ELSEVIER

RECIPIENT OF THE 1999 PIONEER AWARD

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Research Synopsis 1959 - 1999

My scientific career started 40 years ago when I was given the opportunity to participate in the first intercontental transfer of embryos from domestic animals. In addition to starting my career these first experiments were the reason for my moving to Cambridge where I have spent the rest of my research life, initially at the Animal Research Station and then at The Babraham Institute. My science focus has undergone four major restrictions coinciding roughly with each decade. During the first 10 years, which started with my PhD, Tim Rowson and I worked on the whole animal. Our first studies were on the maternal recognition of pregnancy where we demonstrated that the embryo or its protein extracts (now identified as interferons) act at a specific stage in early pregnancy to prevent the uterus from secreting lytic factors which we showed induced lysosomal instability and luteal involution. The studies on early pregnancy were paralleled by experiments on the establishment of the methology and basic principles of embryo transfer in cattle. This exciting work culminated in the production of the first calves by non-surgical cervical embryo transfer.

The focus in the second decade was narrowed from the whole animal to the ovarian follicle. The research was motivated by the realisation that embryo availability was the main limitation to the use of embryo transfer for the exploitation of the genetic potential of superior females. With the unrivalled steroid biochemical expertise of Bob Seamark and structural expertise of Mary Hay we firstly identified both the large array of steroids secreted during antral follicle growth and the haemodynamic and cellular events associated with development and atresia of preovulatory follicles. This was followed by experiments aimed at improving superovulation. Our approach was to analyse the action of exogenous gonadotrophins on the different classes of follicles in the ovaries of livestock. Parallel studies in collaboration with Twink Allen led both to the identification of the cells responsible for the synthesis of the main hormone used for superovulation at that time, namely equine chorionic gonadotrophin (PMGG) and to the determination of clearance rates for this gonadotrophin. However, our most rewarding studies during the 1970s were undoubtedly those associated with intercellular signalling in the granulosa compartment and more particularly experiments that defined the relationship between the follicle cells and the oocyte during maturation.

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The follicular studies outlined above served as the foundation for the third decades' experiments in which we narrowed our focus still further to enable us to concentrate exclusively on the oocyte. It was through the analyses of the nature of in vivo follicular signals, their mode of transmission to the oocyte and their role in reprogramming the oocyte that a group of us including Alan Trounson, Bob Staigmiller and Cesare Galli, devised the foundation techniques for the production of embryos from the ovaries of slaughtered livestock. It was always apparent that the production of embryos in vitro would involve not only oocyte maturation but also fertilization and culture in vitro. In collaboration with Chris Polge and Winston Chen we were also successful in developing the first in vitro fertilization systems for sheep and pigs. The extension of the work to studies on interactions between the newly fertilised egg and the oviduct were carried out with Fulvio Gandolfi and Tiziana Brevini: the results led to a period of considerable interest in co-culture and to an unresolved debate about oviduct secretions and embryonic development.

Our disappointment with the low rates of development and poor quality of embryos produced using in vitro technology has persuaded us in the present decade to become even more narrowly focused: we now work solely on the molecular events underlying maturation and early embryonic development. In particular, we are interested both in the mechanisms by which masked maternal messages are mobilised and translated at precisely defined stages in the oocyte and by the precise role played by each of these oocyte-specific proteins during development. We predict that it will become increasingly evident that events during oogenesis provide the key determinants for subsequent embryonic and fetal development. In conclusion, I wish to thank all my collaborator for the pleasure of working with them. Furthermore, I am deeply indebted to the International Embryo Transfer Society for their generosity in making a Pioneer Award to Tim Rowson in 1985 and in conferring the same honour on me in 1999.