

# [Plant cell biology: with grand challenges come great possibilities](https://assignbuster.com/plant-cell-biology-with-grand-challenges-come-great-possibilities/)

[Health & Medicine](https://assignbuster.com/essay-subjects/health-n-medicine/)

The cell is the basic unit of life, and so it can be argued that cell biologists hold a special place amongst biological researchers in pursuing insight into the most fundamental aspect of what it means to be alive. Starting with the advent of light microscopy and the work of people such as Robert Hooke and Antonie van Leeuwenhoek in the 1600s, a whole new suite of questions as to the workings of the flora and fauna of the Earth flowed from observing biology at magnifications able to reveal its basic building blocks. Although [Hooke (1665)](#B15) originally coined the term “ cell” from the microscopic structure of cork, we now appreciate that all biology, be it a bacterium or an oak tree, shares the cellular basis of its function. This understanding has set the stage for cell biologists to explore some of the most essential questions in biology, such as what are the core features of cells that lie at the heart of life and how do these contrast with the unique aspects of the individual cellular functions that define each organism? Further, how do the interactions of cells with each other and with the environment lead to the diversity of life that is a hallmark of our planet. These are grand challenges not only for plant cell biology but for all biological sciences. Fortunately, we are being presented with an ever-expanding suite of tools and resources to approach some of these basic questions about cellular biology.

Cells are simultaneously characterized by order and by change; herein lies a central challenge for plant cell biology: to capture and explain both the structure and the dynamics of the processes that lead to cellular function. The advent of the era of green fluorescent protein (GFP) technology ( [Sanders and Jackson, 2009](#B24) ; [Zimmer, 2009](#B32) ) has greatly simplified many aspects of live cell imaging and made cell biological analysis accessible to a wide range of researchers. Gone are the days when GFP was simply a tag for following expression patterns and localization of a protein of interest. The color of GFPs now available spans much of the visible spectrum ( [Shaner et al., 2005](#B25) ), allowing for simultaneous labeling of multiple targets in the same cell ( [Stepanenko et al., 2008](#B26) ; [Chudakov et al., 2010](#B8) ). Rigorous techniques for assessing protein localization and interaction such as colocalization indices, fluorescence resonance energy transfer, and bimolecular fluorescence complementation ( [Zhang et al., 2002](#B31) ; [Giepmans et al., 2006](#B13) ; [Ohad et al., 2007](#B21) ; [Kerppola, 2009](#B18) ) are making it possible to bring analysis of, for example, the interactome into the context where it makes most sense to study it, the plant cell itself. GFPs have also been designed to be photoactivated or optically switched in color ( [Stepanenko et al., 2008](#B26) ; [Chudakov et al., 2010](#B8) ) allowing for the following of very complex dynamics within the cell. Other GFP-based sensors have been engineered to be sensitive to specific activities in their environment ranging from the levels of ions (such as Ca 2+ and pH; [Palmer and Tsien, 2006](#B23) ; [Bizzarri et al., 2009](#B3) ; [Swanson et al., 2011](#B27) ) and metabolites (e. g., glucose and glutamate; [Deuschle et al., 2005a](#B9) , [b](#B10) ) to the activity of specific protein kinases ( [Zhang and Allen, 2007](#B30) ), enabling visualization of the biochemistry, metabolism, and signaling within the living cell ( [Frommer et al., 2009](#B12) ). We are in the enviable position of being presented with an increasingly powerful toolkit with which to monitor and manipulate the activities of the living cell. These tools can provide the quantitative glimpse into cellular function upon which we can start to build testable models of plant cell structure and function.

In parallel to the expansion of GFP technology, there has also been a rapid increase in the accessibility to sophisticated cell biological equipment, such as the confocal microscope. Access to such facilities has revolutionized how many researchers approach characterization of their particular protein or process, moving many of the questions being asked into the cellular realm. The technology available to the cell biologist is also rapidly advancing and technical approaches that surpass the diffraction limit of resolution (approximately 200 nm), such as stimulated emission depletion microscopy, 4Pi microscopy, and structured illumination ( [Toomre and Bewersdorf, 2010](#B28) ) now push the boundaries of what we can resolve with the light microscope toward imaging of single molecules and nanometer resolutions. These approaches are opening up new ways to approach problems of molecular kinetics in the cell. The challenge here is to combine this unprecedented view of the dynamics of cells with the host of other approaches at our fingertips ranging from biochemistry and “ traditional” structural biology to approaches that provide a systems-level view of responses such as genomics, proteomics, and metabolomics. Integrating such measurements should help us take one step towards explaining the responses of the organism through cellular-level processes. This is indeed a grand challenge that will require a high-resolution model of cellular functions anchored in the spatial, temporal, and developmental realms. The limit to this comprehensive map of cellular effects is unlikely to be the computational resources to construct the framework of such a model but undoubtedly lies at present in our ability to generate the data sets of cellular processes to populate it.

A further challenge to our understanding of plant cell biology lies in the interactions between the plant and the environment. Plants monitor and respond to a wide array of endogenous and environmental signals. These are perceived by cellular receptors and translated into response first at the cellular level and then propagated throughout the plant as necessary. Recent work has made tremendous advances in the identification of a host of receptors for environmental and endogenous signals ranging from CO 2 sensing via carbonic anhydrase ( [Hu et al., 2010](#B16) ) to auxin perception by the TIR1 F-box protein ( [Calderon-Villalobos et al., 2010](#B5) ). Yet we are far from understanding how the plant senses many of the signals critical to its survival. Even for stimulus–response systems where we have well-defined receptors, the downstream regulatory networks are often poorly understood. For example, three stresses that are predicted to become increasingly important to plants as climate change drives weather to more seasonal extremes are temperature, drought, and flooding stress ( [Ahuja et al., 2010](#B1) ). Although there is a tremendous amount of data detailing plant responses to these factors ( [Kotak et al., 2007](#B19) ; [Ahuja et al., 2010](#B1) ; [Bailey-Serres and Voesenek, 2010](#B2) ; [Mittler and Blumwald, 2010](#B20) ), our knowledge about how these stresses trigger cellular processes, the molecular players that process this information, and then how this network is integrated into the whole plant response remains largely a mystery. Understanding these processes presents a grand challenge recognized by many fields of plant science (for example, see the grand challenges article in our sister journal Frontiers in Plant Physiology; [Frommer, 2010](#B11) ) and can clearly only be met by integrating between these various fields of research.

Indeed, cell biology provides the underpinnings of many other traditional disciplines of plant science such as plant physiology and development. There have been many important advances in our knowledge of cellular processes such as pollination biology and vegetative and reproductive development that blur these traditional distinctions of discipline within the field of plant sciences. Many researchers with interests in physiology and development are approaching their questions at the cellular level. For example, we now have a remarkably detailed model of the cellular events involved in regulating pollen tube growth ranging from ion transport and the cytoskeleton to regulatory networks of lipids, ROS, and G-proteins ( [Cheung and Wu, 2008](#B7) ) and are taking the first steps towards asking how such cellular processes play out in critical aspects of whole plant function such as fertilization and seed set ( [Palanivelu and Johnson, 2010](#B22) ; [Chae and Lord, 2011](#B6) ). Similarly, meristem development is now described at levels from transcriptional networks ( [Kaufmann et al., 2010](#B17) ) to cellular patterns of hormone trafficking ( [Ha et al., 2010](#B14) ; [Vernoux et al., 2010](#B29) ). Yet we are far from understanding these processes, especially in the context of integrating cellular activities to the physiological and developmental plasticity of the whole plant. These cellular processes provide landmarks upon which we can begin to layer the complex networks that provide the flexible response systems that characterize how plants respond to the environment.

One further very significant challenge that we can predict to become an ever more important practical question in the field of cell biology is how we will share the large cell biological datasets that underpin our work. These are often anchored in imaging data. The data are inevitably generated by a huge range of specialized equipment, and although images themselves are often in standard formats, the associated metadata is often not. Indeed, what metadata should be associated with each record is not agreed upon. Yet these data sets have the potential to be rich resources for future analysis, much as microarrays proved to be a key community resource once standards for annotation and archival were agreed upon ( [Brazma et al., 2001](#B4) ). There is ongoing development of the tools and approaches to aid in storage and sharing of imaging datasets, such as the open microscopy environment [1](#note1) and the Bio-Image Semantic Query User Environment (BISQUE) [2](#note2) but it will require the plant cell biology community as a whole to rise to the challenge of determining what we consider appropriate for annotation and archival.

Lastly as cell biologists, we produce some of the most engrossing and fascinating images of the workings of life, providing us with an opportunity to raise broad interest in the fundamentals of the plant sciences. For inspiration, we need look no further than Robert Hooke who published *Micrographia* in 1665. In this book he documented observations made with various magnifying glasses and captured the public’s imagination, making it a best-seller of the day. Indeed, the picture he presented of the intricacies of biology led his contemporary Samuel Pepys, a man who himself chronicled events such as the great fire and great plague of London, to call it “ the most ingenious book that I ever read in my life.” There are hundreds of modern day Hookes in plant cell biology labs throughout the world. Whether it be visualizing the dynamics of single molecules in the cell or mapping their function into the transcriptional, proteomic or metabolomic profile of the plant, modern cell researchers are truly providing the twenty-first century contributions to these “ ingenious” insights into the fundamentals of life.

## Footnotes

1. [^](#note1a) [www. openmicroscopy. org/site](http://www.openmicroscopy.org/site)
2. [^](#note2a) [http://www. bioimage. ucsb. edu](http://www.bioimage.ucsb.edu/)

## References

Ahuja, I., De Vos, R. C., Bones, A. M., and Hall, R. D. (2010). Plant molecular stress responses face climate change. *Trends Plant Sci.* 15, 664–674.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20846898) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20846898) | [CrossRef Full Text](http://dx.doi.org/10.1016/j.tplants.2010.08.002)

Bailey-Serres, J., and Voesenek, L. A. (2010). Life in the balance: a signaling network controlling survival of flooding. *Curr. Opin. Plant Biol.* 13, 489–494.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20813578) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20813578)

Bizzarri, R., Serresi, M., Luin, S., and Beltram, F. (2009). Green fluorescent protein based pH indicators for in vivo use: a review. *Anal. Bioanal. Chem.* 393, 1107–1122.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=19034433) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=19034433)

Brazma, A., Hingamp, P., Quackenbush, J., Sherlock, G., Spellman, P., Stoeckert, C., Aach, J., Ansorge, W., Ball, C. A., Causton, H. C., Gaasterland, T., Glenisson, P., Holstege, F. C., Kim, I. F., Markowitz, V., Matese, J. C., Parkinson, H., Robinson, A., Sarkans, U., Schulze-Kremer, S., Stewart, J., Taylor, R., Vilo, J., and Vingron, M. (2001). Minimum information about a microarray experiment (MIAME) – toward standards for microarray data. *Nat. Genet.* 29, 365–371.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=11726920) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=11726920)

Calderon-Villalobos, L. I., Tan, X., Zheng, N., and Estelle, M. (2010). Auxin perception – structural insights. *Cold Spring Harb. Perspect. Biol.* 2, a005546.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20504967) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20504967)

Chae, K., and Lord, E. M. (2011). Pollen tube growth and guidance: roles of small, secreted proteins. *Ann. Bot.* doi: 10. 1093/aob/mcr015. [Epub ahead of print].

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=21307038) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=21307038) | [CrossRef Full Text](http://dx.doi.org/10.1093/aob/mcr015)

Cheung, A. Y., and Wu, H. M. (2008). Structural and signaling networks for the polar cell growth machinery in pollen tubes. *Annu. Rev. Plant Biol.* 59, 547–572.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=18444907) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=18444907) | [CrossRef Full Text](http://dx.doi.org/10.1146/annurev.arplant.59.032607.092921)

Chudakov, D. M., Matz, M. V., Lukyanov, S., and Lukyanov, K. A. (2010). Fluorescent proteins and their applications in imaging living cells and tissues. *Physiol. Rev.* 90, 1103–1163.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20664080) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20664080)

Deuschle, K., Fehr, M., Hilpert, M., Lager, I., Lalonde, S., Looger, L. L., Okumoto, S., Persson, J., Schmidt, A., and Frommer, W. B. (2005a). Genetically encoded sensors for metabolites. *Cytometry A* 64, 3–9.

[CrossRef Full Text](http://dx.doi.org/10.1002/cyto.a.20119)

Deuschle, K., Okumoto, S., Fehr, M., Looger, L. L., Kozhukh, L., and Frommer, W. B. (2005b). Construction and optimization of a family of genetically encoded metabolite sensors by semirational protein engineering. *Protein Sci.* 14, 2304–2314.

[CrossRef Full Text](http://dx.doi.org/10.1110/ps.051508105)

Frommer, W. B. (2010). Grand opportunities in physiology to address the grand challenges facing the planet. *Front. Physio.* 1: 11. doi: 10. 3389/fphys. 2010. 00011

[CrossRef Full Text](http://dx.doi.org/10.3389/fphys.2010.00011)

Frommer, W. B., Davidson, M. W., and Campbell, R. E. (2009). Genetically encoded biosensors based on engineered fluorescent proteins. *Chem. Soc. Rev.* 38, 2833–2841.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=19771330) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=19771330)

Giepmans, B. N., Adams, S. R., Ellisman, M. H., and Tsien, R. Y. (2006). The fluorescent toolbox for assessing protein location and function. *Science* 312, 217–224.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=16614209) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=16614209) | [CrossRef Full Text](http://dx.doi.org/10.1126/science.1124618)

Ha, C. M., Jun, J. H., and Fletcher, J. C. (2010). Shoot apical meristem form and function. *Curr. Top. Dev. Biol.* 91, 103–140.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20705180) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20705180)

Hooke, R. (1665). *Micrographia: or Some Physiological Descriptions of Minute Bodies Made by Magnifying Glasses with Observations and Inquiries Thereupon* . London: The Royal Society.

Hu, H., Boisson-Dernier, A., Israelsson-Nordstrom, M., Bohmer, M., Xue, S., Ries, A., Godoski, J., Kuhn, J. M., and Schroeder, J. I. (2010). Carbonic anhydrases are upstream regulators of CO2-controlled stomatal movements in guard cells. *Nat. Cell Biol.* 12, 87–93.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20010812) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20010812)

Kaufmann, K., Pajoro, A., and Angenent, G. C. (2010). Regulation of transcription in plants: mechanisms controlling developmental switches. *Nat. Rev. Genet.* 11, 830–842.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=21063441) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=21063441)

Kerppola, T. K. (2009). Visualization of molecular interactions using bimolecular fluorescence complementation analysis: characteristics of protein fragment complementation. *Chem. Soc. Rev.* 38, 2876–2886.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=19771334) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=19771334)

Kotak, S., Larkindale, J., Lee, U., Von Koskull-Doring, P., Vierling, E., and Scharf, K. D. (2007). Complexity of the heat stress response in plants. *Curr. Opin. Plant Biol.* 10, 310–316.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17482504) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=17482504)

Mittler, R., and Blumwald, E. (2010). Genetic engineering for modern agriculture: challenges and perspectives. *Annu. Rev. Plant Biol.* 61, 443–462.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20192746) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20192746) | [CrossRef Full Text](http://dx.doi.org/10.1146/annurev-arplant-042809-112116)

Ohad, N., Shichrur, K., and Yalovsky, S. (2007). The analysis of protein–protein interactions in plants by bimolecular fluorescence complementation. *Plant Physiol.* 145, 1090–1099.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=18056859) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=18056859) | [CrossRef Full Text](http://dx.doi.org/10.1104/pp.107.107284)

Palanivelu, R., and Johnson, M. A. (2010). Functional genomics of pollen tube-pistil interactions in *Arabidopsis* . *Biochem. Soc. Trans.* 38, 593–597.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20298227) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20298227)

Palmer, A. E., and Tsien, R. Y. (2006). Measuring calcium signaling using genetically targetable fluorescent indicators. *Nat. Protoc.* 1, 1057–1065.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17406387) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=17406387) | [CrossRef Full Text](http://dx.doi.org/10.1038/nprot.2006.172)

Sanders, J. K., and Jackson, S. E. (2009). The discovery and development of the green fluorescent protein, GFP. *Chem. Soc. Rev.* 38, 2821–2822.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=19771328) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=19771328)

Shaner, N. C., Steinbach, P. A., and Tsien, R. Y. (2005). A guide to choosing fluorescent proteins. *Nat. Methods* 2, 905–909.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=16299475) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=16299475)

Stepanenko, O. V., Verkhusha, V. V., Kuznetsova, I. M., Uversky, V. N., and Turoverov, K. K. (2008). Fluorescent proteins as biomarkers and biosensors: throwing color lights on molecular and cellular processes. *Curr. Protein Pept. Sci.* 9, 338–369.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=18691124) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=18691124)

Swanson, S. J., Choi, W. G., Chanoca, A., and Gilroy, S. (2011). In vivo imaging of Ca2+, pH and reactive oxygen species using fluorescent probes in plants. *Annu. Rev. Plant Biol.* (in press).

Toomre, D., and Bewersdorf, J. (2010). A new wave of cellular imaging. *Annu. Rev. Cell Dev. Biol.* 26, 285–314.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20929313) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20929313)

Vernoux, T., Besnard, F., and Traas, J. (2010). Auxin at the shoot apical meristem. *Cold Spring Harb. Perspect. Biol.* 2, a001487.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=20452945) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=20452945)

Zhang, J., and Allen, M. D. (2007). FRET-based biosensors for protein kinases: illuminating the kinome. *Mol. Biosyst.* 3, 759–765.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17940658) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=17940658) | [CrossRef Full Text](http://dx.doi.org/10.1039/b706628g)

Zhang, J., Campbell, R. E., Ting, A. Y., and Tsien, R. Y. (2002). Creating new fluorescent probes for cell biology. *Nat. Rev. Mol. Cell Biol.* 3, 906–918.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=12461557) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=12461557)

Zimmer, M. (2009). GFP: from jellyfish to the Nobel prize and beyond. *Chem. Soc. Rev.* 38, 2823–2832.

[Pubmed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=19771329) | [Pubmed Full Text](http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?db=pubmed&cmd=prlinks&retmode=ref&id=19771329)