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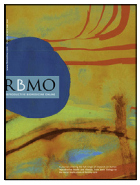

OBITUARY

In memory of Michelle Lane: 1970 – 2020

On 4 February, 2020, one of the world's bright stars in reproductive biology was taken from us all too soon. After fighting a brave battle with illness, we lost Michelle Lane. She was just 49.

Michelle's career spanned 29 years and her contributions to our field can only be described as Herculean. Her basic research helped to lay the foundations of modern embryology, while her clinical translation helped millions of couples worldwide achieve their dream of having a family.

Here, her mentor and some of her students, convey a sense of Michelle to the world. Those of you who were lucky enough to meet her, or hear her talk, will already be aware of her legacy. For those of you who did not know Michelle, we hope that our reflections inspire.

1991– 2003: DAVID GARDNER

Michelle entered my life in 1991 as a 20-year-old undergraduate at a time in embryology when we could not culture mouse embryos reliably past the 2-cell stage (except for F1 hybrid crosses), sheep or cattle embryos past the 8- to 16-cell stage and human embryos past the 8-cell stage. Human IVF at this time was far from successful, with pregnancy rates across the world at around 10%, typically requiring the transfer of 2 or more embryos, meaning implantation rates were considerably below 10%. It was therefore an incredibly exciting period in embryology, with many discoveries to be made.

Michelle's first foray into embryology was a project on the effects of embryo group size in culture, which she took on with incredible energy and developed her skills quickly. This culminated in her first paper (*Lane and Gardner, 1992*). After her undergraduate studies, Michelle worked for a year as my assistant, when along with tackling mice embryo culture, we decided to take on the embryos of both sheep and cattle, and concomitantly both commenced clinical training at Monash IVF.

It was always evident that this young embryologist should undertake a PhD and in 1993 Michelle commenced her graduate studies, my first PhD student, working on the role of amino acids and ammonium in regulating mouse embryo development and programming. Her approach to research was both meticulous and painstaking, working on the metabolism of individual embryos, which was immensely demanding, but provided the data required to understand the embryo's needs as it developed. The amount of data Michelle generated on embryo metabolism and culture during this time was incredible. It was during these studies that it became evident that the culture conditions used in the laboratory had a profound impact on embryo metabolism and the events following transfer (*Lane and Gardner, 1994*), these observations being reported shortly after the inception of the Barker Hypothesis.

It is hard to convey the sense of anticipation and excitement in the lab at this time, as one by one we were able to overcome the developmental blocks in culture of four different species (including the human), and grow their embryos into viable blastocysts (as determined through embryo transfer). Several of these embryo culture milestones we reviewed as early as 1997 (*Gardner and Lane, 1997*). Michelle was integral in so much of this. We fed off each other's scientific creativity and pushed each other harder in the lab.

On completion of her PhD in 1996, Michelle went to Madison, Wisconsin to take up a post-doctoral position with Barry Bavister. In her 3 years with Barry she generated the data for 13 papers on the hamster embryo, again a reflection of her incredible work ethic and ability to generate data, especially as the hamster is a notoriously difficult species to work with!

Our working paths crossed one more time when she joined my team in Denver at the Colorado Center for Reproductive Medicine, where she was the first in the world to successfully vitrify the human blastocyst using a technology she had pioneered, the Cryoloop (*Lane et al., 1999a*; *1999b*).

Before returning to Australia to set up her own laboratory in Adelaide in 2003, Michelle continued to make significant advances in embryo physiology, cryobiology and in clinical translation. I had no idea how many publications we wrote together over the years (although I knew they were many and significant) until I sat down to write this. To my amazement we penned 79 papers, reviews and chapters, and edited two books, which represent only a part of her legacy to the fields of reproductive biology and human IVF. Our last publication together was just last year, a chapter, fittingly on embryo culture (*Gardner and Lane, 2019*).

It is hard to convey the magnitude and impact of her works; going to Google Scholar and looking at the vast number of publications and citations is a good means of assessing her academic impact, but it cannot convey the medical significance of her career. Without doubt, her excellent science contributed significantly to increases in human IVF pregnancy rates.

I shall miss my scientific little sister; she was one of a kind. She used to describe one of my energetic daughters, who she would babysit for, as 'a child that was too much person for one body!'. I actually think her own words are the best description of Michelle herself; so much energy, so many ideas, so much hard work, so special.

2003– 2020: DEIRDRE ZANDER-FOX, HASSAN W BAKOS, NICOLE MCPHERSON AND LEANNE PACELLA-INCE

Michelle moved back to Australia in 2003 to establish the Gamete and Embryo Biology research group at the University of Adelaide in the department of Obstetrics and Gynaecology. At that time the department was based at the Queen Elizabeth Hospital in South Australia and had produced some of the pioneering work in IVF by Professor Lloyd Cox and Professor John Kerin. In addition to overseeing her research group, she stepped into the role of Scientific Director of Repromed (South Australia's largest IVF clinic). Michelle quickly began to attract and identify students, of which we were all fortunate enough to become.

Michelle continued with her research on the sensitivity of the preimplantation embryo to its culture environment. In particular, she was interested in how the embryo responded and adapted to problems with embryo culture systems such as increased ammonium or pH stress. However, she branched out into other areas including female and male reproductive health and reproductive genetics, and developmental origins of adult disease through both parental linages. At the heart of all of this, her primary focus was always on improving IVF success and ensuring that babies born from IVF had the healthiest start to life.

We met Michelle towards the end of our undergraduate studies when we were trying to find our own pathways and careers in science. We were in awe of Michelle, who was a young, enthusiastic and passionate researcher who talked about the beauty of the preimplantation embryo, how sensitive it was to its environment, how important reproductive technology was to society, and how there was so much more to be done. We joined Michelle's team between 2003 and 2008 and have continued to work by her side; initially as students and then as mentees and colleagues.

Working as a young student for Michelle was not an easy task. Her passion and dedication to culturing embryos meant you had to have a very specific skill set before you were allowed to culture on your own. Whilst her leadership style may have appeared to be directive, her intent was to produce the best junior reproductive scientists she could. She was never constrained by norms, relished taking on new challenges and spoke about creating new paradigms.

During her 17 years in Adelaide, she supervised an extraordinary number of honours and PhD candidates and published on a variety of reproductive topics including preimplantation embryo culture and stress (*Zander-Fox et al., 2010*), the impact of paternal obesity (*Bakos et al., 2011*; *Palmer et al., 2012*) and maternal age on reproductive outcomes and offspring health (*Fullston et al., 2012*).

As well as her role in academia, for which she was promoted to the level of Full Professor, Michelle was the Scientific Director of Repromed from 2003 to 2014. During this period she recruited a large number of her students into the field of clinical reproduction as trainee embryologists. She had a unique skill for identifying qualities in young scientists who would not only be excellent embryologists, but would also bring care and empathy to their work and to the patients undergoing IVF treatment. The embryology laboratory at Repromed still has more than 50% of scientific staff that undertook their honours degree with Michelle. After her role as Scientific Director of Repromed she went on to become the Director of Research and Innovation and Chair of the Group Scientific Advisory Committee for the Monash IVF Group.

We cannot begin to imagine a world without Michelle in it. It is incredibly sad that the next generation of young embryologists and scientists will not get to see one of her lectures that contained the most creative science analogies (often involving Australian Rules Football, which was another of her passions) and where her enthusiasm was contagious. We thank Michelle for everything she has taught us over the last 17 years which has helped us become who we are today. We hope that the legacy she has left in us will endure through generations and that we continue to do her proud.

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