Tell us about your early days

I was born and brought up in a small fishing village on the coast of Northumberland in Northern England, called Cullercoats. It has a rich history of local culture and was home to a small artist’s colony in the late 19th century. I spent most of my spare time as a young boy on the beach, swimming in the cold North Sea, clambering over the rocks, and (somewhat perilously) climbing the cliffs. I can date the origin of my interest in science to hours spent examining and catching the varied marine wildlife in rock pools. I attended the nearby Tynemouth Grammar School, receiving a classical education, including Latin, physics, and chemistry. My lifelong interest in chemistry can be attributed to an excellent head chemistry master called Jack Garfoot. I attended Exeter University (over 400 miles away from home) to complete a B.Sc. Hons in chemistry. I then did an M.Sc in enzyme chemistry at the University of Kent at Canterbury, and completed my Ph.D. in synthetic organic chemistry at Trent University in Nottingham. My thesis was on the use of phenolic oxidative coupling to prepare new spirocyclohexadienones, and to elucidate the biosynthetic pathways of the secondary metabolites, isoquinoline alkaloids.

What was your first position after university?

After receiving my Ph.D., I did a series of post-doctoral fellowships in the United Kingdom. The first one was at the University of Ulster in Coleraine, Northern Ireland. Here I worked on the biosynthesis of echinulin. In 1980, I moved to Heriot-Watt University in Edinburgh, Scotland where I worked on the biosynthesis of pyrazofurin and showdomycin. At that time I also met my beautiful wife Angela who was a partner in her family’s antique business in Edinburgh. Angela was an expert in English and European ceramics, and their gallery in Dundas Street reflected her skills as a buyer in this field. Over the years, these skills have widened to include fine Asian ceramics and textiles. At Cambridge University I worked on polyketide biosynthesis. At the University of Leicester I worked on a new method to synthesize myo-inositol phosphorothioates with many applications in the elucidation of the biochemistry of signal transduction pathways. In 1990 I moved to Ninewells Hospital and Medical School in Dundee, Scotland. There, funded by a Cancer Research Campaign fellowship, I worked on what would become one of my lifelong research interests, photodynamic therapy for cancer (PDT).

When and where did you start your own lab?

In 1994, I moved to Massachusetts General Hospital in Boston, Massachusetts, to do junior faculty to work in the Wellman Laboratories for Photomedicine with Professor Tayyaba Hasan. Initially, I worked on conjugates between photosensitizers and monoclonal antibodies to target different kinds of cancer such as ovarian and colorectal. In 1997, I obtained a NIH R01 grant on “Macrophage-targeted Photodynamic Therapy” which allowed me to set up my own lab and be promoted to Assistant Professor at Harvard Medical School. In 2000, I obtained a second NIH R01 grant “Photodynamic Therapy for Localized Infections” which has been repeatedly funded ever since. This was partly based on my original discovery of polycationic photosensitizer conjugates such as those formed between the polymers poly-L-lysine or polyethylenimine and the anionic photosensitizer chlorin(e6), that were able to act as powerful and versatile antimicrobial photosensitizers.

What areas or topics does your lab currently focus on?

My laboratory focuses on the different uses of light to treat a wide variety of human diseases. To a very great extent I believe that almost all types and variety of human diseases can be treated with light (of one kind or another). This credo indeed, is one of the core mission statements of the Wellman Center for Photomedicine, which is what Wellman Labs came to be known in 2000.
Having started out working in PDT, quite a lot of my research is still in this broad area. Some time ago we started working on photodynamic inactivation (PDI) as an antimicrobial technology and as an alternative approach to treat localized infections.

One of the areas we have worked on to a significant extent is that of light-mediated antimicrobial technologies. These include not only PDI, but also the use of ultraviolet C (so-called germicidal UV) as an in vivo treatment for actual infections, and also blue light, which can kill many strains of bacteria and fungi by photoactivating their endogenous porphyrins.

My lab has become deeply involved in nanotechnology since the nanotechnology revolution began some 20 years ago. A lot of our work has involved fullerenes used as photosensitizers, and recently we have developed an interest in photocatalysis, the use of wide-band gap semi-conductors such as titanium dioxide nanoparticles to generate photoexcited reactive oxygen species and kill microorganisms.

In the last few years we have developed an interest in investigating the different photochemical pathways that operate in antimicrobial PDI. These can be divided into Type 1 in which hydroxyl radicals, hydrogen peroxide and superoxide radicals are the most important reactive species responsible for killing the microbial cells. These chemical species are formed via electron transfer from the long-lived triplet state of the photosensitizer. On the other hand singlet oxygen is formed via energy transfer (Type II photochemical pathway) from the long-lived triplet state of the photosensitizer.

Since the early days of PDT for cancer it was realized that in some animal models of cancer (in some strains of mice and rats) that certain particular tumor lines exhibited a remarkable response to PDT. This response included permanent tumor regressions and cures, rejection of a later rechallenge with the same tumor cell line, and spontaneous regressions of distant untreated tumor metastases. We were able to publish several papers shedding light on this intriguing phenomenon and highlighting the role of specific antigens within the tumor, inhibitory function of regulatory T-cells, and possible enhancement by epigenetic reversal drugs.

When we started working on photobiomodulation (PBM) some 15 years ago there was widespread uncertainty about the fundamental mechanisms of action at a molecular and cellular level. It is the first law of photobiology that a photon has to be absorbed by a molecule inside the cell (called a chromophore) in order to have any biological effect. Cytochrome c oxidase is unit IV of the electron transport chain within mitochondria and fulfils most of the requirements for the photoacceptor of mammalian cells. We have also studied the role of ROS generation, dissociation of nitric oxide, activation of transcription factors. Recently we have started to look at the role of light-gated calcium ion channels and the possible role of nanostructured water as a chromophore especially for near infrared wavelengths.

One of the areas that I believe PBM will have the biggest impact in medical science is in its effect on the brain.

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**About Michael R. Hamblin.** Dr. Hamblin is a Principal Investigator at the Wellman Center for Photomedicine at Massachusetts General Hospital, an Associate Professor of Dermatology at Harvard Medical School, and a member of the affiliated faculty of the Harvard-MIT Division of Health Science and Technology. He was trained as a synthetic organic chemist and received his Ph.D. from Trent University in England. His research interests lie in the areas of photodynamic therapy (PDT) for infections, cancer, and stimulation of the immune system, and in photobiomodulation or low-level light therapy (LLLT) for wound healing, arthritis, traumatic brain injury, neurodegenerative diseases, and psychiatric disorders. He directs a laboratory of around a dozen post-doctoral fellows, visiting scientists and graduate students. His research program is supported by NIH, CDMRP, USAFOSR, and CIMIT, among other funding agencies. He has published over 320 peer-reviewed articles, over 150 conference proceedings, book chapters, and international abstracts, and holds 10 patents. He is an associate editor for 8 journals, serves on the editorial board of an additional 30 journals, and also serves on NIH Study Sections. For the past 11 years, Dr. Hamblin has chaired an annual conference at SPIE Photonics West entitled "Mechanisms for low level light therapy" and he has edited the 11 proceedings volumes together with 6 other major textbooks on PDT and photomedicine. He has several other book projects in progress at various stages of completion. In 2011, Dr Hamblin was honored by election as a Fellow of SPIE. He is a Visiting Professor at universities in China, South Africa, and Northern Ireland.
What is your philosophy in scientific pursuits?

One of my research philosophies that has come to prominence in recent years, was first started when I developed a long-lasting interest in PBM, or what was formerly known as “low-level lazer therapy, LLLT.” At the time I became seriously interested in the molecular and cellular mechanisms of PBM, it was considered to have almost the status of “junk science.” The one question everybody was keen to ask me when I described the basic approach was “What’s the mechanism of action then?” So I resolved to find out. While the mechanisms are still not completely elucidated in exquisite detail, we believe we know enough about what is going on to be confident in understanding its role in future medical therapies. Having lived through the convoluted journey of PBM from the crazy fringes of “pseudo-science” to almost mainstream medicine, I believe that the same journey may be in progress with several other “alternative and complementary medicine” approaches. Among these approaches, I would include the following: acupuncture, far-infrared therapy, non-invasive brain stimulation, UV blood irradiation, ozone therapy, and ischemic pre-conditioning. One of the underlying concepts that unifies these disparate approaches is the concept of hormesis as put forward by Professor Ed Calabrese from the University of Massachussetts in Amherst.

What are your most significant scientific accomplishments?

We have recently made some discoveries that I believe could have far-reaching implications for antimicrobial PDI. These include the use of non-toxic inorganic salts such as potassium iodide to potentiate the antimicrobial killing mediated by PDI using electron-transfer type photosensitizers by several logs.

As mentioned above, the use of PBM to benefit the brain is a rapidly growing field, which is likely to have huge benefits for society, and could profoundly help a very large number of patients (not to mention its ability to improve mood and cognition in neurotypical people). We hear an enormous amount these days about the looming burden of Alzheimer’s and other kinds of dementia, as the population ages. Considering the relative failure of most anti-Alzheimer’s drugs, a harmless non-invasive approach such as shining some near-infrared light on the head, delivered from a LED helmet that can be used at home, will be seen as increasingly attractive to millions of sufferers. One of the most widely prescribed classes of all drugs is that of antidepressants. Considering the relative ineffectiveness of these drugs, and the rather troubling side effects of long-term use of these drugs, perhaps PBM using LED light sources could be a viable alternative.

Do you have partners that are important for your research projects?

One of our most significant collaborations was with Dr. Christopher Contag from Stanford University (and later with Xenogen Corp.) who allowed my laboratory access to a range of genetically engineered light-emitting bacteria that could be imaged by a sensitive bioluminescence camera. This innovation dramatically simplified the monitoring of localized infections in small animal models and allowed the Hamblin Laboratory to produce a selection of papers covering the use of antimicrobial PDT to treat infections in wounds, abscesses, burns, and abrasions. Many of these papers covered clinically relevant drug-resistant organisms such as MRSA, Acinetobacter baumanii, and Pseudomonas aeruginosa.

In 2004, I formed a collaboration with (the late) Dr. Tim Wharton, who was a fullerene chemist at Lynntech Inc. in College Station, Texas. Wharton prepared a series of cationic substituted C60 fullerenes that were highly efficient to photoinactivate various different microorganisms and were also highly effective at mediating PDT killing of tumor cells depending on the exact structure and particularly on the number of cationic groups attached to each C60 cage.

Jonathan Lindsey is the Glaxo Distinguished Professor of Chemistry at North Carolina State University, and is one of the world’s foremost experts in porphyrin chemistry. He had devised a novel and versatile synthetic route to stable bacteriochlorins, which allowed the peripheral functionalities of these interesting molecules to be tailored to provide a wide range of groups with varying charge and hydrophobicity. In a series of collaborations, we published several papers showing that these bacteriochlorins could function as extremely powerful, broad-spectrum antimicrobial photosensitizers that absorbed in the near-infrared spectral region.
Professor Long Y. Chiang from U Mass Lowell, Massachusetts, directs a laboratory, which focuses on the design and synthesis of carbon nano-structures. These molecules include the near-infrared absorbing emerald green fullerenes, and the design and synthesis of multi-photon absorptive fullerene-fluorene chromophores for nonlinear photonic sensor protection and optical limiting applications. Chiang has synthesized a range of molecular suprastructures using functionalized C60 or C70 with attached defined polycationic chains to mediate antimicrobial PDI.

Tadeusz Sarna is a professor at Jagellonian University at Krakow, Poland. His laboratory is set up to carry out advanced techniques in photochemistry including electron spin resonance with spin trapping probes, detection of singlet oxygen luminescence at 1270 nm, and flash photolysis studies. I have collaborated on several mechanistic studies of Type 1 and Type 2 photochemical pathways.

Mahdi Karimi spent time in the Hamblin Laboratory during 2012–2013, while he was doing his Ph.D. in the Department of Biophysics, Faculty of Biological Sciences, Tarbiat Modares University in Iran. His research interests included the study of different aspects of nanotechnology in the field of drug and gene delivery. Karimi returned to Tehran, to set up his own laboratory in the Iran University of Medical Science to work on graphene and other nanoparticles as smart stimulus-responsive drug and gene carriers in drug and gene delivery. We have published a range of reviews on this “hot-topic” area.

We have also been fortunate to have had some excellent clinical collaborators in our efforts to move PBM into becoming more of a mainstream clinical therapy for actual patients. These clinicians have included Frederic Schiffer (a psychiatrist), Paolo Cassano (another psychiatrist), and Margaret Naeser (a neurologist).

What were your “highlights” in recent research performed in your field?

I think the most significant highlight that has emerged in my field over the last 20 years has been the emergence of PBM as a generally accepted, almost mainstream, medical therapy. This acceptance can be attributed to several different factors. First, there is the increased scientific understanding of the mechanism of action. Second, is the recent widespread availability of inexpensive LED devices that have largely replaced expensive lazers that were mainly used by “lazer therapists.” LED devices are considered totally harmless with no risk of eye damage or skin burns, and are ideally suited to home use. Third, we can identify the rise of the Internet, which has made it relatively easy for individuals suffering from a range of medical conditions to search for applications of PBM to their particular condition. Moreover, self-help groups have also increasingly taken an interest in this application of PBM.

What makes a good mentor?

I believe that it is one of the most satisfying returns from one’s efforts in running a lab, to see the young folks come into your lab knowing almost nothing, and then blossoming like the most rapidly growing plants and flowers from the farthest Amazon jungle. Sometimes the speed at which these young folks’ progress leaves one totally astonished, peering into the far distance to catch a glimpse of the dust they leave in their wake. Therefore I believe that what makes a good mentor is the ability to recognize this potential before it has even had a chance to poke its head above the surface. Give the best of these young folks their head like a racehorse, and you will be amazed to see them shoot ahead of the field, and win by several lengths.

What advice would you have to junior people entering the field?

I think junior people entering the field should be advised to select their own research area as early as possible, in which they can develop their proprietary ideas, hypotheses, and methodologies. I know for me personally, this did not fully occur until I moved to the U.S. in 1994. It is also important to learn the art of grant writing as early as possible. After all, I tell young folks that their scientific survival will likely depend on their effectiveness in persuading funding agencies to hand over what can initially appear as rather daunting amounts of money. It is also never too early to learn the basics of being an effective Principal Investigator and how to run your own lab. Hiring and firing of lab members are skills that it is not easy to learn, and you should take advantage of any courses that your institution may make available in this regard.