PET Imaging of Glutamine Metabolism in a Colorectal Cancer Co-Clinical Trial

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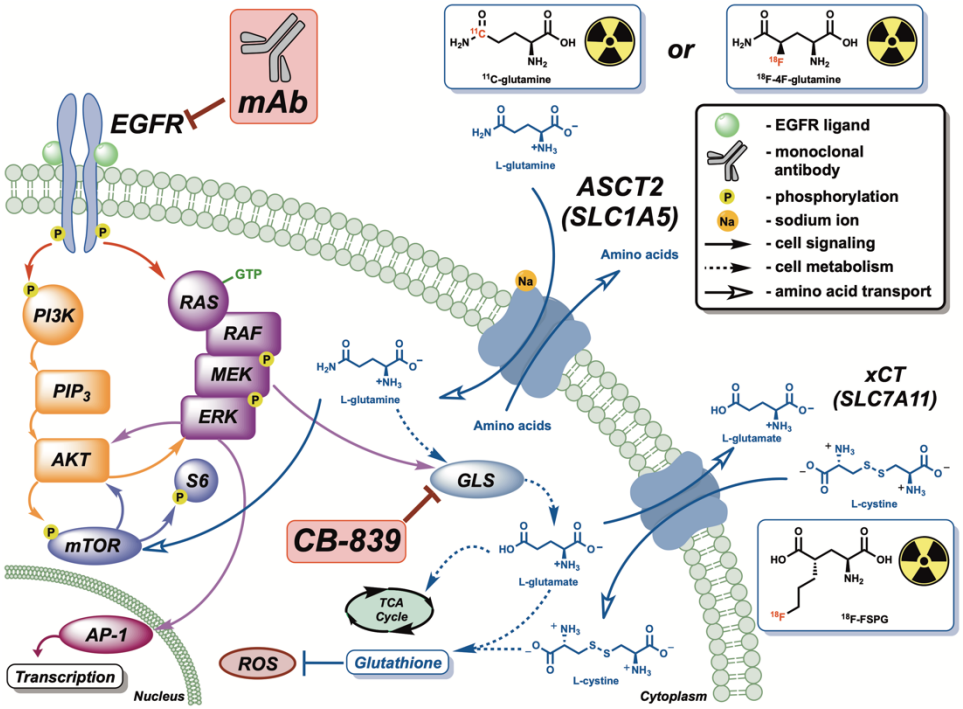

- Altered metabolism is a hallmark of cancer
- Glutamine is used as a carbon source for ATP production, biosynthesis, and as a defense against reactive oxygen species (ROS)
- Glutaminase is a mitochondrial enzyme responsible for catalyzing the conversion of glutamine to glutamate; GLS1 is the predominant isoform expressed in tumor cells
- Epidermal growth factor receptor (EGFR) neutralizing monoclonal antibodies (ie. cetuximab and panitumumab) are approved for treatment of advanced wild-type (*WT*) *RAS* CRC; however, resistance is common
- Non-invasive imaging could enable selection of responders and allow for early detection of therapeutic response

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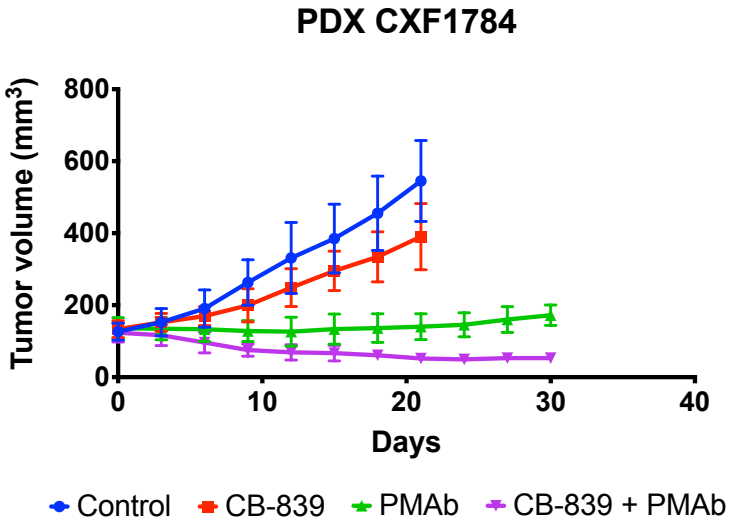
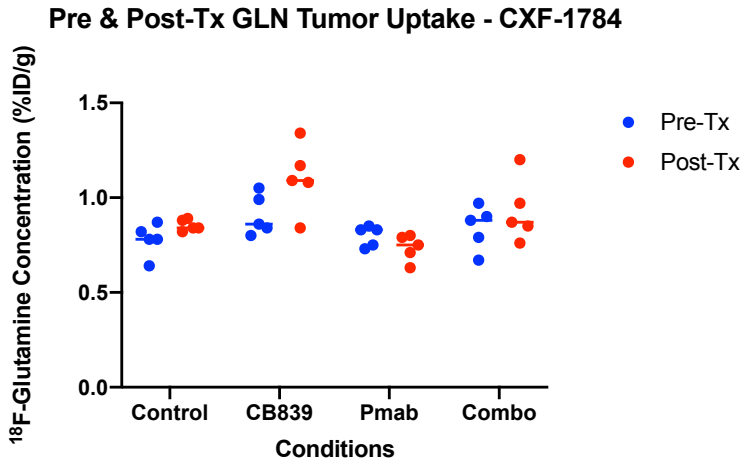
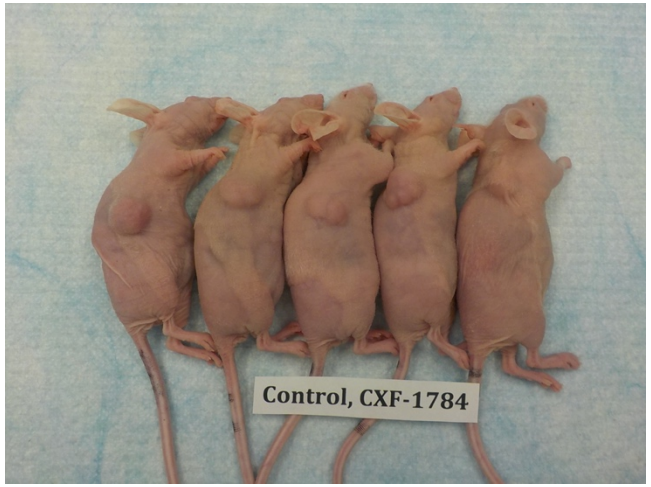
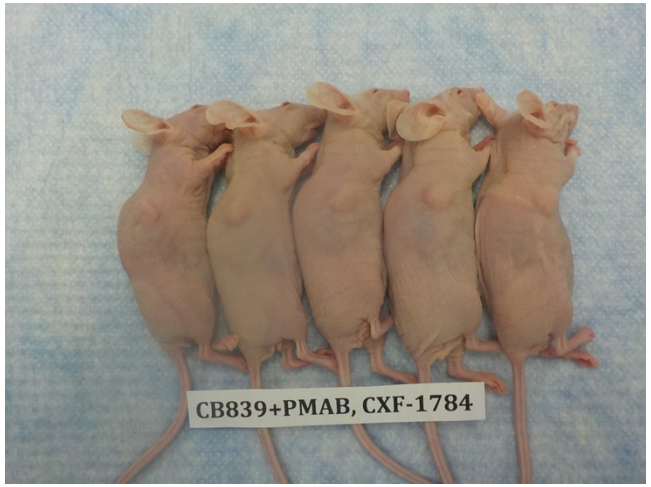
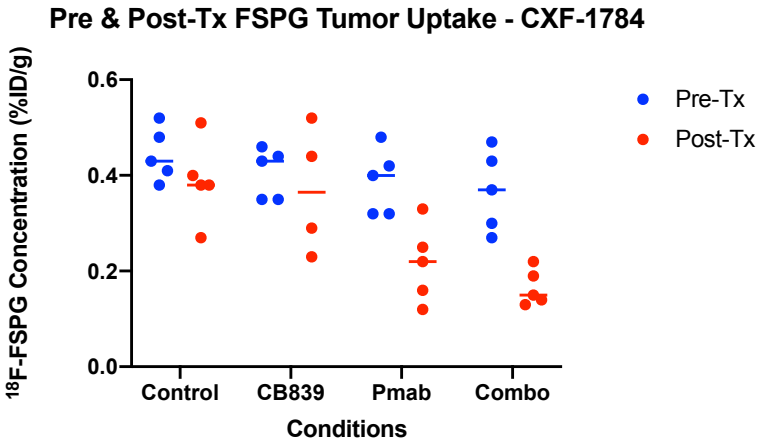
PET Imaging of Glutamine Metabolism in a Colorectal Cancer Patient-derived Xenograft Model











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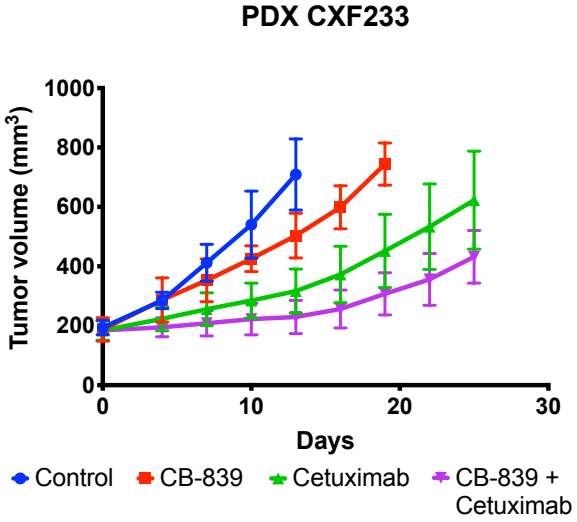

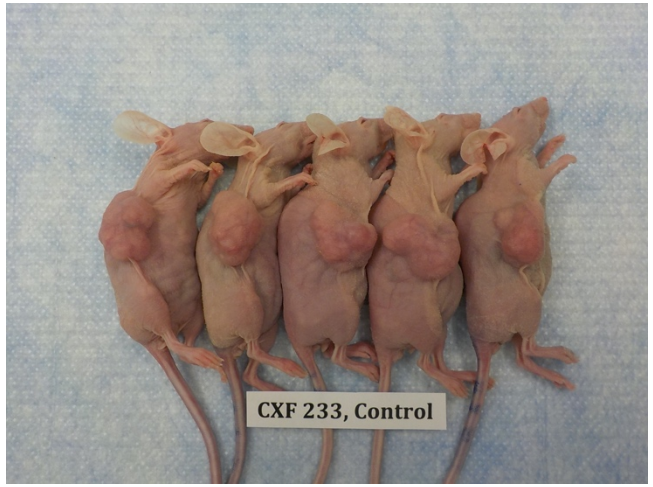

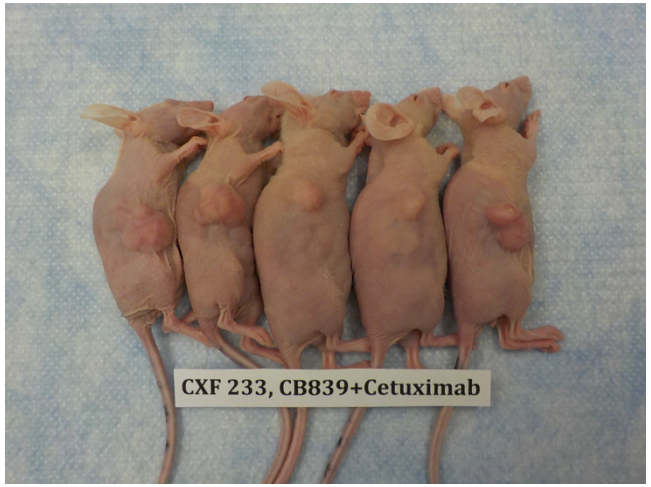

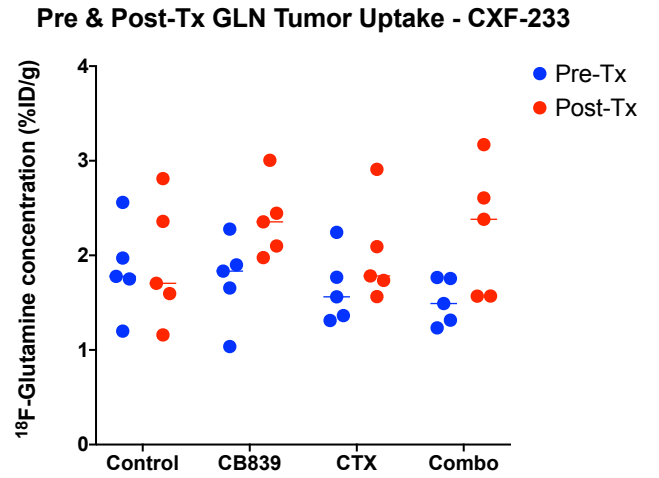

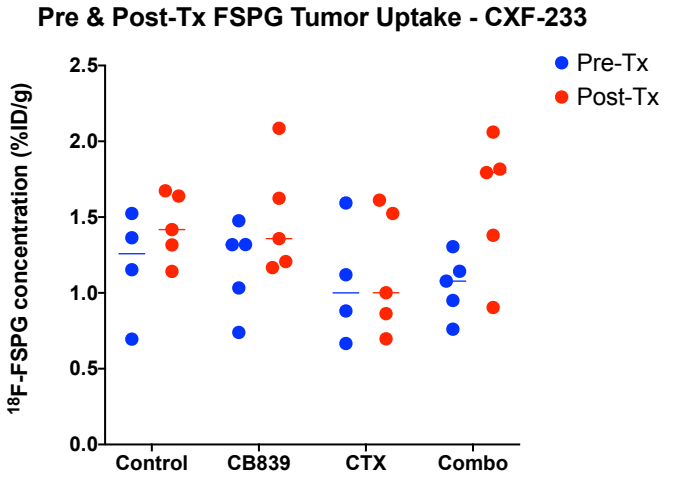

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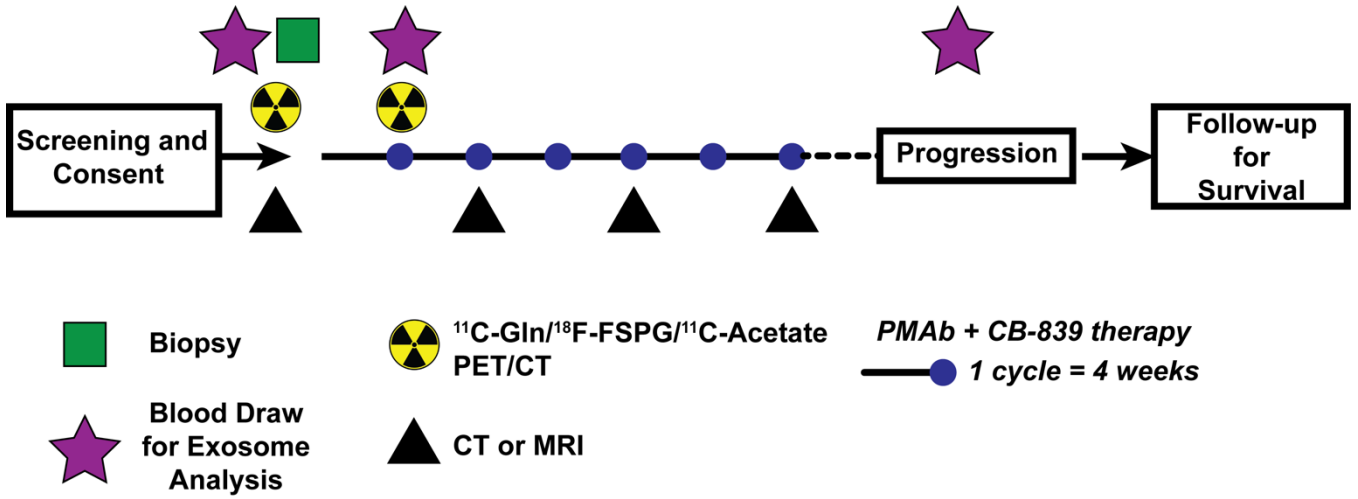
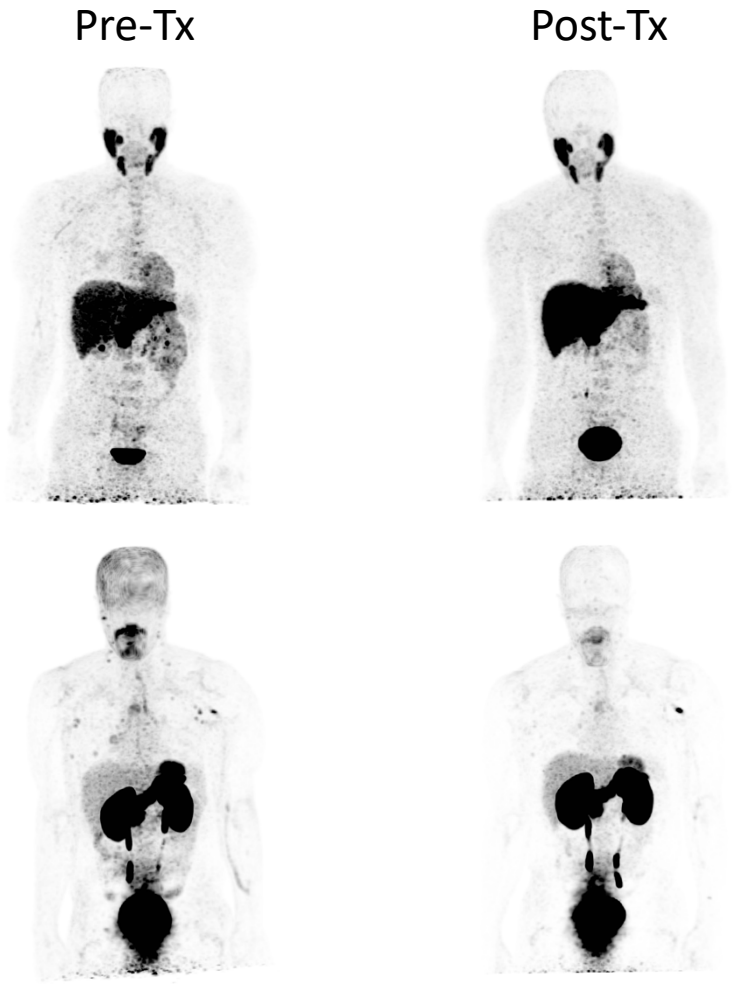
SELECT, PREDICT



Phase II clinical trial (NCT03263429)

- Patients with *RAS* wild-type metastatic colorectal cancer
- Achieved at least stable disease on prior anti-EGFR therapy

- 12 of planned 29 patients enrolled thus far on Phase II
- 5 have completed Pre- and Post-Tx imaging with both tracers



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Conclusions and Future Directions

- Combination of anti-EGFR mAbs and inhibitors of glutamine metabolism represents a new translational approach for treatment of colorectal cancer.
- Noninvasive PET imaging could be a biomarker to select patients likely to respond to treatment and to evaluate therapeutic efficacy.
- PET imaging with ^{11}C-glutamine/^{18}F-4F-glutamine and ^{18}F-FSPG represents a promising strategy for monitoring treatment.
- Preclinically we have evaluated the effect of CB-839 and anti-EGFR antibodies on PET imaging with these tracers in colorectal patient-derived xenograft models.
- PET imaging with ^{11}C-glutamine and ^{18}F-FSPG are also being utilized clinically.
- Future studies will further evaluate the relationship between PET imaging and treatment response as well as biological correlates (gene expression and immunohistochemistry).