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EXPLOITING METABOLIC VULNERABILITIES IN LYMPHOMA: FROM BENCH TO PRECISION THERAPY

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Metabolic rewiring is a defining feature of cancer and a key determinant of therapeutic response. In diffuse large B-cell lymphoma (DLBCL), our work reveals that distinct metabolic states not only dictate sensitivity to standard immunochemotherapy but also uncover targetable weaknesses. Through integrated metabolic and translational studies, we identified how lymphoma cells exploit alternative nutrient pathways—particularly those involving amino acids—to sustain survival under therapeutic stress. Using functional genomics, stable isotope tracing, and patient-derived validation, we demonstrated that disrupting these adaptive metabolic circuits can overcome resistance in otherwise refractory lymphomas. Yet, the same metabolic flexibility that fuels survival also drives secondary resistance, notably through serine biosynthesis-mediated redox adaptation and enhanced DNA repair. Pharmacologic interference with these rescue mechanisms, such as PARP inhibition, restores therapeutic vulnerability and extends efficacy.

During this presentation, we will discuss the importance of measuring cancer metabolism *in vivo* and how effectively it can be targeted in the clinical context. We will also characterize novel metabolic vulnerabilities, as well as the associated escape mechanisms that arise during therapy, which in turn reveal novel targetable weaknesses.

Related references :

- Chiche et al. *Cell Metabolism* 2019 PMID: 30827861
- Grima-reyes et al *Mol Metab.* 2021 PMID: 34256164
- Grima-reyes et al *Sci Adv.* 2022 PMID: 35857457
- Aussel et al. *Nat Com* in press

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