



靶向DGK α /PA轴抑制肿瘤免疫逃逸增强消化道肿瘤对免疫治疗的敏感性

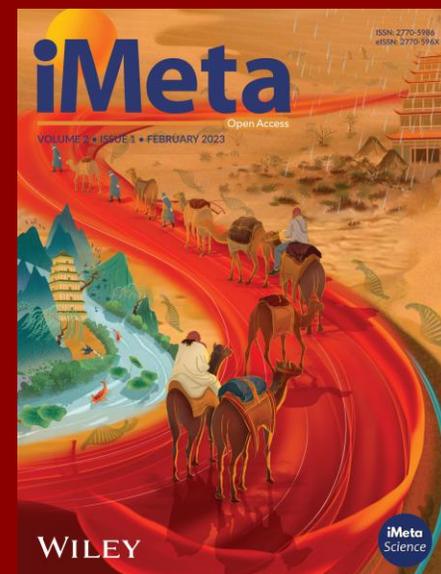
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Jie Chen, Siqi Liu, Ting Peng, Fenglong Wang, Yuheng Zhu, Jingyuan Pang, Qingnan Wu, et al. 2026. Targeting DGK α /PA axis inhibits tumor immune evasion and augments sensitivity to immunotherapy in gastrointestinal cancers.

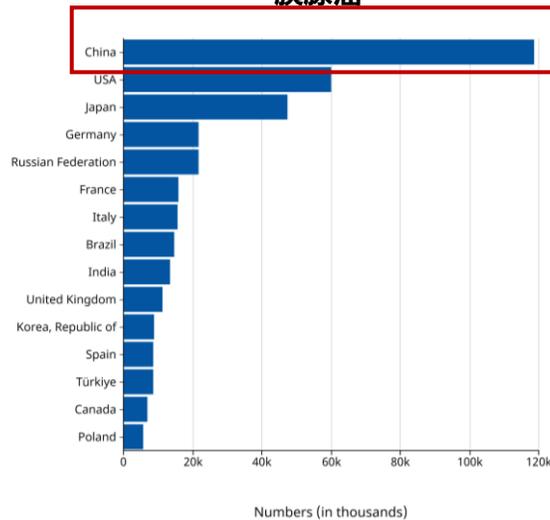
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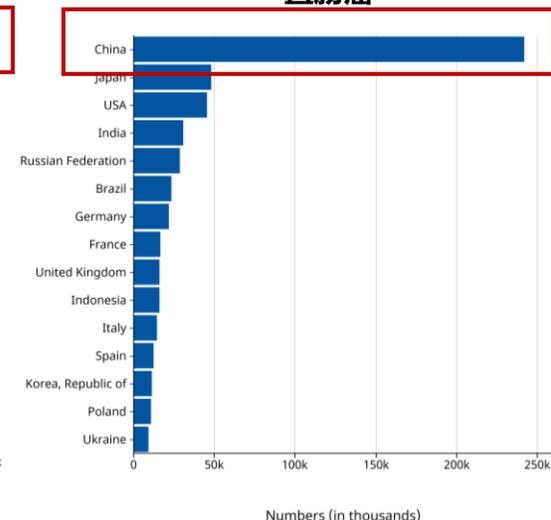
研究背景

- 全球六大消化系统癌症的新发病例占全球癌症总发病人数的约 24.6%;
- 消化道肿瘤是中国高发肿瘤之一，发病人数约占全球同类癌症发病总数的 37%；死亡人数约占全球该类癌症死亡总数的 41%；
- 临床上免疫检查点抑制剂（ICIs）治疗消化道肿瘤仍处于探索阶段；
- 临床研究显示，大量免疫治疗响应的消化道肿瘤患者在缓解期后都会出现不同程度的耐受现象。

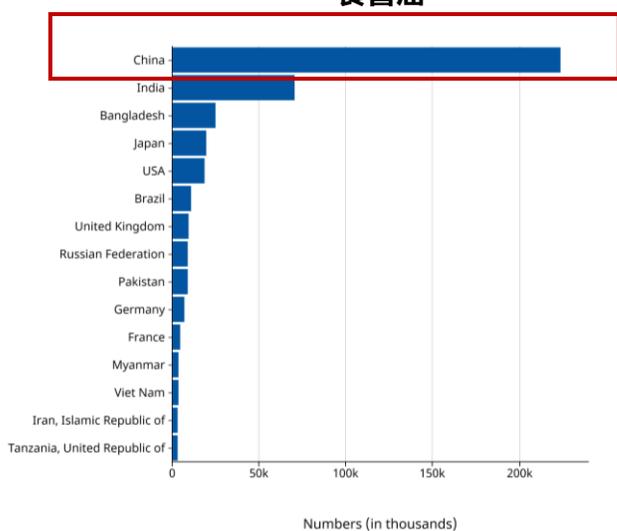
胰腺癌



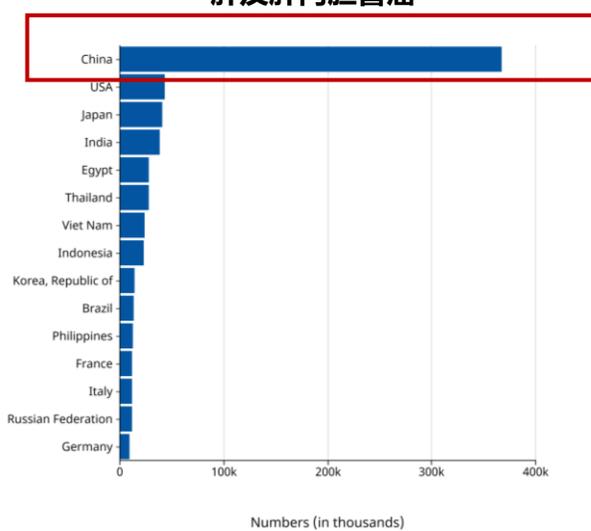
直肠癌



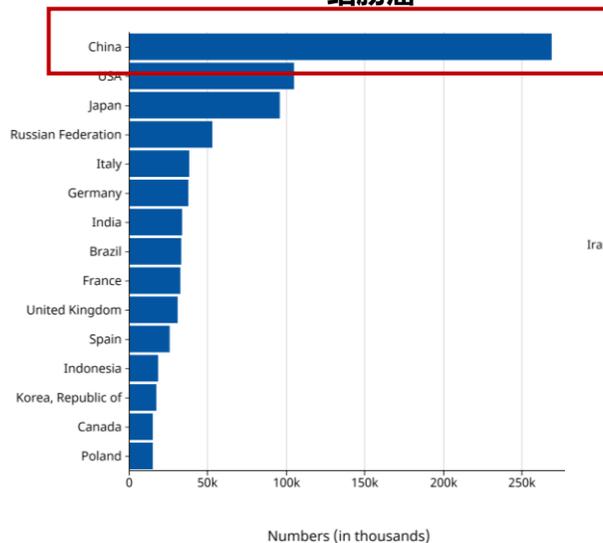
食管癌



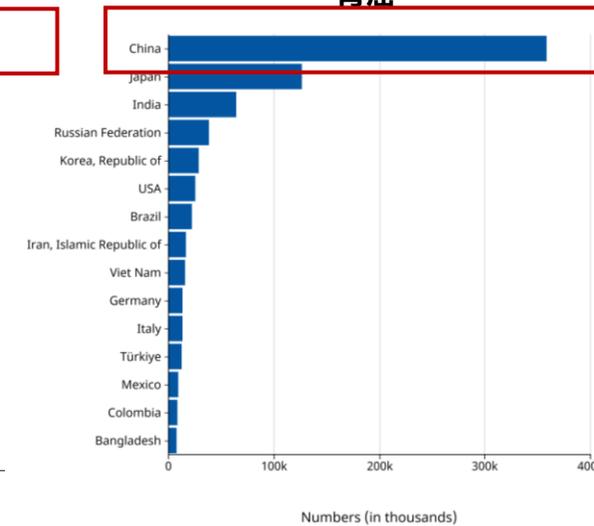
肝及肝内胆管癌



结肠癌

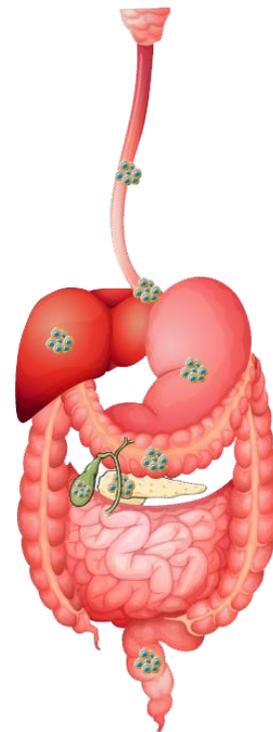
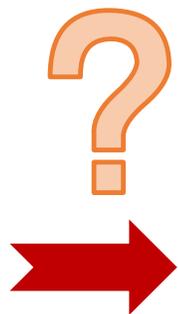
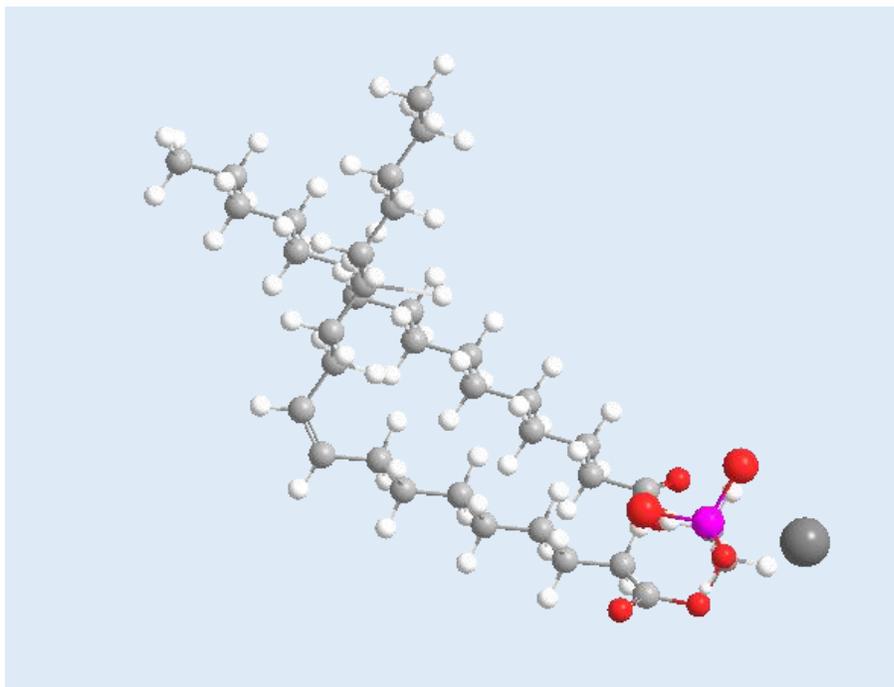


胃癌





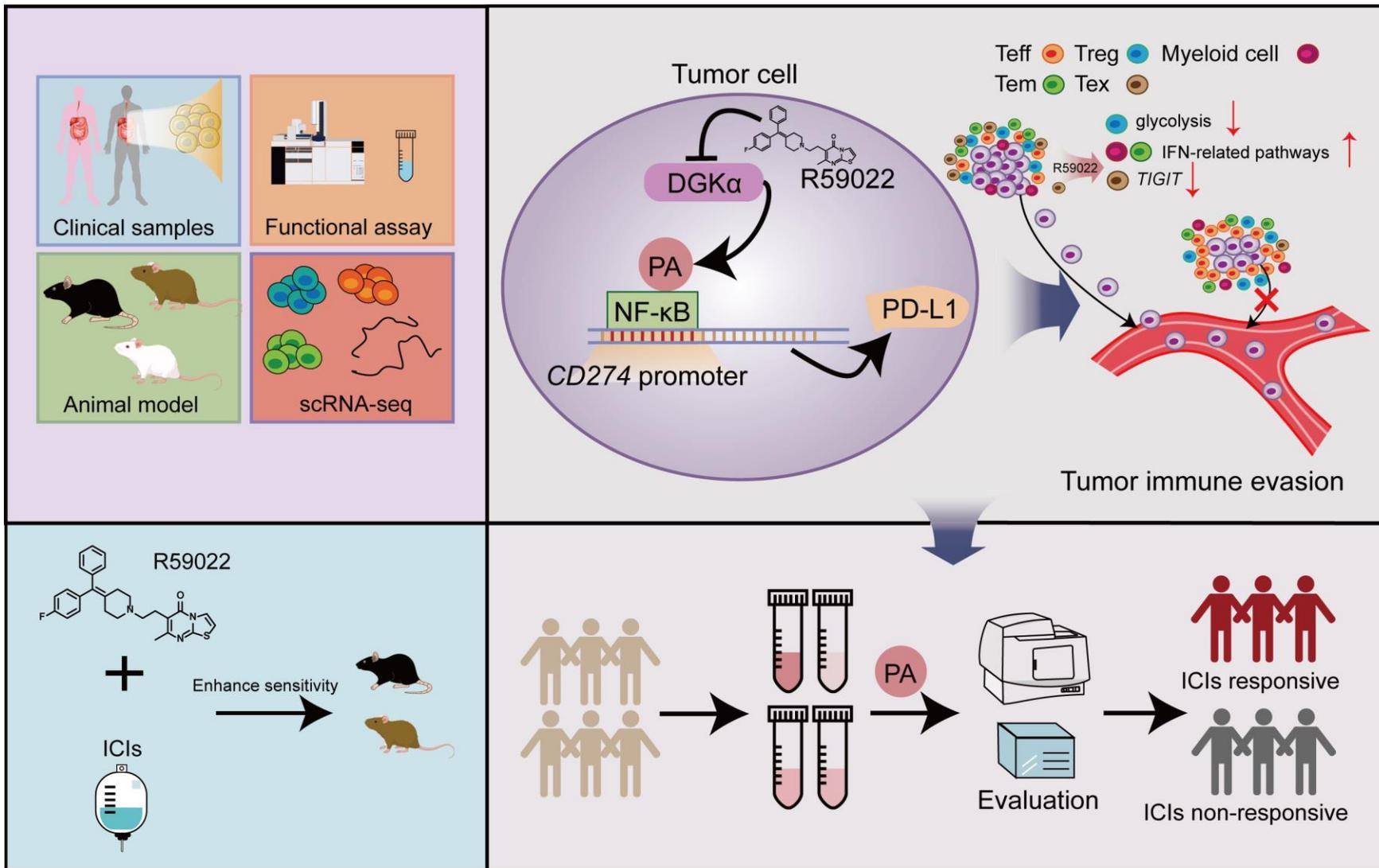
研究背景



- 一直以来脂类代谢产物促癌机制未明确阐述；
- 脂代谢酶DGK α 作为信号枢纽介导多种实体瘤的进展，是肿瘤细胞中重要的癌蛋白，催化二脂酰甘油转化成磷脂酸（PA）；
- DGK α 在消化道肿瘤进展中的作用尚不明确。



亮点

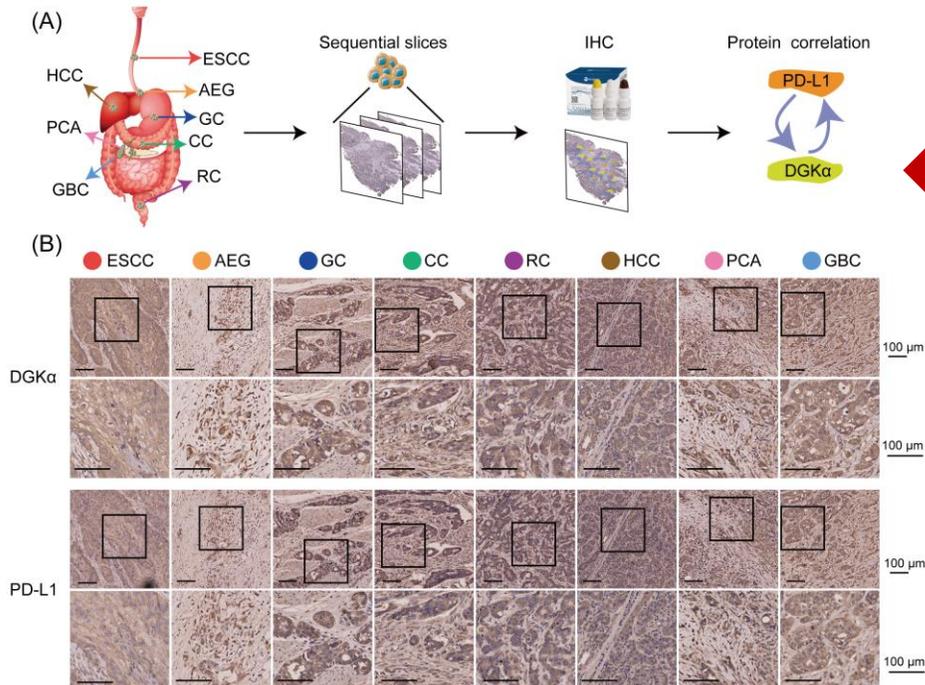


- ◆ 脂类代谢产物PA直接结合NF-κB p65，促进其介导PD-L1表达的效应；
- ◆ 抑制DGKα/PA轴诱导细胞毒性T淋巴细胞在局部肿瘤组织中的浸润；
- ◆ DGKα抑制剂R59022阻断NF-κB轴增强免疫检查点抑制剂的抗癌效应；
- ◆ 血浆PA可用于判断免疫检查点抑制剂在消化道肿瘤治疗中的敏感性。



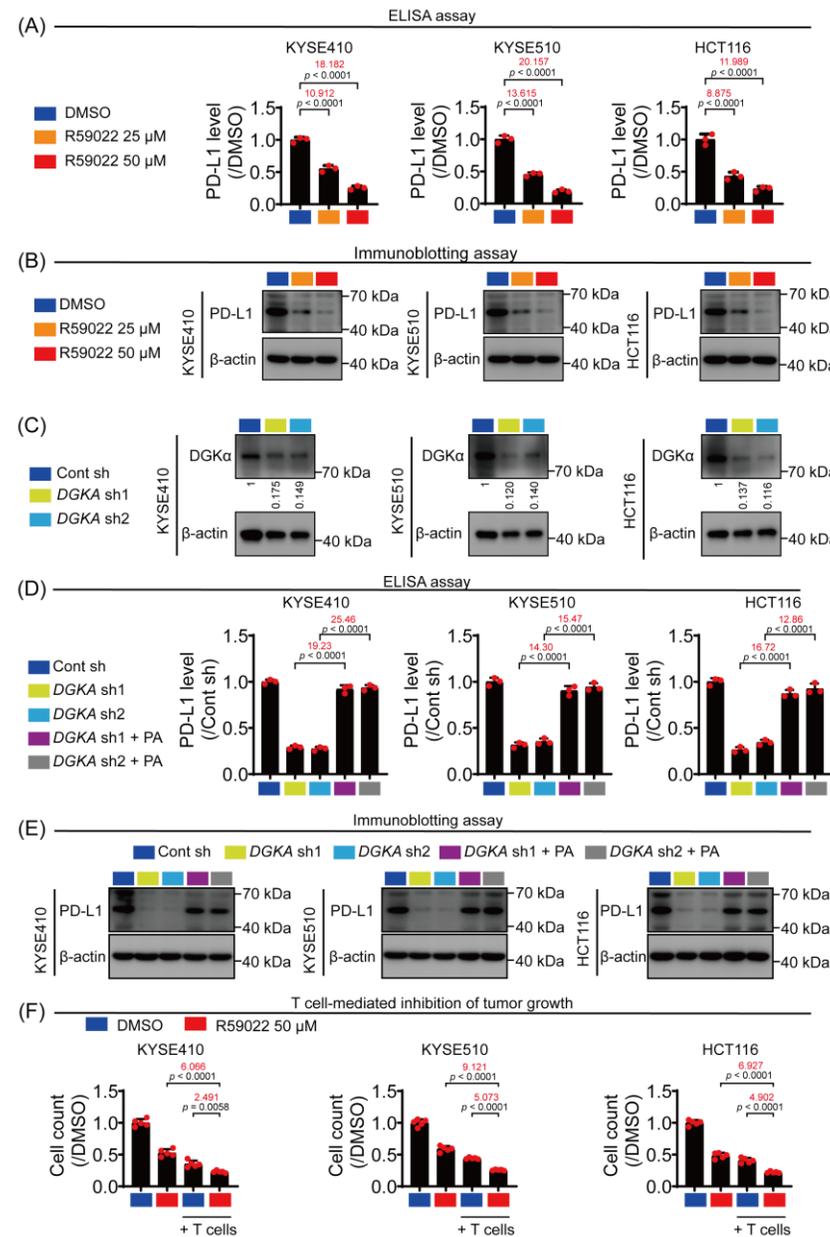
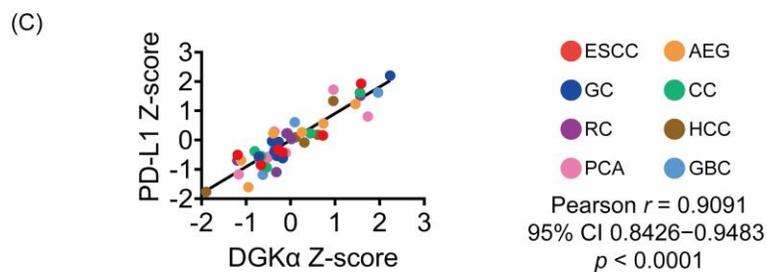
DGK α /PA轴调控PD-L1表达

Correlation between DGK α and PD-L1 in gastrointestinal cancers



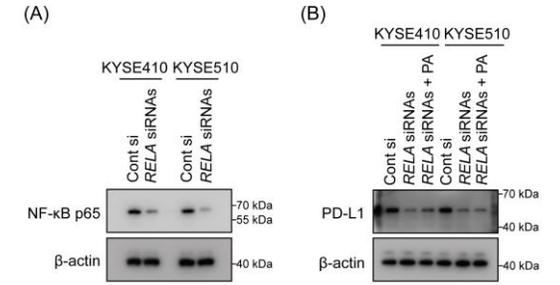
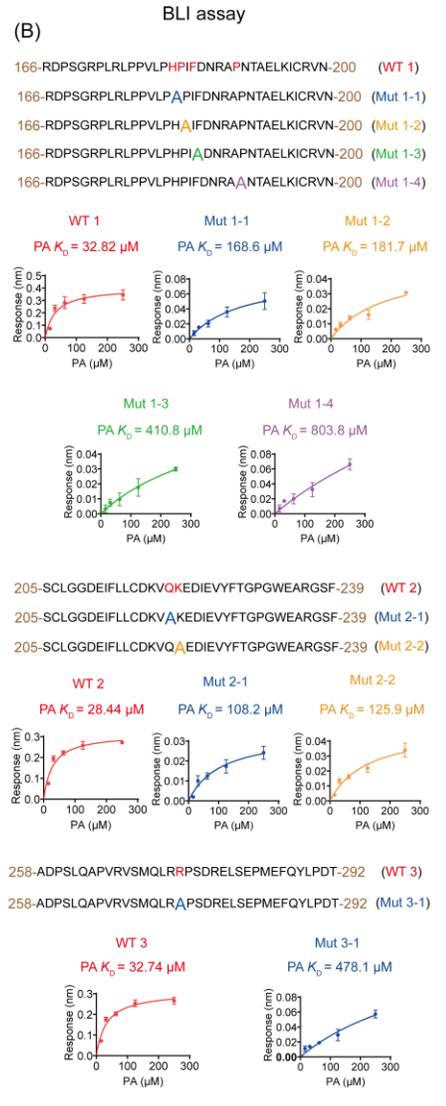
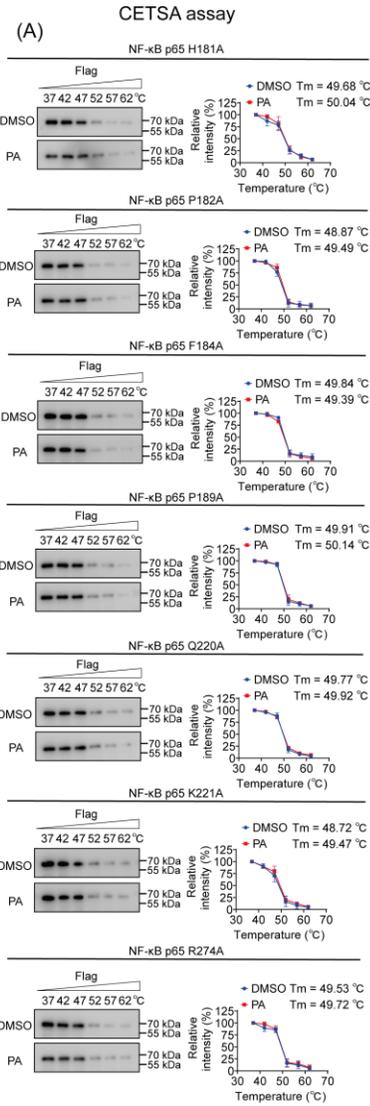
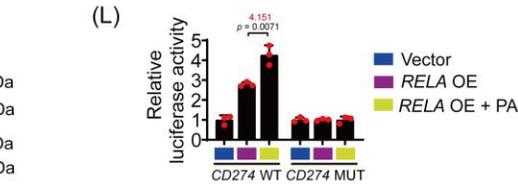
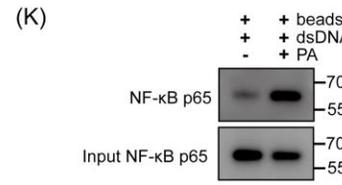
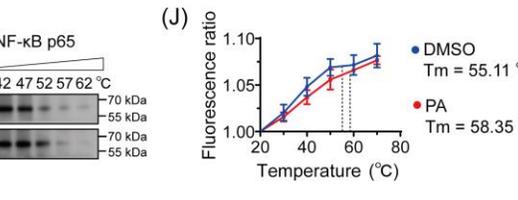
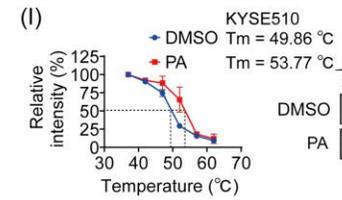
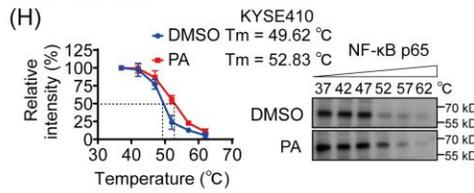
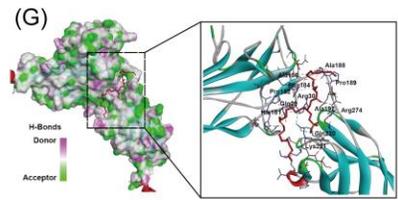
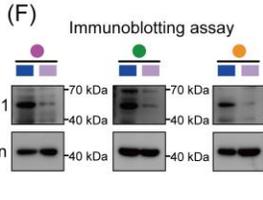
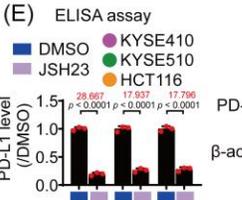
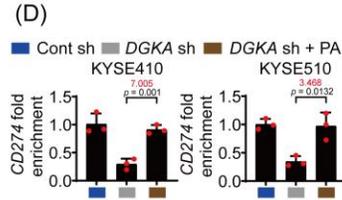
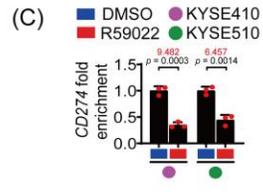
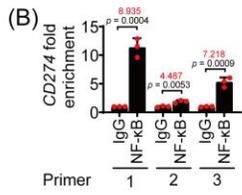
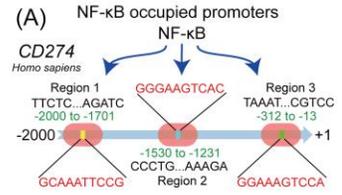
← 消化道肿瘤中 DGK α 的表达与PD-L1表达呈正相关。

肿瘤内 DGK α /PA 轴促进PD-L1表达。 →





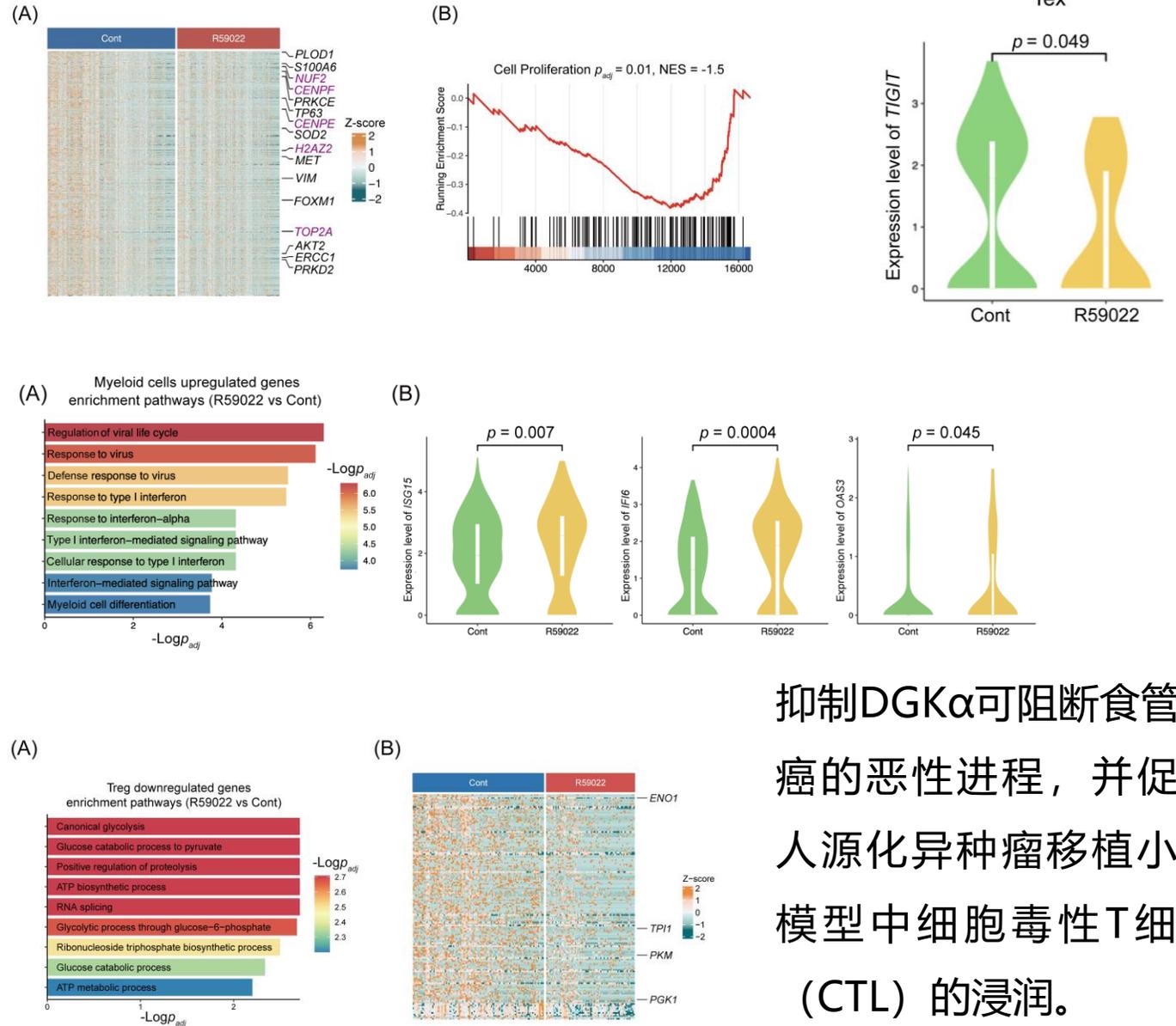
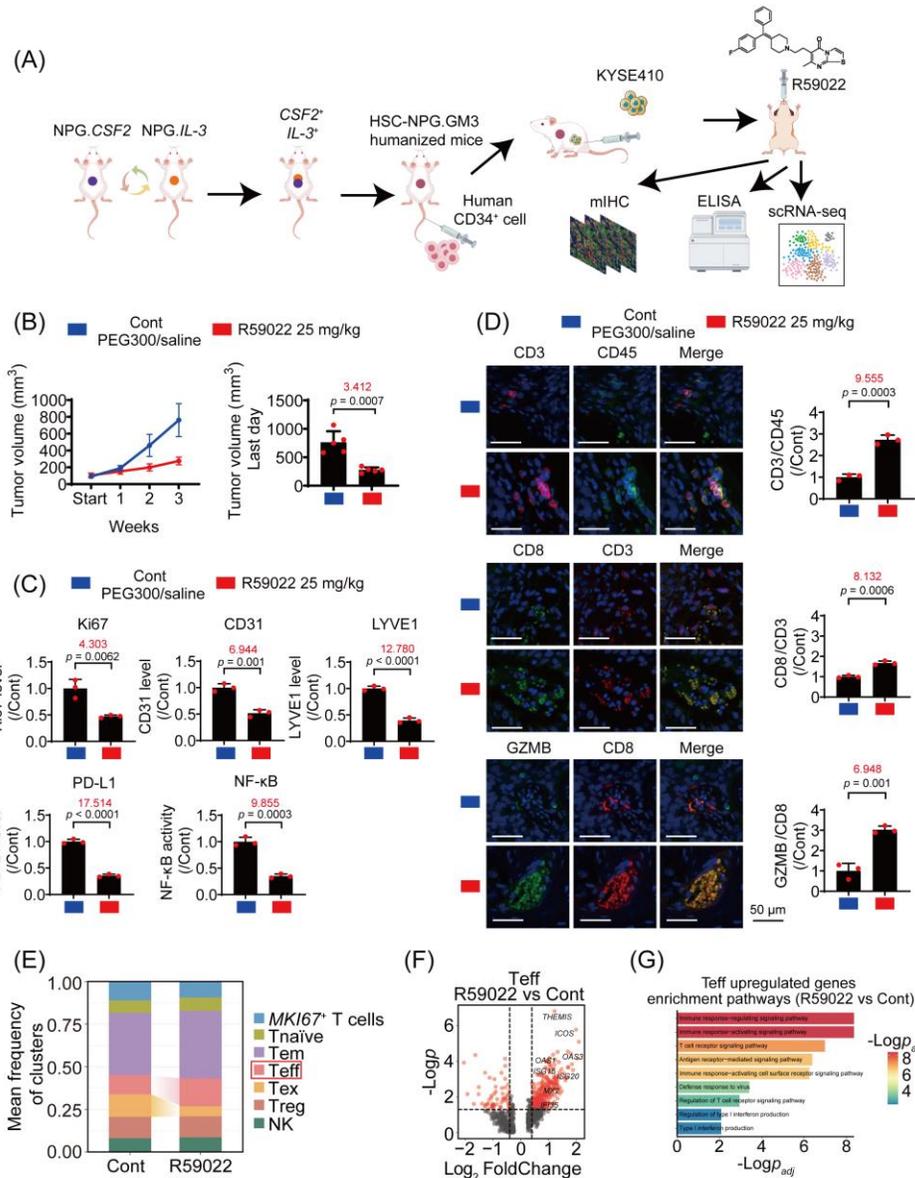
PA直接结合NF-κB p65发挥作用



DGKα来源的PA直接作用于NF-κB p65并激活其转录活性，促进PD-L1的表达。



抑制DGK α 促进CTL浸润

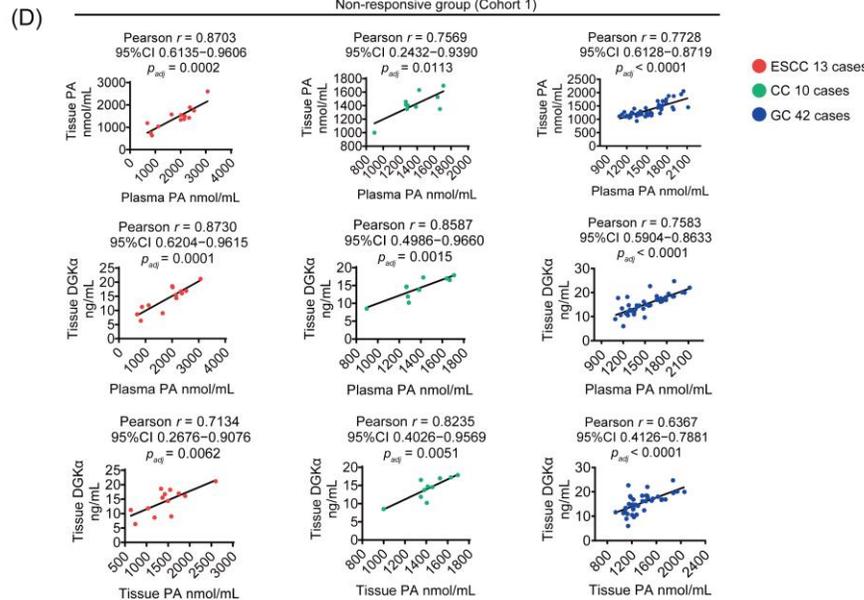
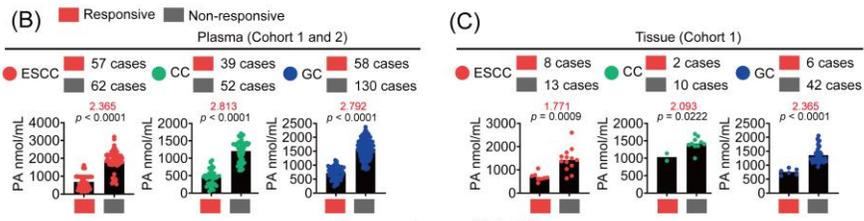
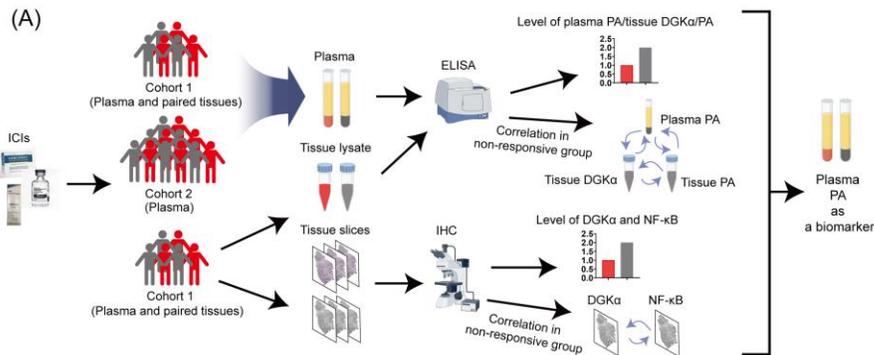


抑制DGK α 可阻断食管鳞癌的恶性进程，并促进人源化异种瘤移植小鼠模型中细胞毒性T细胞(CTL)的浸润。



DGKα/PA轴与消化道肿瘤患者ICIs响应/非响应

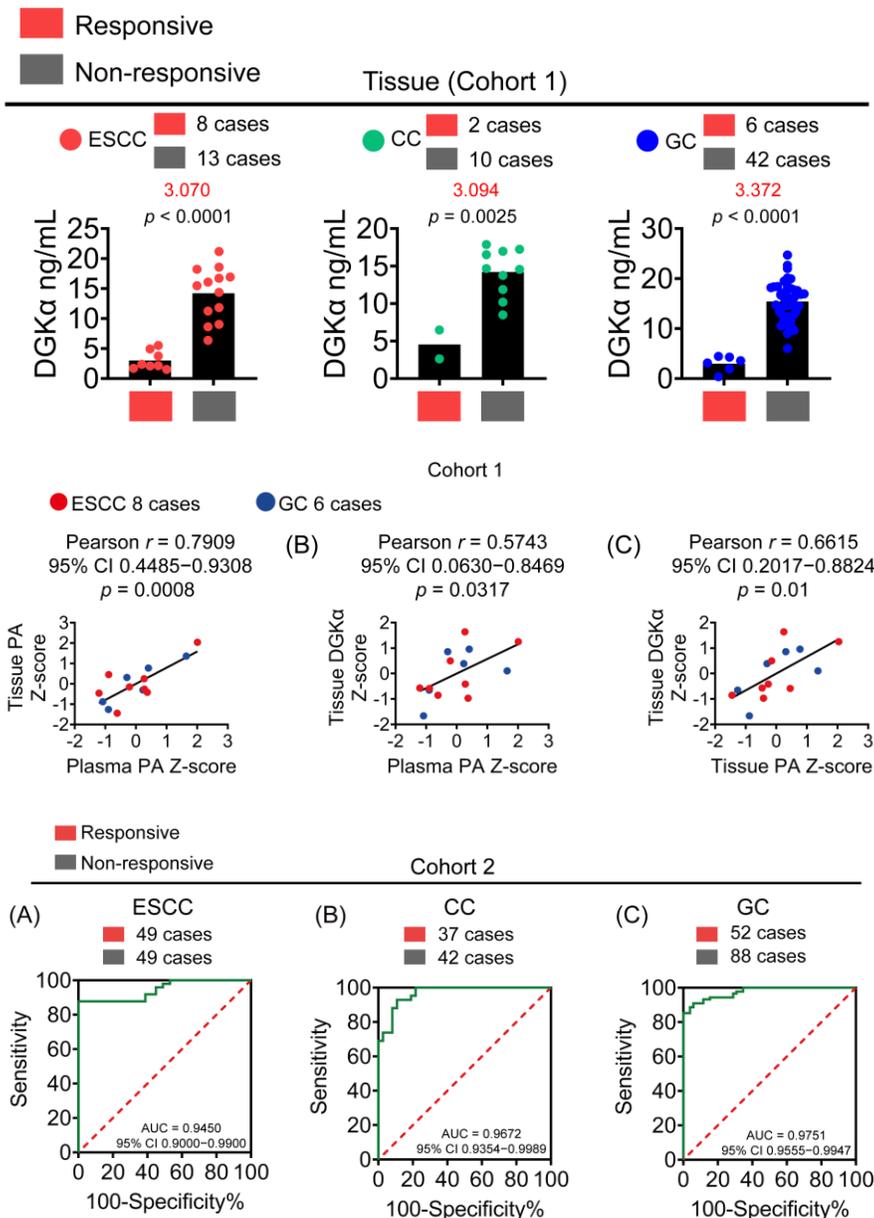
Expression status of DGKα/PA/NF-κB axis in ICIs-treated gastrointestinal cancers



● 血浆PA作为标志物判断消化道肿瘤免疫检查点抑制剂敏感性。



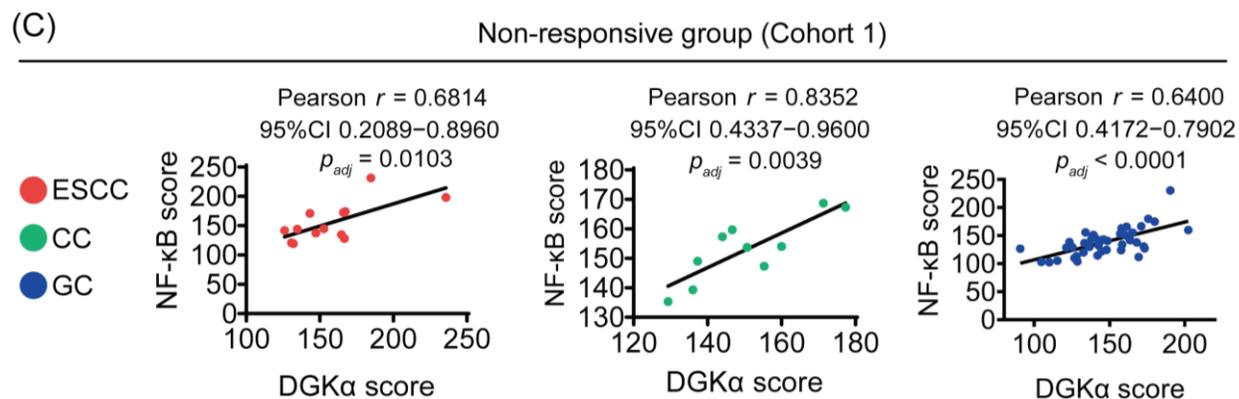
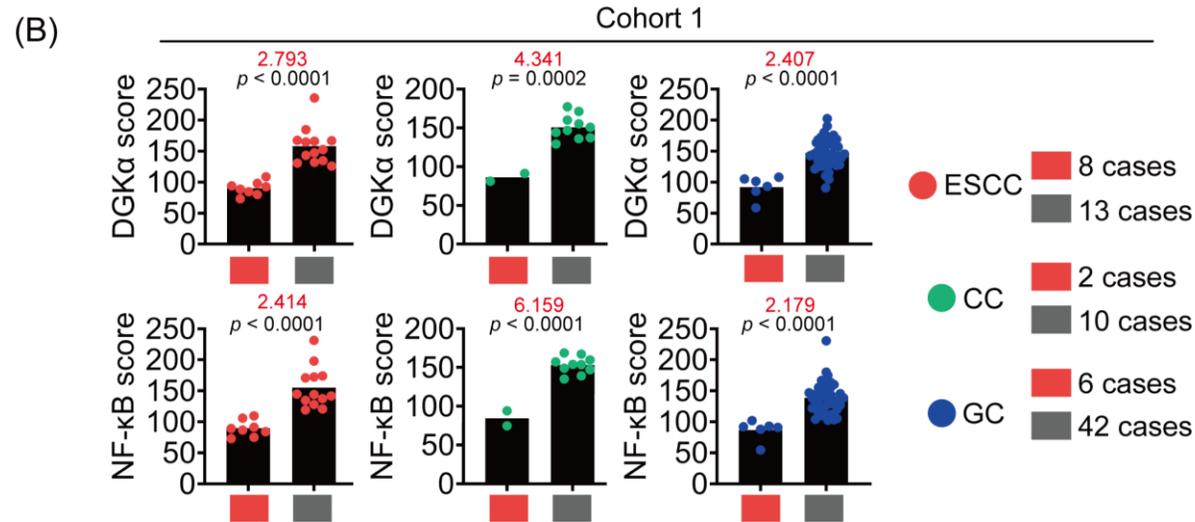
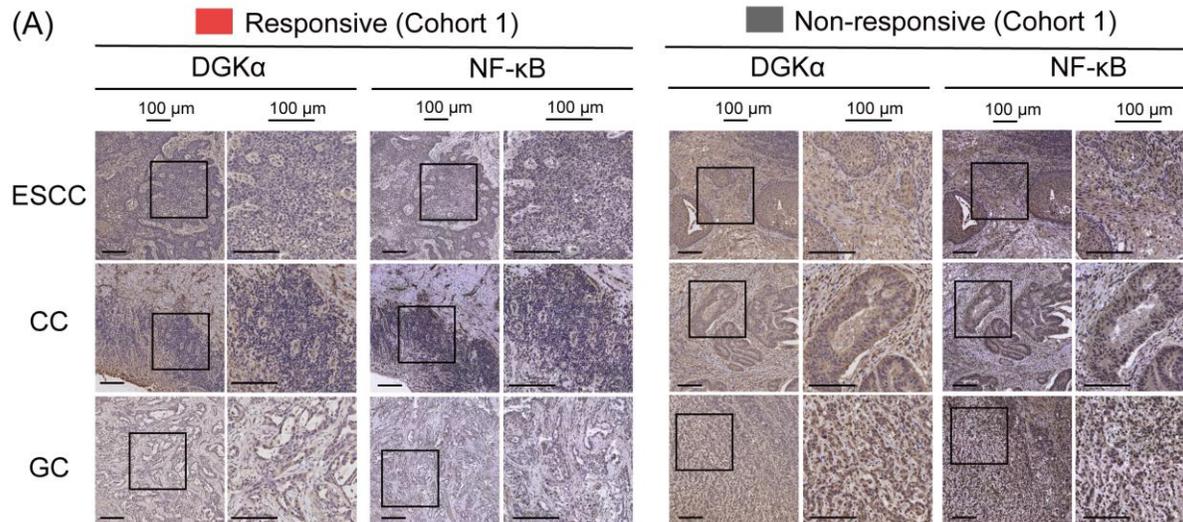
● PA有望成为评估肿瘤进展和治疗反应的可靠生物标志物。





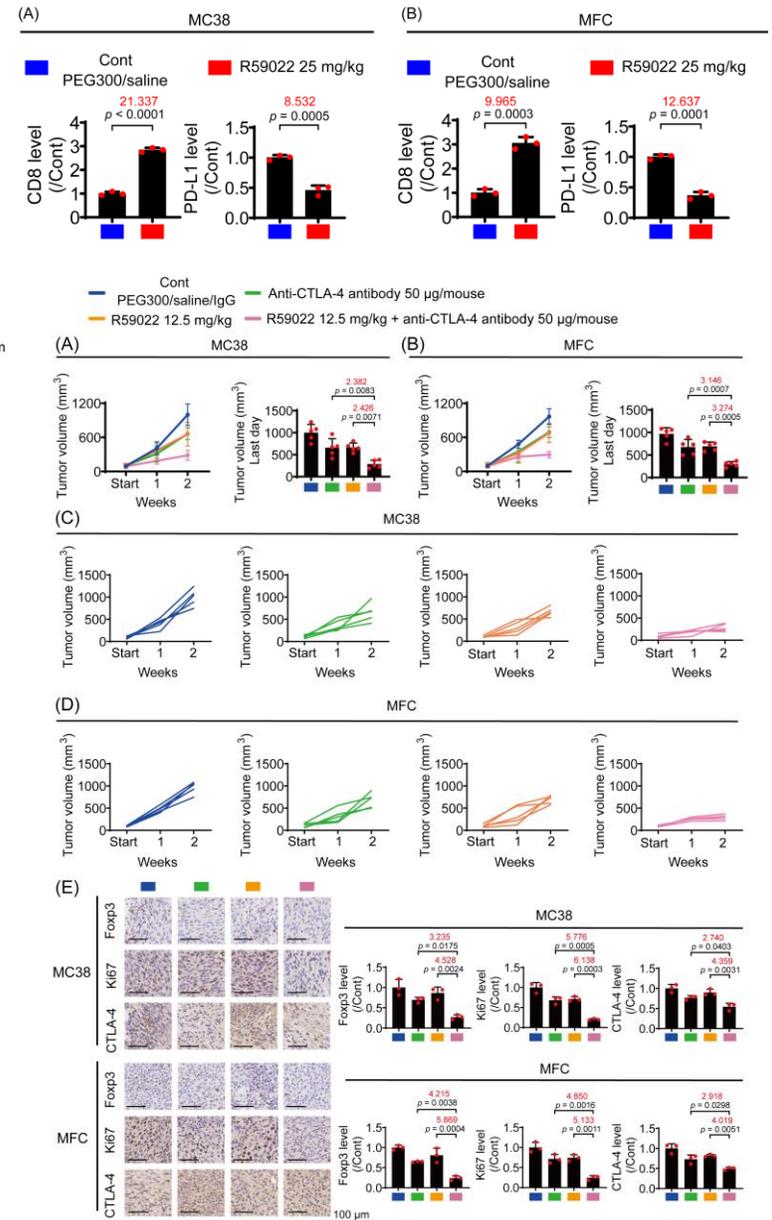
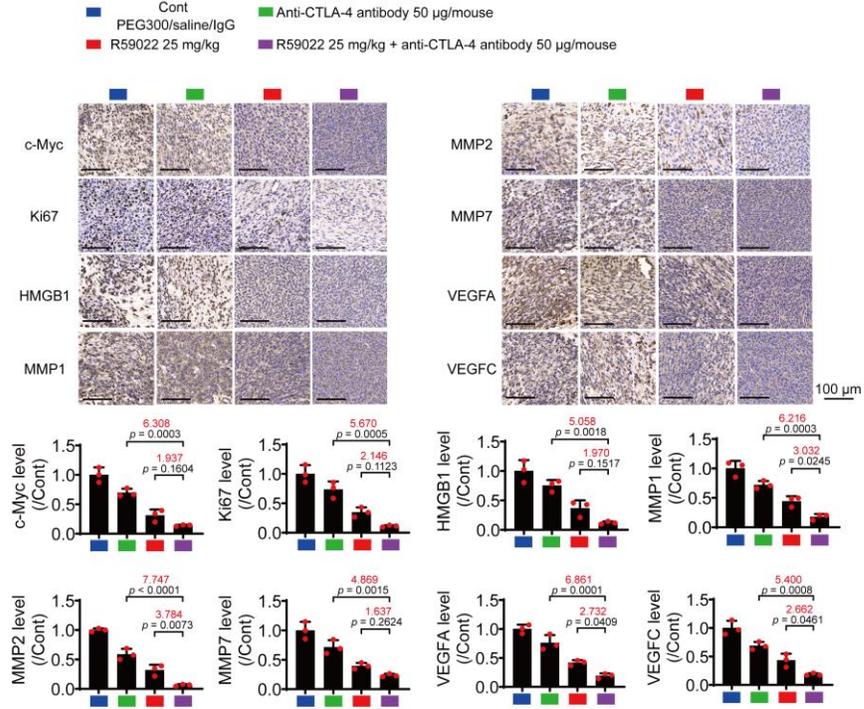
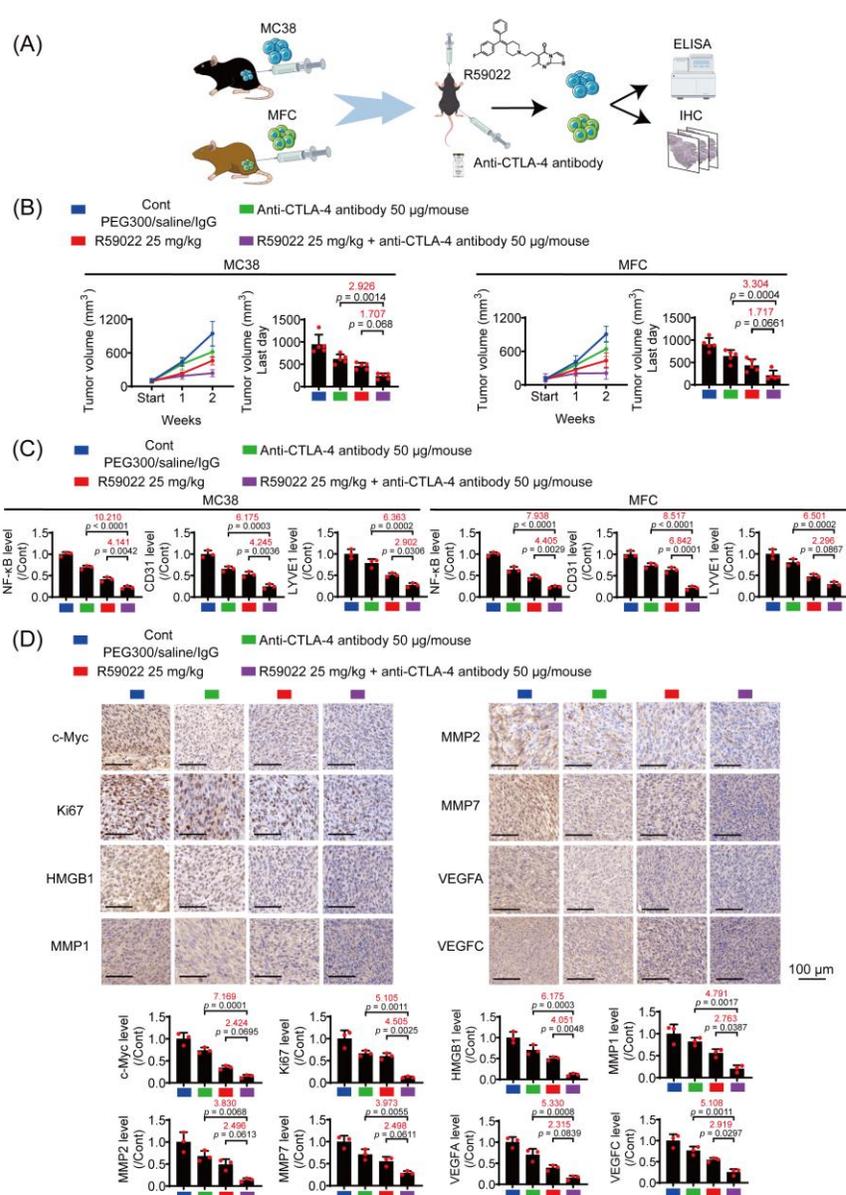
DGK α /PA轴与消化道肿瘤患者ICIs响应/非响应

Correlation between DGK α and NF- κ B in the ICIs non-responsive group



消化道肿瘤ICIs非响应患者中，肿瘤DGK α 与NF- κ B呈正相关。

DGK α 抑制剂与CTLA-4抑制剂联合疗效



DGK α 抑制剂通过调节免疫微环境增强抗CTLA-4抗体的疗效，为开发抗肿瘤药物联合治疗提供了新策略。

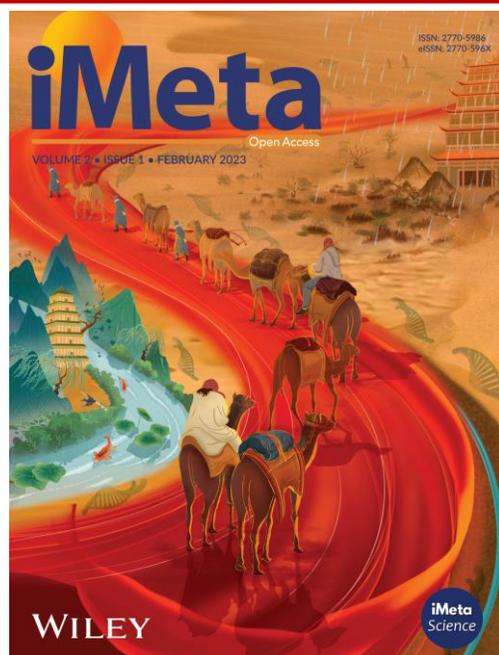
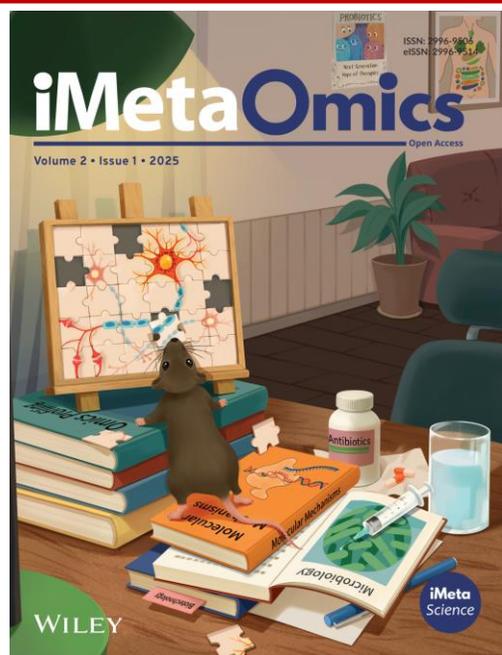
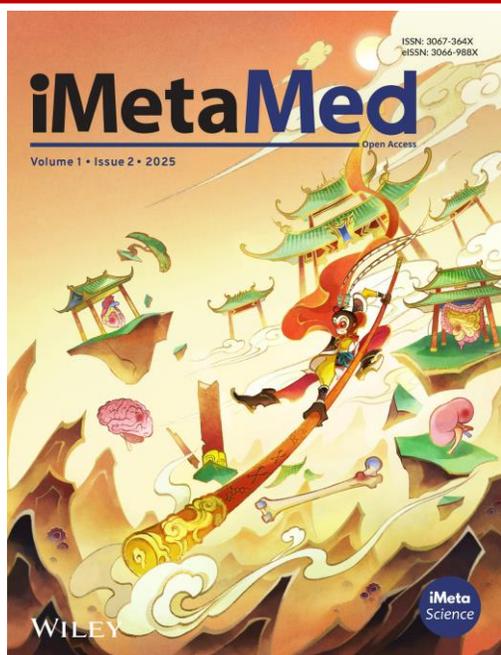


总结

- ❑ DGK α 通过NF- κ B/PD-L1信号轴驱动免疫逃逸;
- ❑ DGK α 抑制剂可调控免疫微环境以增强免疫检查点抑制剂的疗效;
- ❑ 血浆PA可判断免疫检查点抑制剂在消化道肿瘤治疗中的响应情况。

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