S32-2 Detection of small molecules in living animals using Degraton probes

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Fluorescent Proteins show the fluorescence in the absence of exogenous substrates and cofactors, thus they are very useful for monitoring gene expression, localization of proteins and so on, even in living cells, and living transgenic animals. We have proposed a novel imaging technology termed "Degraton probe" based on conditionally regulated protein degradation. This technology was lead by our recent two findings. The red fluorescent protein DsRed1 from *Discosoma* coral showed weak fluorescence because of the ubiquitination and following rapid degradation by the proteasome in mammalian cells. However, tandemly linked dimer of DsRed1 showed bright fluorescence in mammalian cells because the dimer escaped the degradation by proteasome. Taking advantage of this dimerization-dependent stabilization of DsRed1 protein, we have developed new technique to detect protein-protein interactions in living mammalian cells as red fluorescence. The other finding is that fusion protein of a mutant tetracycline repressor (TetR) and EGFP is rapidly degraded through ubiquitin-proteasome pathway in the absence of doxycycline (dox) while the TetR-EGFP escapes the degradation in the presence of dox and shows high intensity of green fluorescence. Using this fusion protein as a probe, we can detect dox as green fluorescence.