관관계가 있으리란 최근의 학설을 뒷받침해 주는 증거라 할 수 있다. 미세결실이 나타나는 유전자 지역과 고환 표현형과의 관계를 알아본 결과 SCOS 환자들에서는 AZF 후보유전자로 제시된 RBM, DAZ 및 SPGY 등이 포함된 AZFb 지역과 AZFc 지역에서 결손이 관찰되었다.

O-32 Phosphodiesterase Type III Inhibitor as a Candidate for a New Contraceptive Pill

Sang-Young Chun* and Hyuk-Bang Kwon

Hormone Research Center, Chonnam National University, Kwangju 500-757

One of the most widely used methods of contraception is the oral contraceptive hormone pill known to disrupt the pattern of gonadotropin secretion and ovulation. Although of undisputed efficacy, the long term exposure to estrogen/progestogen that this method involves is incidentally associated with side effects. Recent medical report issuing that use of conventional contraceptive pills over a long period of time may cause a death by a blood clot prompts the development of a new contraception. Here we describe a novel approach to the control of fertility in the female, based on the prevention of oocyte maturation at the time of ovulation using inhibitors of enzymes involved in cAMP signal transduction.

Mammalian oocyte development is characterized by prolonged meiotic arrest and gonadotropin-induced resumption of meiosis. During most of its growth phase, the oocyte is arrested at prophase I. Meiosis is triggered by the preovulatory surge of luteinizing hormone (LH) in healthy preovulatory follicles during each reproductive cycle. It is well known that the second messenger cAMP plays an important role in meiotic arrest of oocytes. Elevated cAMP levels within the oocyte prevent its maturation and a decrease in intracellular levels of cAMP after LH surge is believed to initiate meiotic resumption. We have demonstrated that the maturation of rodent oocytes *in vitro* can be prevented by addition of inhibitors of phosphodiesterase (PDE) type III (PDE3), the enzyme responsible for the breakdown of cAMP, and that PDE3A is selectively expressed in oocytes (*Dev. Biol.* 1996 178:393). More recent report demonstrating that treatment with PDE3 inhibitors prevents fertilization and pregnancy without disturbing follicle rupture and normal estrous cyclicity in rodents (*J. Clin. Invest.* 1998 102:532) provides a new strategy to develop effective contraception by selective blockage of oocyte maturation. Because PDE3A is also highly expressed in heart and treatment with PDE3 inhibitors induces an increase in heart rate, more studies are necessary to determine if oocyte PDE3A form is different from the PDE3A expressed in heart. Therefore, future studies should aim towards the development of drugs that target only one single cell type, i.e., the oocyte in the preovulatory follicle, during each menstrual cycle. This strategy of oocyte-specific PDE inhibition, when improved, could allow effective contraception by selective blockage of oocyte function without alterations in normal ovulation and reproductive cyclicity.