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PREFACE

One critical difference between an embryo and a machine is that a machine is never required to function until after it is built, whereas every animal has to function as it builds itself.

Scott Gilbert, in "Developmental Biology," 6th ed., 2000

1. THE FOUNDATION OF MAMMALIAN DEVELOPMENT

Development of a fertilized human egg into an adult of 75 kg requires the production of 29 trillion cells or about 60 trillion meters of DNA. That's enough DNA to stretch from the earth to the sun and back 200 times! Include the approximately 1 trillion hematopoietic cells produced each day in adults, together with the turnover in epithelial cell populations, and the number of cell divisions in a human life span is truly astronomical!

Remarkably, the first 7–9 rounds of cell division that follow fertilization, the period termed preimplantation to peri-implantation development, establish the machinery that regulates cell proliferation and differentiation throughout these trillions of cell divisions. Each time a cell divides, it must duplicate its nuclear genome accurately once, but only once. Genes in the fertilized egg must soon be expressed to compensate for the loss of maternally inherited RNA and proteins. A developmental program must be established that determines which genes will become active, in which cells, and at what stage in development. The three primary cell lineages that are established in the blastocyst provide the progenitor cells for the fetus, placenta and adult. They also are the source of stem cells that can be derived, propagated, manipulated and differentiated *ex utero*. Thus, preimplantation development is the foundation on which the adult is built. Unfortunately, mistakes appear to occur frequently at the beginning of human development, because miscarriage during early pregnancy is as high as 31% (Regan & Rai, 2000; Wilcox et al., 1988). This book is dedicated to the proposition that understanding mammalian preimplantation development is critical to understanding fertility, embryonic development, and the birth of healthy offspring.

2. THE UNIQUE GOALS OF PREIMPLANTATION DEVELOPMENT

The mouse has been a popular experimental model, because it is cost-effective, amenable to the tools of genetics, biochemistry, and molecular