

B04 – IMPACT OF MYELOID CELLS ON THE ADAPTIVE IMMUNE RESPONSE IN IDH1-MUTANT GLIOBLASTOMAS

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SUMMARY

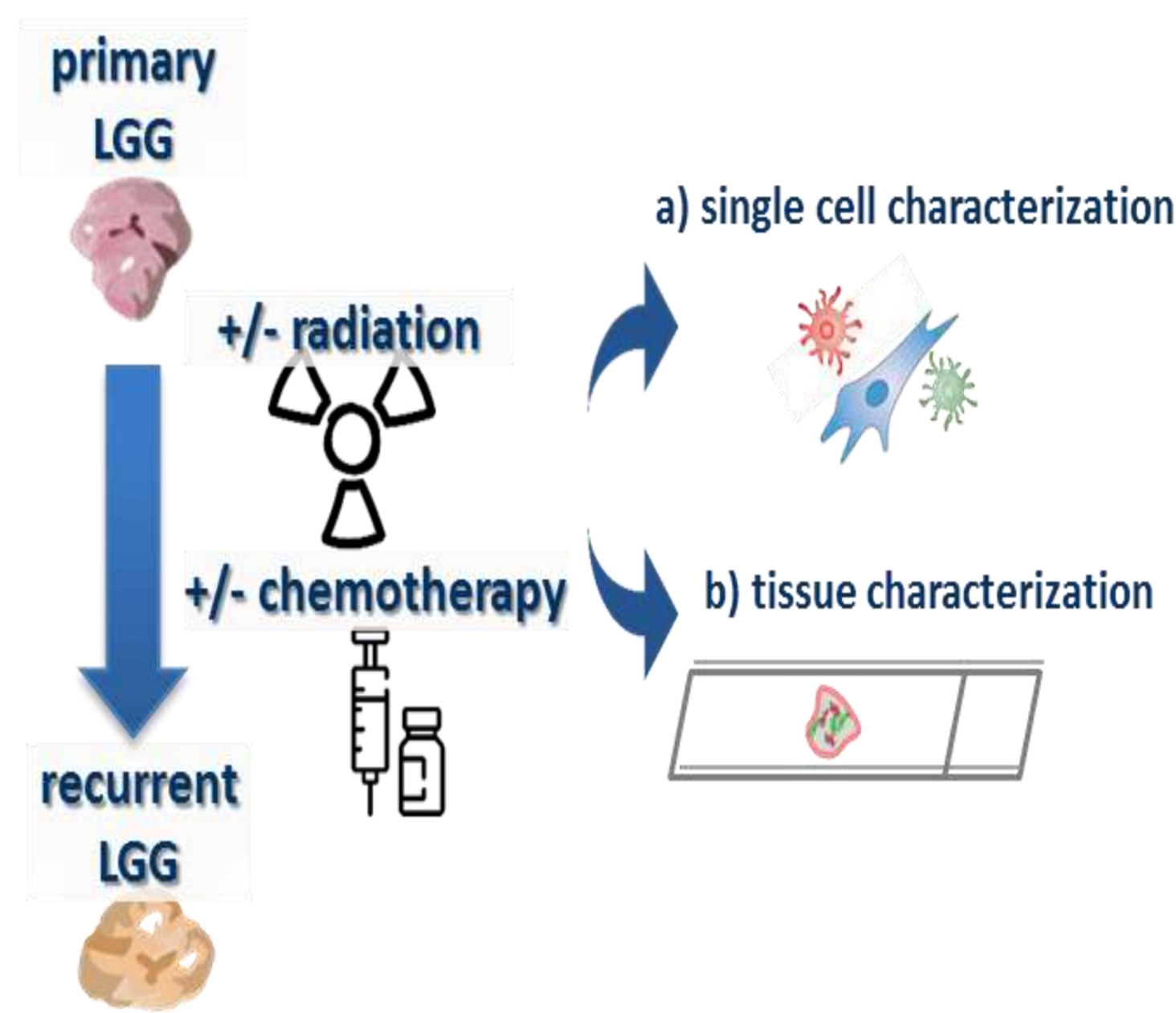
In this project, we will characterize the potential immunosuppressive role of myeloid cells for T-cell based immune response in *isocitrate dehydrogenase (IDH)1* mutant glioblastomas. We will particularly focus on radio- or chemotherapy-induced changes of the immune tumor microenvironment and how this can be improved pharmacologically. We hypothesize that influencing the composition of the intratumoral myeloid compartment might help to better control pre-existing and therapy-induced immunosuppression.

TASK

VISUAL ABSTRACT

WORKFLOW

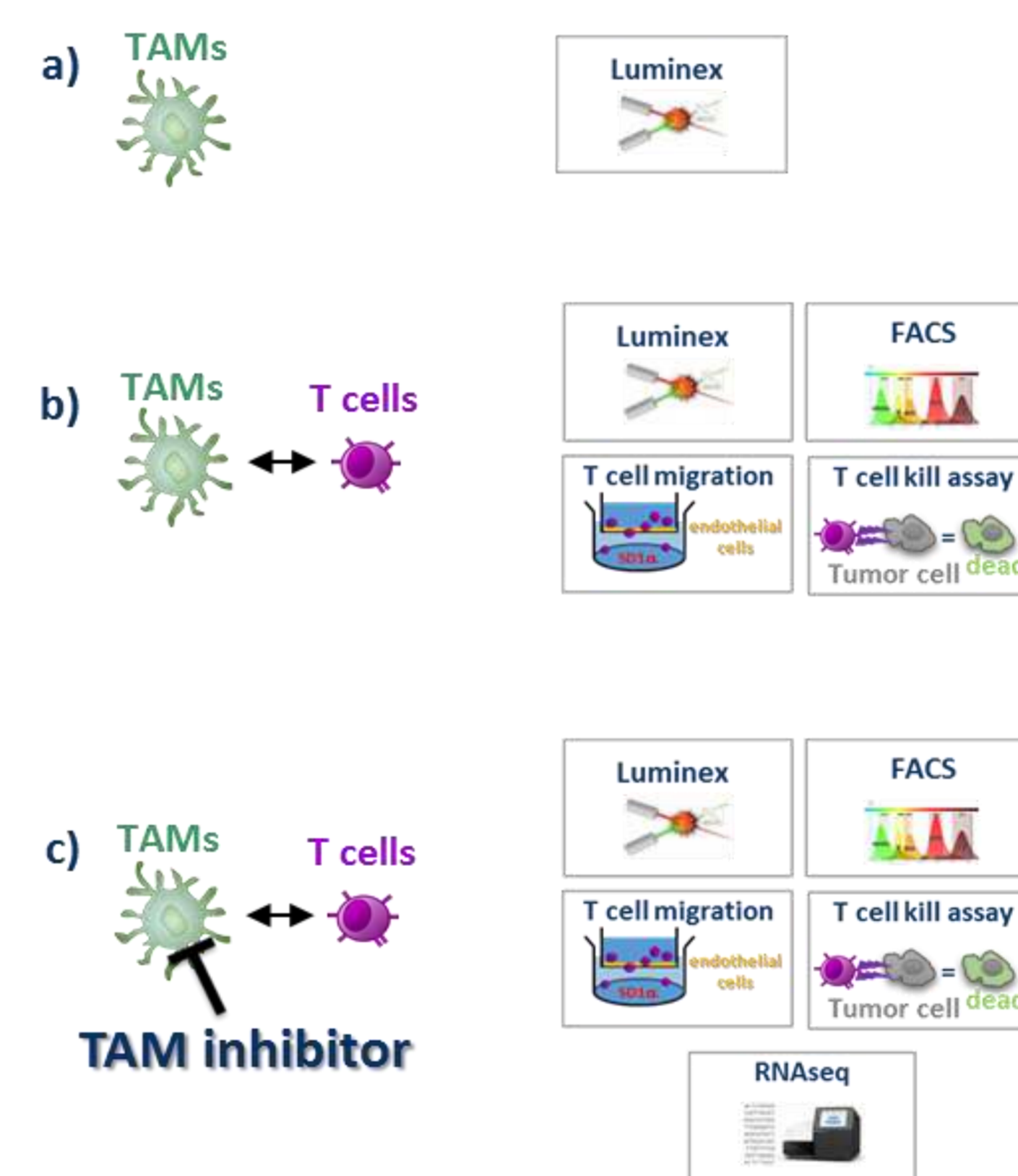
Task 1 –
Characterization of TAMs and TILs



IDH1mut newly diagnosed and recurrent glioma with/without RT or CT

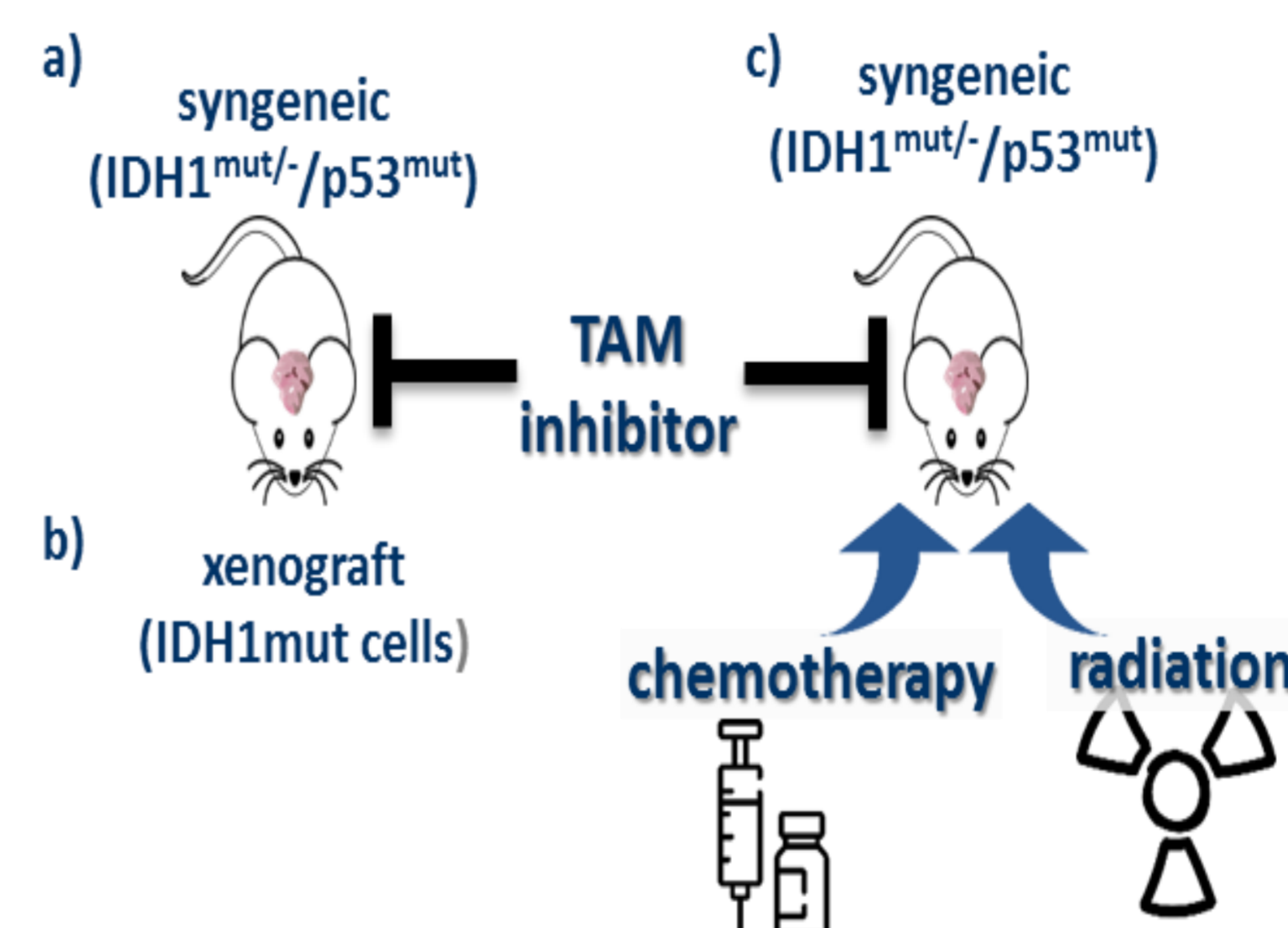
- a) cells
 - isolation of TAM, TIL, EC
 - scRNAseq
- b) tissues
 - multicolor IF stainings (TAM / TIL)
 - novel TAM / TIL subsets by IF or smFISH
 - RNAseq

Task 2 –
Functional role of TAMs *in vitro*



- a) TAM secretome
- b) TAM – T-cell interaction
 - TIL secretome / subset
 - T-cell transmigration
 - T-cell killing
- c) TAM targeting
 - TAM secretome / subset
 - TAM transcriptome
 - TIL phenotype
 - T cell functionality

Task 3 –
Testing of combination therapies *in vivo*



- a) syngeneic mouse model (IDH1mut) +/- TAMi
- b) xenograft mouse model (NCH551b) +/- TAMi
- c) syngeneic mouse model (IDH1mut) +/- TAMi; +/- RT; +/- CT

- analyze a, b, c:
- tumor growth
 - TAM / TIL composition
 - cytokine milieu
 - transcriptome