Summary

Yuji Taketani

We have been fortunate to share in the stimulating and thought-provoking presentations featured at the Takeda-Sponsored 2nd Japan Conference on Endometriosis, held in Kanagawa, Japan on May 8, 1999. There were many significant findings highlighted during the meeting including the role of ovarian hormones and their receptors in the regulation of endometriosis, the regulation of growth factors in the vascular pathogenesis of endometriosis, the role of free radicals in fertility, and new methods of diagnosing endometriosis.

Retinoic acid may act in a manner similar to progesterone in the regulation of endometrial matrix metalloproteinases (MMPs) to reduce the establishment and progression of experimental endometriosis. Professor Kevin Os-teen (Vanderbilt University School of Medicine) noted that retinoic acid is known to be an essential component of normal endometrial function, including the maintenance of normal pregnancy. Developing a better understanding of MMP regulation by both steroids and cytokines may help us to develop more successful treatment strategies for endometriosis.

Assistant Professor Jiro Fujimoto (Gifu University) reported that elevated levels of vascular endothelial growth factor (VEGF) secreted into the peritoneal fluid from activated macrophages may contribute to vascular pathogenesis of endometriosis under the influence of ovarian steroids, while basic fibroblast growth factor (bFGF) might promote endometriosis in autocrine and paracrine manners independent of sex steroids. One likely

autocrine growth factor for stimulation of the angiogenic pathogenesis of endometriosis endometrial stromal cells is IL-8. Dr Fujimoto believes that many angiogenic factors might contribute individually to the advancement of angiogenic lesions.

Endometriotic implants contain both estrogen receptors and P450arom, an enzyme that catalyzes conversion of androgens to estrogens, suggesting that estrogens may be involved in tissue growth through interaction with the estrogen receptors. Assistant Professor Jo Kitawaki (Kyoto Prefectural University School of Medicine) evaluated the clinical usefulness of a diagnostic test for endometriosis by detection of P450arom in endometrial biopsy specimens and found that P450arom is expressed in the eutopic endometria only in patients with endometriosis. It may soon be possible to diagnose the presence of endometriosis by examination of P450arom expression in endometrial biopsy specimens. This technique may be useful as an initial screening for infertility.

Assistant Professor Hirotaka Ota (Akita University School of Medicine) answered the question 'Do free radicals participate in fecundity?'. He noted that in pregnant mice, the administration of a nitric oxide synthetase inhibitor reduced the pregnancy rate in a dose-dependent manner. Histologic analysis of these uteri showed impaired intercellular reactions and retarded 'decidualization' of stromal cells. We can conclude that free radicals appear to participate intimately in implantation, and the optimal levels of free radicals are critical to the process.

The pathogenesis and activity of endometriosis may depend on internal angiogenesis, and may be different in different classifications of pigmented lesions in pelvic endometriosis. Dr. Akira Fujishita (Nagasaki University) reports that high endoglin levels may provoke an increase in the area of the subperitoneal blood vessel network, which may in turn facilitate implantation and viability in the retroperitoneal space. In contrast, lower endoglin levels in black and white lesions could explain the decrease in stromal vascularization and subsequent inactivation of the implant. He noted that immunohistochemical studies of endoglin expression may be better than VEGF expression for understanding the activity and pathogenesis in endometriosis.

Professor Osteen also shared his findings on the possible association between endometriosis and environmen-

tal exposure to dioxin (TCDD). TCDD exposure inhibits the expression of progesterone-associated transforming growth factor (TGF)- β_2 and suppresses associated matrix metalloproteins. Interference with the production of TGF- β_2 may have broad implications to reproductive processes beyond development of endometriosis. It is obvious that a better understanding of progesterone and the role of TCDD is needed.

This symposium included some of the top expert investigators from the field of endometriosis. It is hoped that the studies featured in this supplement will be the basis for a new understanding of cellular and molecular function in the development of endometriosis. These new findings can advance our understanding of this disease and aid in our development of new therapies for the prevention and successful treatment of endometriosis.