Reporting amyloid beta levels *via* bioluminescence imaging with amyloid reservoirs

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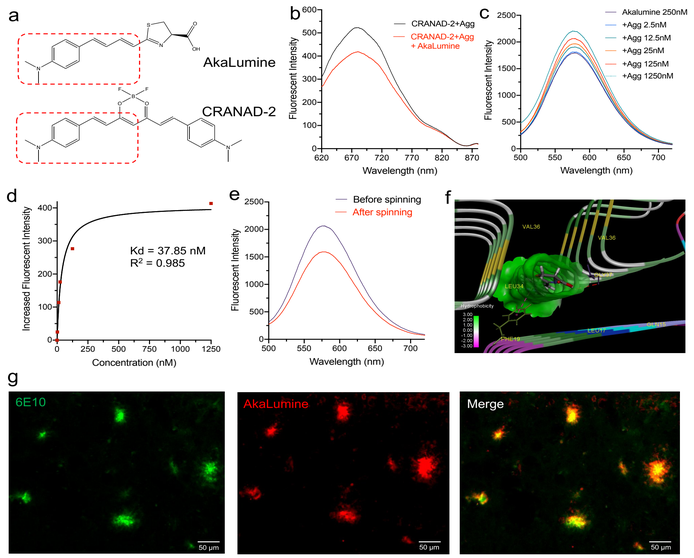
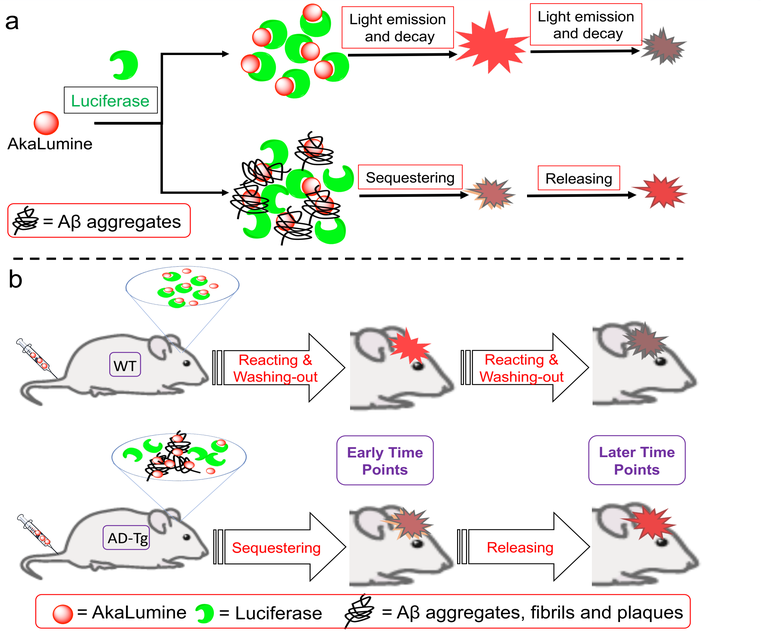
Background and Significance: Bioluminescence imaging has changed daily practice in preclinical research of cancers and other diseases in the last decades; however, it has been rarely applied in preclinical research of Alzheimer's disease (AD). In this report, we demonstrated that bioluminescence imaging could be used to report the levels of amyloid beta (Aβ) species in vivo. We hypothesized that AkaLumine, a newly discovered substrate for luciferase, could bind to Aβ aggregates and plaques. We further speculated that the Aβ species have the reservoir capacity to sequester and release AkaLumine to control the bioluminescence intensity, which could be used to report the levels of Aβs. Our hypotheses have been validated *via in vitro* tests, mimic phantom imaging, and *in vivo* imaging using transgenic AD mice that were virally transduced with aka Luciferase (AkaLuc). As expected, compared to the control group, we observed that the Aβ group showed lower bioluminescence intensity due to AkaLumine sequestering at early time points, while higher intensity due to AkaLumine releasing at later time points.

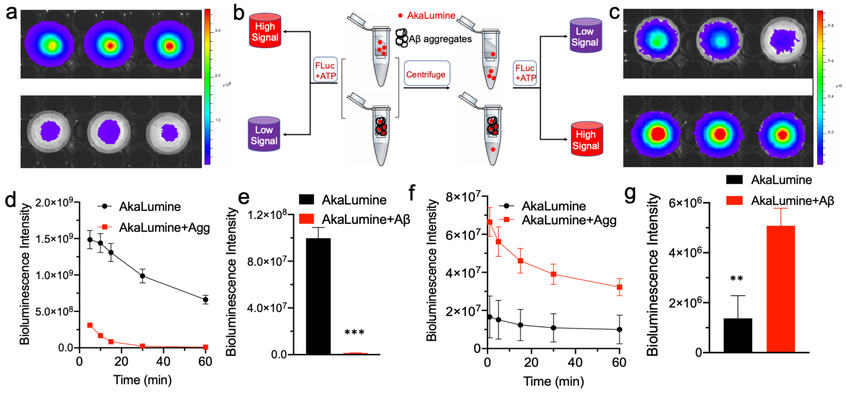
AkaLumine binds to Aβ aggregates and plaques



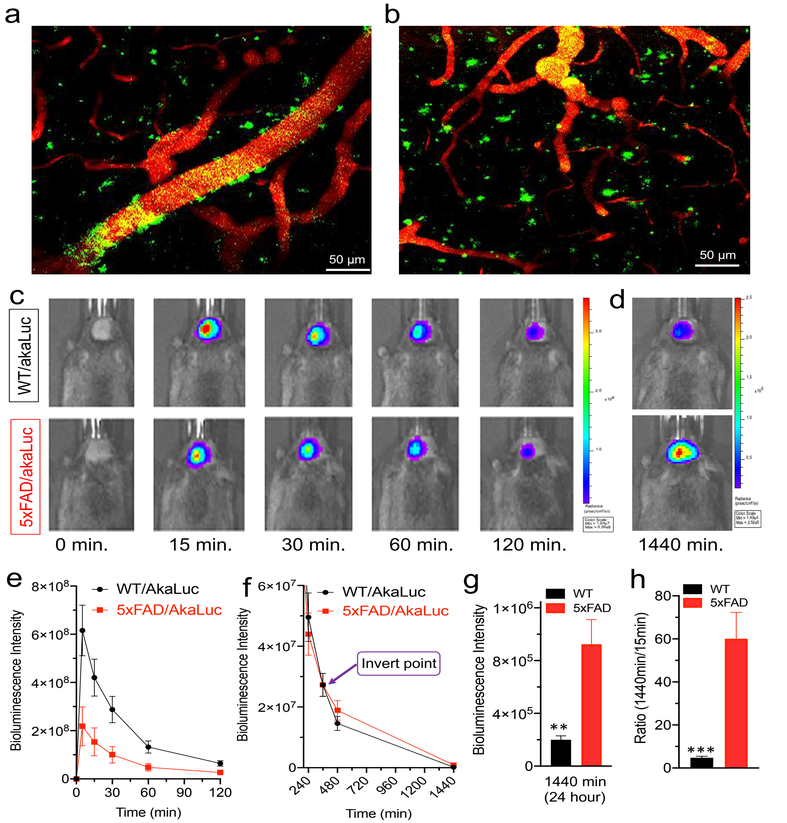
Principle of bioluminescence imaging with amyloid reservoir (BLIAR)



Validation of Aβ aggregates as reservoirs to sequester and release AkaLumine in solutions



In vivo two-photon microscopic fluorescence imaging and in vivo bioluminescence imaging with AkaLumine



Conclusion: In summary, we demonstrated the feasibility of bioluminescence imaging of Aβ species in vivo. Our method can be easily adapted by regular biology laboratories. We believe that this method has the potential to change the daily practice of preclinical AD research and will greatly assist AD drug discovery and development.

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