estradiol somewhat but very little DES. Evidence has been obtained that the 2 binding sites do not belong to the same macromolecule. Results are interpreted as giving a molecular basis for interpreting antihormonal effects and for studying interactions of receptors with the genetic apparatus.

(3) *Regulation of receptors.* A classical phenomenon, the priming of estrogen action by estradiol in uterus, may be explained by the estrogen induction of the progesterone receptor synthesis. Moreover, estradiol induces the synthesis of its own receptor, and progesterone inhibits this induction, while progesterone increases the synthesis of the estrogen receptor in estrogen deprived endometrium. These observations are compatible with results reported under (2), since they suggest the presence of 2 receptors within uterine cells, for estradiol and progesterone, respectively.

The effects of steroid hormones on the intracellular distribution and the apparent half life of their own receptors have also been studied. In particular, progesterone seems to accelerate an apparent "inactivation" of its receptor.

The physiological changes observed in the uterus of the guinea-pig during the estrus cycle, and of the rat during early pregnancy, have been compared to the mechanisms studied in model conditions.

H. Oestrogen and androgen receptors in human breast cancer, H. MAASS, Department of Obstetrics and Gynaecology, University of Hamburg, Hamburg 20, Germany

Oestrogen and androgen receptors are routinely determined in specimens from primary and metastatic breast cancers. Agar gel electrophoresis (Wagner) has been used for determining the cytoplasmic oestrogen and 5α-DHT receptors. Specimens are called "positive" if the difference at the anodic peak is more than 100 c.p.m.

By this definition significant amounts of oestrogen receptors were found in 50% of primary cancers in the premenopausal group and 62% in the postmenopausal group. The rates in metastatic tissue are 22% and 39% respectively. The rate of specimens with 5α-DHT receptors is lower, in our material ranging between 20% and 25%.

Quantitatively the oestradiol binding ranges from 12·0–340·0 fmol/mg tissue protein or 18·0–268·0 fmol/mg DNA. The reference to the DNA content may be helpful in specimens with low receptor content.

Regarding clinical correlations to oestrogen receptor determinations at present 124 treatment trials had been evaluated. The rate of objective remissions in the "positive" group is 43/61, in the "negative" group 3/63. The number of patients who are evaluable regarding correlations to DHT receptors are low: remissions in DHT "positive" 4/5, in DHT "negative" 6/20.

In premenopausal patients there is a low concentration of available cytoplasmic receptor sites following the 12th day of the menstrual cycle.

Experiments on DMBA tumors showed that treatment of the animals with high doses of oestradiol is followed by a heavy decrease of oestrogen receptor contents. There is some evidence that the mechanism for the replenishment of new receptor protein is disturbed.

Similar observations had been made after treatment of the animals with ergocornin.

29. Appearance of nuclear estradiol receptor in perfused chicken liver, U. JOSS, Friedrich Miescher-Institut, P.O. Box 273, CH-4002 Basel, Switzerland

Estradiol causes the appearance of a nuclear estradiol receptor (R_N) in the liver of immature chickens. A significant increase of R_N is observed less than 1 min after administration of 2 μg estradiol/kg chicken into the portal vein. Maximal levels of 80 ± 10 fmol/mg protein are obtained 10 min after the estradiol pulse. The appearance is not sensitive to inhibition of protein synthesis by cycloheximide. The fact that no cytoplasmic receptor has been found in chicken liver prompted us to look for an extracellular receptor or precursor for R_N which would be transported into the liver nucleus and transformed to R_N by the effect of estradiol. In order to test this hypothesis, livers of immature chickens were isolated and perfused with synthetic perfusates. We found that the time course of appearance and maximal levels of R_N were similar to those found in the intact animal even when the synthetic perfusate contained only BSA and purified bovine erythrocytes. From this the existence of an extracellular precursor for R_N can be excluded, unless it is a contaminant of the bovine erythrocytes. The precursor for R_N therefore appears to be intracellularly located.

31. Specific progesterone receptors in DMBA-induced mammary tumors, J. ASSELIN, F. LABRIE, P. A. KELLY and J. P. RAYNAUD, Medical Research Council Group in Molecular Endocrinology, Centre Hospitalier de l'Université Laval, Québec, G1V 4G2, Canada and Centre de Recherches Roussel-UCLAF, Romainville 93230, France

The growing evidence for a correlation between the hormonal dependence of neoplastic tissues and the presence of specific hormone receptors led us to investigate the possible presence of specific progesterone receptors in dimethyl benzanthracene-induced mammary tumors in the rat. After homogenization in 3 vol. (w/v) of 25 mM Tris–HCl (pH 7·4), 1·5 mM EDTA, 10 mM thioglycerol and 10% glycerol (buffer A), the 105,000 *g* supernatant was used for binding studies with the highly potent synthetic progestin [^{3}H] R-5020 (17,21-dimethyl-19-nor-4,9-pregnadiene-3,20-dione). As measured by the charcoal assay after incubation for 15 h at 0°C, a significant level of soluble progesterone receptors is found in approximately 90% of tumors from untreated tumor-bearing animals. The level of progesterone receptors is 80 ± 20 fmol of [^{3}H]-5020 bound/mg of cytosol protein. As evidenced by sucrose gradient analysis, specific binding of [^{3}H]-5020 migrates at 7–8S. Specificity of the progesterone receptor was studied by both sucrose gradient and charcoal adsorption. [^{3}H]-5020 binding is competed by unlabelled R-5020, progesterone and a variety of synthetic progestins in a way very similar to the competition of [^{3}H]-5020 binding to the uterine progesterone receptor in rat. At a 100-molar excess, estradiol-17β and 5α-dihydrotestosterone inhibit [^{3}H]-5020 binding to the 7–8S component by 30 and 20%, respectively, while cortisol and dexamethasone are without effect. The potential significance of the level of progesterone receptors is indicated by our recent findings of a marked decrease of the level of this receptor after ovariectomy, a treatment accompanied by important regression of the tumors, and by the stimulatory effect of progesterone treatment upon tumor development.

32. The determination of the oestradiol receptor in normal and in neoplastic human mammary tissue, S. FUMERO, A. MONDINO, G. ZANOLO, Istituto di Ricerche Biomediche Antoine Marxer, RBM, Ivrea, V. AIMONE, C. CAMPAGNOLI, M. PERONA, II Clinica Ostetrica and Ospedale S. Anna, Torino