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Review

Early embryonic development, assisted reproductive technologies, and pluripotent stem cell biology in domestic mammals

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ABSTRACT

Over many decades assisted reproductive technologies, including artificial insemination, embryo transfer, in vitro production (IVP) of embryos, cloning by somatic cell nuclear transfer (SCNT), and stem cell culture, have been developed with the aim of refining breeding strategies for improved production and health in animal husbandry. More recently, biomedical applications of these technologies, in particular, SCNT and stem cell culture, have been pursued in domestic mammals in order to create models for human disease and therapy. The following review focuses on presenting important aspects of pre-implantation development in cattle, pigs, horses, and dogs. Biological aspects and impact of assisted reproductive technologies including IVP, SCNT, and culture of pluripotent stem cells are also addressed.

Introduction

Over the past decade, the landscape for veterinary research in embryo technology and stem cell biology has reshaped dramatically. The initial focus of embryo technology in the domestic animals was to optimize breeding for improvement of production and health. In some countries, such as Brazil and Argentina, embryo technologies have found extended practical application, and large numbers of bovine embryos are produced in vitro and transferred to recipients in these regions. In most parts of the world, however, the breeding-related use of such technologies is quantitatively limited. Investigations on pluripotent embryonic stem cells (ESCs) were initiated more than two decades ago with the aim of using the technology for the production of genetically-modified domestic animals. However, these initial efforts to establish ESCs in the domestic species were soon abandoned, due to the discouraging results and, more importantly, to the ground-breaking discovery that cultured embryonic or even somatic cells could be reprogrammed into totipotency by the egg cytoplasm, allowing for generation of genetically-modified animals by nuclear transfer.

Recently, however, renewed focus on domestic animal embryo technology and stem cell biology has emerged, due to the need for improved biomedical models for human diseases. This development has sparked in-depth research into fundamental aspects of developmental and stem cell biology in the larger domestic mammals, and thus, the understanding of molecular and cellular aspects of initial embryology and phenomena such as pluripotency and cell differentiation in these species is exponentially evolving.

The understanding of pre-implantation embryonic development is a key to optimizing the use of domestic animals as models for human disease, e.g. via refinement by genetic modification and establishment of different stem cell tools, as well as for optimizing the use of embryo technologies for breeding and production. The present review is an attempt to analyse current knowledge of the molecular aspects of pre-implantation development in pigs, cattle, horses, and dogs as well as to discuss the significance of this knowledge for the practical refinement and utilization of in vitro production of embryos, cloning by somatic cell nuclear transfer, and pluripotent stem cell culture.

The anatomy of pre-implantation embryonic development in domestic mammals

Proper maturation of the oocyte to metaphase II is a prerequisite for fertilization and pre-implantation development. In the sow, cow, and mare maturation occurs in the pre-ovulatory follicle within approximately the last 42, 24, and 36 h before ovulation, respectively. Interestingly, in the dog the oocyte is ovulated with an intact germinal vesicle and completes maturation in the oviduct over a 2–4 day period.

Upon fertilization, major embryonic genome activation, which occurs at the 4-cell stage in pigs and around the 8-cell stage in cat-

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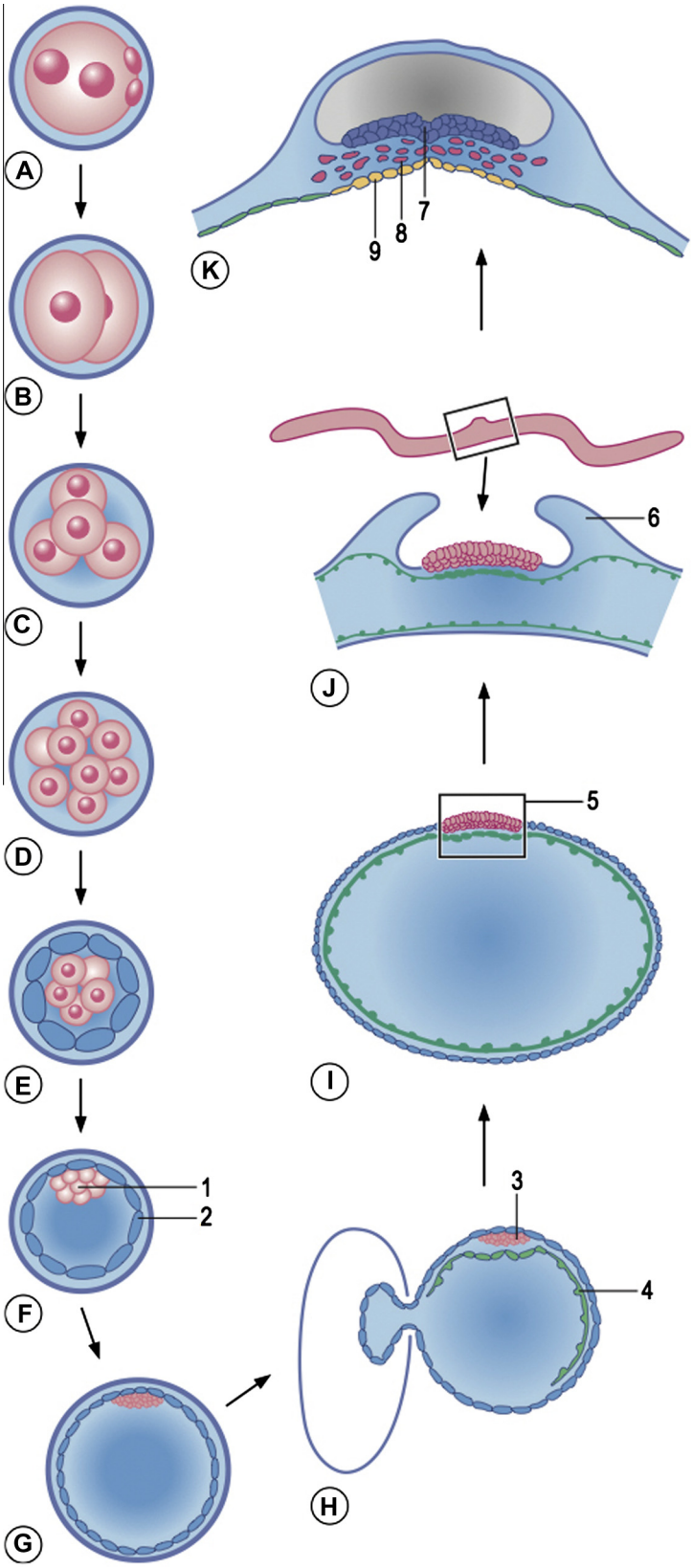

Fig. 1. Initial development of the bovine embryo. A: Zygote; B: 2-cell embryo; C: 4-cell embryo; D: Early morula; E: Compact morula; F: Blastocyst; G: Expanded blastocyst; H: Blastocyst in the process of hatching from the zona pellucida; I: Ovoid blastocyst with embryonic disc; J: Elongated blastocyst; K: Embryonic disc in the process of gastrulation. 1: Inner cell mass; 2: Trophoblast; 3: Epiblast; 4: Hypoblast; 5: Embryonic disc; 6: Amniotic folds; 7: Ectoderm; 8: Mesoderm; 9: Endoderm (from Hyttel et al., 2009).