# 第15屆臨床醫學研究所聯合教學研究研討會

# 2025.6.28(六)

# 第一階段(初審)：

1. **請投稿人注意，建議以Chrome瀏覽器開啟並配合Google帳號雲端上傳附檔，若有其他協助上傳需求請洽: 臺北醫學大學臨床醫學研究所(02)2736-1661#3229。**
2. **投稿表單連結：**
3. **開放投稿時間：**2025年3月5日(三) 12:00
4. **投稿截止日期：**2025年5月10日(六) 24:00
5. **入選結果公布日期：**2025年6月10日(二)後由刊登於臺北醫學大學臨床醫學研究所網頁(https://gicm.tmu.edu.tw/)並將結果將由大會承辦單位發信通知各所辦及投稿者。
6. **請注意**入選證明將依照填寫於系統的內容製作。其他作者若需投稿證明，請務必詳細填寫於其他作者欄位，投稿截止後無法另行修改增加。
7. 學術研討會承辦人：臺北醫學大學臨床醫學研究所蔡坤志所長、鄭朝文老師、張育嘉老師、何佳芸秘書、林美智秘書。
8. 聯絡電話：何佳芸秘書02-2736-1661分機3229

E-mail address: gicm@tmu.edu.tw

**稿件格式**

1. **摘要內容不得超出一頁(約中文1000字或英文字300左右)，並以網頁鍵入資料為主，WORD檔為輔**。
2. WORD版面配置選擇「標準」(上下邊界2.54cm，左右邊界3.18cm)、行距設定為單行行距、英文投稿者請以12號字Times New Roman、中文投稿者請以12號字標楷體。
3. 摘要本文第一字，英文須向後退4格，中文則後退2格。
4. 摘要題目之各英文字第一字母為大寫即可，且**題目以粗體顯示並置中**。
海報展示解說者在其姓名之後附加“＊”，責任作者在其姓名之後附加“＃”號，不同單位用數字表示，**符號請勿設定上下標**。（參考第2、3頁摘要格式及範例）
5. 摘要內容之背景、方法、結果及結論等四大部份，分段或不分段皆可，**請勿設定上下標，令檔案內容與網頁鍵入內容一致。**

**投稿表單注意事項**

1. 投稿時請**先選擇欲投稿之組別並勾選 □是否同意入選大會口頭報告**。
2. **作者資料請確實填寫，入選證明將依照填寫於系統的內容製作。其他作者若需投稿證明，請務必詳細填寫於其他作者欄位，投稿截止後無法另行修改增加。**
3. **請務必勾選□共同作者均同意上傳，以符學術倫理。**
4. 投稿摘要**WORD檔名統一命名為abstract\_單位\_姓名\_投稿組別(1、2或3)**，上傳後由大會給予稿件投稿編號。
5. 入選稿件資料不全或未按規定格式投稿者審查後將予以退稿，請速於三日內修正回覆，逾期視同放棄投稿。
6. 投稿內容應為入學後之研究成果，相關稿件之題目與摘要不應與已接受或發表之期刊內容相同。
7. 若經發現有**違反學術倫理情事**，**將提報懲處**，**責任作者並負連帶責任**。

□同意( □ 不同意)入選大會口頭報告。

**Unveiling the role of NEDD8 upregulation in promoting metastasis and malignancy in BRAF-mutated melanoma**

李宗儒1,2,3\*、林源峰1,4 #

1臺北醫學大學臨床醫學研究所，2臺北醫學大學醫學系皮膚學科，3臺北醫學大學附設醫院皮膚科，4萬芳醫院細胞生理與分子影像研究中心

Background: Melanoma, the most lethal form of skin cancer, exhibits a dismal five-year survival rate of only 22.5% in advanced stages, highlighting the urgent need for innovative therapeutic approaches. Despite recent progress in targeted therapies and immune checkpoint inhibitors (ICIs), challenges such as severe side effects, poor long-term survival rates, and drug resistance persist. This study focuses on NEDD8-mediated neddylation, a crucial post-translational modification in cancer progression, as a potential target for the development of novel anti-melanoma drugs or adjunctive therapies.

Methods: Utilizing The Cancer Genome Atlas (TCGA) cohorts and the GSE30531 dataset, we investigated the transcriptional levels and prognostic significance of neuronal precursor cell-expressed developmentally downregulated protein 8 (NEDD8) in melanoma. Computational simulations via Gene Set Enrichment Analysis (GSEA) assessed the impact of enhanced NEDD8-mediated protein neddylation on melanoma evolution, particularly in cells harboring the BRAF V600E mutation, following treatment of MLN4924, a small molecule of NEDD8-activating enzyme inhibitor. In vitro migration assays and cycloheximide chase assays were employed to examine the consequences of MLN4924 treatment and NEDD8 gene knockdown on cell migration and the protein degradation of TGFBR2, respectively. Additionally, the association of NEDD8 gene expression with the efficacy of ICIs, including anti-PD-1 antibodies, anti-PD-L1 antibodies, and anti-CTL4 antibody, was explored using the Kaplan-Meier Plotter database.

Results: Analysis of TCGA data and cellular experiments revealed that upregulation of NEDD8 is associated with poor prognosis in melanoma, accompanied by the infiltration of myeloid-derived suppressive cells in the tumor microenvironment. Elevated endogenous NEDD8 levels were also correlated with increased migratory capabilities of cancer cells. GSEA suggested that MLN4924 disrupts epithelial-mesenchymal transition, TGF-β signaling, and NF-κB transcription factor activity, influencing transcription factor YBX1 and processes related to cancer proliferation, migration, and invasion. The study explored the impact of NEDD8 expression on existing targeted therapies and immunotherapies, indicating that high NEDD8 expression diminishes the effectiveness of ICIs. Upregulated NEDD8 activated the TGF-β signaling pathway, contributing to a tumor state conducive to metastasis and ICI resistance. Targeting protein neddylation by MLN4924 or repressing NEDD8 transcription showed potential in suppressing the metastatic potentials of melanoma cells with BRAF V600E mutation, possibly through blocking epithelial-mesenchymal transition progression, TGF-β signaling pathway, and NF-κB transcription factor activity.

Conclusions: NEDD8 overexpression impacts specific canonical or non-canonical neddylation substrates, presenting itself as a valuable predictive biomarker and drug target in melanoma. Inhibiting the neddylation pathway, especially non-canonical neddylation (targeting c-CBL [E3]), is anticipated to reduce metastatic capabilities in BRAF mutant melanoma and enhance responsiveness to ICIs, addressing the current bottleneck of poor long-term survival rates. This study provides insights into potential therapeutic strategies for improving melanoma outcomes.