RIKEN Center for Developmental Biology (CDB)
2-2-3 Minatojima minamimachi, Chuo-ku, Kobe 650-0047, Japan

Identification of a mouse maternal effect gene

December 2, 2003 — A gene known to function in the specification of the germline – cells such as sperm and eggs that are capable of transmitting genetic information across generations – has now been shown to function as "maternal effect" gene essential to normal early development in mice. Mice lacking this gene, named *stella*, experience drastic reductions in fertility, as their eggs lack the *stella* protein product and most fail to develop past the first few cell divisions. These findings are the result of collaborative work done by teams at the Wellcome Trust/Cancer Research UK Institute (Cambridge, UK), Osaka University (Osaka, Japan), and Mitinori Saitou, leader of the RIKEN CDB Laboratory for Mammalian Germ Cell Biology (Kobe, Japan).

Maternal effect genes, which have been studied extensively in systems such as flies, fish and frogs, are much less commonly encountered in the mouse. Such genes in these non-mammalian model organisms are expressed in the oocytes and produce messenger RNAs that segregate to specific regions of the egg. These mRNAs typically encode proteins that function to pattern the embryo from the very earliest stages of development. However, mouse embryogenesis is characterized by the equivalency of cells that arise from the first few divisions from the egg, suggesting that in mice maternal effect genes play a limited role at best.

In a study designed to determine *stella's* physiological roles, the Wellcome Trust team and Saitou knocked out the gene, which is specific to nascent germ cells, maturing oocytes and preimplantation embryos in mice, and found that even mice homozygous for the mutation were viable and had no apparent defects in the development of either sperm or eggs. However, they dsicovered that although the knockout males exhibited normal fertility, the females exhibited greatly reduced birth rates, which prompted the investigators to look more closely at development in the mice in the period immediately following fertilization attempts. They found that fertilized oocytes failed to implant in the uterine wall, a critical step in the early embryonic development of the mouse. The dramatic reduction in number of live offspring was consistent regardless of whether the father was a knockout or wild type mouse, a pattern characteristic of maternal effect genes.

The role of *stella* in later development remains a puzzle. The failure of *stella* mutations to produce any discernible effect in germ cells suggests that there may be other proteins capable of compensating for the loss of *stella* function in the developing germline. The Stella protein is known to share structural characteristics with proteins involved in maintaining pluripotency and the development of embryonic and germ cell tumors in humans, and the researchers now expect to focus on the functions of this group of molecules in the earliest stages of development and the establishment of the germline.

Contact: Douglas Sipp sipp@cdb.riken.jp TEL: +81-78-306-3043
RIKEN CDB, Office for Science Communications and International Affairs