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Summary

From bench to bedside: Using multiomics for personalised therapy

Jeroen Dekervel

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Endoscopy | Mechanisms & Personalised Medicine | Hepatobiliary | Digestive Oncology

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Multiomics approaches, particularly single-cell sequencing and TCR analysis, can identify tumor-specific antigens to guide personalized mRNA cancer vaccine development in hepatocellular carcinoma.

KEY POINTS

- The speaker presented work using single-cell sequencing on 90 hepatocellular carcinoma samples to identify immunogenic antigens for personalized vaccines, with analysis of T-cell receptor sequences and phenotypes to select tumor-directed clones.
- In one dramatic responder to checkpoint inhibition, the speaker's team screened 19 TCRs and identified 10 hits corresponding to 6 antigens, finding predominantly tumor-associated transcripts rather than neoantigens and immunodominance against the cancer-testis antigen DCAF4L2.
- The speaker reported that DCAF4L2 expression was stated to be predictive of outcome in the IMbrave150 trial, with the antigen expressed in the speaker's stated 20.26% of liver cancers in TCGA and limited to tumor cells.
- A planned trial (TWIST-FACTS-ON-1) will treat advanced HCC patients with PD-L1 and CTLA-4 inhibition, use the first three months to identify patient-specific antigens via the platform, then add a personalized mRNA vaccine, with primary endpoints of safety and feasibility.
- The speaker disclosed that antigen selection is critical for vaccine efficacy, citing a negative BioNTech phase 2 melanoma trial where only a minority of up to 20 vaccine antigens elicited immune responses, though patients with one or more immunogenic antigens had better outcomes.

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