

A03 – DECIPHERING RESISTANCE AGAINST TARGETED TREATMENTS

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SUMMARY

In this project, preclinical models and NCT Neuro MASTER Match (N²M²) study cohort-derived tissues of patients with newly diagnosed and recurrent glioblastoma will be used to decipher molecular, cellular and imaging determinants of response and resistance to precision treatments in glioblastoma. With this research, patient groups likely to benefit from a molecularly targeted intervention will be characterized, predictive biomarkers selected and prioritized, and parallel as well as subsequent treatments will be developed to enhance therapeutic benefit in selected molecularly defined subgroups.

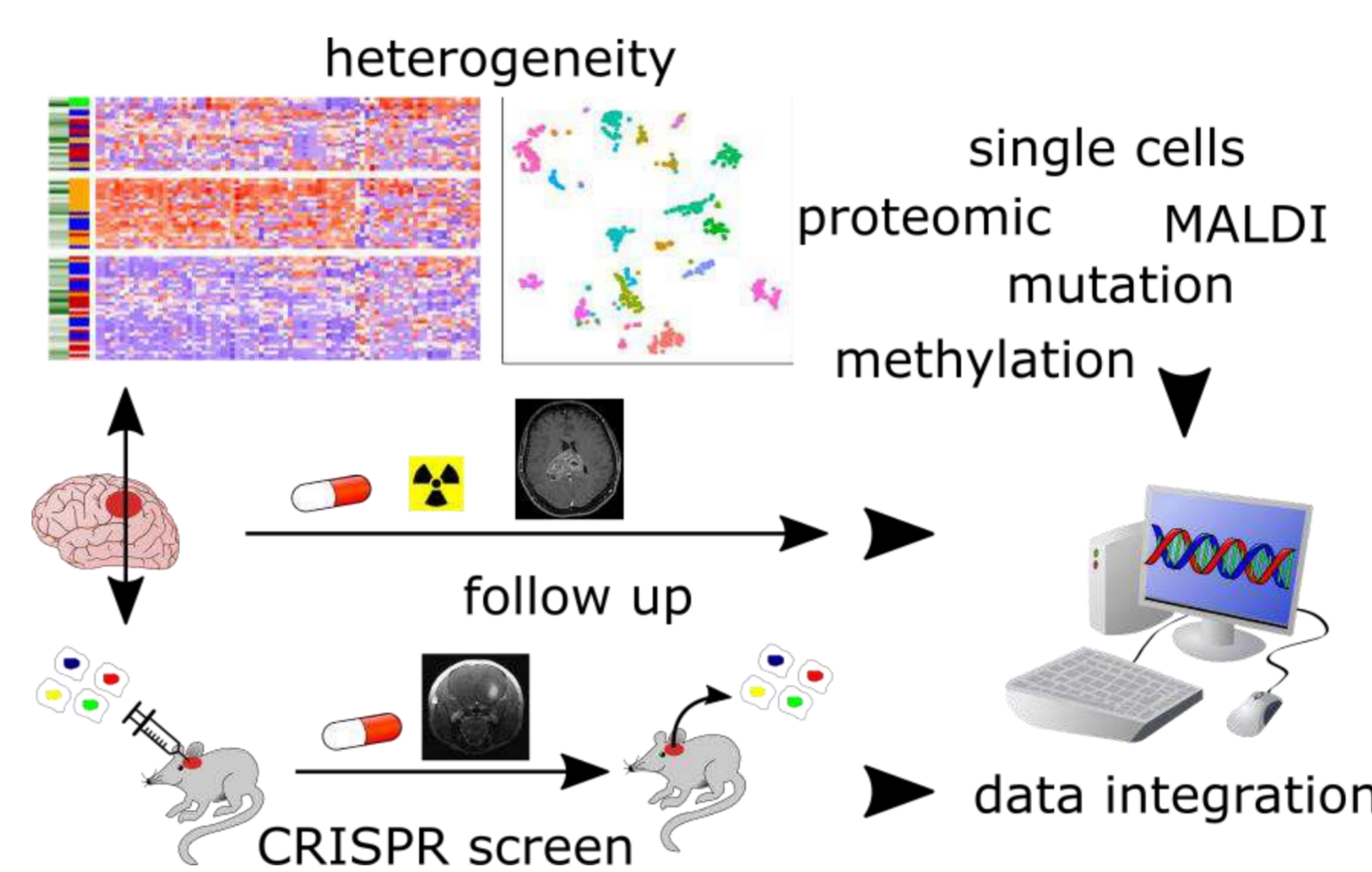
TASK

VISUAL ABSTRACT

WORKFLOW

Task 1 –

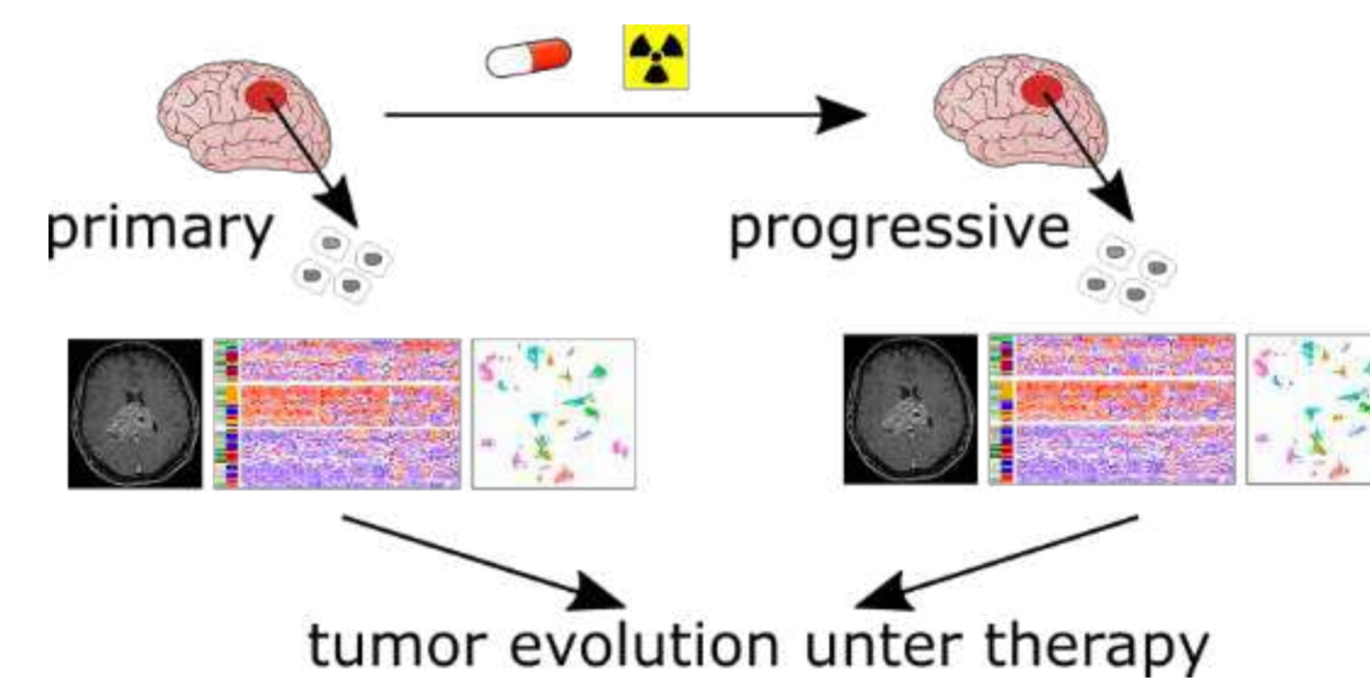
Discovering and understanding mechanisms underlying response and resistance in selected study cohorts and PDX models



1. Molecular, proteomic, metabolomic and single cell analysis of patient samples and PDX
2. Characterization of heterogeneity
3. CRISPR/Cas9 drug screening
4. Integrated data analysis for description of N²M² treatment resistance

Task 2 –

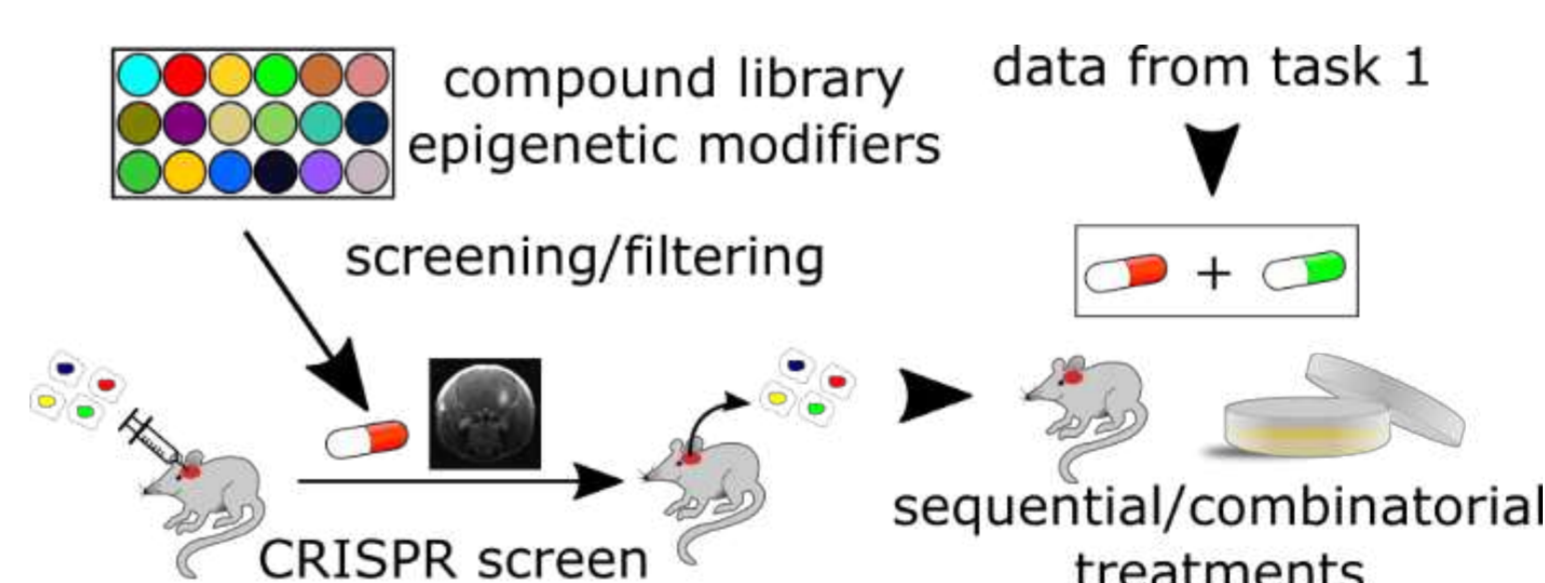
Analysis of primary and recurrent N²M² samples on molecular and radiomic level to study tumor evolution and resistance



1. Molecular, proteomic, metabolomic and imaging data of recurrent tumors after N²M² treatment
2. Identification of patterns of response and resistance against targeted treatments

Task 3 –

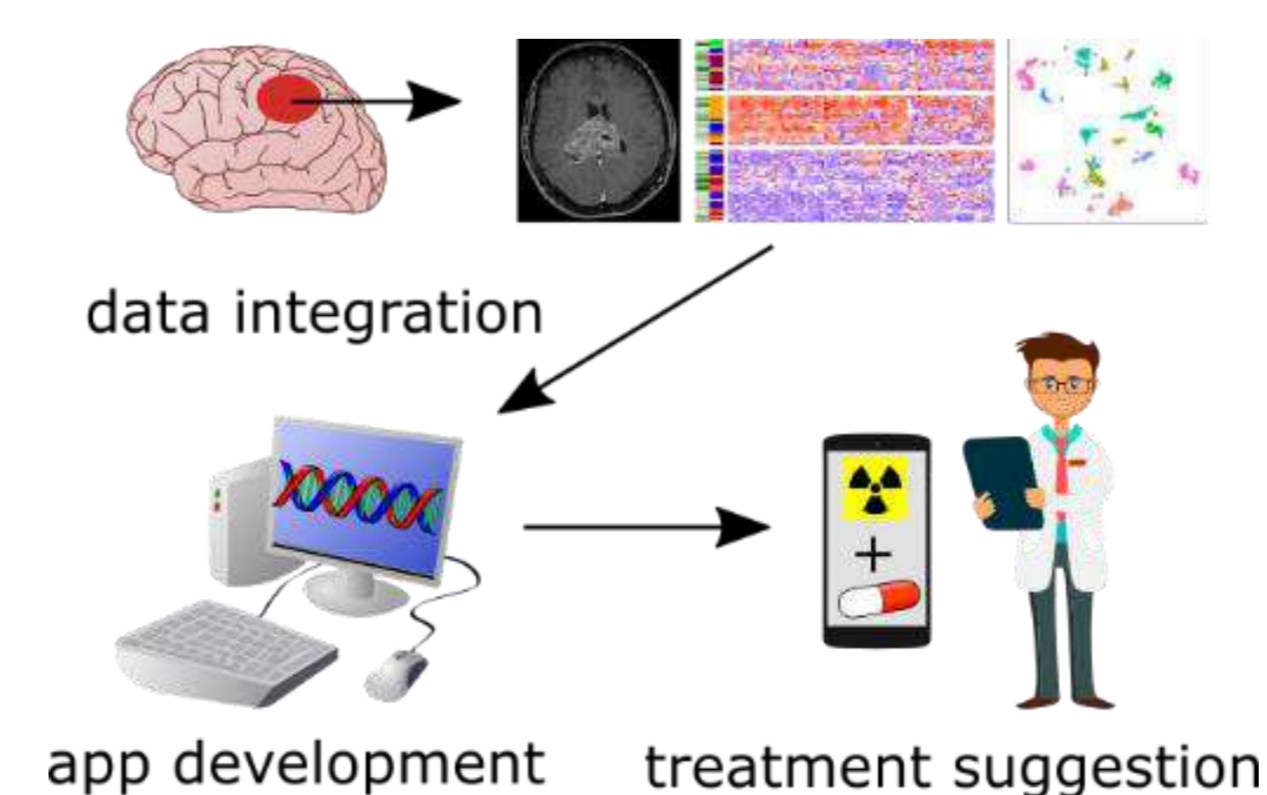
Development of sequential treatment algorithms and discovery of new targets



1. New compounds screening with focus on epigenetic modifiers
2. CRISPR/Cas9 screening to identify resistance markers against new agents
3. Testing of possible sequential treatments

Task 4 –

Developing a sensitivity/resistance molecular and imaging signature and implementation into a multiparametric algorithm for best treatment allocation



1. Literature review and data integration of tasks 1-3
2. Development of a treatment algorithm
3. Bioinformatic implementation into a clinical useful application