

**B01 - MECHANISMS OF RESPONSE AND RESISTANCE
TO CHECKPOINT BLOCKADE IN GLIOMAS**

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SUMMARY

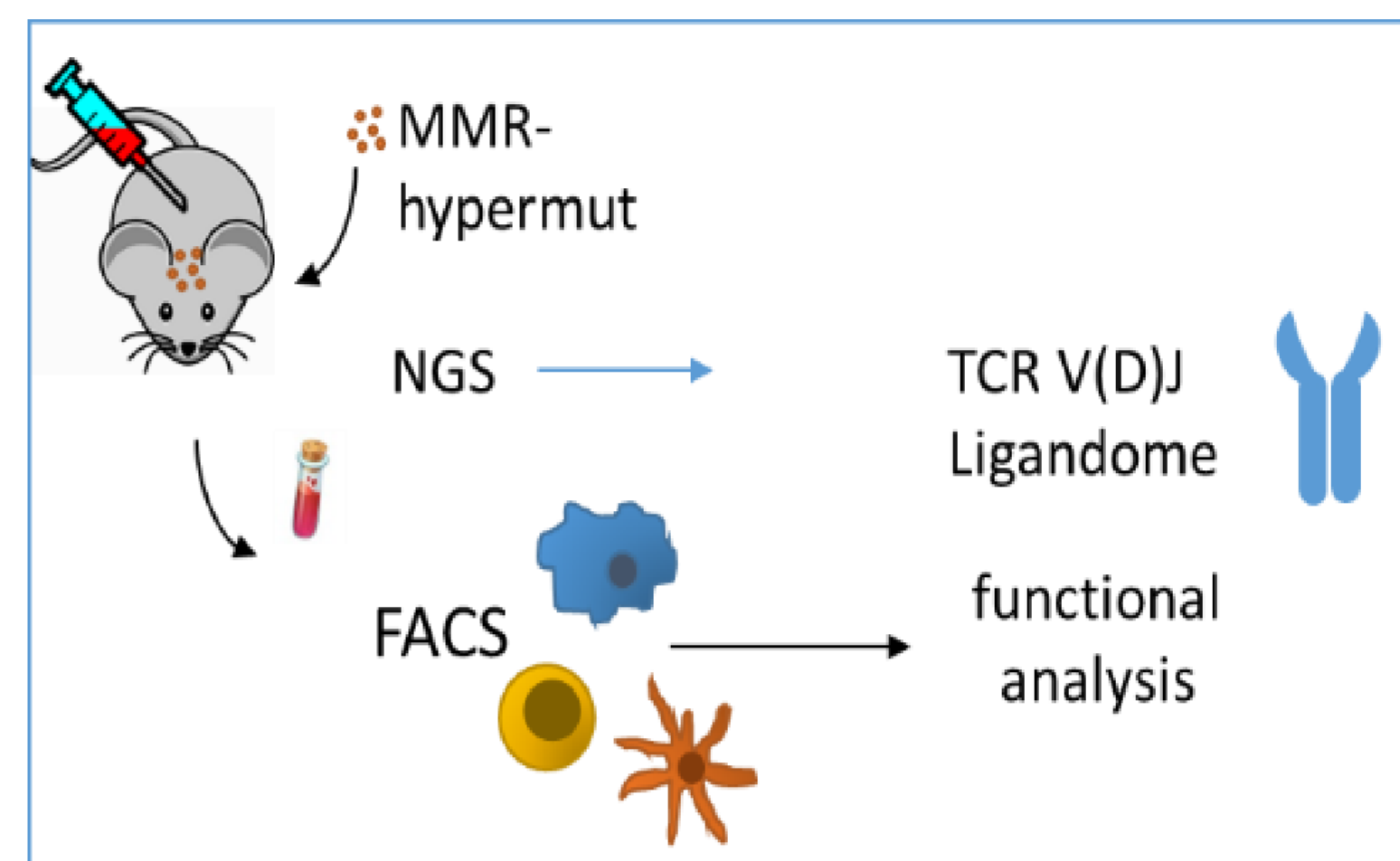
This project aims at identifying cellular, molecular, metabolic and imaging determinants of response and resistance to immune checkpoint blockade in glioma using preclinical animal models and studying cohorts of patients with newly diagnosed and recurrent glioma. The strategic aim is to identify cellular, molecular and imaging biomarkers, which allow to refine the use of checkpoint inhibitors in glioma treatment and to develop rational combinatorial therapies to enhance efficacy.

TASK

VISUAL ABSTRACT

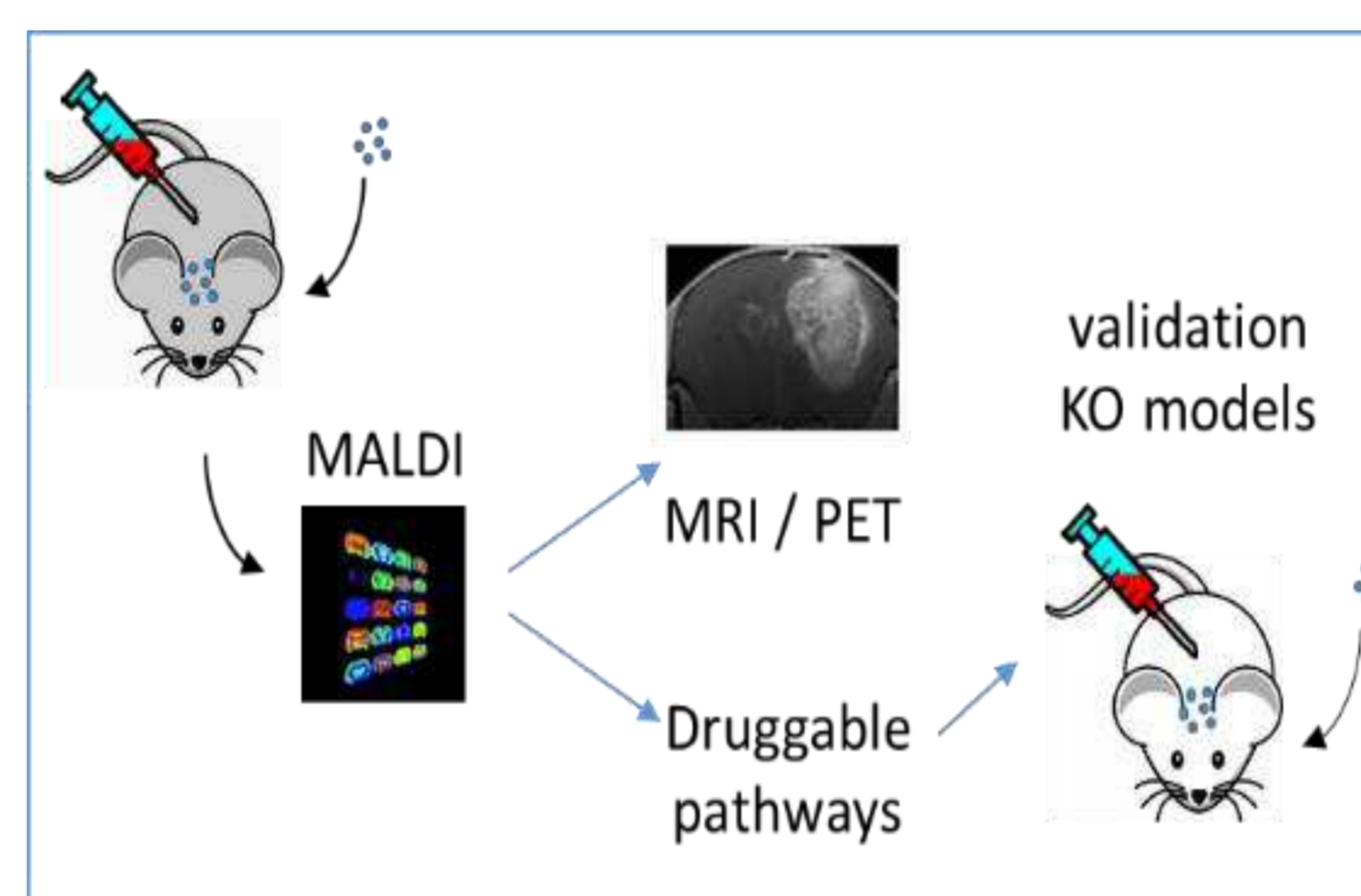
WORKFLOW

Task 1 –
Define immunological determinants of response and resistance to checkpoint blockade



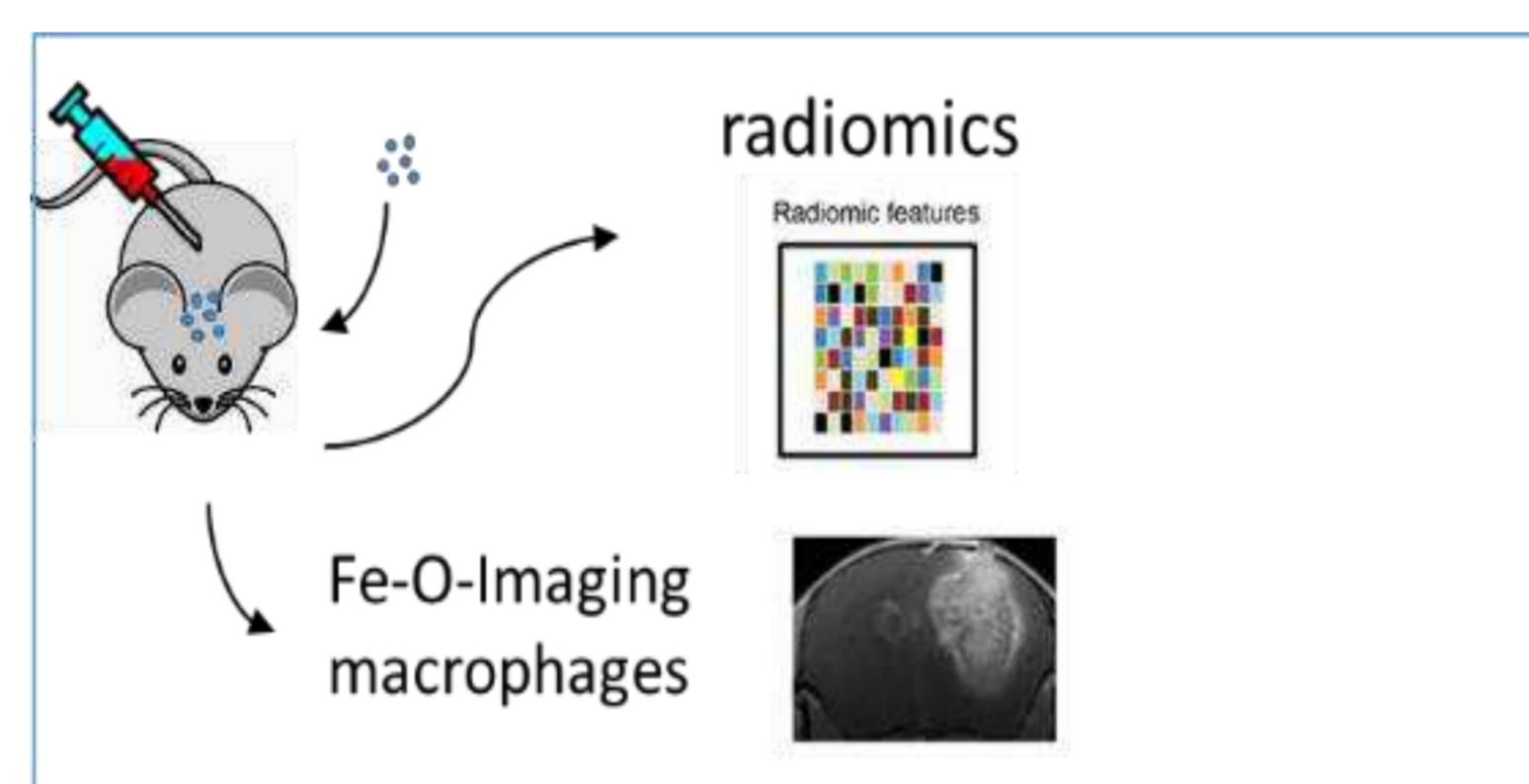
Define relevance of mutational load via CB in hypermutated GBM
a) Define antigens and TCR
b) Molecular and functional profiles of tumor-associated immune cell subsets

Task 2 –
Unravel metabolic determinants of response and resistance to checkpoint blockade



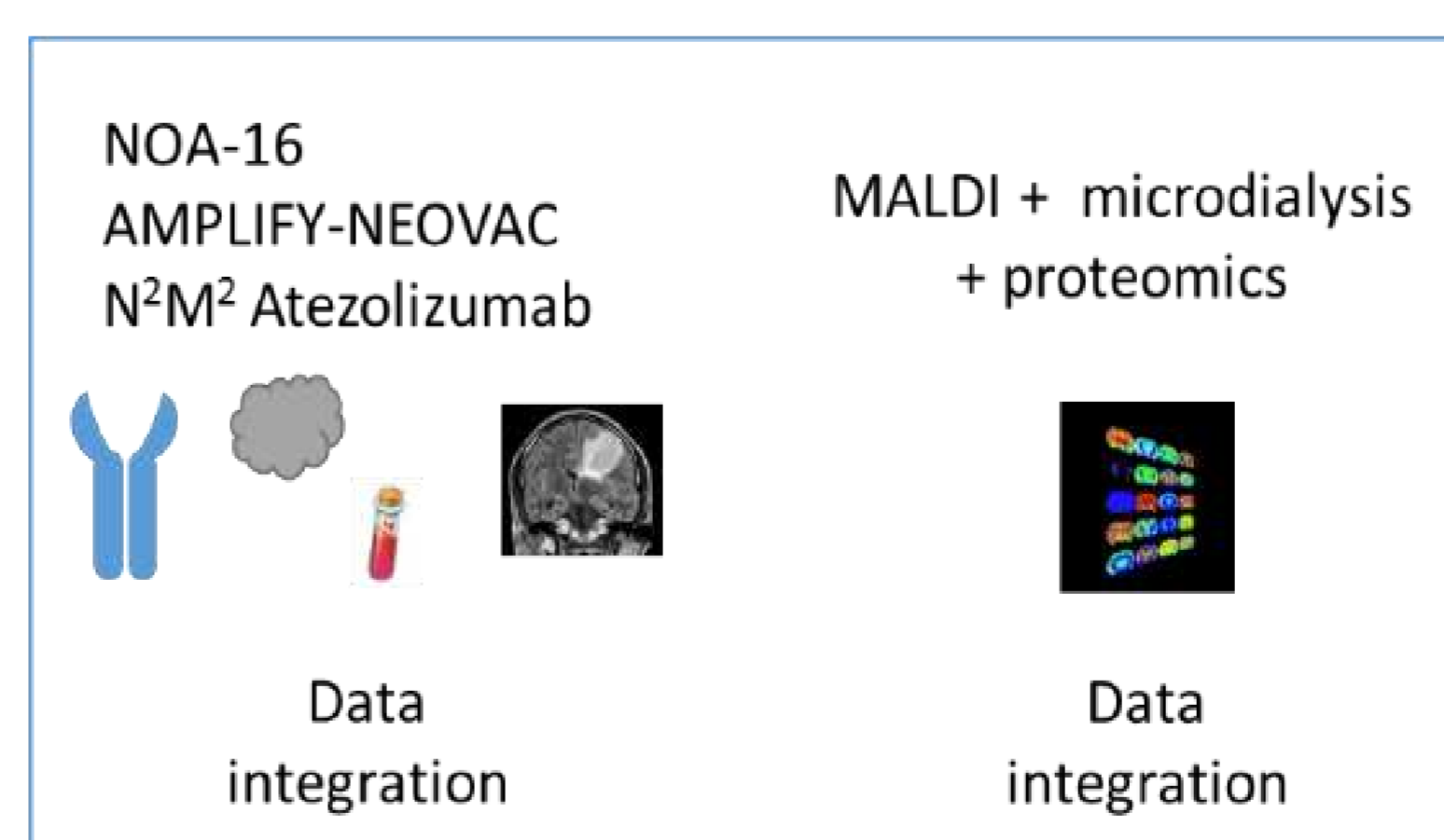
1. MALDI + microdialysis
2. Metabolic biomarkers for resist.
3. Response prediction, novel imaging, druggable pathways
4. Validation

Task 3 –
Define imaging biomarkers of response and resistance to checkpoint blockade



1. Iron oxide imaging to dissect role of macrophages
2. Radiomic profiling
3. Define predictive imaging parameter

Task 4 –
Validate biomarkers of response and resistance to checkpoint blockade in clinical trial cohorts



1. NOA-16: glioma-specific TCRs
2. AMPLIFY-NEOVAC + N2M2 Atezolizumab cohort
3. MALDI + microdialysis + proteomics
4. Refinement of resistance model

Multiparametric model of response and resistance to checkpoint blockade

Rational combinatorial strategies to overcome resistance to checkpoint blockade