Bob Edwards died earlier this year and will be sadly missed by all those who knew him. Recognition of his outstanding contributions came rather late in his career but finally, in 2010, he was awarded the Nobel Prize for Physiology or Medicine. Bob’s achievements have been widely documented on a number of different occasions. Amongst these he set up *Molecular Human Reproduction* (MHR) and as such we wanted to take a slightly different approach to honour his work.

The development of IVF centred on two breakthrough papers. The first described the fertilization in vitro of human eggs (Edwards et al., 1969) and the second was the report of the first birth from IVF (Steptoe and Edwards, 1978). We identified three main challenges, which we believed were fundamental problems faced by Bob to achieve these breakthroughs, namely (i) capacitation for successful fertilization (ii) maturation of eggs in vitro (iii) developing successful stimulation regimes to recover eggs and allow full term development. We invited internationally leading authors to discuss these subjects specifically with the broad remit to provide a background on the challenges Bob faced, hence providing a context to his achievements, and then to speculate how their field is likely to develop.

John Aitken addresses the issue of capacitation. It is difficult now to imagine, when there are a plethora of different media and protocols to capacitate sperm, that it was such a conundrum. Prior to 1969, the focus was to understand how capacitation occurred in the female tract and what factors were involved—the overall aim being to reconstitute the environment in vitro. It is perhaps ironic today that almost all we know about sperm transport comes from work prior to the 1980s with minimal progress since—hopefully this will change. In 1951, capacitation was discovered independently by Austin and Chang yet it took a further 17 years to achieve this in vitro in humans. The importance of the problem is reflected by the sentence in Introduction of the Nature paper in 1969: “a possible solution to the problem of obtaining “capacitated” spermatozoa has emerged from experiments on hamster” (Edwards et al., 1969). Interestingly, despite four and a half decades of research examining capacitation there is still much to learn about this enigmatic process and John expertly guides us through this tricky maze.

A second fundamental challenge was the need to successfully mature human eggs in vitro. Bob made pivotal contributions in this area describing the timing of in vitro maturation (IVM) in humans, which was considerably longer that he first anticipated or was led to believe. Rob Gilchrist and Jeremy Thompson elegantly describe this incredibly productive part of his career and document his critical insight. Although Bob successfully achieved IVM and fertilization, he judged, that for the clinical development of IVF, *in vivo* matured oocytes would be needed. The reason being the limited embryonic developmental capacity of IVM mature oocytes. Remarkably, almost 50 years after successful IVM in humans safe clinical IVM remains a technical challenge and Jeremy and Rob identify six key areas that require urgent attention if the potential of IVM is to be fully realized.

In turning to *in vivo* maturation for the potential to achieve healthy live births, different problems presented themselves. Rudimentary stimulation regimes to achieve conception *in vivo* were available but the control of these processes and the recovery of eggs at the appropriate stages to support development were key issues. Steve Hillier eloquently provides a context to these developments. Remarkably, despite consistent failure Bob deemed it essential to use *in vivo* maturation of eggs and ingeniously turned to the natural cycle. To achieve this it was necessary...
to determine the appropriate time of aspiration and the collection of mature oocytes—no trivial task. Louise Brown was a natural cycle IVF birth which is in contrast to today where stimulation regimes represent the overwhelming majority of cycles. Steve provides key insights into these developments and discusses the concept that more eggs are not necessarily better—a situation he terms ‘back to the future’.

Bob of course made a plethora of key contributions and each person will have a different perspective as to what they believe was central. Personally, I was in awe of his fundamental work in fronting the ethical debate in the early 1970s and 1980s. Characteristically, he took this head on when it would have been so easy to shy away. This had a profound impact formulating the blueprint for subsequent informed debate and allowed the UK to rapidly develop an intelligently regulated but permissive framework for IVF and embryo research. This model—via the HFEA—is widely imitated throughout the world. Additionally, he founded ESHRE and all three journals. In this issue of MHR, we have only concentrated on one aspect—identifying what challenges he faced at the genesis of IVF and providing a summary on what is currently known and a glimpse into the future. His acumen, drive and ability to think years ahead of his time are themes that are continually presented by the three reviews.

Bob, as Editor in Chief of MHR, was instrumental in securing and publishing innovative papers. We have included in this celebratory issue four papers which stand above the others awaiting full publication, in that they have obtained universally high (or in one case exceptional) ratings from every member of the review team. Such complete acceptance from peers is hard to achieve and a convincing indicator of quality. Two of these articles are New Research Horizon reviews and two are primary research papers. All describe the sort of innovative thinking that Bob so energetically encouraged. There seems little doubt that Bob would consider this collection a very fine tribute and be excited that such fundamental basic research, that was the foundation of his work in the 1950s and 1960s, looks set to continue worldwide and even pick up momentum.

References
