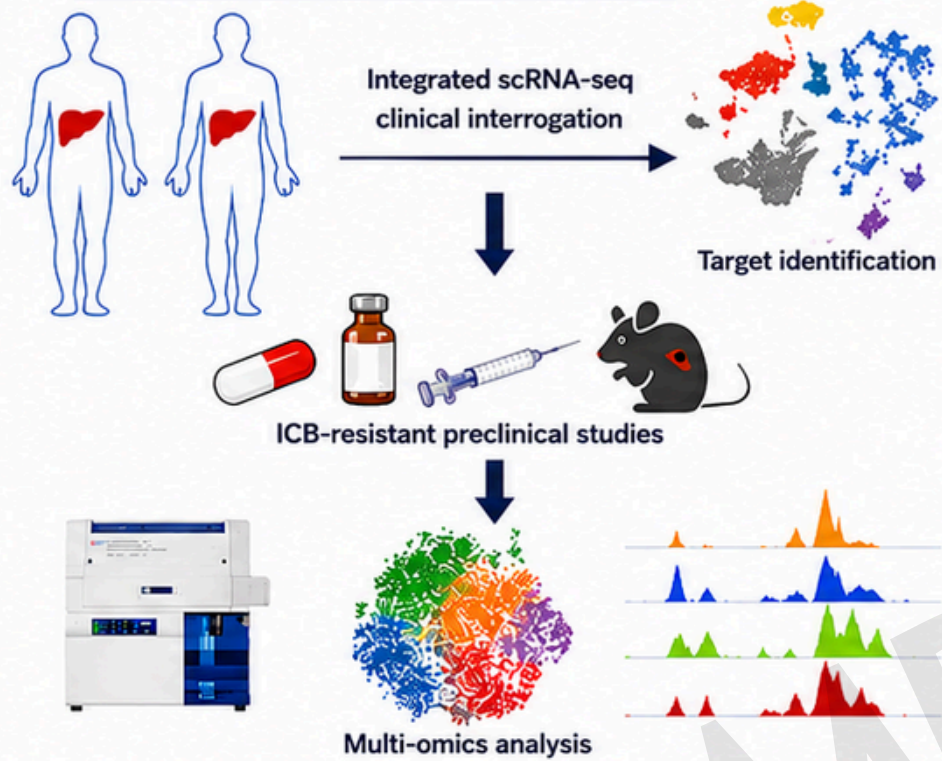


GRAPHICAL ABSTRACT SAMPLE WORK

**Pharmacological activation of STAT1-GSDME pyroptotic circuitry reinforces
epigenetic immunotherapy for hepatocellular carcinoma**

Pharmacological Activation of STAT1-GSDME Pyroptotic Circuitry Reinforces Epigenetic Immunotherapy for Hepatocellular Carcinoma

PD-1 blockade in HCC (NCT03419481)



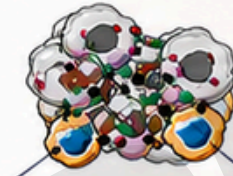
- ✓ HCC patients with **HDAC1/2/3^{high}** tumours exhibited lower levels of **IFN γ** and poorer survival on ICB therapy.
- ✓ A selective class-I HDAC inhibitor **CXD101** re-sensitised **HDAC1/2/3^{high}** tumours to ICB by restoration of the cancer-immunity cycle.
- ✓ This study provides a mechanistic basis of **CXD101** plus **anti-PD-1** treatment in patients with ICB-resistant HCC (NCT05873244).

'Cold' tumor

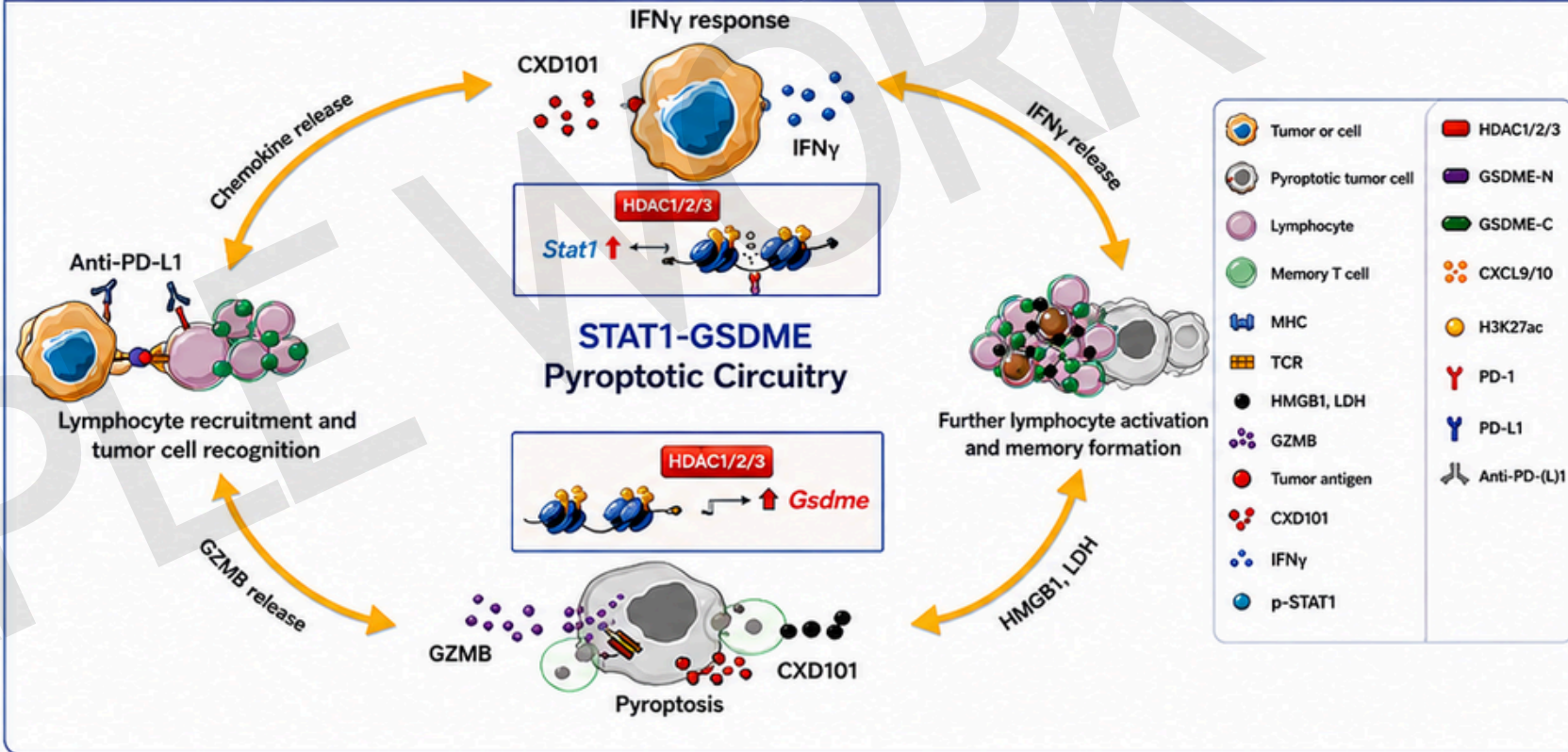


**HDAC1/2/3
targeted ICB therapy**

'Hot' tumor



- ✓ Tumor intrinsic IFN γ response
- ✓ Tumor cell pyroptosis
- ✓ Robust antitumor immunity with T cell memory formation
- ✓ Tumor regression and long-term survival



Epigenetic activation of STAT1-GSDME pyroptotic circuitry underlies successful conversion of the immune-excluded into an inflamed immunotype.