Preface

It has been over four decades since a small group of investigators began making annual pilgrimages to the University of Washington's Friday Harbor Marine Laboratories to embark on studies that would ultimately elucidate the photochemistry responsible for the green light emitted by the crystal jellyfish (*Aequorea victoria* or *Aequorea aequorea*). The group included Frank Johnson (Princeton University), Osamu Shimomura (Princeton University and Woods Hole Oceanographic Institute), Milton Cormier (University of Georgia), and William Ward (then a postdoc with Milton Cormier, now at Rutgers University). Recently, William Ward reminisced to us about his summers spent collecting jellyfish:

> Milt Cormier had great scientific instincts, and before any of the rest of us had the vision, he was convinced of great biochemical similarities between bioluminescent components of the sea pansy and the jellyfish. Soon after joining the Cormier lab in 1973, I was assigned the project of purifying and characterizing green-fluorescent protein (GFP) from the sea pansy *Renilla*. It was to validate Milt's intuitions that I was sent to Friday Harbor in 1975 to collect jellyfish.
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> Every day, at sun-up, the team "hit the floating docks" with their collection of pool skimming nets and dozens of 6-gallon utility pails. The pails were immediately filled with seawater and placed at intervals along the floating docks. No time was wasted as the team quickly began scooping up the jellies and plopping them into buckets—up to 10,000 jellyfish collected each day. The parade of workers carrying pairs of buckets from the docks to the lab always reminded me of the Disney cartoon version of the *Sorcerer's Apprentice*, starring Mickey Mouse. Little did I know, back in 1975, that for 16 additional seasons, I would return to jellyfish "heaven". So much did I enjoy working with bioluminescence, that I chose to make this field of biochemistry my life's work.

Together they caught over a million jellyfish and spent decades investigating the biochemical mechanisms responsible for jellyfish bioluminescence. A crucial event occurred in the 1980s when Douglas Prasher, also working with Milton Cormier, prepared a cDNA library from *Aequorea victoria* mRNA. He used this to obtain a single full-length clone that encoded the complete *Aequorea* GFP sequence. Since no information was available at the time regarding the biosynthetic pathway leading to the chromophore formation necessary for fluorescence, it was not possible to predict whether the jellyfish protein could be produced in other biological systems. Fortunately, it turned out that the GFP chromophore is part of the primary amino acid sequence and forms spontaneously without the need for additional cofactors (described in Parts I and II of this book).

With the demonstration that GFP still fluoresced when produced in other organisms, the astonishing potential of this genetically encoded protein as a tool for studies in cell biology, medicine, and physiology was realized. It is now recognized that the identification of GFP from *Aequorea* was the first step in what has often been described as a "revolution" in cell biology and was ultimately recognized by the 2008 Nobel Prize in Chemistry. What is more, again fulfilling Milton Cormier's intuitions, many other marine organisms were identified in the late 1990s, which produce proteins with amino acid similar to the

Aequorea GFP. Some of these GFP-like proteins have been cloned and engineered for live-cell imaging applications, providing the rainbow of FPs that are described in Part II of this book.

In Part III of this book, the authors present some of the unique applications of the FPs to cell biology. These applications include superresolution microscopy of cellular fine structures and Förster resonance energy transfer (FRET) microscopy to visualize protein interactions and cell-signaling activities inside living cells. The application photobleaching and photoactivation techniques to visualize protein behaviors are discussed, and techniques that exploit the plant and algal photoreceptors to enable light-regulated control of enzymatic activities are described. Finally, the application of FPs to the noninvasive imaging of tumor–host interactions in living animals is presented. We realize the field has grown rapidly and that it is impossible to do justice to all who have contributed to the development and application of many novel FPs. Most importantly, we thank all the authors who have contributed chapters to this book.

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