Jeff Schell (1935–2003): steering *Agrobacterium*-mediated plant gene engineering

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Over the past decade, our knowledge, in molecular terms, of plant growth and development has progressed tremendously. We are starting to understand how plants respond to biotic and abiotic stress. It is still only rudimentary compared to what we should learn in the coming decade, but 30 years ago it was unthinkable that we would have obtained this 'rudimentary knowledge' so fast.

The Ti plasmid was discovered in crown gall-inducing *Agrobacterium* strains 30 years ago and has become the reliable gene vector for creating transgenic plants. Jeff Schell's decision to study why and how *Agrobacterium tumefaciens*, a Gram-negative soil bacterium, induces tumours on plants is key to the progress we have made over the past 30 years.

Jeff studied zoology at the University of Ghent (Belgium) as an undergraduate and bacterial taxonomy for his PhD. A first postdoc with Bill Hayes, the father of bacterial genetics, then at Hammersmith Hospital in London (UK), and some shorter visits to the USA and Canada to discover the world of bacteriophages, particularly phage lambda, prepared him to tackle the mystery of crown gall.

In 1967, he became Associate Professor at his *Alma Mater*. His laboratory was contiguous to mine and we decided to take on together the unusual subject of tumour induction in plants. A large collection of oncogenic and non-oncogenic *Agrobacterium* strains was available at the local taxonomy laboratory. Our expertise was microbial molecular biology, particularly extra-chromosomal elements. Carrot slices, tobacco shoots and some Kalanchoe plants were for a long time the only plant material present in the laboratory. At that time, after identifying the Ti plasmid, which for those days was an unusually large plasmid, most of our effort went into attempting to cure *Agrobacterium* of its Ti plasmid and trying to conjugate the plasmid into non-oncogenic strains. Conjugating the plasmid into non-oncogenic strains became possible thanks to *in planta* conjugation developed by Alan Kerr (University of Adelaide, Australia), a method that took 55 days before one could demonstrate that the exchange had taken place.

George Morel had observed that crown galls synthesized unusual amino acids (the opines) and that the *Agrobacterium* strain determined which opine would be synthesized. Could it be that the genetic determinant, or the genes for opine biosynthesis were linked and were born on Ti plasmids? This led to the bold and daring statement that the Ti plasmid is the causative agent of crown gall induction, the tumour-inducing principle, or TIP as Armin Braun coined it in 1946. The next inspiring hypothesis was that genes encoded by the Ti plasmid were transferred and stably integrated into the plant chromosome – the expression of these 'bacterial genes' in plant cells triggering cell proliferation and opine biosynthesis.

Jeff Schell.

Plant physiologists were highly sceptical about these 'concepts'. Claims without proof are worrying and these concepts did not explain 'genetic tumours', which are proliferations like crown galls that occur spontaneously on offspring of crosses between some *Nicotiana* species. Jeff was not disturbed by these objections; he felt that you should first set the general principle and then explain the exceptions. Luckily, restriction enzymes enabling physical maps to be made of the TI plasmids became available (no sequencing technology had been developed at that time), as did Southern blotting, enabling claims for DNA transfer to be substantiated.

As a charismatic and highly didactical speaker, Jeff Schell did convince some members of the plant community

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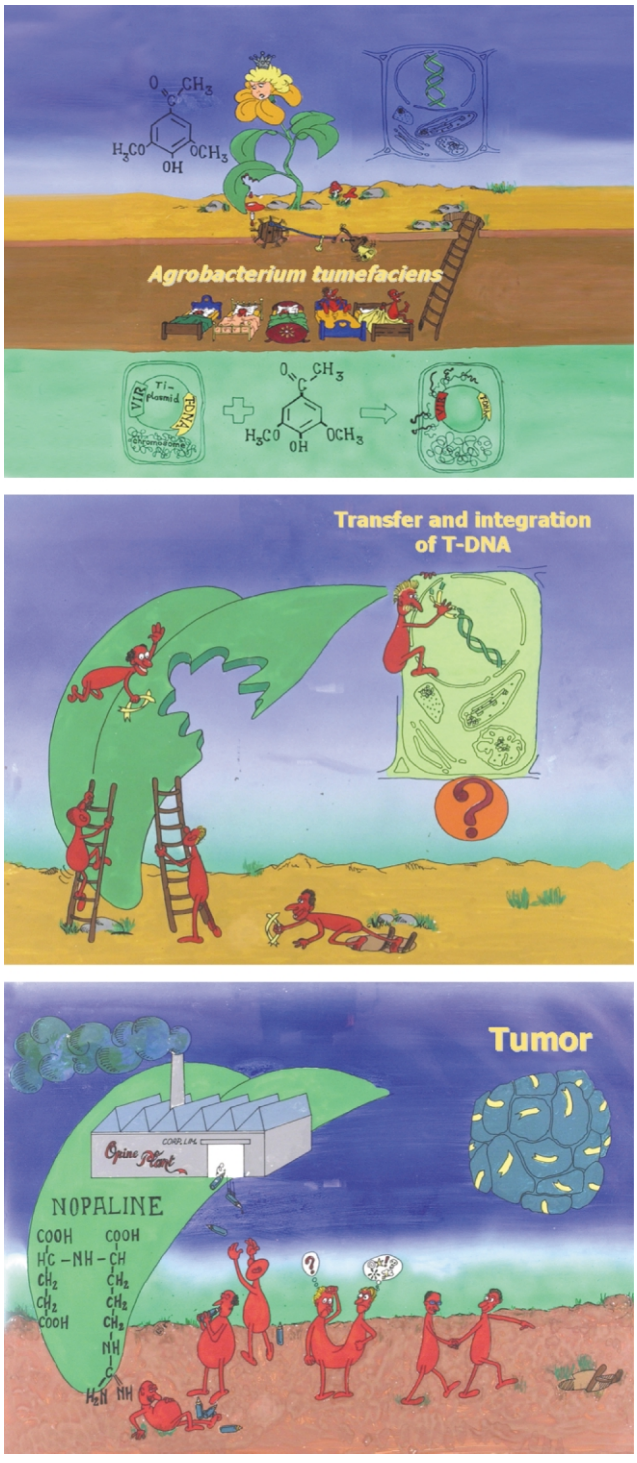

Cartoons by Kan Wang (Iowa State University, Ames, IA, USA).

of the importance of these findings. If some *Agrobacterium* genes could be transferred to and expressed in plant cells, then it should be possible to replace them by man-made genes to confer a new trait to the plant. The race was on to turn *Agrobacterium* into a gene vector for genetically modifying plants.

The approaches used at this time still relied largely on the techniques offered by microbial genetics. Physical maps showed that the transferred genes were located on a well-defined segment – the T-DNA. Recombination techniques allowed the exchange of parts of the T-DNA by other DNA segments. Competition with Mary-Dell Chilton and Eugene Nester was fierce at this time, but stimulating discussions and information exchange remained the rule.

In 1978, Jeff became the director of the Max Planck Institute for Plant Breeding in Cologne. He rapidly turned it into a world-class institute for Plant Sciences. At the same time, he continued to co-direct the laboratory in Ghent. We announced at the 1983 Miami-Winter Symposium, at the same time as the same announcement was also being made by Chilton's and Monsanto's groups, that we had created the first transgenic plants expressing the kanamycin resistance gene – plant gene engineering had started.

The promises were immense, leading start-up companies as well as agrochemical and food-processing companies to invest in the new discipline of plant biotechnology. Jeff Schell played a major role in convincing public and private authorities that we were on the eve of an exceptional breakthrough. To us it was clear that molecular plant sciences would provide a unique opportunity to develop more productive and sustainable agriculture, to solve environmental problems and to create better products.

All his life Jeff paid great attention to the needs of the developing countries, where >80% of the world population lives. He indefatigably participated in lobbying to give them access to the new findings. He hoped that he would be able to convince the major players in international agriculture, such as the Consultative Group on International Agricultural Research (CGIAR) to bring biotechnology to tropical agriculture.

Although the action of some politically inspired groups has caused substantial delay, the best way to honour the memory of Jeff Schell is to participate in establishing the networks that can deliver the new crops that the developing countries so badly need.