ImmunoPET as a Tool for Understanding Resistance Related to Antibody–Drug Conjugates (ADCs): From Biodistribution to the Tumor Microenvironment

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Antibody–drug conjugates (ADCs) combine the specificity of monoclonal antibodies with the potency of cytotoxic payloads. Sacituzumab Govitecan (SG, anti-Trop-2) have shown clinical efficacy in solid tumours, yet many patients fail to respond or relapse, highlighting poorly characterised resistance mechanisms [1,3].

Resistance is driven by heterogeneous antigen expression, uneven intratumoral ADC distribution, aberrant intracellular trafficking and tumoral micro-environment [1]. We hypothesise that resistance arises from interactions vascularization and the treatment inducing a hypoxic and less vascularized environment. We address this with immunoPET imaging in xenograft models, along three objectives [2].

First, we map the intratumoral distribution of SG by immunoPET. ADC was radiolabelled with zirconium-89 ([89Zr]Zr) after DFO conjugation on free lysines; HPLC, DLS and DSF confirmed integrity and preserved stability. Flow cytometry and western blot characterised MDA-MB-468, MDA-MB-231, H1975 and A549 lines, confirming differential Trop-2 expression and establishing matched positive and negative controls. FMISO-PET characterises baseline tumor hypoxia in vivo as a reference for correlating TME state with ADC efficacy.

Second, we assess how the ADCs, and therefore the payloads SN-38, affect TME features: vascularization and hypoxia across Trop-2-targeted models.

Third, we correlate distribution profiles with therapeutic outcome to identify actionable biodistribution barriers.

These findings will support the design of ADCs able to overcome the biodistribution barriers identified, and to reveal predictive biomarkers of resistance linked to tumor vascularisation and antibody distribution [4].

References

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Biosketch

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CURRENT AND PAST POSITIONS

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EDUCATION

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OTHER RELEVANT PROFESSIONAL ACTIVITIES AND ACCOMPLISHMENTS

Oral communication at an international congress of molecular imaging: EMIM 2026, Ljubljana, Slovenia, March 2026.