SYNTHESIS AND CHARACTERIZATION OF THE NEXT-GENERATION CALCIUM-SENSITIVE INFRARED FLUORESCENT INDICATORS

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Intracellular calcium (Ca^{2+}) plays a key regulatory role in the normal physiology of many cellular processes, including muscle contraction and nerve signaling. Spatial and temporal imaging of voltage-altering ions (such as Ca^{2+}) is made possible through voltage sensitive probes, molecules introduced inside the cell for the purpose of imaging the presence of these voltage-altering ions. Current probes have limited applications due to limited penetration of visible wavelengths through tissue. A series of genetically encoded calcium indicators (GECIs) has been engineering with variants of green fluorescent protein (GFP). While these GECIs have shown increased sensitivity to Ca^{2+} in the physiological range, they suffer from low transmittance through tissue, which limits imaging applications to only 7 mm depths of exposed tissue. Using standard molecular biology techniques, we have created a series of novel GECIs that bypass this limitation by modifying probes that emit in the infrared range. These new GECIs will allow for non-invasive *in vivo* imaging, as they will have significantly higher transmittance through tissue. Non-invasive imaging of calcium transients will have a large impact on cell culture imaging by providing an additional wavelength of probes in the molecular toolbox. This work also allows for the *in vivo* study of diseases linked to calcium activation, such as myocardial infarction.