

Redox cycling of iron powers various enzyme functions crucial for life, making the study of iron acquisition, storage, and disposition in the whole organism a worthy topic of inquiry. However, despite its important role in biology and disease, imaging iron in animals with oxidation-state specificity remains an outstanding problem in biology and medicine. Here we report a first-generation reactivity-based probe (termed  $^{18}\text{F}$ -TRX) of labile ferrous iron suitable for positron emission tomography studies in live animals. The responses of  $^{18}\text{F}$ -TRX to systemic changes in labile iron disposition were revealed using iron supplementation and sequestration treatments in mice, while the potential of this approach for in vivo imaging of cancer was demonstrated using genetically and pathologically diverse mouse models, including spontaneous tumors arising in a genetically engineered model of prostate cancer driven by loss of PTEN. Moreover, we show using orthotopic animal models that  $^{18}\text{F}$ -TRX may be very useful for the detection of high grade glioma. In summary, we report herein the first probe for nuclear imaging that can measure the concentration of a highly unstable, but biologically crucial, metabolite in vivo. This probe may have uses for detecting other disorders that require Fe(II), for example infectious or inflammatory diseases. Lastly, this probe may be very useful for identifying diseases that might be likely to respond to therapeutics that conditionally release toxic payloads using the same Fe(II) catalyzed chemistry.