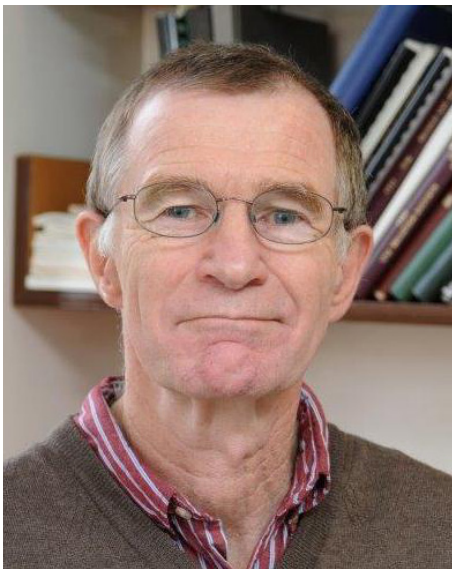
ASPB Pioneer Member

John Browse

How did you spend your career?

I was born in England, where my father was a businessman. But dad wanted to be an orchardist, so when I was eight years old we moved to New Zealand where I spent my teenage years picking fruit and tending lemon and tamarillo trees (later kiwifruit). Despite this apparently auspicious upbringing, I graduated high school and went to university without any developed idea about what scientific discipline I wanted to follow. However, I found that advanced mathematics was obscurely confusing, chemistry was smelly, and lab animals bled, so I graduated with a degree in botany and completed a PhD in 1977 on the physiology of photosynthesis in aquatic plants.

After graduation my then wife and I embarked on an open-ended trip overland through Asia to Europe. Relaxing on a beach in Bali, I wrote manuscripts from my thesis– I can recommend it. A telegram from my PhD supervisor (sent to: Post Restante, Kathmandu, Nepal) induced me to write an application for my first job, which was investigating lipid biochemistry and plant temperature responses with Roger Slack and Grattan Roughan at New Zealand's Department of Scientific and Industrial Research. Grattan and Roger had discovered and characterized the biochemical reactions that drive the two pathways of membrane lipid synthesis in plant leaf cells and described



how these reactions are co-opted to produce triacylglycerol storage lipid in oilseeds.

In 1981, a serendipitous (and frankly implausible) sequence of events led to me hosting Chris and Shauna Somerville when they visited New Zealand. Our discussions induced Chris to begin a screen for chilling-sensitive mutants of Arabidopsis. In 1983, I travelled to Chris's laboratory at Michigan State University to work on these mutants, but they turned out to be rather intransigent. Instead, we devised a screen for fatty acid mutants of Arabidopsis using brute force gas chromatography analysis of leaf samples. The fatty acid mutants made their appearance at an ideal time, since they could be interpreted in the context of Grattan and Roger's two-pathway model, while greatly expanding our understanding of the reactions and regulation involved. In 1987, I spent a year in Chris's lab and began applying for jobs in the United States. I was very fortunate to land a position as Assistant Professor in the Institute of Biological Chemistry at Washington State University, and I have spent the remainder of my career there surrounded by an outstanding group of students and postdoctoral collaborators who have driven our research programs forward with enthusiasm, skill, and perceptive insight.

What do you consider to be your most important contributions to science?

Using mutation genetics to illuminate the biochemistry and cell biology of lipids opened many paths of investigation. To begin with, they quickly helped fill out the details of Grattan and Roger's two-pathway scheme, and to define the substrates, products, and contributions of the enzymes involved. The mutants were also key to isolating genes by map-based cloning and gene-tagging approaches, allowing recombinant enzymes to be expressed and studied in *E. coli* and yeast. This was vital to studying enzymes of lipid metabolism, since many of them are integral membrane proteins recalcitrant to the techniques of biochemistry in the cold room. Most importantly, our collection of mutant lines allowed us to interrogate different mutations about how specific changes in lipid composition affect membrane function and the cell biology and physiology of plants.

Many of our mutants are not readily distinguishable from

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wild type when grown at normal physiological temperatures. Some mutants revealed their phenotypes when the plants were grown at low temperatures or under other extreme conditions. In other cases, the redundancy in enzyme function that is a feature of the two-pathway scheme required us to cross and combine several mutants before phenotypes could be identified. In the late 1990s, we used a similar approach to elucidate lipid biology in *Caenorhabditis elegans*, marking the beginning of the use of biochemical genetics in this animal model.

Several of our early discoveries relate to the impact of fatty acid composition on chloroplast membrane function. Because chloroplasts contain very high levels of the polyunsaturated 18:3 and 16:3 fatty acids, it had been inferred these are essential for maintaining photosynthetic function. However, a triple mutant produced by combining mutations at three loci encoding fatty-acid desaturases, *fad3*, *fad7*, and *fad8*, contained almost no 18:3 or 16:3 fatty acids, but it was indistinguishable from wild type in vegetative growth and development at 22°C. This is not to say that trienoic fatty acids are irrelevant to photosynthetic function. Conservation of the high trienoic content of chloroplasts through the evolutionary time scale attests to their importance, but clearly their role is more subtle than anticipated. The triple mutant revealed instructive photosynthetic phenotypes under different temperature and light conditions, adding to our knowledge of the importance of membrane-lipid structure to photosynthesis function.

A striking feature of the *fad3/7/8* phenotype is that the plants are male sterile. This is because the plant hormone jasmonate is synthesized from 18:3. Our characterization of the fad3/7/8 mutant revealed the role of jasmonate in plant reproduction, and subsequently led to the identification of the mechanism of jasmonate signaling and response. As the result of a fortuitous delivery of *Pythium*-contaminated potting soil, we also discovered that jasmonate is a key regulator of plant defense against necrotrophic pathogens.

To examine plants' ability to survive without any polyunsaturated fatty acids in their membrane lipids, we generated a *fad2 fad6* double mutant that is deficient in desaturation of monounsaturated fatty acids in both pathways of lipid synthesis. The *fad2/6* double-mutant plants are not capable of autotrophic growth, but their growth and development on sucrose media are remarkably normal. This observation indicates the vast majority of receptor-mediated and transport-related membrane functions required to sustain an organism and induce proper development are adequately supported in the absence of polyunsaturated membrane lipids. In terms of vegetative growth, photosynthesis is the one process that absolutely requires highly unsaturated membranes.

One of our most impactful accomplishments was cloning the Arabidopsis *FAD2* gene in 1994, because this led to molecular strategies that successfully reduce the levels of *trans* fats in human diets. Many vegetable oils contain high proportions of polyunsaturated fatty acids that become rancid during storage and processing. The original, industrial-chemistry solution to this problem, initiated in the early 20th century, was to process oils by partial hydrogenation. However, partial hydrogenation leads to the production of unhealthy *trans* fatty acids that medical epidemiologists hold responsible for half a million excess deaths worldwide each year during much of the 20th century. The *FAD2* gene encodes the gateway enzyme of polyunsaturated fatty acid synthesis, and it provided the tools and understanding necessary to engineer high-oleic, low polyunsaturate lines of many oilseed crops that are now widely grown and marketed.

How did ASPB impact your career?

I joined the Society when I moved to the United States in 1987. Following plant biology and the activities of my colleagues through the society, its annual meeting, and the newsletter has been both helpful and enjoyable, but the biggest impact on my career has been the two excellent journals, *Plant Physiology* and *The Plant Cell,* published by the society. A large proportion of

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my laboratory's papers have been published in them. With the help of ASPB members and staff, both journals have the highest possible standards for editing, reviewing and production. As a result, it is always rewarding for me to check the two journals each month for interesting and relevant reports of new discoveries in plant biology.

What important advice would you give to individuals at the start of their career in plant science?

The cardinal rule is to do research for love. As researchers, we are blessed to have the freedom to gather with friends and discuss science and bat around ideas for experimental approaches to understand the world more completely. If you do research for love, you will not be possessive about your discoveries, you won't be jealous of other people's successes, and, importantly, you hopefully won't be tempted to commit scientific fraud. There are many more effective remunerative ways to make a living, and the reward in science lies mainly in watching a new concept unfold as a result of your efforts. If you're making it all up, where is the beauty?

Beyond this, empower the researchers in your laboratory; let them know that they will understand more about their experimental system than you will, and encourage them to use that judgment in making decisions. Never ban anyone from doing that crazy experiment they want to try. It may well be your lab's next big discovery! Recognize that many times discoveries come from a meeting of people from two different fields with different perspectives on the scientific enterprise. Finally, embrace the art of storytelling in your papers, meeting talks, and grant proposals. A scientific paper needs the same story elements as a novel or a play: well-timed introductions and back stories for each of the characters, a hero struggling against adversity who finally breaks through at the climax with the big reveal.