Journal of Clinical Personalized Medicine 临床个性化医学, 2026, 5(4), 478-485
Published Online August 2026 in Hans. https://www.hanspub.org/journal/jcpm
https://doi.org/10.12677/jcpm.2026.54273

SII与PNI对PD-L1阳性胃癌术后复发的预测价值

邹凯迪[1*]，李小宝[1]，毋宇哲[1]，崔登铜[1]，张灏瑜[1]，袁江涛[2#]

[1]延安大学延安医学院，陕西 延安
[2]延安大学附属医院胃肠疝外科，陕西 延安

收稿日期：2026年7月18日；录用日期：2026年8月11日；发布日期：2026年8月24日

摘　要

胃癌仍是预后较差的消化道恶性肿瘤，尽管免疫检查点抑制剂(ICI)的应用为部分患者带来生存获益，但根治术后复发转移风险居高不下，单一PD-L1阳性状态难以满足精准分层需求。近年来，外周血来源的系统性免疫炎症指数(SII)与预后营养指数(PNI)因简便易得而受到关注，分别从炎症负荷与营养－免疫储备维度反映宿主抗肿瘤能力。本综述系统梳理SII与PNI的生物学基础、其在胃癌根治术后复发转移中的预测证据，并聚焦于PD-L1阳性亚组中的适用性，进一步探讨炎症－营养轴通过塑造免疫抑制微环境影响微小残留病灶持续存在的潜在机制。现有证据表明，SII升高与PNI降低均为胃癌术后不良预后的独立危险因素，且在接受ICI治疗的患者中亦具显著判别效能。二者可作为补充PD-L1单一标志物不足的有效工具，为术后个体化辅助治疗与随访策略优化提供新思路。然而，截断值不统一、回顾性研究居多及缺乏直接针对PD-L1阳性术后人群的前瞻性验证仍是当前主要局限，未来需进一步开展多中心研究以推动临床转化。

关键词

胃癌，根治性切除术，系统性免疫炎症指数，预后营养指数，程序性死亡配体1，复发转移

The Predictive Value of SII and PNI for Postoperative Recurrence in PD-L1-Positive Gastric Cancer

Kaidi Zou[1*], Xiaobao Li[1], Yuzhe Wu[1], Dengtong Cui[1], Haoyu Zhang[1], Jiangtao Yuan[2#]

[1]Yan'an Medical College of Yan'an University, Yan'an Shaanxi
[2]Department of Gastrointestinal Hernia Surgery, Affiliated Hospital of Yan'an University, Yan'an Shaanxi

[*]第一作者。
[#]通讯作者。

文章引用: 邹凯迪, 李小宝, 毋宇哲, 崔登铜, 张灏瑜, 袁江涛. SII 与 PNI 对 PD-L1 阳性胃癌术后复发的预测价值[J]. 临床个性化医学, 2026, 5(4): 478-485. DOI: 10.12677/jcpm.2026.54273

Received: July 18, 2026; accepted: August 11, 2026; published: August 24, 2026

Abstract

Gastric cancer remains a digestive tract malignancy with a poor prognosis. Although the application of immune checkpoint inhibitors (ICIs) has brought survival benefits to some patients, the risk of recurrence and metastasis after radical resection remains persistently high, and PD-L1 positivity alone is insufficient to meet the needs of precise risk stratification. SII and PNI are easy to get from routine blood tests. SII tells us about inflammation, and PNI reflects nutrition and immune status. Both are thought to reflect the patient's ability to fight cancer. In this review, we look at their biological background and their role in predicting recurrence after gastric cancer surgery. We pay special attention to PD-L1-positive patients. We also explore how inflammation and nutrition work together to create an immunosuppressive environment, which may help keep residual tumor cells alive. According to current data, high SII and low PNI are both linked to worse outcomes after surgery. They also work well in patients on immunotherapy. So these markers might be useful add-ons to PD-L1 testing, giving us more information for treatment and follow-up decisions. But there are still problems. Cutoff values vary across studies. Most evidence comes from retrospective data. And we lack prospective studies focusing on PD-L1-positive patients after surgery. More multicenter research is needed before we can use them in routine practice.

Keywords

Gastric Cancer, Radical Resection, Systemic Immune-Inflammation Index (SII), Prognostic Nutritional Index (PNI), PD-L1, Recurrence and Metastasis

1. 引言

胃癌作为全球癌症相关死亡的主要原因之一，其治疗策略近年来因免疫检查点抑制剂(ICI)的应用而发生显著变革。程序性死亡配体 1 (PD-L1)阳性状态被视为预测 PD-1/PD-L1 抑制剂疗效的重要生物标志物之一，然而临床实践中 PD-L1 阳性胃癌患者仍表现出显著的预后异质性[1] [2]。部分 PD-L1 高表达患者对免疫治疗反应不佳，而部分低表达者却可获益，提示单一 PD-L1 表达水平难以全面反映肿瘤免疫微环境的复杂动态[3] [4]。目前常用的预后分层工具如 TNM 分期、Lauren 分型或 Ki-67 指数虽具一定参考价值，但在精准识别术后复发转移高风险人群方面仍显不足[3]。尤其在根治性手术后，如何早期甄别具有高复发潜能的 PD-L1 阳性患者，仍是临床亟待解决的关键问题。

1.1. PD-L1 阳性胃癌的临床异质性与现有预后分层工具的不足

PD-L1 在胃癌中的表达受多种因素调控，既包括肿瘤细胞固有的基因组特征(如 EB 病毒阳性、微卫星不稳定性高)，也受到微环境中炎症因子(如 IFN-γ、IL-6)的诱导作用[4] [5]。这种二元来源导致 PD-L1 表达状态与实际免疫应答能力之间存在脱节。例如，炎症驱动的 PD-L1 上调可能伴随免疫抑制性细胞浸润，反而削弱抗肿瘤免疫效应[6]。此外，PD-L1 联合阳性评分(CPS)在活检与术后标本间存在显著差异，进一步限制其作为稳定预后指标的可靠性[3]。尽管 AJCC 分期系统和分子分型(如 TCGA 分类)在整体预

后评估中具有一定价值，但其对个体化复发风险预测的敏感性与特异性仍有限[7]。因此，亟需整合反映宿主系统状态的动态生物标志物，以弥补现有分层体系在预测术后复发转移方面的不足。

1.2. 系统性炎症负荷与营养–免疫储备状态在肿瘤进展中的独立作用路径

系统性炎症不仅促进肿瘤血管生成、侵袭及转移，还可通过重塑免疫微环境诱导 T 细胞耗竭与髓系来源抑制细胞(MDSCs)扩增，从而削弱抗肿瘤免疫应答[5] [8]。与此同时，营养不良与免疫功能障碍在胃癌患者中高度共存，表现为低白蛋白、淋巴细胞减少及肌肉消耗，这些改变不仅影响治疗耐受性，更直接参与免疫监视失效[9] [10]。研究表明，炎症与营养状态并非孤立因素，而是通过“炎症–营养轴”相互耦合：慢性炎症加速蛋白质分解与肌肉流失，而营养储备下降又进一步削弱免疫细胞功能，形成恶性循环[8] [9]。这种双重打击机制在术后恢复期尤为突出，可能为微小残留病灶(MRD)提供免疫逃逸温床，进而驱动复发转移[11] [12]。

1.3. SII (系统性免疫炎症指数)与 PNI (预后营养指数)作为可及性血源性指标的研究基础

系统性免疫炎症指数(SII)基于外周血中性粒细胞、淋巴细胞和血小板计数计算，综合反映促炎与抗炎平衡状态，在多种实体瘤中被证实与不良预后相关[13]-[15]。预后营养指数(PNI)则由血清白蛋白与淋巴细胞计数构成，兼具营养状况与细胞免疫功能的双重信息[16] [17]。多项研究显示，低 PNI 与接受 ICI 治疗的胃癌患者较差的总生存期(HR: 0.530)和无进展生存期(HR: 0.740)显著相关[17]，而高 SII 则独立预测局部进展期胃癌患者在接受新辅助免疫治疗后复发风险增加超过三倍(HR = 3.45) [13]。这些指标仅需常规术前血液检测即可获取，具有成本低、可重复性强、易于临床推广的优势，为基于炎症–营养轴的 PD-L1 阳性胃癌术后复发风险分层提供了可行路径。值得强调的是，尽管 SII 与 PNI 的预测价值已在胃癌总体人群中得到验证，但在 PD-L1 阳性亚组中，系统性炎症与营养不良往往协同加剧免疫抑制微环境，因此二者或可作为 PD-L1 单一评分的有效补充，进一步提升术后复发风险的识别精度。

2. SII 的生物学内涵及其在胃癌中的独立预测价值

系统性免疫炎症指数(Systemic Immune-Inflammation Index, SII)是一种基于外周血中性粒细胞、淋巴细胞和血小板计数计算得出的综合性炎症指标，其公式为 SII = (中性粒细胞 × 血小板)/淋巴细胞。SII 整合机体的促炎与抗炎，从而反映肿瘤相关系统性炎症负荷和免疫监视能力的关联。其中，在肿瘤微环境中，中性粒细胞和血小板可促进血管生成、基质重塑以及免疫抑制，淋巴细胞则能代表宿主抗肿瘤免疫应答情况。因而 SII 升高通常代表促炎状态增强、免疫功能受损[18]。

2.1. SII 的构成与生物学意义

SII 包含外周血的中性粒细胞、淋巴细胞和血小板。中性粒细胞参与急性炎症反应，也能通过分泌多种细胞因子(如 IL-6、TNF-α)促进肿瘤细胞增殖与转移；血小板释放生长因子促进肿瘤细胞远处播散；淋巴细胞数量减少，细胞毒性 T 细胞对肿瘤的清除能力就会下降。三者共同作用下，高 SII 值反映出一种有利于肿瘤逃逸和复发的全身性免疫抑制环境。此外，SII 已被证实与癌症恶病质显著相关，在恶病质患者中水平明显升高，进一步佐证其作为系统性炎症与代谢紊乱耦合指标的生物学合理性[8]。

2.2. SII 在胃癌根治术后复发转移中的预测证据

多项临床研究已验证 SII 在胃癌术后复发风险评估中的独立预测价值。一项针对接受新辅助化疗联合免疫治疗的进展期胃癌患者的研究显示，高 SII (截断值 52.1)与非完全缓解(残余肿瘤 > 50%)、术后并发症增加及总生存率显著降低密切相关(47.6% vs 87.6%, $P < 0.001$)，且是总生存期的独立危险因素(C-

index = 0.82) [19]。另一项纳入 326 例接受新辅助化疗的进展期胃癌患者的回顾性分析发现，术前 SII < 507.45 是获得良好病理反应的独立预测因子，低 SII 组患者生存率显著更高(P < 0.001) [15]。此外，在微卫星稳定(pMMR)胃癌患者中，较低的 SII 亦与更优的无病生存期(DFS)和总生存期(OS)相关，提示其在不同分子亚型中均具预后判别能力[20]。这些证据共同支持 SII 作为胃癌根治术后复发转移的有效预测工具。

3. PNI 的生物学内涵及其在胃癌中的独立预测价值

3.1. PNI 的构成与生物学意义

预后营养指数(Prognostic Nutritional Index, PNI)是一种基于血清白蛋白水平和外周血淋巴细胞计数计算得出的复合指标，其公式为 PNI = 10 × 血清白蛋白(g/dL) + 0.005 × 淋巴细胞总数(/mm^3)。该指标不仅反映机体的营养储备状态，还整合了免疫功能的动态信息，体现了营养–免疫耦合轴的核心特征。血清白蛋白作为肝脏合成的负急性期蛋白，在系统性炎症状态下显著下降，而淋巴细胞计数则直接关联机体细胞免疫应答能力。因此，PNI 本质上是营养状况与免疫功能协同作用的量化表征，在肿瘤微环境中具有独特的生物学解释力。多项研究表明，低 PNI 值往往提示慢性炎症激活、蛋白质能量消耗及免疫监视功能受损，这些病理生理过程共同促进肿瘤进展与治疗抵抗[17] [21]。

3.2. PNI 在胃癌根治术后复发转移中的预测证据

近年来，大量临床研究证实术前低 PNI 与胃癌根治术后不良预后密切相关。一项荟萃分析显示，在接受免疫检查点抑制剂治疗的胃癌或胃食管结合部癌患者中，低 PNI 显著关联较差的总生存期(OS)和无进展生存期(PFS) [16]。另一项纳入 2883 例消化道肿瘤患者的系统评价进一步指出，高 PNI 水平与更长的 OS (HR: 0.530, 95% CI: 0.456~0.616)和 PFS (HR: 0.740, 95% CI: 0.649~0.844)显著相关，且在胃癌亚组中结果一致[17]。此外，PNI ≤ 45 被证实与化疗相关血液学毒性风险增加相关[22]，而术前低 PNI 亦与更低的规范手术完成率及更高的 90 天死亡率相关[11]。值得注意的是，在局部进展期胃癌患者中，PNI > 48.48 是新辅助化疗后获得良好病理反应的独立预测因子，且高 PNI 患者生存率显著更优(P < 0.001) [15]。IINTM 预后评分模型整合 PNI 后，对胃癌术后复发及恶病质的预测 AUC 达 0.858，凸显其在复发风险识别中的实用价值[23]。

4. PD-L1 阳性胃癌的免疫微环境特征与复发转移基础

PD-L1 在胃癌中的表达具有显著的异质性，其来源可分为肿瘤细胞固有性表达与炎症诱导性表达两大路径。固有性表达常由基因扩增、表观遗传调控或信号通路异常(如 CTCF-PD-L1 轴)驱动[24]，而炎症诱导性表达则主要受微环境中细胞因子调控，尤其是 IFN-γ 和 IL-6 等促炎因子可显著上调 PD-L1 表达[4]。例如，迷走神经释放乙酰胆碱通过激活 ILC3 细胞分泌 IL-22，进而触发未折叠蛋白反应并上调 PD-L1 [25]；此外，METTL3 通过 m6A 修饰调控 PD-L1 mRNA 稳定性，也构成外源性调控机制之一[26]。这种二元表达模式不仅决定了 PD-L1 的空间分布异质性[3]，也影响了免疫治疗的响应差异。

4.1. PD-L1 表达的二元来源：肿瘤细胞固有性表达 vs 炎症诱导性表达(IFN-γ、IL-6 通路)

PD-L1 的固有性表达多源于肿瘤细胞内在的遗传或表观遗传改变，如 CDK5 高表达可促进 PD-L1 转录[27]，而 IKZF4/NONO-RAB11FIP3 轴则通过增强 PD-L1 内体循环稳定其膜表面表达[28]。相比之下，炎症诱导性表达依赖于肿瘤微环境中的免疫信号，特别是 IFN-γ 可通过 JAK/STAT 通路强烈诱导 PD-L1 表达，并进一步促进外泌体 PD-L1 (exoPD-L1)的释放，形成系统性免疫抑制[29]。IL-6 亦可通过 STAT3

激活参与 PD-L1 上调[25]。这两种机制常共存于同一肿瘤中，导致 PD-L1 表达呈现时空动态变化，增加了免疫治疗预测的复杂性[30]。

4.2. 肿瘤浸润免疫细胞(TILs)组成及其与 PD-L1 阳性状态的关联格局

PD-L1 阳性胃癌通常伴随特定的肿瘤浸润免疫细胞(TILs)谱型。多重免疫组化分析显示，PD-L1 高表达区域常富集 CD8+ T 细胞、FoxP3+调节性 T 细胞(Tregs)及 M2 型肿瘤相关巨噬细胞(TAMs) [31] [32]。尽管 CD8+ T 细胞浸润增加，但其常呈耗竭表型，表现为 PD-1、TIM-3、CTLA-4 共表达升高及颗粒酶 B 分泌减少[33] [34]。同时，三级淋巴结构(TLSs)的存在与 PD-L1 阳性状态及良好预后相关，提示局部免疫组织化程度影响抗肿瘤免疫效能[35]。值得注意的是，部分研究发现高 CD8+ T 细胞浸润反而与不良预后相关，可能与其功能失活及伴随的髓系抑制细胞浸润增强有关[36]。

4.3. 术后免疫抑制微环境的形成：髓系细胞募集、CD8+ T 细胞功能耗竭

根治术后，残余病灶或微转移灶所处的免疫微环境迅速转向抑制状态。髓系来源抑制细胞(MDSCs)和 M2 型 TAMs 被大量募集，通过分泌 IL-10、TGF-β 及精氨酸酶等抑制因子，直接削弱 CD8+ T 细胞的增殖与细胞毒性[32] [37]。同时，慢性抗原刺激和代谢压力(如乳酸积累)进一步加剧 T 细胞耗竭[38]。单细胞测序揭示，术后复发患者肿瘤中 CD8+PD-1+ T 细胞虽存在，但其克隆多样性下降且效应功能受损[36]。此外，LAG3+ TAMs 通过 CXCL8/CXCR2 轴与肿瘤细胞形成正反馈环路，持续强化免疫抑制[39]。

4.4. 免疫抑制生态位与术后微小残留病灶(MRD)持续存在的关联

免疫抑制性生态位为微小残留病灶(MRD)提供了“庇护所”，使其逃避免疫监视并最终导致复发转移。该生态位特征包括高基质评分、低免疫评分、CAFs 活化及缺氧环境[40]。胃癌干细胞(GCSCs)在此环境中通过与 TAMs、Tregs 等互作维持干性并促进耐药[41]。循环肿瘤细胞(CTCs)动态升高可早于影像学复发近 285 天，提示 MRD 已建立并活跃[42]。此外，外泌体 PD-L1 可系统性抑制外周 T 细胞功能，为远处转移灶的定植创造有利条件[29] [43]。因此，术后免疫微环境的持续抑制状态是 MRD 存活与进展的关键生物学基础。

5. 总结与展望

本文通过系统探讨 SII 与 PNI 在 PD-L1 阳性胃癌根治术后复发转移中的独立预测价值，从而揭示炎症–营养轴与免疫微环境之间的潜在交互机制。SII 和 PNI 分别反映系统性炎症负荷与营养–免疫储备状态，在胃癌术后预后评估中同样具有判别能力。因此，SII 与 PNI 能够补充 PD-L1 阳性胃癌患者的预后指标。

5.1. 临床应用潜力

SII 与 PNI 作为基于常规血检计算的无创、低成本、易获取的指标，具备极强的临床可推广性。在 PD-L1 阳性胃癌这一异质性群体中，二者可有效识别出术后高复发风险亚群，从而指导个体化辅助治疗决策。例如，对于 SII 升高且 PNI 降低的患者，即使 PD-L1 表达阳性，也可能因免疫抑制微环境和营养储备不足而对 ICI 反应不佳，此时应考虑强化营养支持、调控炎症状态或联合其他免疫调节策略。

5.2. 当前研究的主要局限

尽管 SII 与 PNI 展现出良好前景，但当前研究仍存在若干关键局限。首先，多数证据来源于回顾性队列或晚期/转移性胃癌人群[14] [15] [17]，专门针对 PD-L1 阳性、接受根治术后的胃癌患者的前瞻性数

据仍显不足。其次，PNI 和 SII 的截断值尚未统一，不同研究采用的阈值差异较大(如 PNI 截断值在 40~48.48 之间波动) [15] [17] [21]，其异质性源于人群特征(肿瘤分期、治疗方案)、统计方法(ROC 曲线确定)以及地域差异，以上因素导致临床阈值的选择缺乏共识，影响预后判断一致性与跨中心结果可比性[21]，因而亟需多中心、大样本的标准化验证。再者，现有研究多未充分校正混杂因素如肌肉减少症、体成分变化或合并感染等对炎症与营养指标的干扰[44]。此外，SII 与 PNI 虽反映全身状态，但未能直接刻画肿瘤局部免疫微环境的复杂性，如 CD8+ T 细胞耗竭、髓系抑制细胞浸润或 PD-L1 的动态调控机制(如受 IFN-γ、IL-6、m6A 修饰或 circRNA 影响) [25] [26] [28] [45]，因此需结合组织学或液体活检进行多维整合分析。

5.3. 结论与未来方向

综上所述，SII 与 PNI 作为炎症–营养轴的关键量化指标，在 PD-L1 阳性胃癌根治术后复发转移风险预测中具有独立且互补的价值。其临床意义不仅在于预后分层，更在于揭示了宿主系统状态对免疫微环境塑造及治疗反应的深远影响。未来研究应聚焦于：1) 开展前瞻性多中心研究，分别明确 SII 与 PNI 在 PD-L1 阳性胃癌术后人群中的最佳截断值及预测效能；2) 探索 SII/PNI 与肿瘤免疫图谱(如 GMAP 项目所构建的 65 种免疫细胞图谱)、可溶性 PD-L1 水平或神经–免疫代谢通路(如迷走神经-ACh-ILC3 轴)的关联机制；3) 评估基于 SII/PNI 风险分层指导的干预策略(如营养支持、抗炎治疗或仿禁食饮食联合免疫治疗)能否逆转免疫抑制生态位、清除 MRD 并改善长期生存。最终，推动“炎症–营养–免疫”三位一体的综合评估体系进入临床实践，为 PD-L1 阳性胃癌患者提供真正个体化的全程管理方案。

参考文献

[1] Nie, Y., Zhao, W., Lu, L. and Zhou, F. (2023) Predictive Biomarkers and New Developments of Immunotherapy in Gastric Cancer: A 2023 Update. *American Journal of Cancer Research*, **13**, 3169-3184.

[2] Sun, F., Gao, X., Wang, W., Zhao, X., Zhang, J. and Zhu, Y. (2025) Predictive Biomarkers in the Era of Immunotherapy for Gastric Cancer: Current Achievements and Future Perspectives. *Frontiers in Immunology*, **16**, Article ID: 1599908. https://doi.org/10.3389/fimmu.2025.1599908

[3] Chen, X., Zhang, H., Wang, M., Liu, H., Hu, Y., Lin, T., *et al*. (2022) Relationship between Programmed Death Ligand 1 Expression and Other Clinicopathological Features in a Large Cohort of Gastric Cancer Patients. *Frontiers in Immunology*, **13**, Article ID: 783695. https://doi.org/10.3389/fimmu.2022.783695

[4] Zhang, Y., Yang, Y., Chen, Y., Lin, W., Chen, X., Liu, J., *et al*. (2022) PD-L1: Biological Mechanism, Function, and Immunotherapy in Gastric Cancer. *Frontiers in Immunology*, **13**, Article ID: 1060497. https://doi.org/10.3389/fimmu.2022.1060497

[5] Nihira, N.T., Kudo, R. and Ohta, T. (2025) Inflammation and Tumor Immune Escape in Response to DNA Damage. *Seminars in Cancer Biology*, **110**, 36-45. https://doi.org/10.1016/j.semcancer.2025.02.005

[6] Kim, K.T., Lee, M.H., Shin, S., Cho, I., Kuk, J.C., Yun, J., *et al*. (2024) Decorin as a Key Marker of Desmoplastic Cancer-Associated Fibroblasts Mediating First-Line Immune Checkpoint Blockade Resistance in Metastatic Gastric Cancer. *Gastric Cancer*, **28**, 12-26. https://doi.org/10.1007/s10120-024-01567-6

[7] Wang, H., Wang, Z., Yue, B., Luo, X., Yang, Y., Chen, Y., *et al*. (2026) Development of a Prognostic Model Based on Nutritional and Inflammatory Indicators for Predicting Postoperative Survival in Esophageal Cancer: A Retrospective Study. *Frontiers in Immunology*, **17**, Article ID: 1701862. https://doi.org/10.3389/fimmu.2026.1701862

[8] Huang, Y., Zhang, J., Ge, Y., Wang, C., Wang, X. and Zuo, J. (2026) Association between Systemic Inflammation Biomarkers and Cancer Cachexia in Patients with Gastric Cancer: A Cross-Sectional Study. *Frontiers in Nutrition*, **13**, Article ID: 1737375. https://doi.org/10.3389/fnut.2026.1737375

[9] Wang, Z., Ma, L. and Mao, J. (2026) Precision Nutrition in Gastric Cancer: Current Advances and Future Directions. *Frontiers in Nutrition*, **13**, Article ID: 1844696. https://doi.org/10.3389/fnut.2026.1844696

[10] Kono, T., Kasahara, K., Tomisato, S. and Ozawa, H. (2026) Prognostic Impact of CT-Defined Sarcopenia and Prognostic Nutritional Index in Immune Checkpoint Inhibitor-Treated Head and Neck Squamous Cell Carcinoma: A Systematic Review and Meta-Analysis. *Critical Reviews in Oncology/Hematology*, **224**, Article ID: 105375. https://doi.org/10.1016/j.critrevonc.2026.105375

[11] Pelc, Z., Sędłak, K., Mlak, R., Endo, Y., Gockel, I., van Sandick, J., *et al*. (2025) Impact of Prognostic Nutritional Index

on Oncological Outcomes and Mortality among Advanced Gastric Cancer Patients: European GAS-TRODATA Registry Analysis. *International Journal of Cancer*, **157**, 1734-1745. https://doi.org/10.1002/ijc.35489

[12] Zhang, L.K., Shang-Guan, Z.X., Zheng, H.L., Zheng, H.H., Zheng, C.Y., Chen, W.F. and Xie, J.W. (2026) Association of Comprehensive Inflammatory-Metabolic Status and Perioperative Outcomes in Gastric Cancer: Insights from Four Randomized Controlled Trials. *ESMO Open*, **11**, Article ID: 106922. https://doi.org/10.1016/j.esmoop.2026.106922

[13] Li, F., Guo, H., Wu, H., Wu, J., Ma, S., Yang, Y., *et al*. (2026) An Integrated SII-PNI Immune-Nutritional Scoring System Predicts Efficacy and Immune-Related Adverse Events in Locally Advanced Gastric Cancer Patients Undergoing Neoadjuvant Immunotherapy. *Frontiers in Immunology*, **17**, Article ID: 1806537. https://doi.org/10.3389/fimmu.2026.1806537

[14] He, M., Chen, Z.F., Zhang, L., Gao, X., Chong, X., Li, H., *et al*. (2023) Associations of Subcutaneous Fat Area and Systemic Immune-Inflammation Index with Survival in Patients with Advanced Gastric Cancer Receiving Dual PD-1 and HER2 Blockade. *Journal for ImmunoTherapy of Cancer*, **11**, e007054. https://doi.org/10.1136/jitc-2023-007054

[15] Fan, M., Tang, J., Du, W., Du, Y.F. and Liu, H.J. (2024) Systemic Immunoinflammatory Index and Prognostic Nutrition Index for Predicting Pathologic Responses of Patients with Advanced Gastric Cancer after Neoadjuvant Therapy for Advanced Gastric Cancer. *American Journal of Cancer Research*, **14**, 3922-3934. https://doi.org/10.62347/paym2267

[16] Hou, S., Song, D., Hao, R., Li, L., Zhang, Y. and Zhu, J. (2024) Prognostic Relevance of Prognostic Nutritional Indices in Gastric or Gastro-Esophageal Junction Cancer Patients Receiving Immune Checkpoint Inhibitors: A Systematic Review and Meta-Analysis. *Frontiers in Immunology*, **15**, Article ID: 1382417. https://doi.org/10.3389/fimmu.2024.1382417

[17] Zhang, L., Ma, W., Qiu, Z., Kuang, T., Wang, K., Hu, B., *et al*. (2023) Prognostic Nutritional Index as a Prognostic Biomarker for Gastrointestinal Cancer Patients Treated with Immune Checkpoint Inhibitors. *Frontiers in Immunology*, **14**, Article ID: 1219929. https://doi.org/10.3389/fimmu.2023.1219929

[18] Wu, Y., Zhao, J., Wang, Z., Liu, D., Tian, C., Ye, B., *et al*. (2023) Association of Systemic Inflammatory Markers and Tertiary Lymphoid Structure with Pathological Complete Response in Gastric Cancer Patients Receiving Preoperative Treatment: A Retrospective Cohort Study. *International Journal of Surgery*, **109**, 4151-4161. https://doi.org/10.1097/js9.0000000000000741

[19] Huang, J.B., Zhou, Z.Y., Lu, J., Zhu, J.Y., Lai, B., Mao, S.X. and Cao, J.Q. (2025) Inflammatory Burden Index as a Prognostic Marker in Patients with Advanced Gastric Cancer Treated with Neoadjuvant Chemotherapy and Immunotherapy. *Frontiers in Immunology*, **15**, Article ID: 1471399. https://doi.org/10.3389/fimmu.2024.1471399

[20] Zhao, F., Li, E., Shen, G., Dong, Q., Ren, D., Wang, M., *et al*. (2023) Correlation between Mismatch Repair and Survival of Patients with Gastric Cancer after 5-FU-Based Adjuvant Chemotherapy. *Journal of Gastroenterology*, **58**, 622-632. https://doi.org/10.1007/s00535-023-01990-z

[21] Li, Z.T., Sun, M.L., Liu, F.H., Li, Y., Bao, R.H., Jiang, X.F. and Wu, Q.J. (2026) Prognostic Nutritional Index and Cancer Prognostic Outcomes: An Umbrella Review of Systematic Reviews and Meta-Analyses of Observational Studies. *Advances in Nutrition*, **17**, Article ID: 100641. https://doi.org/10.1016/j.advnut.2026.100641

[22] Dong, Y., Yan, X., Ma, Q., Liu, D., Wang, L., Li, M., *et al*. (2026) Association between Pre-Treatment Malnutrition and Chemotherapy Toxicity in Patients with Advanced or Metastatic Gastroenteric Tumors Receiving Systemic Therapy. *Frontiers in Nutrition*, **13**, Article ID: 1780440. https://doi.org/10.3389/fnut.2026.1780440

[23] Du, Y., Li, Y., Tan, Z., Song, J., Jiang, Y., Liu, S., *et al*. (2025) Prognostic Value of Combining Preoperative Immune-Inflammatory-Nutritional Index and Tumor Biomarkers in Gastric Cancer Patients Undergoing Radical Resection. *Frontiers in Nutrition*, **12**, Article ID: 1562202. https://doi.org/10.3389/fnut.2025.1562202

[24] Wang, Q., Huang, C., Ding, Y., Wen, S., Wang, X., Guo, S., *et al*. (2022) Inhibition of CCCTC Binding Factor-Programmed Cell Death Ligand 1 Axis Suppresses Emergence of Chemoresistance Induced by Gastric Cancer-Derived Mesenchymal Stem Cells. *Frontiers in Immunology*, **13**, Article ID: 884373. https://doi.org/10.3389/fimmu.2022.884373

[25] Liao, F., Tong, Y., Sun, H., Chen, S., Wen, S., Du, Y., *et al*. (2026) Nerves Stimulate Cross-Talk between Gastric Cancer and Group 3 Innate Lymphoid Cells to Enhance Immunosuppression. *Cancer Research*, **86**, 1968-1986. https://doi.org/10.1158/0008-5472.can-25-3092

[26] Fang, M., Li, Y., Wang, P., Wang, Y., Wang, X., Wa, X., *et al*. (2025) METTL3 Inhibition Restores PD-L1 Expression and $CD8^+$ T-Cell Cytotoxic Function in Immunotherapy-Treated Gastric Cancer. *Cancer Immunology Research*, **13**, 1037-1052. https://doi.org/10.1158/2326-6066.cir-24-1179

[27] Sun, Y., Chen, Y., Cai, Y., Wang, X., Chen, Q., Fang, S. and Wang, Q. (2023) Discovery of CDK Signature and CDK5 as Potential Biomarkers for Predicting Prognosis and Immunotherapeutic Response in Gastric Cancer Peritoneal Metastases. *American Journal of Cancer Research*, **13**, 4087-4100.

[28] Weng, N., Zhou, C., Zhou, Y., Zhong, Y., Jia, Z., Rao, X., *et al*. (2024) IKZF4/NONO-RAB11FIP3 Axis Promotes

Immune Evasion in Gastric Cancer via Facilitating PD-L1 Endosome Recycling. *Cancer Letters*, **584**, Article ID: 216618. https://doi.org/10.1016/j.canlet.2024.216618

[29] Lu, M.M. and Yang, Y. (2024) Exosomal PD-L1 in Cancer and Other Fields: Recent Advances and Perspectives. *Frontiers in Immunology*, **15**, Article ID: 1395332. https://doi.org/10.3389/fimmu.2024.1395332

[30] Ibrahim, D., Simó, C., Brown, E.L., Shmuel, S., Panikar, S.S., Benton, A., *et al*. (2024) PD-L1 Has a Heterogeneous and Dynamic Expression in Gastric Cancer with Implications for immunoPET. *Frontiers in Immunology*, **15**, Article ID: 1405485. https://doi.org/10.3389/fimmu.2024.1405485

[31] Chen, Y., Jia, K., Sun, Y., Zhang, C., Li, Y., Zhang, L., *et al*. (2022) Predicting Response to Immunotherapy in Gastric Cancer via Multi-Dimensional Analyses of the Tumour Immune Microenvironment. *Nature Communications*, **13**, Article No. 4851. https://doi.org/10.1038/s41467-022-32570-z

[32] He, Y., Hong, Q., Chen, S., Zhou, J. and Qiu, S. (2025) Reprogramming Tumor-Associated Macrophages in Gastric Cancer: A Pathway to Enhanced Immunotherapy. *Frontiers in Immunology*, **16**, Article ID: 1558091. https://doi.org/10.3389/fimmu.2025.1558091

[33] Yu, K., Gu, Y., Zhang, P., Fang, H., Cao, Y., Wang, J., *et al*. (2022) Intratumoral PD-1^{+}CD8^{+} T Cells Associate Poor Clinical Outcomes and Adjuvant Chemotherapeutic Benefit in Gastric Cancer. *British Journal of Cancer*, **127**, 1709-1717. https://doi.org/10.1038/s41416-022-01939-8

[34] Yong, X., Mu, D., Ni, H., Wang, X., Zhang, T., Chang, X., *et al*. (2025) Regulation of the CD8^{+} T Cell and PDL1/PD1 Axis in Gastric Cancer: Unraveling the Molecular Landscape. *Critical Reviews in Oncology/Hematology*, **212**, Article ID: 104750. https://doi.org/10.1016/j.critrevonc.2025.104750

[35] Chen, W., Zhang, L., Gao, M., Zhang, N., Wang, R., Liu, Y., *et al*. (2025) Role of Tertiary Lymphoid Structures and B Cells in Clinical Immunotherapy of Gastric Cancer. *Frontiers in Immunology*, **15**, Article ID: 1519034. https://doi.org/10.3389/fimmu.2024.1519034

[36] Katayama, N., Ohuchida, K., Son, K., Tsutsumi, C., Mochida, Y., Noguchi, S., *et al*. (2025) Tumor Infiltration of Inactive CD8^{+} T Cells Was Associated with Poor Prognosis in Gastric Cancer. *Gastric Cancer*, **28**, 211-227. https://doi.org/10.1007/s10120-024-01577-4

[37] Jiao, F., Wang, Z., Yuan, J., Shi, F. and Zhang, S. (2026) The Tumor Microenvironment Shapes Gastric Cancer Progression by Coordinating Immune Suppression and Metabolic Reprogramming. *Frontiers in Immunology*, **17**, Article ID: 1787060. https://doi.org/10.3389/fimmu.2026.1787060

[38] Zhang, B., Shang, L., Kuang, Z., Wang, C., Sun, B. and Kong, F. (2026) Glycolysis-Driven Immunosuppression in Gastric Cancer: Metabolic Crosstalk between Tumor Cells and the Immune Microenvironment (Review). *International Journal of Oncology*, **69**, 1-21. https://doi.org/10.3892/ijo.2026.5912

[39] Zhou, P., Qu, H., Tang, Y., Shi, K., Zhuang, Z., Qiu, C., *et al*. (2026) Gastric Cancer Cells-Derived Exosomal miR-151a-5p Induces an Immunosuppressive Microenvironment through Promoting LAG3(+)TAMs Infiltration. *Journal of Experimental & Clinical Cancer Research*, **45**, Article No. 115. https://doi.org/10.1186/s13046-026-03703-9

[40] Chen, Y., Sun, Z., Wan, L., Chen, H., Xi, T. and Jiang, Y. (2022) Tumor Microenvironment Characterization for Assessment of Recurrence and Survival Outcome in Gastric Cancer to Predict Chemotherapy and Immunotherapy Response. *Frontiers in Immunology*, **13**, Article ID: 890922. https://doi.org/10.3389/fimmu.2022.890922

[41] Becerril-Rico, J., Alvarado-Ortiz, E., Toledo-Guzmán, M.E., Pelayo, R. and Ortiz-Sánchez, E. (2021) The Cross Talk between Gastric Cancer Stem Cells and the Immune Microenvironment: A Tumor-Promoting Factor. *Stem Cell Research & Therapy*, **12**, Article No. 498. https://doi.org/10.1186/s13287-021-02562-9

[42] Guo, X., Qu, Z., Wang, Y., Huang, L., Cheng, M., Huang, N., *et al*. (2026) Dynamic Monitoring of Circulating Tumor Cells and PD-L1 Combined Positive Score as Prognostic Biomarkers for Adjuvant Immunochemotherapy in Stage III Gastric Cancer: A Prospective Observational Study. *International Immunopharmacology*, **186**, Article ID: 117070. https://doi.org/10.1016/j.intimp.2026.117070

[43] Sun, J.G., Gao, Y., Gao, Y.S., Dai, X.J. and Chen, P. (2024) Identification of the Exosomal PD-L1 Inhibitor to Promote the PD-1 Targeting Therapy of Gastric Cancer. *European Journal of Medicinal Chemistry*, **268**, Article ID: 116182. https://doi.org/10.1016/j.ejmech.2024.116182

[44] Yang, Y.N., Wang, L.S., Dang, Y.Q. and Ji, G. (2024) Evaluating the Efficacy of Immunotherapy in Gastric Cancer: Insights from Immune Checkpoint Inhibitors. *World Journal of Gastroenterology*, **30**, 3726-3729. https://doi.org/10.3748/wjg.v30.i32.3726

[45] Miao, Z., Li, J., Wang, Y., Shi, M., Gu, X., Zhang, X., *et al*. (2023) Hsa_circ_0136666 Stimulates Gastric Cancer Progression and Tumor Immune Escape by Regulating the miR-375/PRKDC Axis and PD-L1 Phosphorylation. *Molecular Cancer*, **22**, Article No. 205. https://doi.org/10.1186/s12943-023-01883-y