Aequorin and GFP: an historical account

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Aequorin and the green fluorescent protein (GFP) were discovered at the same time from the luminous jellyfish *Aequorea*, which displays a bright ring of green light upon stimulation. The luminescence is caused by the calcium-sensitive photoprotein aequorin and the green fluorescent protein (GFP). These two proteins were isolated, purified and cloned. Presently, both the proteins are widely used as important research tools, aequorin as a calcium indicator and GFP as a marker protein. I started the study of the *Aequorea* bioluminescence in 1961 with Dr. Frank H. Johnson. The extraction of aequorin from the light organs was difficult because we did not know that calcium triggers the luminescence of aequorin. The extraction was accomplished only after abandoning the concept of the luciferin-luciferase (substrate-enzyme) reaction. Once aequorin was extracted in a solution, it was a simple work to discover the role of calcium in the luminescence of aequorin. The structure determination of the luminophore of aequorin was a formidable task, because every treatment of aequorin caused an intramolecular reaction that triggers the self-destruction of luminophore. With many years of efforts, the structure of luminophore was finally determined from a fragment of the luminophore, helped by a similarity with the *Cypridina* luminescence system that I had previously studied. The structure determination of the GFP chromophore was accomplished also with the aid of the model compounds of *Cypridina* luciferin. The process of solving these problems and the advance in the understanding of aequorin and GFP are discussed.