484 Expression of P-glycoprotein in human placenta and hydatidiform mole Y.Nakamura, T.Matsumoto, H.Douzono, Y.Nagata,* S.Akiyama** Dept. Obst.and Gynec.* and Dept. Cancer Chemotherapy,Inst. of Cancer Res.**,Kagoshima Univ. Sch.Med.,Kagoshima.

Substantial progress has been made in the development of more effective treatments for cancer. However, the development of drug resisrance, especially of multidrug-resistance to anti-cancer agents has been recognized as one of the major obstracles to successful cancer chemotherapy. Most cell lines with the multidrug-resistance phenotype show increased expression of P-glycoprotein. P-glycoprotein is known to be expressed in normal tissues such as adrenal,kidney,liver & gastrointestinal tract. We examined the expression and localization of P-glycoprotein in human placenta of each gestational period and hydatidiform mole with immunoblot analysis. P-glycoprotein was expressed in all placenta and hydatidiform mole. Expression of P-glycoprotein in hydatidiform mole was weaker than that in placenta. There was no correlation between gestational period and expression of P-glycoprotein in placenta. Monoclonal antibody MRK16 was used to determine the location of P-glycoprotein in placenta and hydatidiform mole by immunohistchemistry. P-glycoprorein in placenta and hydatidiform mole was detected on the trophoblast.

485 The function of Gp170, the multidrug resistance gene products, in human placenta villous membrane vesicles. S. Ikeda, H. Dozono, Y. Nakamura, T. Matsumoto, S. Akiyama * , Dept. Obst. and Gynec., Kagoshima Univ. Sch. Med., * Dept. Cancer Chemotherapy, Institute of Cancer Research.

Gp170 (also known as P-glycoprotein) is a trans-membrane glycoprotein which is overexpressed in multidrug-resistant tumor cells and is also found in villi of human placenta. Gp170 has been postulated to function as an energy-dependent efflux pump for cytotoxic drugs. Villous membrane vesicle contained a ~ 160-KDa protein which reacts with anti-Gp170 monoclonal antibody and manifest ATP-dependent [^{3}H] vincristine transport which is osmotically sensitive.

The photoactive dihydropyridine calcium channel blocker, azidopine, reversed multi-drug resistance, and [^{3}H] azidopine photolabelled Gp170 in membrane vesicle from human placenta. The labelling was completely inhibited by reserpine, but was slightly inhibited by progesterone.

ATP-dependent [^{3}H] vincristine transport was inhibited by cytotoxic drugs, and other drugs such as verapamil and reserpine, but was slightly inhibited by progesterone.

These results suggested that Gp170 in human placenta is an ATP-dependent efflux pump for cytotoxic drugs. And in human placenta, Gp170 is slightly associated with a transport of progesterone.

486 Evidence for a role of Plasminogen Activator and Plasmin in ovulation in *in vitro* perfused rat ovaries, N. Morioka, M. Mukaida, Y. Sagara. Dept. of Obst. and Gynec., Kochi Medical School, Kochi.

The role of Plasminogen activator (PA) and Plasmin in the ovulatory process has been studied extensively, but remained controversial, We demonstrated that tranexamic acid (AMCHA), a potent inhibitor of PA and Plasmin, inhibit ovulation in a dose-dependent manner in *in vitro* perfused rat ovaries. In this study, we investigated whether there is a critical time for AMCHA to inhibit ovulation. The addition of LH(NIAMMD-oLH-23, 0.1 ug/ml) + 3-isobutyl-1-methylxanthin (IBMX, 0.2mM) to the perfusion medium induced ovulation consistently (18.9 ± 1.8 per ovary, n=7). When 5 mM of AMCHA was added to the perfusion medium at different times (1-7 hours), the effective times to inhibit ovulation were 1, 2 and 3 hours after stimulation with LH+IBMX (4.6 ± 2.2,n=7; 6.0 ± 1.6, n=5; 10.0 ± 2.9, n=5; respectively). An exchange method, in which the ovary was perfused with AMCHA at 5mM and then placed into a second apparatus with fresh medium, showed that the exposure to AMCHA from 2 to 4 hours after stimulation with LH+IBMX, inhibit ovulation sufficiently. These data suggest that there may be a critical hours for PA and Plasmin to influence the ovulatory process.