Translocator Protein 18 kDa (TSPO), a Potential *In-Vivo* Biomarker of Space Radiation Induced CNS Injury

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The Guilarte laboratory has pioneered the validation and application of Translocator Protein 18 kDa (TSPO), formerly known as the peripheral benzodiazepine receptor (PBR), as an early, sensitive and predictive biomarker of brain injury, neuro-inflammation and neurodegeneration and has been a leader in determining the function of TSPO in glial cells. NASA seeks "*An approach…to extrapolate existing observations to possible cognitive changes, performance degradation, or late CNS effects in astronauts*. (Cucinotta, *et al.,* 2009). We believe non-invasive TSPO imaging may help provide a method and approach that could be utilized today, in pre-flight and post-flight testing of astronauts.

Our translational research has established that TSPO can be utilized to define specific regions of brain injury *in-vivo* using PET or SPECT imaging in both human subjects and animal models. We now have preliminary findings in rodent models that radiation exposure is correlated with temporal changes in TSPO expression in the brain. We hypothesize that specific brain regions and glial cell types are most susceptible to space radiation induced changes in TSPO expression and that dose related increases in TSPO expression precede and predict future specific regional neuropathology and neurodegeneration. Because of the limited availability of direct human epidemiological data for neurological risks arising from space travel, *in-vivo* TSPO imaging could provide an innovative new approach for determining quantitative risk estimates for cognitive or behavioral deficits and/or long-term CNS degenerative effects during long-term space flight. This approach also suggests a methodology for evaluating future neuroprotective pharmacological strategies specifically targeting this receptor to prevent or reduce CNS risk associated with space travel.

In summary: 1) TSPO is a validated biomarker of brain injury and inflammation, 2) it is the only biomarker of brain injury and inflammation that can be imaged and quantitatively measured in the living human brain using non-invasive techniques such as Positron Emission tomography (PET) and Single Photon Emission Computed tomography (SPECT) or in experimental animals such as mice, rats and non-human primates and 3) TSPO is actively being used as a biomarker of brain injury and inflammation for a number of human neurological and neurodegenerative diseases. These characteristics make TSPO an exceptional molecular biomarker of brain injury and inflammation that can also be used to assess recovery from injury and the effectiveness of therapeutic strategies. There is no other biomarker of brain injury and inflammation that possess all of these characteristics and strengths, notably the non-invasive imaging and quantification in the living human brain.

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