FEATURED PUBLICATION

[18F]CFA as a Clinically Translatable Probe for PET imaging of Deoxycytidine Kinase Activity

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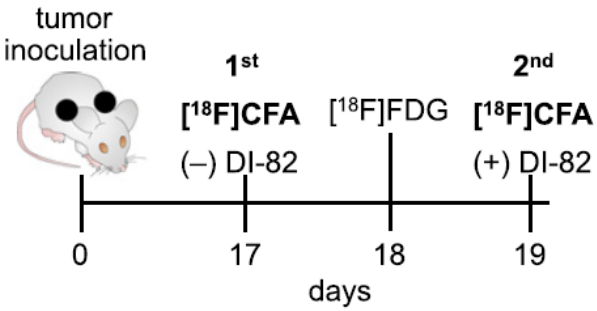
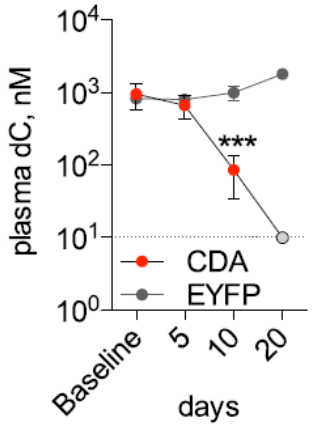
Enzyme deoxycytidine kinase (dCK) has been recognized as a new therapeutic target in hematological malignancies. Kim et al. have identified [18F]CFA is an exciting new Positron Emission Tomography (PET) probe for dCK. This allows [18F]CFA PET to become a new cancer biomarker for therapeutic interventions, treatment stratification and monitoring for hematological malignancies.



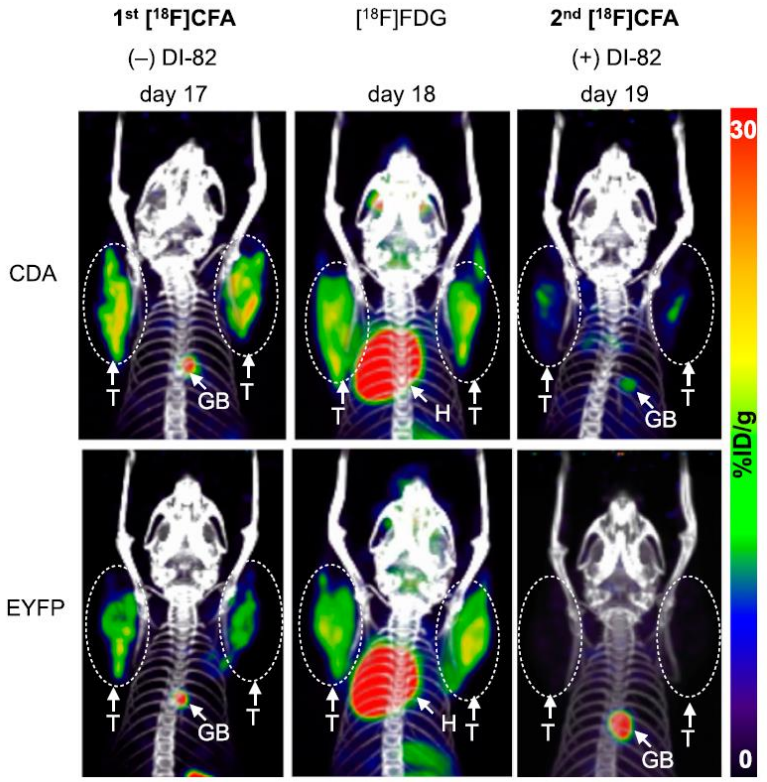


- dCK is a rate-limiting enzyme in the cytosolic deoxyribonucleoside (dN) salvage pathway. This pathway synthesizes deoxyribonucleoside triphosphates (dNTPs) which are required for accurate DNA replication.
- Kim et al. have identified [18F]Clofarabine; 2-chloro-2′-deoxy-2′-[18F]fluoro-9-β-D-arabinofuranosyl-adenine ([18F]CFA) as a new potential PET imaging tracer for the enzyme dCK.

Competition between PET probes for dCK and endogenous metabolites often reduces the sensitivity of PET assays. To investigate how cytidine deaminase (CDA) expression influences CFA accumulation, mice bearing bilateral tumors expressing CDA or a negative control (EYFP) were serially imaged with PET (G8 PET/CT Preclinical Imaging System, PerkinElmer and Sofie Biosciences) with [18F]CFA (day 17), with [18F]FDG (day 18), and then again with [18F]CFA on day 19, 2 hours after treatment with DI-82 (a dCK inhibitor). CDA tumors had reduced plasma deoxycytidine (dC) concentrations (CFA accumulation is inhibited in a dose-dependent manner by dC, the physiological substrate of dCK) that decreased with time in mice with CDA tumors but not EYFP tumors.

- Mice bearing CDA tumors accumulated significantly more [18F]CFA than mice bearing EYFP tumors, as indicated by day 17 PET scans. [18F]FDG PET scans performed on day 18 revealed similar metabolic activity in both CDA and EYFP tumors. On day 19, mice were treated with DI-82 followed by a second [18F]CFA PET scan, which confirmed that tumor probe accumulation was dCK-dependent. (Key: T, tumor; GB, gallbladder; H, heart; %ID/g, percentage injected dose per gram)
- Results indicate that competition with endogenous dC reduces the sensitivity of [18F]CFA PET imaging and tumor [18F]CFA accumulation in vivo requires dCK activity.

Preclinical PET imaging may be used to validate the translational capabilities of PET probes such as [18F]CFA for tissues with high dCK expression, e.g. hematopoietic bone marrow and secondary lymphoid organs.



Kim et al. (2016). [18F]CFA as a clinically translatable probe for PET imaging of deoxycytidine kinase activity.
PNAS, 15, 4027–4032, April 12, 2016.

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