ASPB Pioneer Member

Ming-Che Shih

How did you spend your career

In Taiwan

I attended Tunghai University in Taiwan as an undergraduate between 1972 and 1976. After graduation, I had to serve two years in the military and was stationed in the Penghu Islands, which is a group of small islands off Taiwan. With a routine daily life and no clear career plan, I decided to take the GRE exams and apply for admission to graduate schools in the US. Luckily, I was offered scholarships from several universities and chose to attend the Genetics Ph.D. program at the University of Iowa.

To the US

In August 1978, with only US$1500 in my pocket, I took my first overseas flight and arrived in Iowa City to start life as a graduate student. Iowa City is a beautiful city and very friendly to international students, so I was able to settle down quickly. I joined Gary Gussin's lab to study the regulation of transcription initiation of λ P_{RM} and P_{RE} promoters. It was an exciting time for molecular biology and the dawn of the recombinant DNA era. I had to learn a lot of new stuff, such as DNA fragment purification, protein purification, including that of RNA polymerase and restriction enzymes. Once in a while, Gary would come in and say, "there is a new technique that can be used in your research, why don't you try it…." I had to work hard, but it was rewarding. I completed my

Ph.D. study in a reasonable time period and published papers in Cell, PNAS and the Journal of Molecular Biology.

In January 1984, I joined Howard Goodman's lab in the Department of Molecular Biology, Massachusetts General Hospital, as a postdoctoral fellow, which became my base between1984 and1988. Howard had just moved from UC San Francisco to MGH and was forming a plant biology group in his lab. He gave us a lot of freedom in deciding which project to pursue. I chose to investigate how light regulates nuclear genes encoding chloroplast glyeraldehyde-3-phosphate dehydrogenase (GAPDH). When I obtained full-length tobacco cDNA clones for two chloroplast subunit genes, GAPA and GAPB, and cytosolic GAPC, I realized their sequences would allow me to answer a question on the evolutionary origin of nuclear genes encoding chloroplast functions. I found that tobacco GAPC has much higher identity to animal and yeast GAPDH than to tobacco GAPA and GAB. However, I had no idea how to do evolutionary analyses. I went to Howard and asked him to give me several months in the library reading about evolution. Howard looked puzzled, probably not understanding why I wanted to read evolution papers, but just said okay. After three months, I completed a manuscript "Evidence in favor of the symbiont origin of chloroplasts: Primary structure of tobacco glyeraldehyde-3-phosphate dehydrogenase". The manuscript was submitted to *Cell* and the review was back in two weeks with minor editorial comments. I managed to publish another evolution paper, "Introns existence predated the divergence of prokaryotes and eukaryotes" in *Science*. With these two papers and one gene regulation paper in *EMBO*, I was able to get faculty position offers from several universities. I decided to take the offer from the Biology Department at the University of Iowa and moved back to Iowa City in 1988.

In Iowa, my lab started working on light regulation of GAPA and GAPB in Arabidopsis. Surprisingly, we found that GAPC could be regulated by hypoxia and heat stress, which became a second project. I was lucky to have stable funding and now had a reasonable number of publications under my belt. Life seemed to become a bit routine at that time; however, soon large-scale

continued on next page

Ming-Che Shih *continued*

DNA sequencing techniques started to appear, which have subsequently kept making quantum leaps in terms of improvement, right up to the current NGS era. These advances led me into the field of omics and changed the nature of the research in my lab.

Back to Taiwan

I returned to Taiwan in 2008 to join the Agricultural Biotechnology Research Center (ABRC) at Academia Sinica as a Distinguished Research Fellow/Professor and was the Director of ABRC between 2008 and 2016. This was the busiest but the most enjoyable time of my scientific career. ABRC was officially established in 2006 and had an interim Director until I took over as the Director in January 2008. I was lucky when I joined ABRC as it was already endowed with a group of talented and dedicated research fellows. We put our efforts together and were able to establish ABRC as the best research institute in agricultural biotechnology in Taiwan and gained an international reputation. In my own research, my lab published a series of findings that I believe contribute to understanding the plant response to hypoxia at the cellular and molecular levels.

My lab also participated in generating genomic resources for important crops in Taiwan. We have created an orchid transcriptomic database and completed high quality draft genomic sequences of *Phalaenopsis aphrodite*, the breeding parent of most white flowered orchids on the market in Taiwan. These genomic databases also include genetic linkage maps and high-resolution pachytene karyotypes, which are the first such data for orchid species.

What do you consider your most important contributions to plant sciences

I consider three findings to be my most important contributions to plant sciences:

First, my 1986 *Cell* paper that provided the molecular evidence that nuclear genes encoding chloroplast functions originated from cyanobacterium-eukaryote endosymbiosis and transferred from the chloroplast to the nuclear genome during evolution.

Second, we showed that dual mechanisms control plant-specific hypoxia translation.

It is well known that in both animal and plant cells under hypoxia, translation of the majority of mRNAs is inhibited, but a group of mRNAs that encode proteins essential for cell survival is selected for translation. How these specific mRNAs are selected for the protein synthesis that occurs under hypoxia remained unclear for a long time. My lab provided evidence that in Arabidopsis plants under submergence the protein kinase SnRK1.1 directly phosphorylates eIFiso4G1, a plant specific translation initiation factor, to select specific mRNAs for translation. The activation of SnRK1 is triggered by the energy crisis at the early stages of hypoxia. In addition, we found that during submergence, entrapped ethylene leads to the activation of GCN2/eIF2α, which in turn inhibits global translation.

Third, SUB1A-1, ERF66 and ERF67 form a regulatory cascade involving transcriptional and N-end rule control, which allows rice to distinguish flooding from other SUB1A-1-regulated stresses. Group VII ERFs are regulated by an N-end rule proteolysis pathway which is believed to be the oxygen sensing mechanism. Sub1*A*-1 is a member of the group VII ERFs and confers the majority of submergence tolerance to rice. Despite having the canonical N-degradon sequences, Sub1A1 appears to able to evade N-end rule protease degradation under normoxia. We found that two other *ERFVIIs*, *ERF66* and *ERF67*, are transcriptionally up-regulated by SUB1A under submergence and are the substrates of the N-end rule pathway, and may be responsible for triggering a stronger transcriptional response to promote submergence survival. Our results suggest that Sub1A and ERF66/67 form a regulatory cascade to regulate submergence responses.

What advice would you offer to someone contemplating a career in plant science.

Being a plant biologist has been an enjoyable journey. I would say that in the era of dealing with global warming, sustainability, and food security, having a career in plant science can be fulfilling and rewarding.