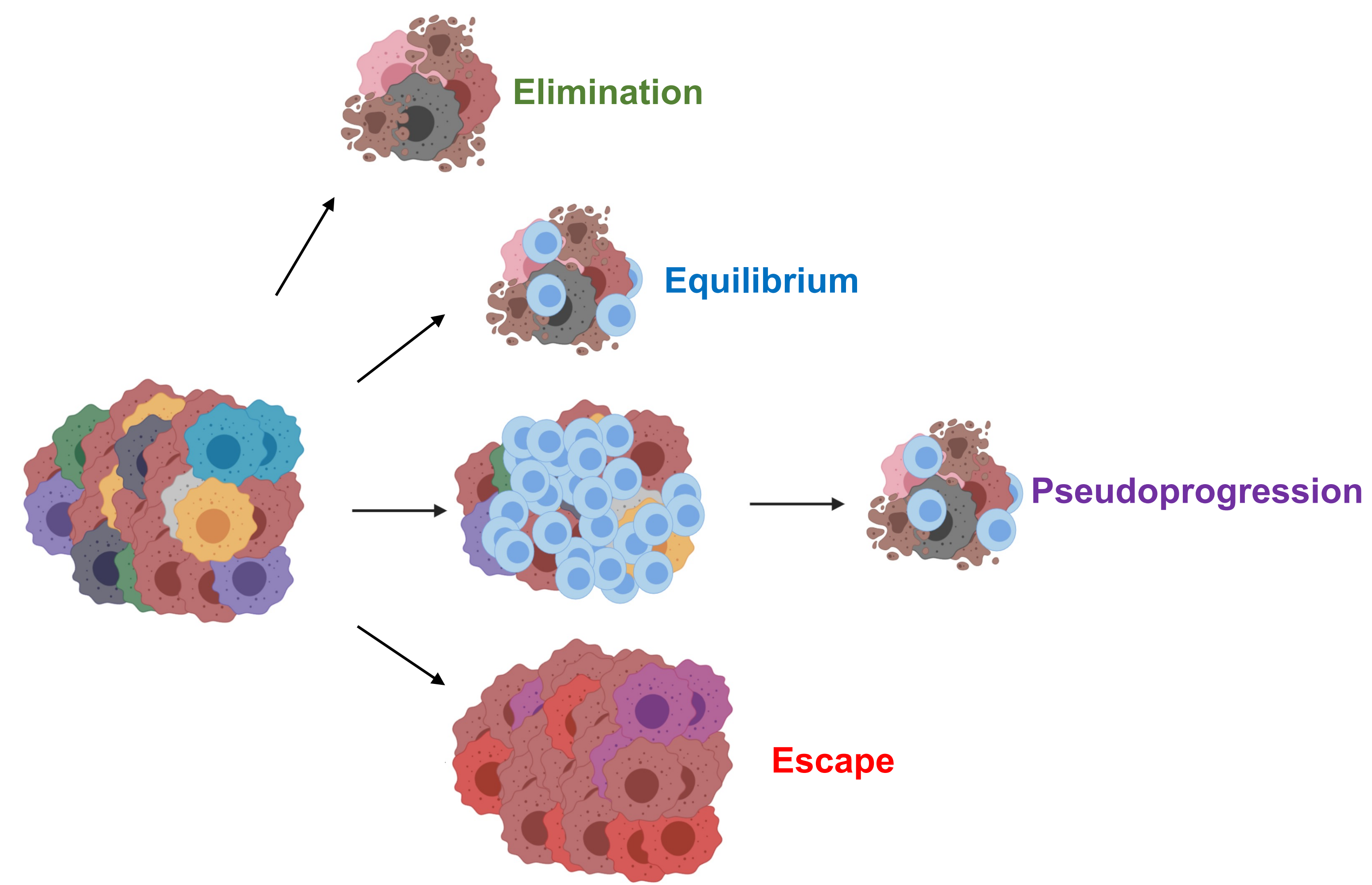


Background: Monitoring Response to Immunotherapy in HNSCC

Assessment of treatment response by standard RECIST or 'immune-sensitive' RECIST (iRECIST) criteria is confounded by the complex tumor-immune dynamics driven by ICI therapy. Unlike traditional cytotoxic therapies, which stereotypically reduce the size of sensitive tumors, ICIs can provoke a variety of responses:



- Elimination** - Immediate tumor rejection
- Equilibrium** - Grossly Stable Disease Burden
- Pseudoprogession** - Initial, Paradoxical Increase in Disease Burden Followed by Regression
- Escape** - Rapid Progression Secondary to Selection Against Immunogenic Tumor Clones with Promotion of Non-Immunogenic Clones

Clinical Relevance Mischaracterizing tumor response to ICI confounds management:

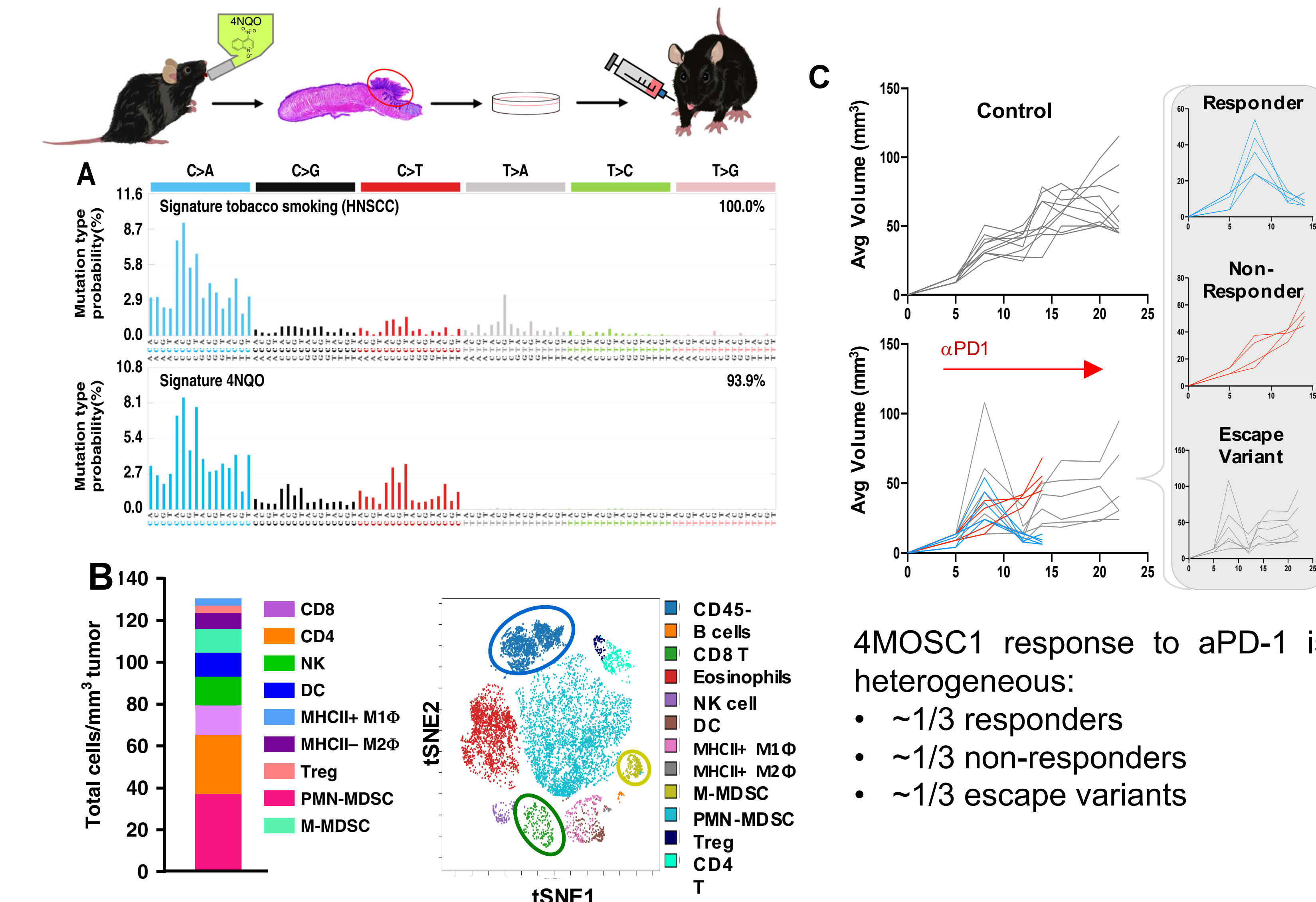
- Early discontinuation of therapy in responders
- Delayed reassignment in non-responders

There is an urgent need for reliable, non-invasive metrics of tumor response to ICI that do not depend on serial measurement of overall tumor burden.

Preclinical Model to Identify Novel Imaging Biomarkers of Treatment Response:

4MOSC (4NQO-murine oral squamous carcinoma) Model

4-nitroquinoline-1 oxide (4NQO) leads to DNA adduct formation and oral cancer with a (A) tobacco-signature mutanome, (B) immune infiltrate and (C) α PD-1 response as seen in human HNSCC.



Functional Imaging with Diffusion-Weighted MRI

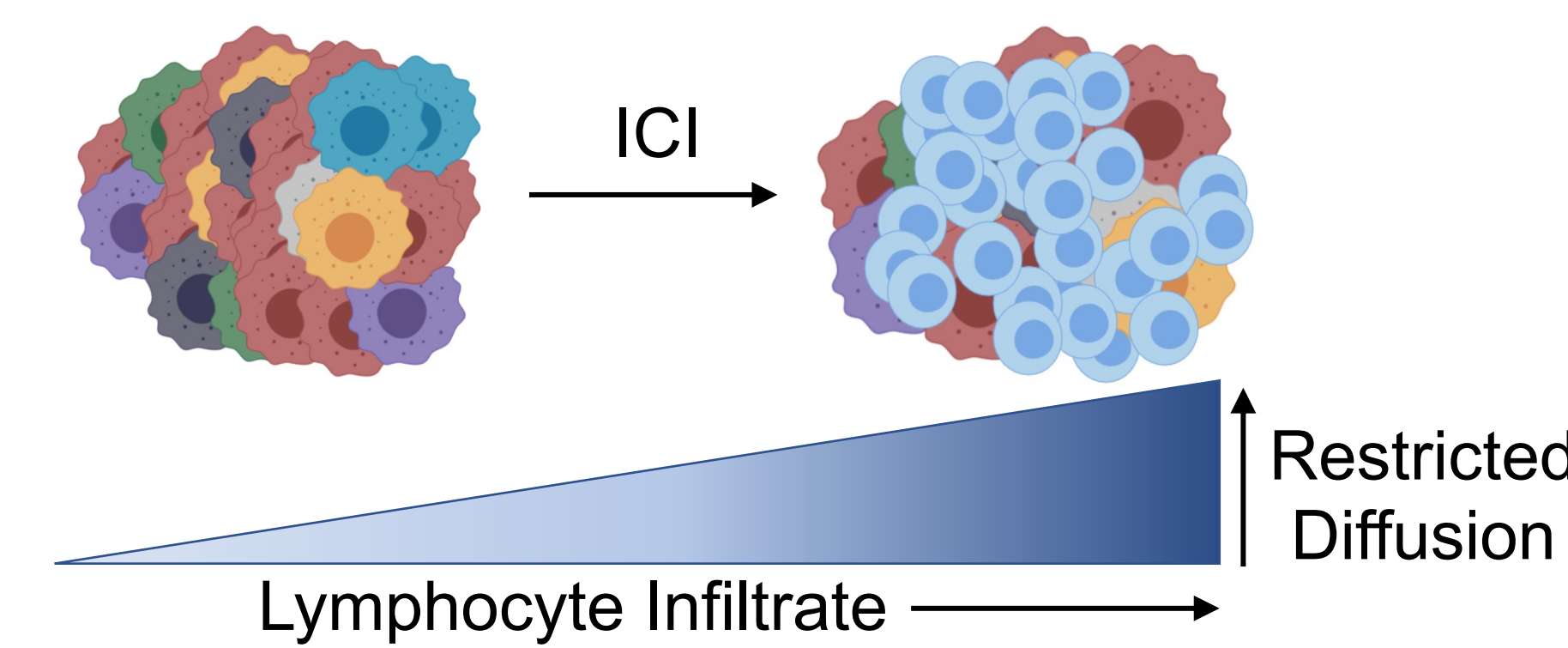
DW-MRI - related to the motion of water molecules within tissues - is sensitive to cellular composition and structural architecture.

- MRS3000, 3T small animal magnet
- 64 shot SE-EPI, 128x64
- Slice: 1mm



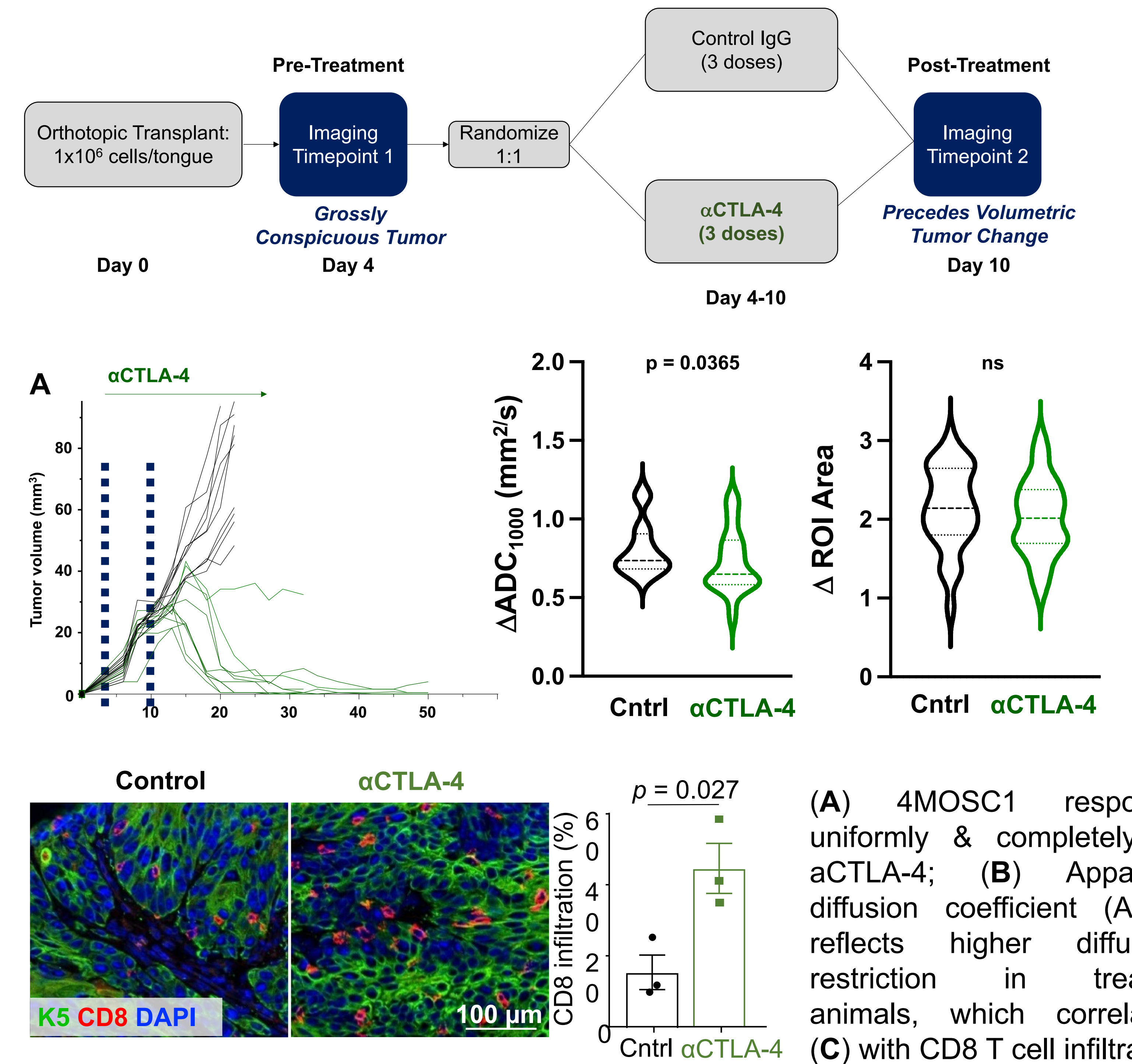
DW-MRI can serve as a non-invasive method to monitor tumor response to ICI.

Diffusion Correlate of Lymphocyte Infiltrate



Experimental Design and Results

Hypothesize that changes in intratumoral diffusion properties, measured by DW-MRI, predict tumor response to ICI before anatomical changes manifest.



Conclusions and Future Directions

- Novel Application of DW-MRI as a Surrogate for Intratumoral Lymphocyte Infiltration
- Development of a Non-invasive Functional Imaging Biomarker to Predict Tumor Response to ICI

Future Directions:

- Apply the DW-MRI Functional Imaging Biomarker to Predict the Heterogenous Tumor Response to α PD-1 in the 4MOSC1 Murine HNSCC Model
- Examine DW-MRI against Gold-Standard Biomarkers to Predict ICI-Response