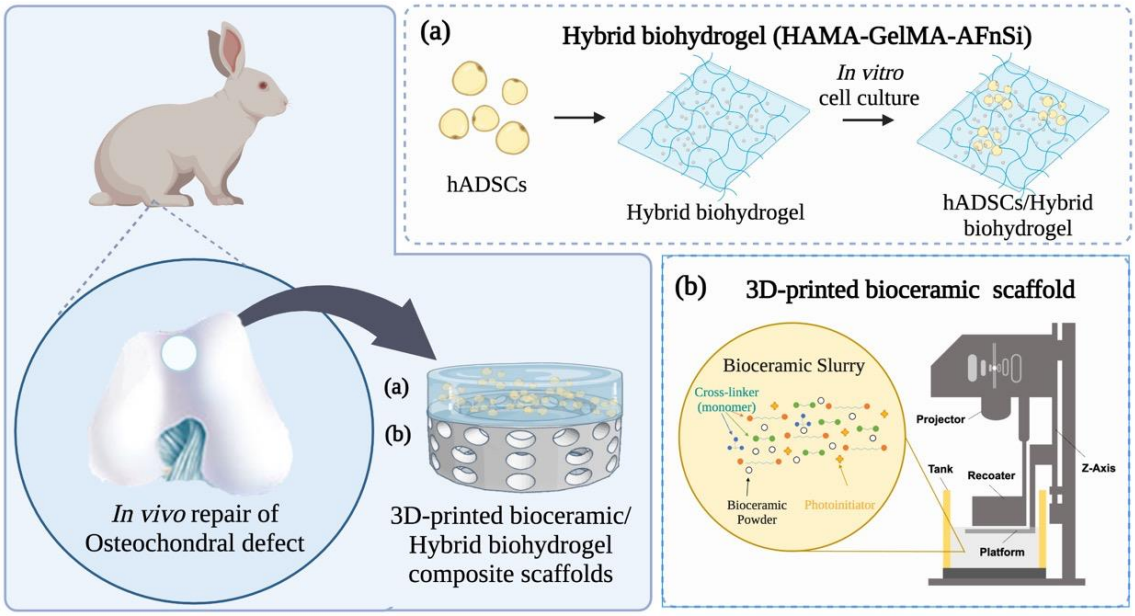
王志光 教授

生命科學院/醫藥暨應用化學系

再生醫學與細胞治療研究中心

▶目前擁有三項佈局全球的負溫感陶瓷漿體的專利系統，致力發展「更快癒合、具支撐性 3D 生物陶瓷骨材」的積層製造技術，應用於個人化骨癒合的精準骨移植替代物，以促進人類健康福祉為首要任務。

本團隊設計一種新穎骨與軟骨雙層支架，該支架下層使用 3D 列印的 β-磷酸三鈣(β-tricalcium phosphate, β-TCP)生物陶瓷支架，即通過數位光處理(digital light processing；DLP)技術和新型光敏與負溫感雙功能之專利生物陶瓷漿料製成，這 3D 生物陶瓷支架不僅能提供必要的軟骨下骨組織的機械支撐與再生，還能延緩其生物降解，為軟骨再生提供穩定的基質。雙層支架的上層是三維仿生混合水凝膠，主要由透明質酸甲基丙烯酸酯(hyaluronic acid methacryloyl；HAMA)與明膠甲基丙烯酸(gelatin methacryloyl；GelMA)共聚組成，並創新穎運用無機奈米氧化矽交聯劑(acrylate functionalized nano-silica；AFnSi)增強混合光固化水凝膠的機械性能並減緩生物體的降解速度，其體外具有細胞相容性和促進軟骨分化的優異結果。並且我們也已申請此混合光固化生物水膠系統在軟骨生成的專利佈局(中華民國專利號：798084)。研究結果顯示，當這 3D 生物陶瓷支架與富含人體脂肪幹細胞的光固化混合水凝膠組成的雙層骨軟骨支架，在兔子膝蓋骨軟骨缺損模型中展現了良好的骨軟骨缺損修復效果，能夠加速骨形成並促進與鄰近骨組織的融合。上述研究證實了 3D 列印技術在組織修復領域具有廣泛應用潛力，團隊有幸於 2021~2024 年獲得國科會育苗計劃的支持，並以此 3D β-磷酸三鈣生物陶瓷支架為基礎衍生出新創公司「品醫生技」，專注於開發積層製造 3D 生物陶瓷骨移植替代物個人化的骨缺損適應症。



▲雙層骨軟骨支架示意圖，引導幹細胞軟骨細胞和成骨分化，為骨軟骨組織修復提供有前景的解決方案。(a) 由透明質酸甲基丙烯酰（HAMA）/明膠甲基丙烯酰（GelMA）（1/1）和 0.5%（w/v）丙烯酸酯官能化奈米矽膠（AFnSi）交聯劑組成的人體脂肪幹細胞（hADSCs）載體光固化混合生物水凝膠，為軟骨再生提供了合適的環境。(b) 利用數位光學處理（DLP）技術與新型光敏與負溫感雙功能（NTR）生物陶瓷漿料，製作出凹頂圓盤結構的軟骨下支架，其中間層較為緻密，3D 列印的生物陶瓷支架具有良好的開放性孔道結構。

【具體成果】

具體成果：獲獎經歷

1. 110；111；112 學年度 優秀論文
2. 110；111；112 學年度 教師研究論文獎勵
3. 112 學年度 技術移轉—卓越獎
4. 110；111；112 學年度 專利獲證—優良獎、績優獎、優良獎
5. 111；112 學年度 產學合作—特別卓越獎、卓越獎

- **SCI 論文**

1. Che-Wei Lin, Yu-Feng Su, Chih-Yun Lee, Lin Kang, Yan-Hsiung Wang, Sung-Yen Lin, Chih-Kuang Wang*, 3D printed bioceramics fabricated using negative thermoresponsive hydrogels and silicone oil sealing to promote bone formation in calvarial defects, Ceramics International, 47, 5464-5476, 2021, (IF:5.1 at 2023)

2. Swathi Nedunchezian, Parikshit Banerjee, Chih-Yun Lee, Su-Shin Lee, Che-Wei Lin, Che-Wei Wu, Shun-Cheng Wu, Je-Ken Chang, Chih-Kuang Wang*, Generating adipose stem cell-laden hyaluronic acid-based scaffolds using 3D bioprinting via the double crosslinked strategy for chondrogenesis, Materials Science and Engineering: C, 124, 112072, 2021. (IF: 8.04 at 2023)
3. Swathi Nedunchezian, Che-Wei Wu, Shung-Cheng Wu, Chung-Hwan Chen, Je-Ken Chang, Chih-Kuang Wang*, Characteristic and Chondrogenic Differentiation Analysis of Hybrid Hydrogels Comprised of Hyaluronic Acid Methacryloyl (HAMA), Gelatin Methacryloyl (GelMA), and the Acrylate-Functionalized Nano-Silica Crosslinker, Polymers, 14, 2003, 2022. (IF: 4.7 in 2023)
4. Che-Wei Lin, Chih-Yun Lee, Sung-Yen Lin, Lin Kang, Yin-Chih Fu, Chung-Hwan Chen, Chih-Kuang Wang*, Bone targeting nanoparticles of dendritic (aspartic acid)$_3$-functionalized PEG-PLGA biopolymer encapsulated simvastatin treated for the osteoporosis rat models, International Journal of Molecular Sciences, 2022, 23, 10530. (IF:4.9 at 2023).
5. Chih-Yun Lee, Swathi Nedunchezian, Sung-Yen Lin, Yu-Feng Su, Che-Wei Wu, Shun-Cheng Wu, Chung-Hwan Chen, Chih-Kuang Wang*, Bilayer osteochondral graft in rabbit xenogeneic transplantation model comprising sintered 3D-printed bioceramic and human adipose-derived stem cells laden biohydrogel, Journal of Biological Engineering,17,74, 2023. **(IF:5.6 at 2023)**
6. Pavanchandh Atturu, Sunaina Mudigonda, Chau-Zen Wang, Shun-Cheng Wu, Jhen-Wei Chen, Mary Fornica Francis Forgia, Hans-Uwe Dahms, Chih-Kuang Wang*, Adipose-derived stem cells loaded photocurable and bio printable bioinks composed of Methacrylated Gelatin, Methacrylated Hyaluronic acid and Polyethylene glycol diacrylate crosslinker to differentiate into smooth muscle phenotype, International Journal of Biological Macromolecules, 265: 130710, 2024. (IF:.7.7 at 2023)

- **產學專利獲證**

1. 王志光, 何美泠, 潘力誠, 傅尹志, 陳崇桓, 張瑞根, 積層製造 3D 列印物品的方法, WO(EP)-世界專利(歐盟) 核准通知獲證通 3385057。2021/02/24
2. 王志光, 何美泠, 潘力誠, 傅尹志, 陳崇桓, 張瑞根, 積層製造 3D 列印物品的方法, WO(CN)-世界專利(中國) 獲證號 4274912。2021/02/26
3. 王志光, 何美泠, 潘力誠, 傅尹志, 陳崇桓, 張瑞根, 積層製造 3D 列印物品的方法, WO(US)-世界專利(美國) 獲證號 111,111,84。2021/09/07

4. 王志光, 李之昀, 李宜蓁, 劉哲維, 林哲緯, 用于光固化 3D 打印的浆料、其制备方法及其使用方法, PCT (CN), 獲證號 5682329. 2023/01/06
5. 王志光, 李之昀, 李宜蓁, 劉哲維, 林哲緯, 用于光固化 3D 打印的浆料、其制备方法及其使用方法, PCT (JP), 獲證號 7255915. 2023/04/03
6. 王志光, Swathi Nedunchezian, 羅振綸, 複合水凝膠組合物、其製備方法及其用途, 中華民國專利號：I798084。2023/04/01

7. 王志光, 李之昀, 王郁惠, 王潔瑩, 齊俐安, 蘇裕峯, 陳崇桓, 林松彥, 一種顱骨修復結構, 中華民國專利號：M648441。2023/11/21.

- **產官學合作計畫：**

1. 載有脂肪幹細胞之3D列印新穎複合組織工程氣管移植物結合氣管腔內上皮細胞片於氣管再生研究(II-III), 國科會, 2024/08/01至2026/07/30 (總核定1,660,000; 1,540,000 NT)。(NSTC 113-2314-B-037 -024 -MY2)(主持人)
2. 評估仿生物水凝膠系統與間質幹細胞(mesenchymal stem cells；MSCs)的增生與分化活性研究, 順臻生物科技有限公司產學合作計畫, 2022/09/01-2024/12/31. (核定15,000 NT)(主持人)
3. 載有脂肪幹細胞之3D列印新穎複合組織工程氣管移植物結合氣管腔內上皮細胞片於氣管再生研究(I), 國科會, 2023/08/01至2024/07/30 (總核定978,600 NT)。(NSTC 112-2314-B-037-078)(主持人)
4. 產業前瞻-應用型研究育苗專案計畫之「積層製造3D生物陶瓷顱骨鑽孔蓋骨移植替代物 (II)」, 科技部, 2022/01/01至2024/03/31 (總核定9,150,000 NT)。(NSTC 112-2622-B-037-001 -)(主持人)
5. 產業前瞻-應用型研究育苗專案計畫之「積層製造3D生物陶瓷顱骨鑽孔蓋骨移植替代物 (I)」, 科技部, 2021/11/01至2022/12/31 (總核定8,500,000 NT)。(MOST 110-2622-B-037-002 -)(主持人)
6. 新穎性生物墨水系統進行組織工程化血管移植物的3D生物列印研究, 科技部, 2021/08/01至2022/07/30 (總核定1,140,000 NT)。(MOST 110-2314-B-037-032)(主持人)

- **重要成就事項**

1. 110 年度教育部「U-start 創新創業計畫」第一階段獲補助團隊名單-品醫生技 (共計 75 隊), 2021 年 05 月 20 日核准成立品醫生技有限公司。(王志光 教授技術發明人與創辦人) 。

2. 第十八屆戰國策全國創新創業競賽，品醫生技有限公司榮獲 育成企業類 第一名，2023 年 06 月 29 日。

3. 品醫生技有限公司於 2023 年 06 月 30 日完成與高雄醫學大學的技術作價合約，總金

額為新台幣 2,000 萬元。首期 1,000 萬元技術轉移資金已於 2023 年 11 月完成。

【3D 生物陶瓷研究團隊】

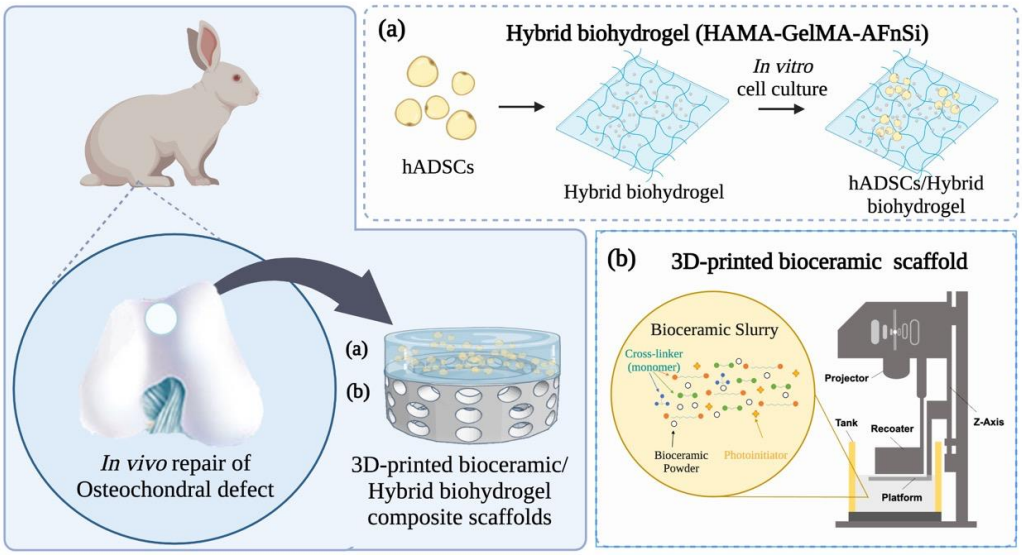
團隊成員：王志光教授、李之昀、齊俐安、王潔瑩、林莉芳

團隊簡介：目前擁有三項佈局全球的負溫感陶瓷漿體的專利系統，致力發展「更快癒合、具支撐性 3D 生物陶瓷骨材」的積層製造技術，應用於個人化骨癒合的精準骨移植替代物，以促進人類健康福祉為首要任務。

研究聯繫 Email：ckwang@kmu.edu.tw ； j020900@yahoo.com.tw 20900@yahoo.com.tw

Our team designed a novel osteochondral osteochondral double-layer scaffold. The lower layer of the double-layer scaffold uses a 3D printed β-tricalcium phosphate (β-TCP) bioceramic scaffold, which uses digital light processing (DLP) technology and photo-cured and negative thermoresponsive (NTR) bifunctional bioceramic slurry achieved. This 3D bioceramic scaffold not only provides the necessary mechanical support and regeneration of subchondral bone tissue, but also delays its biodegradation and provides a stable matrix for cartilage regeneration. The upper layer of the double-layer scaffold is a three-dimensional bioinspiral hybrid hydrogel, which is mainly composed of hyaluronic acid methacryloyl (HAMA) and gelatin methacryloyl (GelMA) copolymers. Acrylate functionalized nano-silica (AFnSi) is innovatively used to enhance the mechanical properties of the hybrid light-cured hydrogel and Slows down the degradation rate of organisms, has excellent results in cytocompatibility in vitro and promotes cartilage differentiation. However, we have also applied for a patent layout of this hybrid light-curing biohydrogel system for cartilage generation (ROC patent number: 798084). The research results show that when the double-layer osteochondral scaffold composed of this 3D bioceramic scaffold and photo-cured hybrid hydrogel rich in human adipose stem cells (hADSCs) showed good osteochondral defect repair effects in the rabbit knee cartilage defect model, Can accelerate bone formation and promote fusion with adjacent bone tissue. The above research has confirmed that 3D printing technology has broad application potential in the field of tissue repair. The team is fortunate to receive the NSTC Grant's two-year industry perspective for Applied Research Incubation Project (I) (II) (Cranial burr hole cover of 2021~2024) 3D bioceramic bone graft substitute using the additive manufacturing method), and based on this 3D

bioceramic scaffold bone graft material product technology, "Precisely Printed Medical Co., Ltd." a new start-up company, which focuses on the development of active materials Layer-fabricated 3D bioceramic bone graft substitutes for personalized bone defect indications.



▲A schematic diagram of the well-integrated bilayer osteochondral scaffold is expected to guide stem cells' chondrogenic and osteogenic differentiation and provide a promising solution for osteochondral tissue repair. The human adipose-derived stem cell (hADSCs) laden photocured hybrid biohydrogel comprised of hyaluronic acid methacryloyl (HAMA)/gelatin methacryloyl (GelMA) (1/1) and 0.5% (w/v) acrylate-functionalized nano-silica (AFnSi) crosslinker, which provide a suitable environment for cartilage regeneration. **a** The concave-top disc structure of the subchondral scaffold with the denser intermediate layer and the well-open interpenetrating pore channels structure of the 3D-printed bioceramic scaffold is made using digital light processing (DLP) technology and the novel photocurable negative thermo-responsive (NTR) bioceramic slurry.

【Concrete Results】

- **Award experience**

1. Excellent papers in 110; 111; 112 academic years respectively
2. Research paper awards in 110; 111; 112 academic years respectively
3. Technology Transfer - Excellence Award in the 112 academic year
4. Patent certification—Excellence Award, Merit Award, and Excellence Award in the 110; 111; 112 academic years respectively
5. Industry-university cooperation - Special Excellence Award and Excellence Award in the 111 and 112 academic years respectively

- **Main SCI papers**

1. Che-Wei Lin, Yu-Feng Su, Chih-Yun Lee, Lin Kang, Yan-Hsiung Wang, Sung-Yen Lin, Chih-Kuang Wang*, 3D printed bioceramics fabricated using negative thermoresponsive hydrogels and silicone oil sealing to promote bone formation in calvarial defects, Ceramics International, 47, 5464-5476, 2021, (IF:5.1 at 2023)
2. Swathi Nedunchezian, Parikshit Banerjee, Chih-Yun Lee, Su-Shin Lee, Che-Wei Lin, Che-Wei Wu, Shun-Cheng Wu, Je-Ken Chang, Chih-Kuang Wang*, Generating adipose stem cell-laden hyaluronic acid-based scaffolds using 3D bioprinting via the double crosslinked strategy for chondrogenesis, Materials Science and Engineering: C, 124, 112072, 2021. (IF: 8.04 at 2023)
3. Swathi Nedunchezian, Che-Wei Wu, Shung-Cheng Wu, Chung-Hwan Chen, Je-Ken Chang, Chih-Kuang Wang*, Characteristic and Chondrogenic Differentiation Analysis of Hybrid Hydrogels Comprised of Hyaluronic Acid Methacryloyl (HAMA), Gelatin Methacryloyl (GelMA), and the Acrylate-Functionalized Nano-Silica Crosslinker, Polymers, 14, 2003, 2022. (IF: 4.7 in 2023)
4. Che-Wei Lin, Chih-Yun Lee, Sung-Yen Lin, Lin Kang, Yin-Chih Fu, Chung-Hwan Chen, Chih-Kuang Wang*, Bone targeting nanoparticles of dendritic (aspartic acid)$_3$-functionalized PEG-PLGA biopolymer encapsulated simvastatin treated for the osteoporosis rat models, International Journal of Molecular Sciences, 2022, 23, 10530. (IF:4.9 at 2023).
5. Chih-Yun Lee, Swathi Nedunchezian, Sung-Yen Lin, Yu-Feng Su, Che-Wei Wu, Shun-Cheng Wu, Chung-Hwan Chen, Chih-Kuang Wang*, Bilayer osteochondral graft in rabbit xenogeneic transplantation model comprising sintered 3D-printed bioceramic and human adipose-derived stem cells laden biohydrogel, Journal of Biological Engineering,17,74, 2023. **(IF:5.6 at 2023)**
6. Pavanchandh Atturu, Sunaina Mudigonda, Chau-Zen Wang, Shun-Cheng Wu, Jhen-Wei Chen, Mary Fornica Francis Forgia, Hans-Uwe Dahms, Chih-Kuang Wang*, Adipose-derived stem cells loaded photocurable and bio printable bioinks composed of Methacrylated Gelatin, Methacrylated Hyaluronic acid and Polyethylene glycol diacrylate crosslinker to differentiate into smooth muscle phenotype, International Journal of Biological Macromolecules, 265: 130710, 2024. (IF:.7.7 at 2023)

- Patent certified

1. Method for additive manufacturing of 3D-printed articles, WO(EP)-European Union, 3385057, 2021/02/24.
2. Method for additive manufacturing of 3D-printed articles, WO(CN)-China, 4274912, 2021/02/26.
3. Method for additive manufacturing of 3D-printed articles, WO(US)- United States, 111,111,84, 2021/09/07.
4. Slurry for photocuring 3D printing, preparation method therefor, and method of use thereof, PCT (CN)-China, 5682329, 2023/01/06.
5. Slurry for photocuring 3D printing, preparation method therefor, and method of use thereof, PCT (JP)-Japan, 7255915, 2023/04/03.
6. Inorganic nanosilica-crosslinker mixed with bio-ink to promote cartilage differentiation of adipose stem cells, ROC (Taiwan), I798084, 2023/04/01.
7. A skull repairing structure, ROC (Taiwan), M648441, 2023/11/21.

- Industry-government-academic cooperation project:

1. Adipose stem cells laden 3D-printed novel composite tissue-engineered tracheal grafts combined with tracheal luminal epithelial cell sheets for tracheal regeneration (II-III), National Science and Technology Council, 2024/08/01~2026/07/30 (1,660,000; 1,540,000 NT)。(NSTC 113-2314-B-037 -024 -MY2) (PI)
2. Evaluate the proliferation and differentiation activities of biohybrid hydrogel system and mesenchymal stem cells (MSCs), Industry-Academic Cooperation Project (順臻生物科技有限公司), 2022/09/01-2024/12/31. 15,000 NT) (PI)
3. Adipose stem cells laden 3D-printed novel composite tissue-engineered tracheal grafts combined with tracheal luminal epithelial cell sheets for tracheal regeneration (I), National Science and Technology Council, 2023/08/01~2024/07/30 (978,600 NT)。(NSTC 112-2314-B-037-078) (PI)
4. Industry Perspective - Applied Research Incubation Project—「Cranial burr hole cover of 3D bioceramic bone graft substitute using the additive manufacturing method (II)」, National Science and Technology Council, 2022/01/01 至 2024/03/31 (9,150,000 NT)。(NSTC 112-2622-B-037-001 -) (PI)

5. Industry Perspective – Applied Research Incubation Project—「Cranial burr hole cover of 3D bioceramic bone graft substitute using the additive manufacturing method (I)」, Ministry of Science and Technology, 2021/11/01 至 2022/12/31 (8,500,000 NT)。(MOST 110-2622-B-037-002 -) (PI)

6. Study on 3D bioprinting of tissue-engineered vascular grafts with novel bioinspired bioink, Ministry of Science and Technology, 2021/08/01 至 2022/07/30 (1,140,000 NT)。(MOST 110-2314-B-037-032) (PI)

- **Important achievements**

1. Award the "U-Start Plan for Innovation and Entrepreneurship" in the manufacturing technology category (500,000 NT dollars) and established a startup company (Precisely Printed Medical Co., Ltd.), 2021/04/30.
2. The startup company achieved championship in the Incubates category at the 18th Strategies of Warring States Period National Innovation & Entrepreneurship Competition, 2023/07/03.

3. In 2023, We raised NT$20 million in technology investment stock for the Precisely Printed Medical startup company, and the first phase of technology transfer fund of NT$10 million has been completed in November 2023.

【Research Team】

Team Members: Prof. Chih-Kuang Wang, Chih-Yun Lee, Li-Ann Chi, Jie-Ying Wang, Li-Fang Lin

Research Team Introduction: The team has three patents for negative temperature-sensitive bioceramics system that are deployed around the world. We have been committed to the development of " healing faster, and supportive 3D bioceramic aggregates" 3D printing technology. Precision bone graft substitutes for personalized bone healing with the primary mission of promoting human health and well-being.

Research Contacts Email: ckwang@kmu.edu.tw ;j020900@yahoo.com.tw

▲積層製造 3D 陶瓷(磷酸鈣、氧化鋁、氧化鋯等)的各式 3D 燒結後陶瓷形體樣態展示。未來除了醫療領域外、在航空航太和半導體等產業中也有很大的潛力應用。

Display various 3D sintering ceramic shapes of additional manufacturing 3D ceramics (calcium phosphate, alumina, zirconia, etc.). In addition to the medical field, it will also have great potential applications in the aerospace and semiconductor industries.

▲蕭美琴副總統出席 2024 台灣國際醫療暨健康照護展，高雄醫學大學專館備受矚目，也特別參觀了高醫大衍生新創公司-品醫生技與衡心科技。

Vice President Bi-khim Hsiao attended the 2024 Taiwan International Medical and Health Care Exhibition. The Kaohsiung Medical University Pavilion attracted much attention. She also visited the new spin-off companies of Kaohsiung Medical University - Precisely Printed Medical Co., Ltd. and Cardio Metrics Co., Ltd.