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**Spatial single-cell profiling and neighbourhood analysis reveal the determinants of immune architecture connected to checkpoint inhibitor therapy outcome in hepatocellular carcinoma**

*Salié H, Wischer L, D’Alessio A, et al. Spatial single-cell profiling and neighbourhood analysis reveal the determinants of immune architecture connected to checkpoint inhibitor therapy outcome in hepatocellular carcinoma. Gut 2025; 74: 451-466. doi: 10.1136/gutjnl-2024-332837.*

A large proportion of patients with hepatocellular carcinoma (HCC) do not respond to current immunotherapies. Previous classifications of HCC based on immune features identified by transcriptomic and proteomic analysis have not been able to predict outcomes to immunotherapy therapy. The spatial organisation of the anti-tumour immune response is emerging as a determinant in the response to immunotherapy.

In this study, Salié et al., utilised highly multiplexed imaging mass cytometry (IMC) to characterise the immune architecture of the tumour microenvironment of 101 HCC tissues. IMC is a novel advanced technique to analyse the spatial distribution and molecular composition of tissues. They found significant heterogeneity between HCC specimens and within the specimen between the tumour parenchyma and the stroma. They employed bioinformatic techniques to identify three major immune architectures with different immune cell and checkpoint patterns.

The team developed a simplified spatial immune classification which accounted for the amount and distribution of CD8 (cluster of differentiation 8) T cells and the stromal/parenchymal distribution. They validated this in an independent cohort and examined the ability to predict outcomes in response to immunotherapy and found that spatial immune architecture correlated with therapy outcome.

They postulate that their spatial immune classification may be translated into a clinical prediction tool for immunotherapy response in HCC patients and therefore guide rational therapy selection.