Targeting Mistranslation in Cancer and Neurodegenerative Disease Therapies

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A growing body of evidence suggests that failures in aminoacyl-tRNA editing lead to perturbation of protein homeostasis, damaging the cellular environment. Studies in human cells lines have shown that expression of editing-defective AARSs leads to changes in cell morphology, decreased vitality, protein misfolding, and apoptotic responses. In order to decipher these identified links between protein mistranslation and genome stability, a sensor capable of directly detecting mistranslation in the cells will be developed. This technology will allow the correlation of areas with translational errors and pathological origin, such as tRNA mischarging, DNA damage, and cell death. The ultimate super-EGEMs sensor will also be able to identify the linkage between mistranslation and oncogenesis. Through a combination of imaging, histology and signaling studies, we will define the extent to which mistranslation plays a role in the progression of DNA damage, cell death and tumorigenesis. An EQTV double mutant from the original EGFP showed a large shift in fluorescence intensity compared to wild type GFP. Testing fluorescence of cell lysate from transfected HEK 293T cells showed that expression of E222Q gave a 10-fold higher signal than EQTV. Transiently transfected 3T3 cells were also imaged and the fluorescence of E222Q and EQTV was quantified. As in cell lysate, EQTV cells showed lower fluorescence than E222Q. Similar fluorescence differences were also observed when EQTV and E222Q variants were imaged in live and fixed fish embryos. As the research is still being conducted, initial data supported that EQTV should serve as the targeted mutation of my ultimate mistranslation sensor.

Awards Won:

Third Award of $1,000