋巴癌
Keyword	Haploidentical HSCT, Hodgkin
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片檔案，經部份修改後轉成 PDF 檔格式，掛於血液病學會網站上供該會會員瀏覽下載。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	白血球介素-6 C-572G 基因多型性與血小板抗體產生沒有關聯
Title	No association between interleukin-6 C-572G gene polymorphism and platelet antibody production
性質	原著(original article)
內容	Hemostasis, Transfusion
報告方式	壁報論文
作者	林炯熙, 李立旋, 劉學玫, 陳瀅如, 邱宗傑
Author	Jeong-Shi Lin, Li-Hsuan Lee, Hsueng-Mei Liu, Ying-Ju Chen , Tzeon-Jye Chiou
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Affiliations	Divisions of Transfusion Medicine and Hematology, Department of Medicine, Taipei Veterans General Hospital; National Yang-Ming University School of Medicine

Abstract	Purpose: Interleukin-6 (IL-6) is an important inflammatory cytokine. IL-6 promotes antibody production by promoting the B cell helper capabilities of CD4+ T cells. We explored the association between IL-6 C-572G gene polymorphism and platelet antibody production. Materials and Methods: Thirty subjects with platelet antibodies and 20 subjects without platelet antibodies were studied. Antiplatelet antibody tests were performed using a solid phase red cell adherence assay technique with the MASPAT kit (Sanquin, Amsterdam, The Netherlands). The data including age, sex, diseases, amount of platelet transfusion, G/C polymorphism of the IL-6 gene at position -572 and platelet antibody were analyzed. Results: Although subjects who had platelet antibodies was transfused less platelets pheresis than those without platelet antibody (18.9±14.6 vs. 54.0±59.8 units, P = 0.026), the two groups of subjects showed similar age, sex, proportion of benign diseases, and proportion of homozygotes for the C allele at position -572 of the IL-6 gene. The total transfusion amounts of platelets pheresis were similar between CC genotype and G positive genotype (CG and GG) in patients with platelet antibodies, as well as in patients without platelet antibodies. The relative risk of platelet antibody production in patients with the -572 G positive genotype was the same with that of patients with -572 CC genotype, (1.0 vs. 1.0, P = 1.0). Conclusion: There is no association between IL-6 C-572G gene polymorphism and platelet antibody production.
關鍵字	白血球介素-6、單核苷酸多型性、血小板抗體、輸血
Keyword	interleukin-6, single-nucleotide polymorphism, platelet antibody, transfusion
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	C 型肝炎相關與原發性免疫性血小板低下之抗血小板抗體的比較
Title	Comparison of antiplatelet antibody profile in hepatitis C virus-associated and primary immune thrombocytopenia
性質	原著(original article)
內容	Hemostasis, Transfusion
報告方式	口頭報告
作者	黃慈恩 1,3, 陳慰明 2,3, 吳育穎 1, 沈建亨 2, 李芊霈 1, 許家禎 1, 陳苡揚 1, 呂長賢 1, 陳志丞 1,4* *通訊作者
Author	Cih-En Huang1,3, Wei-Ming Chen2,3, Yu-Ying Wu1, Chien-Heng Shen2, Chian-Pei Li1, Chia-Chen Hsu1, Yi-Yang Chen1, and Chih-Cheng Chen1,4* *corresponding author
單位	1 嘉義長庚醫院血液腫瘤科，2 嘉義長庚醫院肝膽胃腸科，3 長庚大學臨床醫學研究所， 4 長庚大學醫學院
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	of Clinical Medical Sciences, and 4College of Medicine, Chang Gung University, Taoyuan, Taiwan
Abstract	Purpose Immune thrombocytopenia (ITP) is an autoimmune disorder characterized with increasing bleeding risk induced by the immunologic destruction of platelet. In the secondary ITP, hepatitis C virus (HCV) infection is an important etiology and assumed as a distinct entity named HCV-associated immune thrombocytopenia (HCV-ITP) when compared to primary ITP. The pathophysiology and mechanism are complex. In this study, we focused on the impact of antiplatelet autoantibodies on the HCV-ITP. Materials & Methods Initially, we included 120 patients with HCV-ITP, primary ITP, and HCV without thrombocytopenia and normal volunteers. After excluding severe bleeding episode or drug related thrombocytopenia, platelet count between 100-149 x109/L in thrombocytopenic groups, co-infected chronic hepatitis B, severe cirrhosis Child-Pugh B and C, Helicobacter infection in ITP cohort, the case numbers were 45, 21, 19, and 18 in HCV-ITP, primary ITP, HCV without thrombocytopenia, and normal control, respectively. We checked complete blood cell count, biochemistry, multiple autoimmune associated markers, and spleen size. For antiplatelet antibody examination, we used two kinds of enzyme-linked immunosorbent assay (ELISA) kit. One is qualitative solid-phase ELISA kit, the PakPlus assay (IMMUCOR, USA). This sandwich ELISA method can identify autoantibodies to the platelet glycoprotein IIb/IIIa, Ia/IIa, Ib/IX, IV, and HLA Class 1. The other one is unselective competitive Human anti-platelet antibody (anti-PA Ab) ELISA kit (CUSABIO, China) Results The mean platelet counts were 53.67, 52.81, 222.05, and 235.28 x109/L in HCV-ITP, primary ITP, HCV, and normal group, respectively. About the autoimmune markers, HCV-ITP patients had significantly increasing proportion of abnormal antinuclear antibody, C3, cryoglobulin profile, and anti-cardiolipine antibody profile compared to the other groups. In the antiplatelet antibody subtype analysis, the positive rates were 64.4%, 38.1%, 36.8%, 5.6% in HCV-ITP, primary ITP, HCV, and normal group, respectively. The antibody profile in HCV-ITP was different from primary ITP, with more proportion of antibody to glycoprotein Ib/IX and HLA Class 1. In HCV without thrombocytopenia group, there have been development of antiplatelet autoantibodies before clinical thrombocytopenia. But they had relatively simple antibody profile with 1 or 2 types of antibodies. In the unselective antibody ELISA exam, there were 71.1%, 47.6%, 52.6%, 0% of positive antiplatelet antibody in HCV-ITP, primary ITP, HCV, and normal group, respectively, when using more than mean + 2.5SD of normal group as positive antiplatelet antibody level. These two methods were compatible. Conclusion Our study had documented the distinct characteristics of HCV-ITP compared to primary ITP. In addition to clinical parameters, the associated autoimmune effect and antiplatelet antibodies profile were also different from primary ITP. Interestingly, the antiplatelet antibody developed before clinical thrombocytopenia. And the complexity of antibody profile seems to be dynamic and as evolution. Further mechanism needs more studies to clarify.
關鍵字	免疫性血小板低下，慢性 C 型肝炎，C 型肝炎病毒，抗血小板抗體，自體免疫
Keyword	immune thrombocytopenia, chronic hepatitis C, hepatitis C virus, antiplatelet antibody, autoimmune
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)

中文標題	兩位遺傳性抗凝血胸原缺乏患者之新基因錯意突變導致疾病分子機制
Title	Molecular Mechanism of Two Patients with Inherited Anti-Thrombin Deficiency with Novel Missense Mutations
性質	原著(original article)
內容	Hemostasis, Transfusion
報告方式	口頭報告
作者	陳宇欽 1,2、胡淑霞 1、黃秋萍 1
Author	Yeu-Chin Chen1,2 , Shu-Hsia Hu2, Chiew-Peng Huang2
單位	國防醫學院 三軍總醫院 血液腫瘤科 1 血友病中心 2
Affiliations	1Division of Hematology/Oncology, Department of Medicine 2Hemophilia Care & Research Center Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
Abstract	Purpose: We have reported two missense point mutations (c.663G>T, W221C; c.851T>G, M284R) of antithrombin (AT) gene in patients with venous thromembolisms resulted from antithrombin (AT) deficiency. We aimed to characterize the molecular mechanism of the two novel mutations by bioinformatics analysis and cell expression study. Patients and Methods: One 40-year-old male patient with deep venous thrombosis was found to have 633G>T mutation, the other 23-year-old male patient with intracranial venous thrombosis was identified to harbor 851T>G mutation. Wild type and the two mutant AT cDNA expression plasmid were transfected into Human embryo kidney 293 (HEK293) cells. The cells were collected at Days 3 & 6 and lysed in M-PER buffer (Thermo scientific, USA). AT antigens in the culture medium and cell lysates were measured using ELISA kits (R&D Systems, Inc., USA) and Western blotting analysis. Results: The AT antigen in supernatant and cell lysate of the 663G>T mutant type was 296.8 ng/mL and 968.5 ng/mL, which were higher than those of wild type (149.0 and 290.8 ng/mL) and higher than those of 851T>G mutant type (2.5 and 55.4 mg/mL). The average of AT excretion ratio (supernatant/cell lysate) of mutant type 851T>G on days 3 & 6 was 0.045 0.007, which was lower than 0.440 0.098 in the mutant type 851T>G and significant lower than 0.255 0.077 in the wild type (p=0.0301). The bioinformatics analysis revealed substitution of Try221 by cysteine eliminated these interactions, which may destabilize the central -sheet and led to functional loss. The Met284 substitution may affect the conformational stability of the central -sheet and the interaction of reactive center loop with thrombin as well. Conclusions: Our study demonstrates that the two missense mutation can impair the AT excretion as compared to wild type by protein expression study, which are novel mutation of inherited AT deficiency.
關鍵字	遺傳性抗凝血胸原缺乏，錯意突變，細胞表現

Keyword	Inherited antithrombin deficiency, Missense mutation, Cell expression.
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	胃癌病人之輸血需求及靜脈血栓栓塞
Title	Transfusion requirement and venous thromboembolism in gastric cancer patients
性質	原著(original article)
內容	Hemostasis, Transfusion
報告方式	壁報論文
作者	林炯熙 1,2,3 陳瀅如 1 邱宗傑 1,2,3
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Affiliations	Divisions of 1Transfusion Medicine and 2Hematology, Department of Medicine, Taipei Veterans General Hospital; 3National Yang-Ming University School of Medicine
Abstract	Purpose: Gastric cancer patients may have bleeding-induced iron deficiency anemia. Transfused blood can disrupt the balance of coagulation factors. Packed red blood cell (PRBC) transfusion may be associated with the development of venous thromboembolic phenomena. We queried the Taiwan health insurance database to study the transfusion requirement and the relationship between transfusion and development of venous thromboembolism (VTE) in gastric cancer patients. Materials and Methods: We conducted a nationwide population-based study using data retrieved from the Taiwan Longitudinal Health Insurance Database 2005 which contained claims data of one-million beneficiaries randomly selected from the Registry of Beneficiaries of NHIRD in 2005. We analyzed the data from 2005 to 2010 for patients with gastric cancer (ICD-9-CM code 151.0 – 151.9). VTE includes deep vein thrombosis (DVT) (ICD-9-CM code 453.8) and pulmonary embolism (PE) (ICD-9-CM code 415.1; not including iatrogenic PE [ICD-9-CM code 415.11]). Results: Of the1,036 patients with gastric cancers randomly selected, the median age was 71 years (range: 22 to 100 years) and 61.1 % were male. PRBC transfusion was prescribed in 662 patients (662/1036 = 63.9%), and median total PRBCs requirements was 4 units, (95% confidence interval: 6.3 – 7.7 units) in transfused patients. The amounts of PRBC transfused was the following: 0 unit in 374 patients, 1 unit in 11 patients, 2 units in 186 patients, 3 units in 13 patients, 4 units in 147 patients, and higher than 4 units in 305 patients. Fourteen patients (1.35 %) developed VTE; DVT alone: 11 patients (1.06%), PE alone: 2 patients (0.19 %), and both DVT and PE: 1 patient (0.1%). Eight out of 14 patients with VTE received PRBC transfusions after VTE occurrence, but none of them received transfusion before VTE episodes.

	Conclusion: The incidence of VTE in gastric cancer is low in Taiwan population. Transfusion is not identified as risk factor for VTE. Small PRBC requirement was found in most gastric cancer patients. Screening for iron deficiency and iron therapy in iron-deficient patients may avoid unnecessary transfusion.
關鍵字	輸血、靜脈血栓栓塞、胃癌
Keyword	transfusion, venous thromboembolism, gastric cancer
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	淋巴管內播散於瀰漫性大 B 細胞淋巴瘤併淋巴結外侵犯是一少見的病理表徵卻代表不佳預後
Title	Intralymphatic spread is a rare finding associated with poor prognosis in diffuse large B-cell lymphoma with extranodal involvements
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告
作者	鄭傑隆 1,2,3 ，蘇勇誠 4,5 ，趙祖怡 4,6，林中梧 7，周聖傑 1，姚明 1，郭頌鑫 8，尤善琦 7,9
Author	Chieh-Lung Cheng 1,2,3 、Yung-Cheng Su 4,5 、Tsu-Yi Chao 4,6、Chung-Wu Lin 7、 Sheng-Chieh Chou 1、Ming Yao 1、Sung-Hsin Kuo 8 and Shan-Chi Yu 7,9
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Abstract	Purpose Intralymphatic spread is common in solid cancers, but has been rarely studied in lymphomas. To date, little is known about the frequency and clinical implications of intralymphatic spread in diffuse large B-cell lymphoma (DLBCL). In this study, we reviewed a large number of specimens of extranodal DLBCL to evaluate the prevalence and clinicopathologic features of intralymphatic spread. The prognostic significance of extranodal intralymphatic spread in DLBCL had also been investigated.

	Materials & Methods All cases of DLBCL with extranodal specimens (except bone marrow and effusions) diagnosed at National Taiwan University Hospital (NTUH) between 2005 and 2015 were selected from the archive of the Department of Pathology, NTUH. The pathologic features of specimens and the clinical characteristics and outcomes of patients were reviewed. Only those receiving frontline rituximab-containing chemoimmunotherapies for curative-intent treatment were included in survival analyses. Results A total of 635 extranodal specimens from 475 DLBCL patients were analyzed. Intralymphatic spread was identified in 10 surgical resection specimens from 10 patients including: 9 de novo DLBCL and one Richter transformation. The prevalence in de novo DLBCL with extranodal involvements was 1.65%. The most common involved site of intralymphatic spread was the gastrointestinal tract, followed by the female genital tract and breasts. Lymphatic vessels, lined by D2-40-positive endothelial cells, were expanded by lymphoma cells, reminiscent of intravascular lymphoma or tumor emboli. None of the involved lymphatic vessels were located in the mucosa. There was no significant difference in clinical features between patients with and without intralymphatic spread. Patients with intralymphatic spread had a trend of lower overall response rate and a trend of higher progressive disease than those without intralymphatic spread. Compared with patients without intralymphatic spread, those with intralymphatic spread had a shorter median overall survival (OS) (14.3 months vs. 96.2 months, P=0.004, Figure 1A) and a shorter median progression-free survival (11.2 months vs. 64.2 months, P=0.01, Figure 1B), respectively. Multivariate analyses showed that the presence of intralymphatic spread was an independent poor prognostic factor for OS (hazard ratio: 3.029; 95% confidence interval, 1.315 to 6.978; P=0.009) irrespective of the National Comprehensive Cancer Network-international prognostic index, B symptoms, and serum albumin levels. Among patients who underwent surgical resection, intralymphatic spread was still an independent prognostic factor. Conclusions Our study demonstrated the presence of intralymphatic spread in extranodal DLBCL. Inspiringly, this rare morphologic finding may serve as a new negative prognostic indicator in extranodal DLBCL with extranodal involvements.
關鍵字	淋巴管內播散，淋巴結外，瀰漫性大 B 細胞淋巴瘤，預後
Keyword	Intralymphatic spread, extranodal, diffuse large B-cell lymphoma, prognosis
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。
	*本篇有附圖(參見附件)

分類	第 168 次聯合學術研討會(107 年會)
中文標題	濾泡型淋巴瘤治療後的正子斷層掃描完全緩解率及下一線治療期間對預後之影響
Title	The Impact of First Complete Remission by PET-CT and Time to Next Treatment on Survival of Follicular lymphoma Patients
性質	原著(original article)

內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告
作者	譚傳德(1)，吳茂青(1)，邱倫瑋(1)，陳鵬宇(1)，吳佳興(2)，李明媛(3)，曹美華(3)，黃玉儀(4)，李佩瑛(4)，陳行素(5)
Author	Tran-Der Tan(1), Mau-Ching Wu(1), Lun-Wei Chiou(1), Peng-Yu Chen(1), Ja-Shing Wu(2), Ming-Yuan Lee(3), Mei-Hwa Tsao(3), Yu-Yi Huang(4), Pei-Eng Lee(4), Shing-Su Chen(5)
單位	和信治癌中心醫院血液淋巴及幹細胞移植團隊 (1)血液及腫瘤內科; (2)放射腫瘤科; (3)病理科; (4)核子醫學科; (5) 放射診斷科
Affiliations	Hematology and Medical Oncology(1), Radiation Oncology(2), Pathology(3), Nuclear Medicine(4); Radiology(5); Multidisciplinary Team of Leukemia, Lymphoma, and Stem Cell Transplant; Koo Foundation Sun Yat-Sen Cancer Center
Abstract	Purpose Rituximab alone or combined with chemotherapy is the treatment choice for follicular lymphoma and we retrospectively analyzed the impact of PET-CT complete remission (CR) and time to next treatment (TTNT) on outcome of follicular lymphoma patients. Materials & Methods Between 2002 and 2014, we have 174 follicular patients treated at our institute and 150 patients can be evaluated the treatment response and long-term outcome. Results The CR after first line treatment with either R-COP or R-CHOP is 89% and PR 7% and 10-year overall survival is 89.7%. Eleven percent of patients died of lymphoma and 3% died of other causes. Forty seven patients (31%) underwent second line of treatment with 19 (40%) TTNT shorter than 24 months and 28 (60%) longer than 24 months. There is no difference of overall survival between R-COP (98%) versus R-CHOP (92%) in 5 years, but there is trend to have more next treatment event in R-COP group as compared with R-CHOP group (60% vs 35% on 8-year follow up). There is no difference of overall survival between with or without rituximab maintenance. For PET-CT response, there is significant overall survival difference between CR and PR patients (98% vs 90%, p<0.001), and longer TTNT is seen in initial CR patients. TTNT longer than 24 months have better overall survival as compared with shorter than 24 months patients (100% vs 79% on 5-year). Conclusions: Initial PET-CT CR patients have better overall survival as compared with PR patients and PET-CT CR should be the treatment goal on initial treatment. Besides, TTNT longer than 24 months patients have better outcome as well.
關鍵字	濾泡型淋巴瘤，正子斷層掃描反應率
Keyword	Follicular lymphoma, PET-CT response
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。
	*本篇有附圖(參見附件)

分類	第 168 次聯合學術研討會(107 年會)

中文標題	莫須瘤維持性療法改善濾泡性淋巴瘤病人存活: 台灣癌症登記資料庫之回溯性研究
Title	Rituximab Maintenance Improves Survival in Follicular Lymphoma: A Retrospective Nationwide Real-world Analysis from Taiwan Cancer Registry
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告或壁報論文任擇一均可
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Abstract	Background: Follicular lymphoma (FL) is the most frequent type of indolent lymphoma in western countries, but it is less frequent in Asia. Several trials have demonstrated the progression-free benefit of rituximab maintenance (R-maintenance) in FL in western countries. However, the overall-survival benefits of R-maintenance in Asian FL patients remain uncertain. Aims: We utilized the Taiwan Cancer Registry Database (TCRD), the National Death Registry Database (NDRD), and the National Health Insurance Research Database (NHIRD) to investigate the clinical importance of R-maintenance for newly diagnosed FL patients in Taiwan. Methods: From TCRD, we identified 836 patients with newly diagnosed FL during 2009 to 2012. We retrieved the clinical information from NHIRD, and the survival status from NDRD. We enrolled patients with stage II-IV diseases and receiving 4-8 cycles of rituximab containing frontline chemotherapies. We excluded those who died or received chemotherapies again within 180 days after the end date of the frontline therapies. Total 396 patients were included. Their demographics, clinical parameters, overall survival (OS), and time to next treatment (TTNT) were subjected for analysis. Results: Among the 396 patients, 260 underwent R-maintenance, and 136 served as the observation group. Compared with the observation group, the R-maintenance group had similar distribution in age, gender, Ann Arbor stages, Charlson Comorbidity scores and the sites of the practice setting. However, those with R-maintenance underwent less intensive frontline chemotherapies (less R-CHOP receiving rate; 53.5% in R-maintenance, versus 66.2% in observation; p value 0.0150) and less cycles of rituximab-containing frontline therapies (the rate of receiving 7-8 cycles frontline therapies, 25.8% in R-maintenance, versus 41.9% in observation; p value 0.0010). The patients receiving R-maintenance had a significantly better OS in univariate analysis (hazard ratio (HR), 0.43; 95% confidence interval (CI), 0.20-0.91), and even in multivariate analysis (HR, 0.42; 95% CI, 0.19-0.91). In the multi-variate analysis, age older more than 60 years and stage IV disease also showed negative impacts on OS. On the other hand, the TTNT was similar in the R-maintenance and observation groups (multivariate analysis, HR, 0.96; 95% CI, 0.65-1.42). Conclusion: Our study is the first real-world study to demonstrate the OS benefit of R-maintenance after the frontline therapies in newly diagnosed FL patients of Asian population.
關鍵字	濾泡性淋巴瘤, 莫須瘤, 台灣癌症登記資料庫
Keyword	follicular lymphoma, rituximab maintenance, Taiwan Cancer Registry Database
著作權授權同	本人不同意將本次投稿主題之會員演講幻燈片掛網。

意書	

分類	第 168 次聯合學術研討會(107 年會)
中文標題	瀰漫性大 B 細胞淋巴瘤的病人接受合併莫須瘤的引導性化療時女性是好的預後因子
Title	Female gender is a favorable prognostic factor in DLBCL patients receiving rituximab containing induction chemotherapies
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告或壁報論文任擇一均可
作者	黃懷萱, 陳俐如, 陳合旻, 蕭斐元, 柯博升
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Abstract	Background: Diffuse large B cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma. The treatment response and overall survival (OS) improved after the incorporation of rituximab with chemotherapies. Previous studies had demonstrated the benefit of rituximab in women with DLBCL. However, the patient numbers are limited, or the results are based on the post-hoc analysis from previous prospective trials. It is remained uncertain about the gender difference of rituximab for patients with DLBCL in the real world. Aims: We demonstrate the benefit of rituximab in a population-based national wild database from Taiwan Cancer Registry Database (TCRD). Methods: From TCRD, We included patients older than 20 years and diagnosed as DLBCL during 2009 to 2013, and excluded those with unknown stage or without treatments. Total 4490 patients, including 2048 women, have been included. Results: The baseline characteristics of female patients were similar to those of male patients, except that female patients had lower Charlson Comorbidity scores (CCS). The median age at diagnosis was 65 years for males and 64 years for females. In the detailed CCS, the female patients had lower incidences of cardiovascular events, chronic obstructive pulmonary disease, and renal disease, but higher incidence of rheumatoid diseases. About the frontline treatments, females had lower cumulative dose of rituximab than males, and less females received R-CHOP as the frontline chemotherapy. In the survival analysis, females had better overall survival (OS) and longer time to treatment failure (TTF). Three-year OS rate was 61.76% for females and 55.14% for males ($p < 0.0001$; Fig. a). Three-year TTF was 47.02% for females and 44.07% for males ($p = 0.0182$; Fig. b). The multivariate analysis of OS showed that the female gender remained to be an independent favorable prognostic factor regardless of Ann Arbor stages, age, frontline treatments, CCS, and practice settings (male, HR 1.18, 95 % CI 1.07-1.29). However, there was no

	significant gender differences in the multivariate analysis of TTF. In the subgroup analysis, the female gender was a favorable prognostic factor among the patients receiving R-CHOP (Fig. c), but not among those receiving non-rituximab containing frontline regimens (Fig. d). In the patients receiving standard dose of rituximab (600 mg or less per cycle), the female gender was a favorable prognostic factor (Fig. e). But, this benefit diminished in the patients receiving higher dose of rituximab (more than 600 mg rituximab per cycle, Fig. f). It was compatible with the theory that female patients had better response to rituximab because females had lower clearance of rituximab than males. Conclusions: From our population-based study, women had more survival benefit from the use of rituximab-containing induction chemotherapies for DLBCL, especially in the subpopulation of patients who received standard dose rituximab or R-CHOP.
關鍵字	莫須瘤，性別差異，瀰漫性大 B 細胞淋巴瘤，台灣癌症登記資料庫
Keyword	rituximab, gender difference, diffuse large B cell lymphoma, Taiwan Cancer Registry Database
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	對於年老瀰漫性大細胞淋巴癌病人口服化療藥物的追蹤觀察報告
Title	The outcome of first-line oral chemotherapy in the elderly patient diagnosed with Diffuse Large B cell Lymphoma
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告
作者	廖碧涵
Author	Pihan Liao
單位	高雄長庚血液科
Affiliations	Kaohsiung Chang Gung hospital, Hematology
Abstract	未完稿
關鍵字	瀰漫性大細胞淋巴癌
Keyword	diffuse large B cell lymphoma
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	原發性中樞神經淋巴瘤: 台北榮民總醫院治療經驗分享
Title	Primary CNS Lymphoma: experience in Taipei Veterans General Hospital
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告
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Abstract	[Background]: Primary central nervous system lymphoma (PCNSL) accounts for up to 1% of non-Hodgkin lymphoma (NHL). It is notorious for high rate of recurrence and the lake of standard treatment. Here we present our experience in treating this challenging entity. . [Methods]: Non-HIV adults with newly diagnosed PCNSL at Taipei Veterans General Hospital were enrolled between January 1, 2002 and December 31, 2016. Patients without histological confirmations, or those diagnosed with secondary CNS lymphoma were excluded. The cohort was followed up until the end of February, 2018. . [Results]: PCNSL was finally diagnosed in 113 patients, with a median age of 65 years. All patients' histological pathology showed diffuse large B-cell lymphoma. The median progression-free survival (PFS) and overall survival were 21.3 (95% confidence interval, 18.6-24.0) months and 100.8 months, respectively. Of note, only 17 patients had PFS more than 3 years and escaped from any recurrent episode. Among these 17 patients, 13 patients had been exposed to rituximab, 10 patients had received whole-brain radiotherapy, and 2 patients undertook frontline high-dose chemotherapy with autologous stem-cell rescue. . [Conclusion]: Given patients' older age and poor prognosis, a high unmet need still exists for effective and long-standing treatments for PCNSL.
關鍵字	非何杰金氏淋巴瘤； 原發性中樞神經淋巴瘤·
Keyword	Non-Hodgkin Lymphoma； Primary central nervous system lymphoma·
著作權授權同	本人不同意將本次投稿主題之會員演講幻燈片掛網。

意書	

分類	第 168 次聯合學術研討會(107 年會)
中文標題	Clinicopathological characteristics and survival outcomes of subcutaneous panniculitis-like T-cell lymphoma: A single-center analysis
Title	皮下脂層炎樣 T 細胞淋巴瘤的臨床與病理特徵 - 單一機構研究
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告
作者	林庭安 楊靜芬 蕭樑材 洪君儀 顏秀如 余垣斌 邱宗傑 高志平
Author	Ting-An Lin, Ching-Fen Yang, Liang-Tsai Hsiao, Giun-Yi Hung, Hsiu-Ju Yen, Yuan-bin Yu, Tzeon-jye Chiou, Jyh-Pyng Gau
單位	台北榮民總醫院內科部血液科
Affiliations	Taipei Veterans General Hospital Division of Hematology
Abstract	Purpose: Subcutaneous panniculitis-like T cell lymphoma (SPTCL) is a rare form of cytotoxic T-cell lymphoma. Previous studies have reported that cases with an alpha beta phenotype usually have an indolent clinical course, while cases with gamma delta phenotype typically have an aggressive clinical behavior. Based on previously described differences in immunophenotypic and clinical features, the 2017 WHO classification has now separated these two entities into SPTCL for alpha beta phenotype and primary cutaneous gamma delta T-cell lymphoma (PCGD-TCL). In this study we assessed the clinicopathological features and outcomes of 10 Taiwanese patients with SPTCL defined by the latest WHO classification. Methods: 11 patients with biopsy-confirmed diagnosis of SPTCL at our institution between June 1994 and April 2015 were retrospectively reviewed. Beta F1 staining was requested, if not previously performed. One patient with gamma delta phenotype was excluded from the study. Pathologic and clinical data of the remaining 10 patients were described and analyzed. Results: The mean patient age was 22.5 years (range: 11-39 years). Only one patient presented with ulcerative skin lesions, all other patients (9/10) presented with nodules or plaques. Most patients (7/10) had multifocal skin lesions, 6 patients had T3 disease at diagnosis using ISCL/EORTC TNM classification. Hemophagocytic syndrome (HPS) was seen in 5 patients (50%), a much higher percentage than previously reported. Most patient had a CD4- (9/10), CD8+ (9/10), CD56- (8/10), beta F1+ (10/10) immunophenotype. One patient received interferon-alpha and steroid as initial treatment, but disease progressed within 2 months. 9 patients received chemotherapy as initial treatment. Complete remission (CR) was achieved in only 2 patients (2/9, 22%), both of them had solitary skin lesion as initial presentation. Most patients (8/10) experienced disease progression after initial treatment, in addition, time to progression after initial treatment was short (median: 3.9 months, range: 1-12 months).

	4 patients failed second-line salvage chemotherapy; one subsequently failed the third line treatment. A total of 8 patients underwent hematopoietic stem cell transplant (HSCT). One patient reached CR after initial chemotherapy and underwent front-line autologous HSCT. 7 patients underwent allogenic HSCT because of refractory or relapsed disease. 6 of them achieved long-term remission after transplant. The 3-year survival rate of the total group was 80% (8/10). None of the 3-year survivors had ongoing skin lesions at the time of last follow-up (mean follow-up: 51 months, range: 8-263 months). Conclusion: While evidence suggests that most SPTCL patients follow an indolent course, our study demonstrates a group of patients following a rather aggressive course with early progression. Hemophagocytic syndrome was also more common (50%) than previously reported. We also showed excellent effectiveness of allogenic HSCT in SPTCL. Allogenic HSCT is a potentially curative option for eligible SPTCL patients.
關鍵字	皮下脂層炎樣 T 細胞淋巴瘤，皮膚 T 細胞淋巴癌，免疫表現分型，治療成效，造血幹細胞移植，世界衛生組織分類
Keyword	subcutaneous panniculitis-like T-cell lymphoma, cutaneous T cell lymphoma, immunophenotyping, treatment outcome, hematopoietic stem cell transplant World Health Organization classification
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。
	*本篇有附圖(參見附件)

分類	第 168 次聯合學術研討會(107 年會)
中文標題	以競爭性定量雙重聚合酶連鎖反應搭配客製化質體去偵測並定量 JAK2V617F 突變基因 ---一個高敏感且精確的全新方法 方法
Title	Development of a Highly Sensitive Assay for Precise Quantitation of JAK2V617F Mutant Allele Burdens
性質	原著(original article)
內容	Myelodysplastic syndromes, Myeloproliferative neoplasms
報告方式	口頭報告
作者	陳志丞，許家禎，黃慈恩，吳育穎，李芊霈，鄒幸宜，陳怡珊，蔡佩彣，莊韋軒
Author	Chih-Cheng Chen, Chia-Chen Hsu, Cih-En Huang, Yu-Ying Wu, Chian-Pei Li, Hsing-Yi Tsou, I-Shan Chen, Pei-Wen Tsai, Wei-Hsuan Chuang
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Affiliations	Division of Hematology and Oncology, Department of Medicine, Chang Gung Memorial Hospital, Chiayi, Taiwan; College of Medicine, Chang Gung University, Tao-Yuan, Taiwan
Abstract	Background: Detection of the JAK2V617 mutation has become a prerequisite in the diagnostic work-up of myeloproliferative neoplasms (MPN). With steady advances

	in the management of MPN, there are increasing needs in precise quantitation of the mutant allele burdens (AB), especially in the setting of monitoring minimal residual disease. Methods: To improve the accuracy of JAK2 mutant AB quantitation, we developed a highly sensitive quantitative competitive allele-specific TagMan Duplex PCR (qCAST-Duplex PCR) assay. Key features of this refined assay include: the addition of a 3'-dideoxy oligonucleotide blocker, duplex PCR in one reaction tube, and use of diluted DNA from constructed plasmids as standards. Exon 21 of JAK2 was chosen as the reference PCR control. Results: The qCAST-Duplex PCR assay consistently showed reproducible results on clinical sample analyses. When tested with purified DNAs containing known proportions of JAK2V617F (including those with 100% wild-type DNA), there was a superb concordance between the observed and expected mutant AB, indicating the high sensitivity and specificity of this method. The assay reliably quantified as few as 0.01% of the JAK2V617F allele. In contrast, we found significant copy number variations in different batches of JAK2V617F-positive HEL and UKE-1 cells, and DNA standards from these cells yielded discrepant results on mutant quantitation. We considered both cells inappropriate standards for the measurement of JAK2V617F AB. Conclusion: In conclusion, our refined qCAST-Duplex PCR method yields highly accurate and reproducible results with both low false-positive and false-negative rates. Our innovation represents a significant progress in the molecular diagnostics of MPN.
關鍵字	突變偵測，JAK2V617F，競爭性定量雙重聚合酶連鎖反應，阻斷物，骨髓增生性腫瘤
Keyword	Mutation detection, JAK2V617F, Duplex PCR, Quantitative Competitive Allele-Specific PCR, qCAST-Duplex PCR, 3'-dideoxy blocker, Myeloproliferative neoplasms,
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	以血癌幹細胞標誌計分系統評估骨髓化生不良症候群之整體及無白血病存活期
Title	A leukemic stem cell signature-based scoring system for prognostication in myelodysplastic syndromes helps predicting prognosis for overall and leukemia-free survival.
性質	原著(original article)
內容	Myelodysplastic syndromes, Myeloproliferative neoplasms
報告方式	口頭報告
作者	王昱弘 1、姚啟元 2、蔡承宏 3、林建嶔 2、侯信安 1、周文堅 2、田蕙芬 1
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Abstract	Leukemic stem cells (LSCs) possess biological properties of stemness share with normal hematopoietic stem cells, and render chemo-resistance and relapse in acute myeloid leukemia (AML). Although myelodysplastic syndrome (MDS) has traditionally been regarded as a "stem cell disease", the clinical and biological significance

	of LSCs in MDS is less defined. In this study, we used Affymetrix HTA 2.0 microarray to profile 16 out of the 17 stemness genes reported in a recent study (Ng et al. Nature 2016) on 160 adult primary MDS patients. (1 gene, ARHGAP22, could not be mapped). We retrained the 16 genes on overall survival (OS) in our cohort, and identified 4 (LAPTM4B, NGFRAP1, NYNRIN, EMP1) whose expression levels significantly correlated with OS; an LSC4 score was constructed based on the weighted sum. Higher LSC4 scores were associated with higher-risk subgroups of MDS, complex cytogenetics, and higher incidences of RUNX1, ASXL1, TP53, SRSF2 and ZRSR2 mutations. High-score patients also had significantly shorter OS and higher AML transformation rate. LSC4 score could successfully stratify normal karyotype MDS patients into different risk groups. In multivariate analysis, higher LSC4 score remained an independent unfavorable factor for OS. High-score patients'expression profiles formed a distinct cluster separate from low-score patients'by principle component analysis. We could validate the prognostic significance of the scoring system in an independent cohort of 30 MDS patients. In conclusion, we demonstrate that a simple scoring system related to stem cell biology correlates with distinctive clinical and genomic features of MDS and serves as an independent prognostic factor for overall and leukemia-free survival.
關鍵字	血癌幹細胞標誌、計分系統、骨髓化生不良症候群、預後、整體存活期、無白血病存活期
Keyword	Leukemic stem cell signature, scoring system, myelodysplastic syndromes, prognosis, overall and leukemia-free survival
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	鐵質傳遞、血紅素合成及骨髓化生不良症候群
Title	Iron transport, heme biosynthesis and MDS
性質	原著(original article)
內容	Myelodysplastic syndromes, Myeloproliferative neoplasms
報告方式	口頭報告
作者	楊文祺，林勝豐
Author	Wen-Chi Yang, Shang-Fung Lin
單位	義大醫院血液腫瘤科
Affiliations	Division of hematology and medical oncology, Department of internal medicine, E-DA hospital
Abstract	Purpose\Materials & Methods\Results\Conclusions:(最多 450 字) Purpose: Myelodysplastic syndrome (MDS) is a hematological disease characterized by reduced blood cell production and dysplasia. This disease can progress from cytopenia(s) to acute myeloid leukemia (AML) through several intermediate morphological subgroups. Although several genes and splicing pathway mutations have been associated with MDS, genetic changes associated with the pathogenesis of MDS still remain unclear. MDS patients are unable to generate new red blood cells from iron that is liberated from transfused cells. It is also responsible for increased progression to AML.

	Dysregulation of hepcidine, a key iron regulation hormone, is one of important pathogenesis of iron overload in MDS patients. Under array based sequence capture followed by next generation sequence (NGS) gene expression analysis, iron metabolism and mitochondrial function had highest number of genes deregulated in RARS patients, compared to controls. In our previous study, BDH2, a cytosolic type 2-hydroxybutyrate dehydrogenase, and LCN2, lipocalin 2, those control iron trafficking in cells, showed up- and down-regulation separately during leukemia progression in MDS patients. We want to find out the other genes related to iron metabolism and MDS. Materials and Methods: We collected MDS patients' bone marrow before and after treated with Azacitidine (AZA). The samples are including MDS, with leukemia change, AZA responder and AZA resistant patients. We used next-generation sequence for RNA to survey the differences between them. Furthermore, we pick up genes up- or down-regulation during disease progression and expand patients' number using qRT-PCR. Results: Under NGS study, we also found that genes related to mitochondrial metabolism and iron metabolism dys-regulate when MDS patients got resistance to Azacitidine or leukemia change. After expansion patients' samples, we found that genes related to iron utility and mitochondrial function in heme synthesis, including ABCB1 and FXN show up regulation in more advanced status of MDS. Conclusion: Genes related to iron metabolism and mitochondrial function show important roles in MDS patients.
關鍵字	骨髓化生不良症候群，鐵質，血紅素，粒線體
Keyword	myelodysplastic syndrome, iron, heme, mitochondiral
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	台灣骨髓增生性腫瘤病人的基因突變特徵:頻率及臨床相關性研究
Title	Mutational Profiles of Classic Myeloproliferative Neoplasms in Taiwanese Patients: Frequency and Clinical Correlation
性質	原著(original article)
內容	Myelodysplastic syndromes, Myeloproliferative neoplasms
報告方式	口頭報告
作者	張育誠 1,2,3、林煥超 1,3、江翊豪 1,3、黃齡 3、王瑋婷 1,3、程俊嘉 1,3、蘇迺文 1,3、陳功深 1,2,3、林炯森 1、謝瑞坤 1、張明志 1,2、張義芳 1,2,3、黃道揚 4、林建鴻 1,2,3
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Abstract	Purpose: JAK2V617F, CALR exon 9 and MPL exon 10 mutations are three major driver mutations in classic BCR-ABL1-negative myeloproliferative neoplasms (MPNs). MPN patients can also harbor other non-driver mutations such as TET2, DNMT3A, AXSL1 and TP53. The aims of this study were to determine the mutational profiles of MPN in a cohort of Taiwanese patients, and to correlate the mutations with clinical characteristics. Materials & Methods: MPN patients seen at MacKay Memorial Hospital from Oct 2009 to Oct 2015 were enrolled into this study. The clinical and laboratory characteristics at the time of diagnosis or referral were determined retrospectively by chart review. Patient genomic DNA was derived from bone marrow or peripheral blood. Targeted next-generation sequencing (NGS) was carried out using a customized myeloid-related panel including 33 genes. The Illumina MiSeq system was used to run NGS experiment. MiSeq Reporter Software and the Burrows-Wheeler Aligner were used for bioinformatics analysis. Results: A total of 155 MPN patients were enrolled (median age at diagnosis 57 years; 51.6% females) including 95 essential thrombocythemia (ET, 61.3%), 50 polycythemia vera (PV, 32.3%) and 10 primary myelofibrosis (PMF, 6.5%). Frequencies of the 3 driver mutations were 67.1% for JAK2V617F, 11.6% for CALR and 1.3% for MPL. 22.6% of patients were classified as triple-negative. The frequencies of major non-driver mutations were 15.5% for TP53, 9% TET2, 8.4% DNMT3A, 7.7% ASXL1, 5.8% BCOR, and 3.9% RUNX1. The frequencies of mutations in other 11 genes occurred in less than 3% of patients. Median number of mutation was 1 (range 0-5): 12.9% no mutation, 40% 1 mutation, 27.1% 2 mutations, 14.2% 3 mutations, 3.9% 4 mutations, and 1.9% 5 mutations. Mutations in an epigenetic regulation gene (TET2, DNMT3A, IDH1/2) were most frequently detected (20%, one patient harbored both TET2 and DNMT3A mutations) in this cohort. 9% mutations in a gene involved in histone modification/chromatin regulation (ASXL1, EZH2, one patient harbored both mutations). JAK2V617F mutation was significantly associated with older age at diagnosis (median 62 vs 54, P=0.02), higher hemoglobin level (median 14.7 vs 13g/dL, P=0.02) and higher leukocyte count (median 13.3 vs 8.5/uL, P<0.001). Whereas, CALR mutations were significantly associated with higher platelet count (median 1119 vs 731/uL, P<0.01) and lower hemoglobin level (median 11 vs 14.7g/dL, P<0.01). Patients with PMF had inferior overall survival (OS) (median 3.4 years vs. not reach vs. not reach; P<0.001). ASXL1 mutations were associated with inferior OS (median 8.7 years vs. not reach; P<0.001). Mutations in an epigenetic regulation gene or an increased number of somatic mutations were not associated with worse OS. Conclusions: In this cohort of Taiwanese MPNs, driver mutations correlate with clinical features. Consistent with the results from Western populations, ASXL1 mutations have prognostic significance in MPNs.
關鍵字	骨髓增生性腫瘤, 突變, 次世代定序, AXSL1
Keyword	Myeloproliferative neoplasms, mutation, next-generation sequencing, AXSL1
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	高通量單細胞 RNA 定序分析原發性血小板增生症

Title	Single-Cell RNA Sequencing Discloses Distinct Transcriptomic Profiling in Essential Thrombocythemia
性質	原著(original article)
內容	Myelodysplastic syndromes, Myeloproliferative neoplasms
報告方式	口頭報告
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Abstract	Background Myeloproliferative neoplasm (MPN) is a heterogeneous group of stem cell-derived clonal disorders of the hematopoietic system. The underlying mechanisms of pathogenesis, especially in subtype specification and stochastic malignant transformation, are still largely unknown. Single-Cell RNA sequencing (scRNA-seq), a novel tool that can be used to identify the transcriptomic signature of individual cells, is gaining wide popularity in our dissection of the molecular pathogenesis of human cancers. In the current study, we aim to employ scRNA-seq to analyze genetic profiling of individual cells at different hematopoietic hierarchy in patients with essential thrombocythemia (ET). Methods: We enrolled seven previously untreated ET patients (two JAK2-mutated, three CALR-mutated, and two triple-negative) and one healthy adult in the current study. Individual CD34+ progenitor cells were enriched from peripheral blood. Harvested viable cells were barcoded and sequenced with the Illumina HiSeq 4000. Data was visualized with 10x Genomics Loupe software, and gender-related RNAs were removed during analysis. We performed t-distributed stochastic neighbor embedding (t-SNE) plotting to dissect the scRNA-seq data and cluster cells with transcriptional similarity. On the other hand, Gene Set Enrichment Analysis (GSEA) and the Reactome were employed to delineate pathway activation. Cellular sub-populations, such as multipotent progenitors (MPPs) and common myeloid progenitor (CMPs), were stratified by the surface markers. Results: Integrative analysis of the expression data showed significant activation of JAK-STAT pathways in patients with ET, which was in contrast comparison with that seen in the healthy control. The seven ET patients, even among those who harbored the same driver mutation, exhibited heterogenous t-SNE transcriptome pattern with distinct expression profiles. In the two JAK2-mutated patients, one had enhanced expression in interferon-related genes and genes participating in proliferation and cell cycle propagation, whereas the other one had significant up-regulation of TGF singling pathway. Surprisingly, two months after blood sampling for scRNA-Seq, the latter patient developed secondary myelofibrosis. In the two samples harboring type II CALR mutation, one exhibited dysregulation of P53 signaling pathway, yet the other had up-regulation of DNA replication stress genes. By combining the information with the data obtained from targeted deep sequencing in those same patients, we were able to uncover unique transcriptome pattern in samples carrying specific somatic mutations. This in turn helped us identify candidate genes for further investigation on their potential roles in the mechanism of ET. Conclusion: We demonstrate that scRNA-seq extends our knowledge of clonal diversity and inter-individual heterogeneity in patients with ET. The obtained information could

	potentially leapfrog our effort in the elucidation of the pathogenesis of ET.
關鍵字	原發性血小板增生症，單細胞 RNA 定序分析，驅動突變基因
Keyword	Essential thrombocythemia, Single-cell RNA sequencing, Transcriptome, Targeted deep sequencing, Driver mutations
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	鐵質過度沈積對男性重度海洋性貧血病患生殖能力之影響
Title	Effect of iron overload on impaired fertility in male patients with transfusion-dependent beta-thalassemia
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
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Abstract	Purpose： To investigate the fertility of male patients with transfusion-dependent beta-thalassemia, and use MRI as a novel method to assess the iron overload status of testis in such patients. Materials & Methods： Twenty-one male patients with transfusion-dependent beta-thalassemia and 5 normal male controls enrolled in this study. Hormonal profiles, iron levels, MRI testicular dimension, MRI T2 values, parameters for sperm quality, sperm DNA fragmentation (SDF) of participants were measured. Results： The MRI T2 values of the testis were significantly lower in transfusion-dependent beta-thalassemia patients than normal controls (P=0.027) and correlated to serum ferritin levels in all enrolled subjects (R square=0.258, P=0.008). There were significantly lower sperm concentrations (P=0.037), a lower percentage of sperm with normal morphology (P=0.001), and a higher percentage of SDF (P=0.009) in transfusion-dependent beta-thalassemia patients without hypogonadotropic hypogonadism

	and with spontaneous spermatogenesis compare to normal controls. The percentage of SDF was significantly correlated with serum ferritin levels in transfusion-dependent beta-thalassemia male patients with spontaneous spermatogenesis (R square=0.48, P=0.009). Conclusion： Our study is the first demonstration of iron deposition in the testis of patients with transfusion-dependent beta-thalassemia based on imaging and such findings might explain the high prevalence of impaired fertility in above patients with normal pituitary function.
關鍵字	重度海洋性貧血, 鐵質沈積, 生殖能力
Keyword	thalassemia, iron-overload, fertility
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片檔案，經部份修改後轉成 PDF 檔格式，掛於血液病學會網站上供該會會員瀏覽下載。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	兒童期慢性骨髓性白血病以 Imatinib 為第一線治療的分子基因反應及成果報告：台灣多中心的合作研究
Title	Molecular Responses and Outcomes of Pediatric CML Treated with Front-line Imatinib: a Multi-center Study in Taiwan
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
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Abstract	Background and Purpose Chronic myeloid leukemia (CML) is a rare disease in children and constitutes 2% to 3% of pediatric leukemia. Imatinib (IM), a potent tyrosine kinase inhibitor (TKI), is well established as a standard treatment for newly diagnosed adults with CML in chronic phase. The aim of this multi-center study in Taiwan was to assess the treatment responses and outcomes of front-line IM therapy in pediatric CML. A comparison between pediatric and adult CML patients was also performed. Patients and Methods Between 2002 and 2017, there were 53 newly diagnosed children, age < 18 years old, with CML in chronic phase receiving front-line IM therapy with a daily dosage of 300 mg to 400 mg. Fifty-two patients with b3a2 (32, 61.5%), b2a2 (19, 36.5%) and b3a2+b2a2 (1, 2%) BCR-ABL1 transcripts were enrolled in this study. Peripheral blood BCR-ABL1 levels expressed as International Scale (IS) were measured by TaqMan RQ-PCR assay every 3 months in a central laboratory. The criteria of the European LeukemiaNet regarding optimal response were adopted: major cytogenetic response (MCyR, IS < 10%) at 3 months, complete cytogenetic response (CCyR, IS < 1%) at 6 months and major molecular response (MMR, IS < 0.1%) at 12 months (Blood 2013). Molecular response of a patient was censored if the patient received hematopoietic stem cell transplantation (HSCT), switched to 2nd-generation TKI, or died. An adult cohort of 685 patients who had molecular measurements in the same central laboratory, presented partly in ASH 2014 (Blood 2014. 124: 4544a), was updated for the comparison analysis. Results The clinical features, molecular responses and outcomes of the pediatric cohort are summarized in Table 1. Eight patients underwent HSCT, and 20 were shifted to 2nd-generation TKIs (14 dasatinib, 6 nilotinib), including 3 achieved optimal responses but IM intolerance. Optimal responses at 3 months, 6 months and 12 months following IM were achieved in 52.0%, 39.1% and 21.7%, respectively. The cumulative incidence of MMR in pediatric patients was inferior to that in adult cohort (P < 0.0001) (Figure 1). The IS levels at 3 months among three different Sokal risk groups did not differ in pediatric CML. The 10-year progression-free survival (PFS) and overall survival (OS) were not significantly different between pediatric and adult cohorts (PFS, 90.4 ± 4.7 vs. 93.0 ± 1.3, P = 0.533; OS, 90.6 ± 4.7 vs. 94.3 ± 1.6, P = 0.176). Conclusions The molecular responses in pediatric CML patients receiving front-line IM therapy were inferior to those of adult cohort, but the PFS and OS did not differ between the two cohorts. The Sokal scores did not predict outcome in pediatric CML.
關鍵字	兒童期，慢性骨髓性白血病，酪胺酸激酶抑制劑，基利克

Keyword	childhood, chronic myeloid leukemia, Tyrosine kinase inhibitor, Imatinib
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。
	有附圖

分類	第 168 次聯合學術研討會(107 年會)
中文標題	小兒橫紋肌肉瘤病患之治療成績與分析 - 單一醫學中心報告
Title	Outcomes of pediatric patients with newly diagnosed rhabdomyosarcoma - A single institution report
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
作者	周書緯 1, 張修豪 1, 盧孟佑 1, 楊永立 1,2, 林東燦 1, 2, 林凱信 1, 周獻堂 1
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Abstract	Purpose: Taiwan Pediatric Oncology Group (TPOG) initiated two consecutive protocols for treating pediatric patients with rhabdomyosarcoma since 1995. However, the results have not been analyzed and reported yet. The aim of this study is to investigate the treatment results of these two protocols in our hospital and to assess whether the results are comparable to other large-scaled studies. Materials & Method: Treatment of pediatric patients with rhabdomyosarcoma according to TPOG protocols at National Taiwan University Hospital began in 1995. Between 1995 and 2006, patients were treated by TPOG RMS 95 protocol, which was based on IRS-III/IV. After 2007, patients were treated by TPOG RMS 2007 protocol which was adapted from IRS-V study. The clinical data of patients were obtained retrospectively by reviewing medical records. The date of the latest follow-up was December 31, 2016. Results: Thirty-seven patients were enrolled in this study. The 5-year overall survival (OS) and event-free survival rates of them were 54.7±8.8% and 48.5±8.6%, respectively. The 5-year OS rates for patients treated by TPOG RMS 95 and TPOG RMS 2007 protocols were 55.0±11.1% and 55.9±14.0%, respectively. Age at diagnosis of less

	than ten years old and receiving operation with gross total or subtotal tumor resection were identified as independent prognostic factors that predicted better outcomes in the multivariate analysis. Conclusions: The clinical outcomes of pediatric patients with rhabdomyosarcoma in Taiwan improved dramatically after incorporating two consecutive protocols from TPOG. In addition, the treatment results of these two protocols were comparable to large-scale studies of other countries.
關鍵字	化學治療，治療成績，小兒病患，橫紋肌肉瘤，台灣
Keyword	chemotherapy, clinical outcomes, pediatric patients, rhabdomyosarcoma, Taiwan.
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	台灣兒童原發性縱膈腔大 B 細胞淋巴瘤的治療成果
Title	Clinical features and treatment outcome of children with primary mediastinal large B-cell lymphoma in Taiwan
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
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Abstract	Purpose: Primary mediastinal large B-cell lymphoma (PMBL) is a rare subtype of non-Hodgkin lymphoma in children. Event-free survival rate of children with PMBL in western counties was around 80%. Studies of childhood PMBL are less reported from East Asian countries. We would like to analyze the clinical features and treatment outcomes of children with PMBL in Taiwan. Material and Methods: Patients aged 18 years or younger with newly diagnosed PMBL between January 1998 and December 2017 were identified from Taiwan Childhood Cancer Foundation registry. The clinical features and the treatment outcomes were analyzed. Results: Forty-two patients with PMBL were eligible for analysis. All patients were teenagers. The median age at diagnosis was 16.3 years (range 12.8 – 18.0). Twenty-five patients were females, and 17 were males. Eighteen (18/37, 48.6%) patients had high LDH level (2 upper normal limit) at diagnosis. All were in stage III based on Murphy’s staging. Patients were treated with various chemotherapy regimens throughout the study period, including DA-EPOCH (1)/DA-EPOCH-R (13)

	in 14, CHOP (5)/R-CHOP (7) in 12, NHL-BFM in 10, MACOP-B in 1, CEOP in 1, and uncertain regimen in 4. Twelve patients received radiotherapy for local residual disease post chemotherapy. Six patients had recurrent or progressive disease. Two of the six patients achieved long-term remission after salvage chemotherapy and hematopoietic stem cell transplantation. The remaining four patients died due to disease progression. The 5-year event-free survival and overall survival rates were 85.4% and 90.0%, respectively. Sex, age, and LDH level were not associated with treatment outcome. Conclusions: The treatment outcome in children with PMBL in Taiwan compared favorably to those from western countries. Further studies, including molecular analysis, are warranted.
關鍵字	原發性縱膈腔大 B 細胞淋巴瘤、兒童、治療成果
Keyword	Children, Primary mediastinal B-cell lymphoma, Treatment outcome
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	兒童 B 細胞急性淋巴性白血病特定基因之套數變化
Title	Copy number profiling of childhood B-cell acute lymphoblastic leukemia
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
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Abstract	Purpose: The use of Multiplex Ligation-dependent Probes Amplification (MLPA) has been mainly for searching copy number alterations of genes and subtelomeric sequences for aneuploidy detection. This study demonstrated how MLPAs help the diagnosis of genetic classifications of childhood acute lymphoblastic leukemia (ALL). Materials & Methods: There are total 145 B-cell ALL patients enrolled in this study. DNA was analyzed by the SALSA MLPA kits (P335-A4 ALL-IKZF1

	probemix, P327 for iAMP21-ERG probemix and P329 for CRLF2-CSF2RA-IL3RA probemix) (MRC-Holland, Amsterdam, the Netherlands). The chromosomal gains and/or losses were detected by the SALSA MLPA P036 Subtelomere Mix 1 probemix. These numerical chromosomal alterations were correlated with DNA index (DI) and cytogenetics if data were available. Results: There are 13 patients with IKZF1 deletions, five patient with ERG deletions and four patients with isochrome 21. Sixty-three bone marrow samples were available for analysis by flow cytometry to determine the DI. The chromosomal number matched in 93 out of 115 samples between MLPA and karyotype (R2 = 0.5718, p < 0.0001), 63/63 between MLPA and DI (R2 = 0.9582, p < 0.0001), and 37/46 between karyotype and DI (R2 = 0.5045, p < 0.0001). MLPA results correlated with DI and cytogenetics, especially DI. Four patients were identified to have isochrome 21 and all of them suffered from disease relapses under the protocols proposed by TPOG (Taiwan Pediatric Oncology Group), making the identification of this subtype of ALL necessary in Taiwan. In addition, the deletion status of several genes, including IKZF1, TCF3, ERG, CRLF2 deletions are helpful for the diagnosis of some other types of ALL, such as Ph-like, DUX4, CRLF2 and TCF3 rearrangement fusions. Conclusions: MLPAs are able to identify ALL patients with IKZF1 deletions, isochrome 21 and aneuploidy. The above genetic alterations have prognostic and clinical significances. MLPAs help the risk-directed therapy of childhood ALL.
關鍵字	Childhood ALL, MLPA, isochrome 21, DNA index (DI), IKZF1 deletion, aneuploidy
Keyword	Childhood ALL, MLPA, isochrome 21, DNA index (DI), IKZF1 deletion, aneuploidy
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	TP53 基因變異在復發兒童急性淋巴性白血病的意義
Title	TP53 alterations in relapsed childhood acute lymphoblastic leukemia
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
作者	楊永立 1,2,張婉婷 3,游智翔 4,林子剛 5,6,林倩伃 7,林凱信 2,周獻堂 2,盧孟佑 2,陳淑惠 8,巫康熙 9,王士忠 10,張修豪 2,蘇怡寧 5,洪加政 5, 林東燦 1,2,陳璿宇 7
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	Pediatrics, Changhua Christian Hospital, Changhua, Taiwan
Abstract	Purpose: TP53 alterations are frequent relapsed acquired mutations in childhood ALL. This study is to investigate its clinical significance in relapsed childhood acute lymphoblastic leukemia. Materials & Methods Diagnostic and/or relapsed bone marrow (BM) or peripheral blood was obtained from 101 children with relapsed acute lymphoblastic leukemia from January 1997 to December 2015. Mutational status of coding regions of TP53 was determined by Sanger sequencing in 101 pediatric patients with relapsed ALL. The status of deletions was measured by Multiplex Ligation-dependent Probes Amplification (MLPA) in 68 cases. The associations between mutation status and clinicopathological features at the time of relapse, treatment outcome and survival were assessed. Univariate and multivariate survival analyses were performed to identify independent prognostic factors associated with overall survival (OS), event-free survival (EFS). Results: A mutation rate of 22.8% was identified in this cohort. Acquired TP53 alterations (relapse-only) was associated with lower OS (5-year OS: median 23 months vs 38 months, P-value=0.00316). Multivariate analysis showed more than two TP53 alterations and the onset age less than 1-year were independent poor prognostic factors (HR=4.0, P-value=0.004 and HR=2,6, P-value=0.02, respectively). Forty-three patients received hematopoietic stem cell transplantations after disease relapses. Patients with TP53 alterations (9/43) had inferior 5-year OS in comparison with patients without TP53 alterations after transplants. Multivariate analysis also showed more than two TP53 alterations and the onset age less than 1-year were independent poor prognostic factors (HR=2.3, P-value=0.042 and HR=3.0, P-value=0.02, respectively) for relapsed patients who received transplants. Conclusions: TP53 alterations were enriched in childhood ALL when disease flare-up. TP53 alterations were prognostic markers in relapsed childhood ALL.
關鍵字	TP53, relapsed acute lymphoblastic leukemia
Keyword	TP53, relapsed acute lymphoblastic leukemia
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	NUDT15 同基因型變異在急性淋巴性白血病病童導致嚴重 mercaptopurine 不耐
Title	Homozygous variants of NUDT15 indicate extreme mercaptopurine intolerance in children with acute lymphoblastic leukemia
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
作者	王德勳 1,2,3、游智翔 1,4、林凱信 1、周獻堂 1、盧孟佑 1、張修豪 1、陳淑惠 5、張裕享 6, 7、林倩伃 8、林淑華 4、林東燦 9, 1、陳璿宇 8、楊永立 9, 1

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Abstract	Propose Inherited NUDT15 variant is a genetic determinant of mercaptopurine intolerance in children with acute lymphoblastic leukemia (ALL). This study investigated the extreme mercaptopurine intolerance and prolong neutropenia are related with children with homozygous variant of NUDT15 in ALL. Materia and Method From Sep. 1, 1997 to Dec. 31, 2017, total 300 children diagnosed as ALL were enrolled in this study. Germline DNAs were prepared by standard methods from peripheral blood mononuclear cells. The coding regions of the NUDT15 gene were first amplified by PCR from germline DNA, followed by Sanger sequencing. Clinical data were correlated with these genetic variants. Result: There are six children with homozygous variants of NUDT15 and 70 children with heterozygous variants. Children with homozygous variants account 1-2 % in this study. The average daily dose of 6MP on maintaince phase of six homozygous mutation is 4.6 mg/m2/day (7.6% intensity of protocol design). That much lower than 60mg/m2/day protocol designed. Three of six patients have completed TPOG-ALL treatment and followed more than 5 years without relapse. The other three patients are undergoing treatment. One of these patients has suffered from 10 episodes neutropenic fever during the maintain phase treatment. In the continuation phase beginning, two patients with homozygous variants has suffered from prolonged neutropenia while we did not know their NUDT15 coding. Their neutropenia periods are 14 days and 26 days respectively. The average daily dose of 6MP on maintaince phase of 70 patients with heterozygous mutation is 18.72 mg/m2/day (31.2% intensity of protocol design). The average daily dose of 6MP in ALL children with wild type NUDT15 37.14 mg/m2/day (61.9% intensity of protocol design). Conclusion: Patients with variant NUDT15 take less dose of 6MP than patient with wild type variant. Furthermore, patients with homozygous NUDT15 variants extremely take much less dosage. If 6MP is administrated with unknown patient NUDT15 coding variants, it may induce prolong or frequent neutropenia. It is suggested that genetic analysis should be performed before the administration of mercaptopurine to avoid the complications of myelosuppression, especially for patients with homozygous variants.
關鍵字	NUDT15, Mercaptopurine (6MP), Children, Acute lymphoblastic leukemia
Keyword	NUDT15, Mercaptopurine (6MP), 兒童急性淋巴性白血病

著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	依據微量殘餘疾病調整的治療方案改善青少年急性淋巴性白血病的治療成績：單一醫學中心之報告
Title	Improved treatment outcome of adolescents with acute lymphoblastic leukemia by minimal residual disease-based therapy: a single center report
性質	原著(original article)
內容	Pediatric hematology and Oncology
報告方式	口頭報告
作者	1 陳世翔，1 江東和，1 楊兆平，1 洪悠紀，1 張從彥，2 黃盈蓉，2 施麗雲
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Abstract	Purpose: Adolescents with acute lymphoblastic leukemia (ALL) have been reported as having a poorer prognosis compared to younger patients. Recent studies have demonstrated that personalized treatment based on minimal residual disease (MRD) can improve outcome in children with ALL by identifying patients who require intensified treatment to avert relapse. The aim of our study was to evaluate the impact of MRD-based therapy on treatment outcome of adolescents with ALL in a single center. Material and Methods: Between 1996 and 2016, 355 pediatric ALL patients, including 47 adolescents aged 12 to 18 years, had genetic/cytogenetic analysis at diagnosis and were treated with consecutive TPOG-ALL protocols at Linkou Chang Gung Memorial Hospital. In earlier TPOG-ALL protocols, risk stratification was based on presenting clinical features and leukemic cell genetics. In the latest TPOG-ALL-2013 protocol, we started to determine MRD by multiparameter flow cytometry, PCR analysis or both in bone marrow specimens, and the MRD level was used to guide further treatment intensity. Results: The 47 adolescents were significantly more likely to have T-cell ALL, the t(9;22)(BCR-ABL1), and the t(1;19)(E2A-PBX1); they were less likely to have the t(12;21)(ETV6-RUNX1) and hyperdiploidy compared with younger patients. Thirty-two adolescent patients were treated with earlier TPOG-ALL protocols. The distribution of patients by risk classification was standard risk (SR) in 0 (0%), high risk (HR) in 24 (75.0%), and very high risk (VHR) in 8 (25.0%). Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) had been applied to 3 of 32 adolescent patients in the first complete remission. Fifteen adolescent patients underwent chemotherapy with TPOG-ALL-2013 protocol. There was a significant difference ($P < 0.05$) in definitive risk group allocation compared to earlier TPOG-ALL protocols: SR in 1 (6.7%), HR in 3 (20.0%), and VHR in 11 (73.3%). Six patients in the provisional HR group with MRD > 1% on day 15 of remission induction were assigned to the definitive VHR group. Two had MRD <= 0.01% upon completion of remission induction and continued further chemotherapy. The remaining 4 patients had MRD > 0.01% upon completion of remission induction: 2 had MRD level <= 0.01% at continuation week 7 and continued further

	chemotherapy; 2 with persistent MRD received Allo-HSCT. The overall treatment outcome was better in patients treated with TPOG-ALL-2013 protocol: 4-year event-free survival rates 86.7% vs. 65.6% (P = 0.20); 4-year overall survival rates 85.6% vs. 68.8% (P = 0.39). Conclusions: Although the case number was small and the follow-up duration was short, more adolescents with ALL seemed to be cured with MRD-based risk-adjusted intensive chemotherapy.
關鍵字	急性淋巴性白血病，青少年，兒童，微量殘餘疾病，治療成果
Keyword	Acute lymphoblastic leukemia, Adolescents, Children, Minimal residual disease, Treatment outcome
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	接受異體骨髓移植 17 年後發生骨髓外漿細胞瘤 ： 是延遲性復發還是源自捐者細胞的腫瘤?
Title	Plasmacytoma after allogeneic HSCT seventeen years ago : Late recurrence or Donor cell-derived malignancy
性質	病例報告(case report)
內容	Hematopoietic stem cell transplantation including stem cell biology
報告方式	口頭報告
作者	蕭宇廷, 楊文祺, 林勝豐, 張肇松, 蘇裕傑
Author	YT Hsiao, WC Yang, SF Lin, CS Chang, YC Su
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Abstract	We report a 51-year-old female who had history of plasma cell myeloma (IgG type), diagnosed 17 years ago in Sep. 2000. She recieved thalidomide base treatment followed by allogeneic peripheral blood stem cell transplantation from her brother in May, 2002. Grade 2 GVHD was noted then and the disease were free condition for 15 years. Left side abdominal pain, vomiting with no stool passage were noted and abdominal computed tomography revealed transverse colon tumor with adjacent soft tissue involved in Nov. 2017. Left hemicolctomy was performed and pathology reported plasmacytoma (IgG). The blood type (B) still remains as ″donor type.″ Further bone marrow examination showed only 2% of plasma , cytogenetic study of bone marrow aspiration showed male result with XY sex chromosomes which represents still chimerism.cell. But the flow cytometry showed abnormal kappa/lambda ratio(60.5%:18.1%). Further discussion about the late relapse plasma cell neoplasms or donor cell-derived plasma cell malignancy will be done.
關鍵字	骨隨瘤,異體骨髓移殖,
Keyword	Myeloma, allogeneic HSCT.
著作權授權同	本人不同意將本次投稿主題之會員演講幻燈片掛網。

意書	

分類	第 168 次聯合學術研討會(107 年會)
中文標題	Ixazomib 用於復發/難治性多發性骨髓瘤之經驗--台灣單一醫院中的四個病例報告
Title	Experience of Ixazomib for patients with relapsed/refractory multiple myeloma – 4 cases in single institute in Taiwan
性質	病例報告(case report)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告
作者	黃敬元，洪家燕，蔡官哲，廖柏年，周桂芳，張育誠，蘇迺文，林煥超，蘇穎文，張義芳，陳功深，林炯森，張明志，林建鴻
Author	Jeffrey Peng Huang, Chia-Yen Hung, Guan-Jhe Cai, Po-Nien Liao, Kuei-Fang Chou, Yu-Chen Chang, Nai-Wen Su, Huan-Chau Lin, Ying-Wen Su, Yi-Fang Chang, Caleb Gon-Shen Chen, Johnson Lin, Ming-Chih Chang, Ken-Hong Lim
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Affiliations	Mackay Memorial hospital, Taipei, Taiwan
Abstract	Introduction Ixazomib is an oral form proteasome inhibitor used in patients with relapsed/refractory multiple myeloma. According to the TOURMALINE-MM1 trial, adding ixazomib to lenalidomide/dexamethasone (Rd) regimen resulted in better overall response rate and longer progression free survival. Common side effects include cytopenia, skin rash, GI upset, peripheral neuropathy. Here, we present 4 cases with relapsed/refractory multiple myeloma treated with Ixazomib/lenalidomide/dexamethasone (iRd) regimen in our institute. Case report Case 1 A 72-year-old female was diagnosed with multiple myeloma, IgA-kappa type, ISS stage III on June, 2014. The patient received velcade/thalidomide/dexamethasone (VTD) for 6 months. Complete response was achieved 2 months after treatment. Disease relapse was noted in April, 2016. Rd was given since May, 2016. iTd was switched to control disease progression since June, 2017. Her disease was stable since then. Thalidomide was replaced to lenalidomide in November, 2017. Severe thrombocytopenia refractory to platelet transfusion was noted in December, 2017. Bone marrow examination showed residual plasmacytosis. Thrombotic thrombocytopenia purpura (TTP) was suspected. Plasma exchange was performed but in vain. The patient died of infection on January, 2018. Case 2 A 56-year-old male was diagnosed with multiple myeloma, lamda light chain type, ISS stage II in February, 2014. The patient received VTD for 7 months. Complete response was achieved 3 months after treatment. Disease relapse was noted in March, 2016. Rd was given since March, 2016. Ixazomib was added since January, 2017. Serum IFE still showed monoclonal lamda band 4 months later. Hyperammonemia was noted since 2014 and aggravated after adding ixazomib. He finally developed to

	comatose status with intermittent seizure. The patient died in December, 2017. Case 3 A 62-year-old male was diagnosed with multiple myeloma, IgA-lamda type, ISS stage III in December, 2012. The patient received VTD for 12 months. Complete response was achieved 3 months after starting treatment. Disease relapse was noted in December, 2015. Rd was given since December, 2015. ASCT was performed in July, 2016. Disease relapse was noted in September, 2017. Ixazomib was added on Rd since December, 2017. Hand cellulitis and ischemic stroke occurred after starting Ixazomib. Present response to iRd is VGPR after 2 courses of iRd. Case 4 A 63-year-old female was diagnosed with multiple myeloma, IgG type, Durie-Salmon stage IIIA in May, 2008. The patient received Td, MPT and VTD since June 2008 to September, 2013. Complete response was achieved. Relapse was noted in October, 2017 due to left mandible and left knee plasmacytoma. Rd was given since November, 2017. iRd was switched in January, 2018. Skin lesions were noted after starting Ixazomib. Conclusion Although iRd regimen gives a better overall response and progression-free survival, we should keep in mind that this probably yields rare side effects including hyperammonemia and TTP.
關鍵字	蛋白酶體抑制劑，多發性骨髓瘤，復發，難治
Keyword	proteasome inhibitor, multiple myeloma, relapse, refractory
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	年齡及性別與紅血球細胞指數的關聯性: 台灣單一醫學中心之研究
Title	Age and gender-related changes in red blood cell indices: a single center study in Taiwan
性質	綜論 (reviews)
內容	Anemia and other RBC disorders
報告方式	口頭報告
作者	李純慧 1、曾潤煜 2、蘇勇曄 1、陳嫈文 1、顏志傑 1、許雅婷 1、李欣學 1、鍾為邦 1、葉裕民 1、陳雅萍 1、楊孔嘉 3、陳彩雲 1
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Abstract	Purpose Numerous studies have shown significant differences of red blood cell indices between age and gender. However, in Taiwan, we lack of our own hematological reference range in different age group and gender from healthy adult. Materials and methods We retrospectively reviewed data of hemogram red blood cell indices from adult health examination in our institute between Jan 2006 to May 2017. Thirty-two thousand and three hundred fifty-nine cases were obtained and reviewed from centralized digital data base. The red blood cell indices were analyzed at the institution central laboratory using Coulter LH 750. Results Thirteen thousand and eight hundred sixty-seven cases comprising age greater or equal to twenty and both genders were included for analysis. There are significant differences of red blood cell indices distribution between men and women. Besides, impacts on red blood cell (RBC), hemoglobin (HBG), hematocrit (HCT), mean corpuscular volume (MCV) and mean cellular hemoglobin (MCH) can be observed from different age groups. Conclusion Our results confirmed the importance of age and gender-related changes in red blood cell indices for the healthy adult. This supports the need to establish local reference interval or cutoffs rather than adoption of generalized reference values.
關鍵字	年齡，性別，紅血球細胞指數，貧血
Keyword	age, gender, red blood cell indices, anemia
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片檔案，經部份修改後轉成 PDF 檔格式，掛於血液病學會網站上供該會會員瀏覽下載。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	後天再生不良性貧血之治療策略和臨床結果- 單一中心之治療經驗與臨床困境
Title	TREATMENT STRATEGIES AND OUTCOME OF ACQUIRED APLASTIC ANEMIA: REAL-WORLD INFORMATION WITH SINGLE-CENTER EXPERIENCE
性質	原著(original article)
內容	Anemia and other RBC disorders
報告方式	口頭報告
作者	顏志傑，李欣學，許雅婷，李純慧，陳建旭，鄭兆能，陳雅萍，陳彩雲
Author	Chih-Chieh Yen, Sin-Syue Li, Ya-Ting Hsu, Chun-Hui Lee, Chien-Hsu Chen, Chao-Neng Cheng, Ya-Ping Chen, Tsai-Yun Chen
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Affiliations	Division of Hematology/ Oncology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung

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Abstract	Acquired aplastic anemia (AA) is a life-threatening hematological disorder featured by pancytopenia and hypocellular bone marrow. It is reported rare with the annual incidence of 1.5 to 7.0 cases per million persons per year. The introduction of upfront allogeneic hematopoietic stem cell transplantation (HSCT) and immunosuppressive therapy (IST) has transformed the dismal outcomes into substantial improvements. However, contemporary information concerning treatment strategies and outcomes in real-world practices is lacking and the responses vary from different treatment eras. Here we performed a retrospective study for patients with acquired aplastic anemia from 2002 to 2017 in a referral medical center in Taiwan. A total of 87 patients were analyzed with median age of 33 years (range 1-90). Very severe aplastic anemia (VSAA) and severe aplastic anemia (SAA) accounted for 68.2% of patients. Primary treatment included IST (39.1%), HSCT (11.5%), danazol (25.3%), transfusion (21.8%) and erythropoietin stimulating agent (2.3%). In the total follow up time of 194 months, 5-year survival rate was 78% and 10-year survival was 71%. Only 4.8% of patients over 60 years of age received IST. Age was the most prevalent predictive factor for treatment response and overall survival. In comparing from the contemporary cohort to the 1991 to 2001 cohort in the same institute, patients with primary treatment of IST had significantly improved response rate (53.6% vs 39.5%, p<0.05). However the difference was not significant after age-matched adjustments (39.5% vs 33.3%, p=0.65). In conclusion, the single center information revealed the treatment paradigm is distinctive in different age groups and age remained the most prevalent factor for treatment strategies and responses. The response to IST was similar from different treatment eras and the elderly population is the potential group undertreated by current optimal management.
關鍵字	再生不良貧血，治療，免疫抑制療法，抗胸腺球蛋白
Keyword	APLASTIC ANEMIA, TREATMENT, IMMUNOSUPPRESSIVE THERAPY, ANTITHYMOCYTE GLOBULIN
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片轉成 PDF 檔格式後，掛於血液病學會網站上供該會會員瀏覽下載
	附圖

分類	第 168 次聯合學術研討會(107 年會)
中文標題	**台灣型血友病患之基因型分析**
Title	Successful Mutational Analysis in Mild/Moderate-type Hemophilia A Genotype Analysis of Hemophilia B Patients in Taiwan
性質	原著(original article)
內容	
報告方式	口頭報告
作者	張家堯，邱世欣，林珮瑾，胡淑霞，陳宇欽*

Author	Chia-Yau Chang[1,2]、Shyh-Shin Chiou[3,4]、Pei-Chin Lin[3,4]、Shu-Hsia Hu[5]、Yeu-Chin Chen[5,6*]
單位	三軍總醫院 國防醫學中心 內科部 血液腫瘤科
Affiliations	(1) Taipei Medical University, Graduate Institute of Clinical Medicine, School of Medicine (2) Taipei Medical University Hospital, Division of Pediatric Hematology/Oncology, Hemophilia Center (3) Division of Hematology and Oncology, Department of Pediatrics, Kaohsiung Medical University Hospital Department of Pediatrics, School of Medicine, College of Medicine, Kaohsiung Medical University (4) Tri-Service General Hospital, Hemophilia Care and Research Center Tri-Service General Hospital, National Defense Medical Center, Department of Internal Medicine, Division of Hematology/Oncology, Taipei, Taiwan
Abstract	**Purpose:** Hemophilia B (HB) is a congenital coagulation factor IX (FIX) defect or deficiencyThe genetic defect of HB have been reported in different ethnical populations, but very limited genetic study on HB had been reported from Taiwan. The objectives of our study was to report our experience on the F9 gene mutation analysis and to characterize the spectrum of genetic defects in our Taiwanese HB patients. **Materials & Methods:** From 2014 to 2017, there were 28 HB patients from 26 unrelated families enrolled for genotype analysis from Tri-Service General Hospital, Taipei Medical University Hospital, and Kaohsiung Medical University Hospital. Genomic DNA is extracted from peripheral blood buffy coat cells according to QIAamp DNA Mini Kit (USA) after each patient's signed inform consent was obtained. The promoter region of the F9 gene and all entire coding region, the 5' untranslated region, the 3' untranslated region and the splicing site boundaries were amplified by polymerase chain reaction (PCR). When a large deletion or duplication is suspected after amplification failed repeatedly, multiplex ligation-dependent probe amplification (MLPA) reaction is performed using the SALSA F9 Kit. **Results:** Twenty of the 28 patinets (71.4%) were severe type, followed by moderate type in 6 patients (21.4%) and two patients with mild type HB (7.1%). None of the patients had inhibitors. There were totally found 29 types of mutation including 20 (70%) missense point mutations, 5 (17.2%) non-sense mutation, two (6.9%) small deletion, one (3.4%) small insertion and one (3.4%) large deletion. In terms of the frequency of mutation sites, six patients had exon 8 mutations, five patients had exon 4 mutations, each four patient had mutations on exon 2 or exon 6, three patients had exon 7 mutations, two patients had mutations on exon 5, one had exon 3 mutation and one had exons 4-5 deletion. There were two patients with severe-type HB, who had double missense mutation located at exons 4 & 6 in one patient and at exons 6 & 8 in another. One missense mutation of exon 8：c.1271T>G; TTC>TGC was proved as a novel mutation. **Conclusions:** With regard to the genotype analysis of our 28 Taiwanese HB patients, missense mutation (70%) and nonsense mutation (17.2%) were more common in our cohort and the most common mutation sites were exon 8, followed by exon 4, then followed by exons 2 & 6.
關鍵字	B型血友病，第九凝血因子基因，基因型，多組接合探針放大
Keyword	Hemophilia B, Factor 9 gene, Genotype, dHPLC, Multiplex Ligation-Dependent Probe Amplification
著作權授權同意書	

分類	第 168 次聯合學術研討會(107 年會)
中文標題	新診斷骨髓瘤病患骨髓血中高濃度之肝細胞生長因子與較差的預後有關
Title	High levels of hepatocyte growth factor in bone marrow plasma are associated with inferior outcome in patients with newly diagnosed multiple myeloma
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma
報告方式	口頭報告
作者	林耘曲，陳羿汎，黃聖懿
Author	Lin Yun-Chu, Chen Yi-Fan, Huang Shang-Yi
單位	臺大醫院內科部血液科
Affiliations	Division of Hematology, Department of Internal Medicine, NTUH Taipei
Abstract	Background: Hepatocyte growth factor(HGF) is a multifunctional growth factor to promote cellular growth and mobility, as well as tissue angiogenesis. HGF plays role in pathophysiology of multiple myeloma(MM) as a paracrine and/or an autocrine. High HGF in MM patients has been reported to associate with poor prognosis. However, the clinical characteristics and significance of HGF in our myeloma patients are unclear. Method: By using enzyme-linked immunosorbent assay (ELISA), we examined levels of HGF in bone marrow (BM) plasma obtained from our 268 patients with newly diagnosed MM (NDMM). The clinical salient features and outcomes including response to induction therapy, progression free survival(PFS) and overall survival(OS) were evaluated and correlated to the levels of HGF. Results: Based on the levels of HGF, we divided our patients into three groups, namely high HGF group (HGF >3.8ng/mL; N=90), intermediate HGF group (HGF: 1.04~3.8ng/mL; N=89) and low HGF group(HGF<1.04ng/mL; N=89). Compared to the low HGF group, patients in the high HGF group have significantly lower hemoglobin, higher beta2-microglobulin(β2-MG), higher creatinine, more ISS stage III ($p< 0.05$). Notably, we found that patients in the high HGF group had higher incidence of amyloidosis than those who did in the low HGF group (68.8% vs. 3.1%, respectively; $p< 0.05$). Regarding to the treatment response, there was no significant difference between the high and low HGF group. Only a trend of lower HGF level were seen in the responder compared to the non-responders. However, patients in the high HGF group had significantly shorter OS compared to those who in the low HGF group (med, 86 months vs. 39 months, respectively; $p= 0.003$); patients in the high HGF group also had significantly shorter (PFS for induction compared to those who in the low HGF group (med, 30 months vs. 22 months; $p= 0.027$). Multi-variate analysis confirmed that high level HGF was an independent prognostic factor for OS (Hazard ratio:1.66, 95% CI:1.012-2.723, $p=0.045$). Conclusion: Higher levels of HGF in BM plasma are associated with more advanced diseases and inferior outcome in patients with NDMM. Higher incidence of

	amyloidosis noted in patients with high HGF warrants further study.
關鍵字	肝細胞生長因子，多發性骨髓瘤，類澱粉沉積症
Keyword	Hepatic growth factor(HGF), multiple myeloma, amyloidosis
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	台灣血液疾病半相合移植之總體成果分析
Title	Transplant outcomes of haploidentical activities for hematological disorders in Taiwan: results from TBMTR
性質	
內容	原著(original article)
報告方式	口頭報告
作者	李啟誠
Author	Chi-Cheng Li
單位	[1]花蓮佛教慈濟醫院幹細胞移植中心 [2]國立臺灣大學台成幹細胞治療中心 [3]臺大醫院內科部血液科骨髓移植病房
Affiliations	Center of Stem Cell Transplantation, Hualien Tzu Chi Hospital[1]
Abstract	
關鍵字	免疫基因半相合，骨髓，週邊血幹細胞，移植後 cyclophosphamide 使用
Keyword	Haploidentical, Bone marrow, Peripheral blood stem cells, Post-transplant cyclophosphamide
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片檔案，經部份修改後轉成 PDF 檔格式，掛於血液病學會網站上供該會會員瀏覽下載。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	使用次世代定序研究 CD5 表達黯淡的淋巴球增多症
Title	A new look on CD5-attenuated T lymphocytosis using NGS-based T cell receptor rearrangement analysis
性質	原著(original article)
內容	Lymphoma, CLL, and Myeloma

報告方式	口頭報告
作者	張裕享、黃泰中、翁佩芳、林詠容、劉驥揚、薛佳雨、莊其蓁、李啟誠、孫珣懿 、唐季祿
Author	Yu-Hsiang Chang, Tai-Chung Huang, Sophie Weng, Chi-Cheng Li, Jih-Luh Tang
單位	台成幹細胞治療中心、臺大醫院內科部血液腫瘤科
Affiliations	Tai-Cheng Stem Cell Therapy Center、Division of Hematology, Department of Internal Medicine, National Taiwan University Hospital
Abstract	Purpose\Materials & Methods\Results\Conclusions:(最多 450 字) Purpose Human CD5, a membrane glycoprotein, is normally expressed on the majority of circulating T cells and inhibits TCR activating signaling in T cells interacting with antigen-presenting cells. It has been reported that a subpopulation of CD8+ T cell clonal expansion with CD5 down-regulation and bright human leukocyte antigen (HLA)-DR expression was found in patients with Epstein-Barr virus (EBV)-associated hemophagocytic lymphohistiocytosis (HLH). Materials and Methods Thirteen patients with abnormal CD5dim T lymphocytes detected by flow cytometry were investigated using next generation sequencing (NGS)-based T cell receptor rearrangement analysis. Results Of the thirteen patients, six patients were diagnosed with T large granule lymphocyte leukemia (T-LGLL), one with B and T cell lymphoma; one with HTLV-1 carrier; two with aplastic anemia; one with autoimmune hemolytic anemia, and two with unknown T-cell lymphocytosis. The average mean fluorescence intensity of CD5high, CD5dim and CD5- cells in these thirteen patients were 136, 23 and 4, respectively. NGS-based T cell receptor rearrangement analysis showed a positive clonal population of T-cells in five patients with T-LGLL, one with B and T cell lymphoma and one with HTLV-1 carrier. The clonality was markedly increased in sorted CD5dim cells, and decreased in sorted CD5bright cells in samples from two patients, which indicated the clonality originated from CD5dim cells. The results showed weak positive in one patient with T-LGLL and two with unknown T-cell lymphocytosis. Importantly, NGS-based clonality analysis was negative in patients with non-malignant disease, including two patients with aplastic anemia and one with autoimmune hemolytic anemia. Conclusions NGS-based strategy to determine T-cell clonality has superior diagnostic sensitivity compared with traditional approach, such as PCR-based clonality assay or southern blot analysis. According to our preliminary results, NGS-based T cell receptor rearrangement analysis can help us distinguish between reactive and malignant lymphoproliferation. Furthermore, the specific clonal population of T cells can be enriched using Fluorescent Activated Cell Sorting (FACS) to confirm the clonal origin in patients with T-cell lymphocytosis.
關鍵字	淋巴球增多症、次世代定序
Keyword	lymphocytosis、NGS
著作權授權同意書	本人不同意將本次投稿主題之會員演講幻燈片掛網。

分類	第 168 次聯合學術研討會(107 年會)
中文標題	去除初始 T 細胞週邊血液幹細胞移植之病例報告
Title	Outcomes of acute leukemia patients transplanted with naive T cell–depleted stem cell grafts in CMUH
性質	病例報告(case report)
內容	Hematopoietic stem cell transplantation including stem cell biology
報告方式	口頭報告
作者	陳姿婷，林精湛，葉士芃
Author	Tzu-Ting Chen, Ching-Chang Lin, Su-Peng Yeh
單位	中國醫藥大學附設醫院血液腫瘤科
Affiliations	Hematology and oncology, China medical university hospital
Abstract	Graft-versus-host disease (GVHD) is a major cause of morbidity and mortality following peripheral blood allogeneic hematopoietic stem cell transplantation (HCT). In mice, naive T cells (TN) cause more severe GVHD than memory T cells (TM). We hypothesized that selective depletion of TN from human allogeneic peripheral blood stem cell (PBSC) grafts would reduce GVHD and provide sufficient numbers of hematopoietic stem cells and TM to permit hematopoietic engraftment and the transfer of pathogen-specific T cells from donor to recipient, respectively. We transplanted three patients with high-risk leukemia with TN-depleted PBSC grafts following conditioning with myeloablative conditioning regimen. GVHD prophylactic management was with sirolimus immunosuppression alone. Subjects received CD34-selected PBSCs and a defined dose of TM purged of CD45RA+ TN. Two recipients of TN-depleted PBSCs engrafted.One patient sufferred from primary graft failure and died of infection.One had disease relapse one month after stem cell transplantation. Ant-GvHD medication was withdrawed and salvage chemotherapy was given. The patient was died of infection. One patient had disease relapse after TN-depleted PBSCs transplantation. The patient received CAT-T cell therapy in China and died of CRS. None of these patient had acute GVHD.
關鍵字	初始 T 細胞，週邊血幹細胞移植，急性白血病，排斥
Keyword	Naive T cell, peripheral blood stem cell transplantation, acute leukemia，graft-versus-host disease
著作權授權同意書	本人同意將本次投稿主題之會員演講幻燈片轉成 PDF 檔格式後，掛於血液病學會網站上供該會會員瀏覽下載