Embryo Implantation

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Preface

Embryo implantation - coordination of maternal and embryonic adaptations

Viviparity is the process of a fertilized egg growing and developing within the mother (Amoroso, 1968). The process has inherent benefits, including a level of protection from predators and need-based delivery of nutrients. The opportunity of the embryo to develop within the female reproductive tract is met with many challenges. These challenges are addressed with specializations within the embryo and uterus and an elaborate system of controls. Research has focused on the female reproductive tract and its transformation into a safe haven facilitating embryonic and fetal development and on the extraembryonic specializations derived from the embryo. Collectively these events comprise embryo implantation. Coordination of parallel processes in maternal and embryonic compartments is a necessity. This Special Issue of the *International Journal of Developmental Biology* provides a forum for a talented group of experimentalists actively pursuing research addressing a range of scientific questions related to embryo implantation. Each contribution consists of a short review of the relevant literature and insightful perspectives with the goal of stimulating future research.

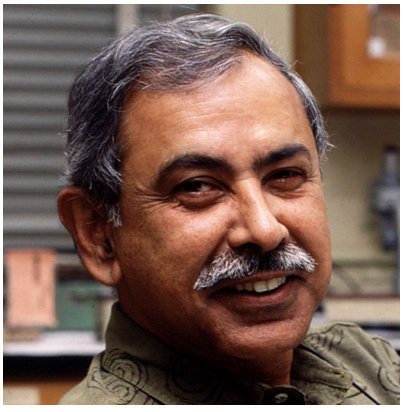

Fig. 1. Sudhansu K. Dey, *Ph.D., Cincinnati Children's Hospital, Ohio, USA.*

Ivan Damjanov provides a special historical perspective highlighting the biology of the human decidua and the contributions of the noted pathologist, Arthur H. Hertig, to our understanding of human embryo implantation. Professor Damjanov's scientific accomplishments are especially noteworthy. He is an eminent pathologist whose efforts in embryo implantation grew from early observations on the extrauterine growth of embryos and their formation of teratocarcinomas (Solter *et al.*, 1970; Damjanov *et al.*, 1973; Damjanov and Solter 1974a,b). His elegant experiments published over forty years ago spurred research in the fields of cancer biology, developmental biology, and reproduction and led to the emergence of stem cell biology as a discipline.

The research of two individuals has epitomized excellence in the field of embryo implantation. Sudhansu K. Dey, Lova Riekert Chair and Professor of Pediatrics and Director of the Division of Reproductive Sciences at Cincinnati Children's Hospital, has dedicated his scientific career to research on embryo implantation (Fig. 1). Professor Dey's research has made remarkable progress in defining and translating the molecular language used in embryo-uterine communication. The impact of his efforts is far-reaching and illuminated in a personal interview presented in the Special Issue. This article is followed by an interview with Susan J. Fisher, Professor, Departments of Obstetrics, Gynecology, and Reproductive Sciences and Anatomy and Director of the Human Embryonic Stem Cell Program at the University of California, San Francisco (Fig. 2). Professor Fisher has made seminal discoveries that have enhanced our understanding of trophoblast cells, the embryonic specialization facilitating interactions with the uterus, and their involvement in the establishment of pregnancy and in pregnancy-related diseases. Both scientists are exceptional mentors. Their interviews are punctuated with personal reflections and thoughtful advice. Readers of this Special Issue are also directed to the scientific works of Professor Dey and Professor Fisher, including their own outstanding reviews on embryo implantation. References for a sampling of some of their reviews are provided in the reference list at the end of this introduction (Norwitz *et al.*, 2001; Paria *et al.*, 2002; Red-Horse *et al.*, 2004; Wang and Dey 2006; Maltepe *et al.*, 2010; Cha *et al.*, 2012).

Fig. 2. Susan J. Fisher, *Ph.D., University of California, San Francisco, USA.*

The short reviews in the Special Issue address subjects related to embryo implantation and are subdivided into thematic sections (uterine biology, epithelial-stromal interactions, and decidualization; embryo-uterine interactions; maternal immune/inflammatory cells and the establishment of pregnancy; trophoblast development and actions on the maternal interface; epigenetics of development and disease). There was not an attempt to be all-inclusive in terms of topics related to embryo implantation, but instead the goal was to assemble a timely collection of provocative discourses on the theme.

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Initial presentations focus on the preparation of the uterus for the embryo, which is critical for the establishment of pregnancy. These uterine changes are driven by an assortment of signaling systems involving hormones, growth factors, and cytokines and their actions on defined cellular compartments. Effective communication between the uterine cellular constituents is essential for embryo implantation. In concert with these preparatory events, the embryo acquires specialized attributes facilitating the transformation of the female reproductive tract. Evolutionary and comparative aspects of embryo implantation are also addressed in the Special Issue and include discussions of the origin of the decidual cell, embryonic diapause, delayed embryo implantation, and hemochorial placentation.

Among the various maternal adaptations characterizing the onset of pregnancy are those associated with the immune system. Precise uterine trafficking and activities of immune and inflammatory cells are coordinated by a complex set of signals originating from the mother, father and fetus. These efforts allow the semiallogeneic embryo to prosper in a potentially harmful environment. Reviews address the resident uterine immune/inflammatory cells, including their actions and regulation during the establishment of pregnancy and how their dysfunction can contribute to pregnancy-associated disease.

The penultimate section of the Special Issue contains reviews discussing the derivation of the trophoblast cell lineage and its participatory efforts in transforming the uterine interface and maternal milieu. Molecular mechanisms and signaling pathways controlling trophoblast cell development are presented, including an overview addressing the complexities of investigating human trophoblast development. Examinations of trophoblast-uterine communication and the actions of trophoblast cells on the uterine vasculature and immune system are included. The final review in this section discusses the exciting recent discovery of a microRNA-based system used by trophoblast cells as protection against viral infection (Delorme-Axford *et al.*, 2013).

The final chapter represents a presentation on the role of epigenetics and imprinting in development and disease. Genomic imprinting is an example of epigenetic regulation and is fundamental to mammalian embryogenesis, including development of the trophoblast lineage. Disruptions in genomic imprinting alter development and lead to disease.

Collectively, it is hoped that readers of this Special Issue will gain a useful resource of not only facts, but also of ideas that will propel research on embryo implantation for the next several years.

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Michael J. Soares
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