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# Plasma soluble CD147 levels in sepsis: the association with disease severity and the prediction for clinical outcome

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To the editor,

CD147, also known as extracellular matrix metalloproteinase inducer (EMMPRIN) or Basigin, is mainly expressed on activated immune cells, such as T cells, monocytes and neutrophils, and it exists in both membrane-bound and soluble isoforms [1]. The soluble isoform, sCD147, which is generated via proteolytic cleavage of the membrane-bound form, has been shown to induce matrix metalloproteinase (MMPs) exacerbating inflammatory responses [2]. Elevated sCD147 levels are linked to disease progression and worse survival in hepatocellular carcinoma, multiple myeloma and breast cancer [3–5]. However, the role of plasma sCD147 in sepsis, particularly its association with disease severity and prognostic potential, remains unclear.

Available frozen plasma samples were obtained from 268 individuals, with 245 samples from the First Hospital of China Medical University and 23 samples from the First Affiliated Hospital of Zhejiang University School of Medicine. These individuals included 165 septic patients admitted to the intensive care unit (ICU), 55 non-septic ICU controls, and 48 healthy donors. All blood samples were collected within 24 h of the patients' admission to the ICU. Plasma levels of soluble CD147 (sCD147) were determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit. Clinical and demographic characteristics are summarized in Table S1. In our non-sepsis control cohort, the proportion of tumor patients was high, which is not consistent with other control cohorts; however, there is no significant difference of sCD147 level between tumor and non-tumor patients (Fig. S2A). Similarly, abdominal infection predominated in our sepsis cohort, in contrast to most studies where pulmonary infection is more common, we didn't find any difference of sCD147 levels between septic patients with abdominal infection and those with pulmonary infection (Fig. S2B). Plasma sCD147 levels in septic patients were significantly higher at ICU admission (834.80 [IQR: 548.20–1210.00] pg/mL) than in non-septic ICU controls (319.50 [111.50-551.10] pg/mL; $P < 0.001$) and healthy donors (undetectable [the detectable level < 31.25 pg/mL]; $P < 0.001$) (Fig. 1A). Receiver operating characteristic (ROC) curve analysis revealed discriminatory capacity, with sCD147 achieving an

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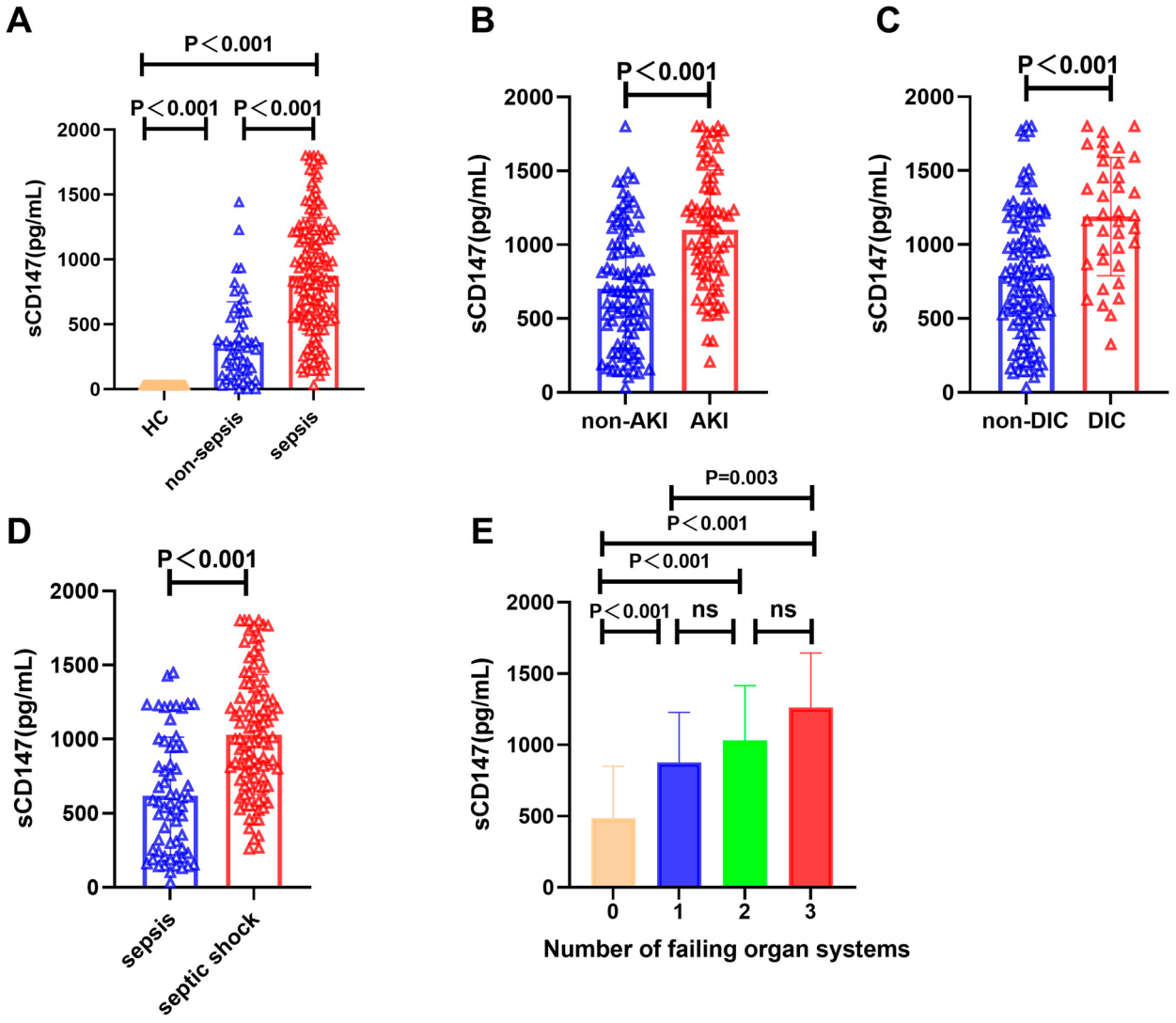


**Fig. 1** Comparison of plasma sCD147 levels across clinical groups in Sepsis (**A**) Comparison of the levels of plasma sCD147 among healthy controls (HC, $n=48$), non-septic ICU patients ($n=55$), and septic ICU patients ($n=165$) at admission. Group comparisons were analyzed using the Kruskal-Wallis test ($P<0.001$). Pairwise comparisons were performed with the Mann-Whitney U test, and the significance level was adjusted using the False discovery rate (FDR) analysis across the healthy, non-septic ICU controls and sepsis groups. (**B**-**D**) Comparison of sCD147 levels between patients with AKI ($n=72$), DIC ($n=37$), and septic shock ($n=103$), and those without AKI ($n=93$), DIC ($n=128$) and septic shock ($n=62$). Groups were compared by Mann-Whitney U test. (**E**) Comparison of the levels of plasma sCD147 among septic patients with different numbers of failing organ systems. Groups were compared by the Kruskal–Wallis test

area under the curve (AUC) of 1.000 ($P<0.001$) for distinguishing septic patients from healthy donors, and maintained favorable diagnostic accuracy (AUC = 0.830 [0.766–0.888], $P<0.001$) when differentiating sepsis from non-septic ICU cases, with sensitivity of 70.91% and specificity of 84.24% (Fig. S1). Moreover, sCD147 levels were elevated in patients developing acute kidney injury (AKI) compared to those without septic AKI (1097.50 [806.63-1384.25] vs. 675.60 [361.50–1002.00] pg/mL, $P<0.001$) (Fig. 1B). Septic patients who disseminated intravascular coagulation (DIC) exhibited elevated sCD147 levels compared to those without DIC (1196.00 [881.80–1558.00] vs. 786.65 [484.03-1118.75] pg/mL, $P<0.001$) (Fig. 1C), and septic patients with septic shock exhibited higher sCD147 levels than those without shock (1001.00 [724.30–1290.00] vs. 570.90 [239.03-946.85] pg/mL, $P<0.001$) (Fig. 1D). sCD147 levels also increased with the number of failing organ systems (Fig. 1E). In addition, significant positive correlations were observed between sCD147 and SOFA scores ($r=0.359$; $P<0.001$; Fig. 2A), as well as with key inflammatory mediators: procalcitonin (PCT: $r=0.266$; $P=0.001$), interleukin-6 (IL-6: $r=0.200$; $P=0.015$), and IL-10 ($r=0.335$; $P<0.001$) (Fig. 2B). Further, sCD147 levels were correlated with markers of organ injury, including renal impairment (creatinine: $r=0.494$, $P<0.001$; urea: $r=0.524$, $P<0.001$)

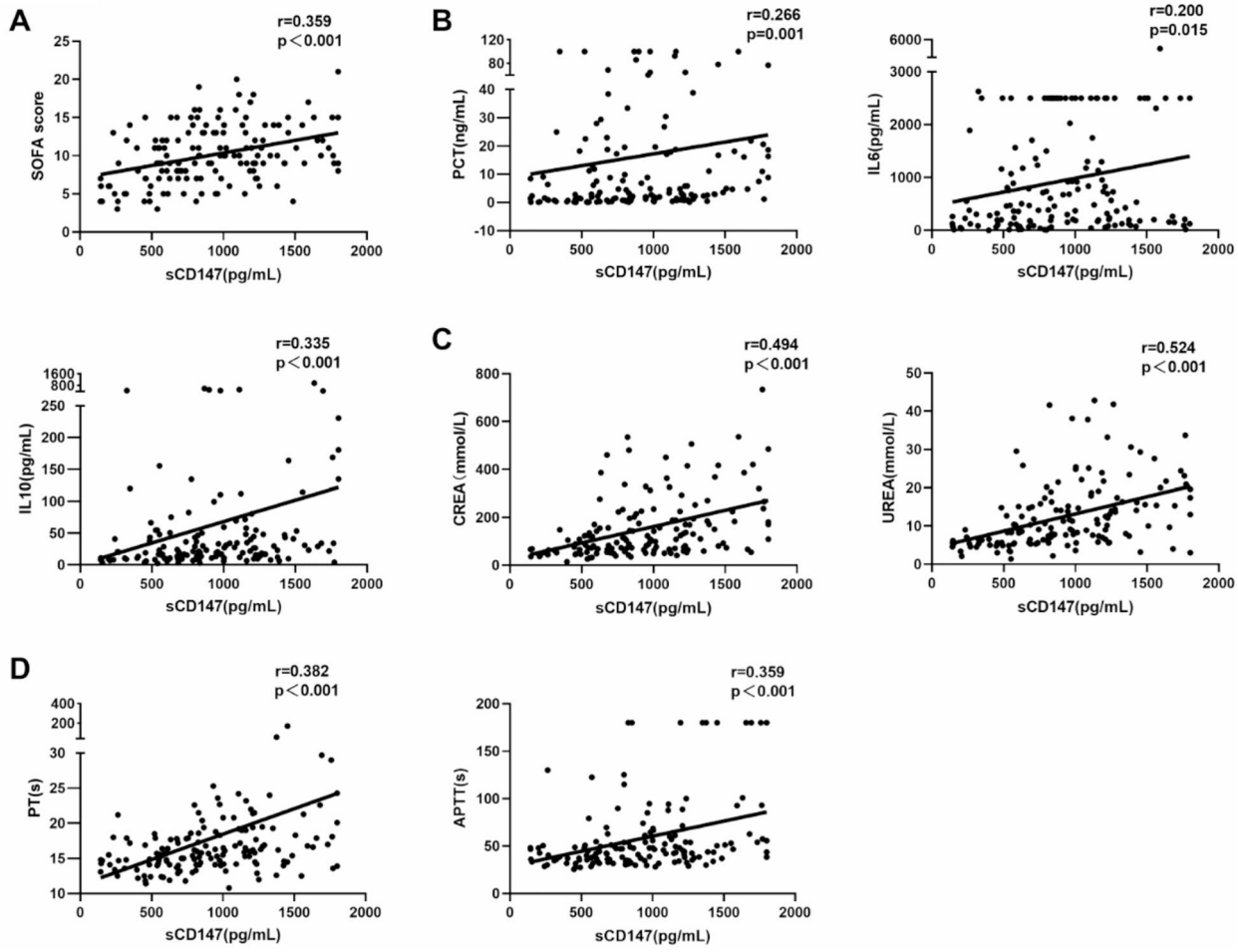


**Fig. 2** sCD147 was associated with disease severity (**A**) Correlation of plasma sCD147 with SOFA scores ($n = 149$). (**B**) Correlations of plasma sCD147 with procalcitonin (PCT, $n = 149$), interleukin-6 (IL-6, $n = 149$) and interleukin-10 (IL-10, $n = 149$). (**C**) Correlations of plasma sCD147 with Creatinine (Crea, $n = 149$), Urea ($n = 149$). (**D**) Correlations of plasma sCD147 with prothrombin time (PT, $n = 149$), activated partial thromboplastin time (APTT, $n = 149$). Bivariate correlations were assessed via Spearman's rank correlation analysis. FDR analysis was used to correct for multiple testing in the correlation analyses, and the adjusted p-values for all panels remained statistically significant. *Values exceeding the assay detection limit were assigned the upper limit value

and coagulation dysfunction (prothrombin time [PT]: $r = 0.382$, $P < 0.001$; activated partial thromboplastin time [APTT]: $r = 0.359$, $P < 0.001$) (Fig. 2C and D). These findings suggest that sCD147 levels are associated with inflammatory markers and disease severity in sepsis.

Notably, sCD147 demonstrated predictive ability for mortality. Non-survivors exhibited significantly higher sCD147 levels at ICU admission than survivors (1157.50 [833.00-1461.25] vs. 684.85 [399.13-1004.50] pg/mL; $P < 0.001$; Fig. 3A). Among nine significant univariate predictors, multivariable logistic regression (with no collinearity) identified sCD147 as an independent predictor of mortality (odds ratio [OR] = 1.216, 95%CI [1.085–1.363]; $P = 0.001$) (Table S2). Comparative ROC analysis revealed higher predictive accuracy of sCD147 over SOFA scores (AUC 0.770 [0.701–0.845] vs. 0.710 [0.628–0.790]; Fig. 3B). The optimal cut-off of sCD147 was 805.20 pg/mL. Integration of both parameters further improved prognostic performance with sensitivity of 79.63% and specificity of 64.81% (AUC = 0.790 [0.718–0.859]; Fig. 3B). Septic patients with high sCD147 levels (> 805.20 pg/mL) had significantly lower 30-day survival than those with low levels (< 805.20 pg/mL) (high-risk: 56.64% vs. low-risk: 43.36%; HR = 3.532, 95% CI [1.936–6.444]; $P < 0.001$). This prognostic stratification persisted at 90 days (57.04% vs. 42.96%; HR = 3.466; 95% CI [1.990–6.037]; $P < 0.001$), as demonstrated in Fig. 3C and D. Furthermore, internal validation using 10-fold cross-validation revealed that sCD147 exhibited a reliable AUC of 0.772 (95% CI: 0.769–0.774) for mortality prediction (Fig. 3E). These results suggest that sCD147 is a prognostic biomarker for sepsis-related mortality.

Our findings demonstrate that plasma sCD147 levels are associated with sepsis severity and may predict clinical outcome. Infection-related stimuli (such as LPS and poly: IC) can upregulate the expression and activity of

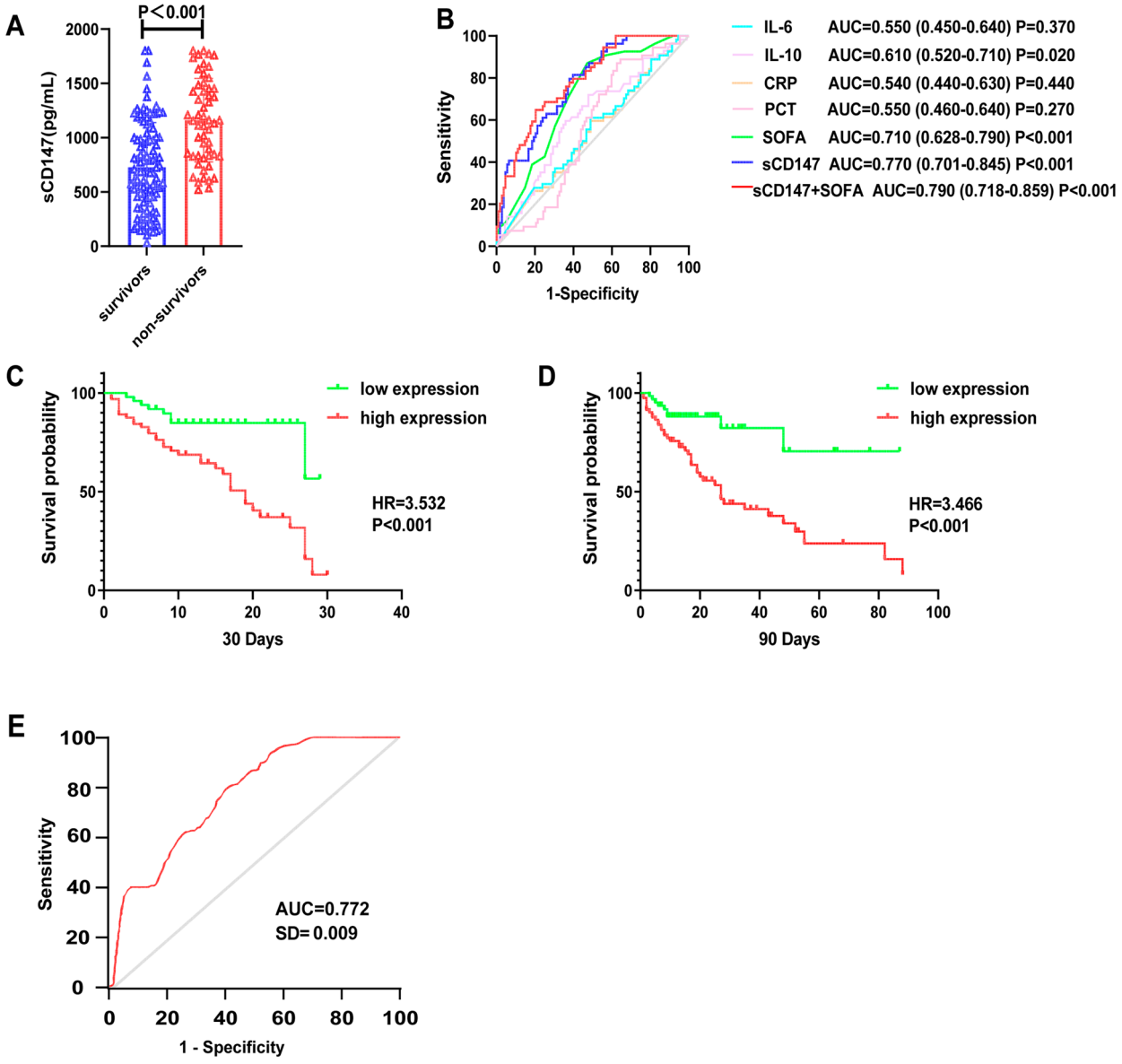


**Fig. 3** Predictive value of plasma sCD147 for sepsis mortality. (**A**) Comparison of the levels of plasma sCD147 between survivors ($n=108$) and non-survivors ($n=54$). Groups were compared by Mann-Whitney U test. $P<0.001$. (**B**) Efficacy in predicting mortality. Comparison of the area under the ROC curve of sCD147 and SOFA scores and other current biomarkers (IL-6、IL-10、CRP、PCT). (**C**) Kaplan-Meier survival curves stratified by sCD147 cut-off (805.20 pg/mL) for 30-day mortality and 90-day mortality(**D**). (**E**) Mean ROC curve of sCD147 for predicting mortality using 10-fold cross-validation

matrix metalloproteinases (MMPs). The activated MMPs further cleave membrane-bound CD147 to generate soluble CD147 (sCD147). Subsequently, sCD147 binds to its membrane-bound counterpart, thereby triggering immune cells to secrete cytokines. This process establishes a positive feedback loop that drives cytokine storm. This cascade may contribute to microcirculatory impairment and organ failure, ultimately leading to adverse outcomes. Moreover, as an easily measurable secretory protein, sCD147 will draw attention as a promising biomarker and potential therapeutic target in future sepsis research and therapeutic development.

There are several limitations in our findings. First, our non-sepsis control cohort with high proportion of tumor patients is discordant with other control cohorts, although we didn't find any significant difference of sCD147 levels between tumor and non-tumor patients. Second, the distribution of anatomical sites of infection in our cohort dominant with abdominal infection is discordant with most sepsis cohorts dominant with pulmonary infection, although we didn't find any significant difference of sCD147 levels between abdominal and pulmonary sepsis. These two points might limit the generalizability of our findings. Third, because of relatively

small cohort recruited from a single country, further validation in large cohorts and in other countries is urgently needed.

**Abbreviations**

| | |
|---|---|
| sCD147 | Soluble CD147 |
| EMMPRIN | Extracellular matrix metalloproteinase inducer |
| MMPs | Matrix metalloproteinases |
| ICU | Intensive care unit |
| ROC | Receiver operating characteristic |
| AUC | Area under the curve |
| AKI | Acute kidney injury |
| DIC | Disseminated intravascular coagulation |
| OR | Odds ratio |
| SOFA | Sequential organ failure assessment |

## Supplementary Information

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Supplementary Material 1.

**Author contributions**

JC: Writing – original draft, Methodology, Investigation, Data curation. HZ: Writing – design, review & editing, Funding acquisition. YS, YC and ST: data curation, sample collection. YX: validation. XY, PW, ZZ: formal analysis, sample collection. YF: Funding acquisition, review. QH: methodology. YJ and HS: design, review, Supervision, Funding acquisition. All authors read and approved the final manuscript.

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**Data availability**

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate**

The work was supervised by the Research and Ethics Committee of the First Hospital of China Medical University. Not applicable.

**Competing interests**

The authors declare no competing interests.

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**References**

1. Yang XM, Bian H, Chen ZN. CD147/Basigin: From Integrative Molecular Hub to Translational Therapeutic Target. Adv Sci (Weinh). 2026;13(8):e18884.
2. Albrechtsen R, Wewer Albrechtsen NJ, Gnosa S et al. Identification of ADAM12 as a novel basigin sheddase[J]. Int J Mol Sci, 2019, 20(8): 1957.
3. Lee A, Rode A, Nicoll A, et al. Circulating CD147 predicts mortality in advanced hepatocellular carcinoma[J]. J Gastroenterol Hepatol. 2016;31(2):459–66.
4. Łacina P, Butrym A, Frontkiewicz D, et al. Soluble CD147 (BSG) as a prognostic marker in multiple myeloma[J]. Curr Issues Mol Biol. 2022;44(1):350–9.
5. Kuang YH, Liu YJ, Tang LL, et al. Plasma soluble cluster of differentiation 147 levels are increased in breast cancer patients and associated with lymph node metastasis and chemoresistance[J]. Hong Kong Med J. 2018;24(3):252–60.

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