Steroid hormones activate gene expression by interaction of their receptors with hormone-responsive DNA elements and tissue-specific or ubiquitous factors. To monitor the molecular changes on the promoter of the rabbit uteroglobin gene during early pseudopregnancy in vivo, we have applied the genomic footprinting methodology to endometrial tissue. Estrogen induction results in the simultaneous occupancy of an estrogen-responsive element and an adjacent GC/GT box in the promoter. DNA binding assays demonstrate that the corresponding regulatory factors are the ligand-induced estrogen receptor and the ubiquitous transcription factor Sp1. Both factors functionally synergize in primary endometrial cells, showing that the GC/GT box is an essential part of a composite estrogen-responsive unit. However, the estrogen receptor and Sp1 do not bind cooperatively to their sites in vitro, suggesting that other mechanisms might be responsible for the hormone-dependent binding of Sp1 in vivo. Since hormone treatment leads to the appearance of a distinct DNase I-hypersensitive site over the promoter chromatin, an estrogen-induced change in the local chromatin structure could facilitate binding of Sp1 in vivo.

Gene expression is controlled by combinatorial arrangement of sequence-specific transcription factors that interact with each other and with components of the transcription initiation complex. Modulation of gene transcription is achieved by factors whose activity is reversibly influenced by ligands or post-translational modifications, such as phosphorylation. The transcriptional effects of ligand-inducible steroid hormone receptors represent a typical example. To attain efficiency and specificity in gene regulation, steroid hormone receptors interact with ubiquitous or tissue-specific factors as well as with co-activators, which bridge to the general transcriptional apparatus.

The particular combination of factors and the nature of the interactions required for regulated expression of a gene is specified in the form of complex arrays of cis-acting elements in its enhancer and promoter regions. These elements are usually identified through gene transfer experiments and in vitro DNA binding studies. However, the binding of factors to cognate DNA elements, as well as interactions with other factors, is conditioned by the native organization of DNA in chromatin, which imposes defined topological constraints. Therefore, demonstration of the functional relevance of DNA elements requires a genomic analysis of the chromosomally organized gene in intact cells.

To approach these issues, we have studied the steroid hormone-dependent regulation of the rabbit uteroglobin gene. In female animals, the gene is transcriptionally active in epithelial cells of the endometrium during the preimplantation phase of pregnancy (3, 4). Estrogen and progesterone exert a stimulatory effect on transcription (5). Whereas the action of progesterone is probably mediated by an upstream enhancer region containing two clusters of progesterone receptor binding sites (6), estrogen might function via a noncanonical estrogen-responsive element (ERE),1 as suggested by gene transfer and in vitro binding assays (7).

We have analyzed the promoter of the endogenous uteroglobin gene by genomic footprinting in endometrial epithelium from uterus in situ. Upon hormone treatment, we detect endometrium-specific occupancy of the noncanonical ERE in the promoter. Concomitantly, we observe estrogen-dependent recruitment of Sp1 to an adjacent site, which proved to be functionally essential for estrogen induction of the promoter. We provide evidence that Sp1 but not the related transcription factor Sp3 (8) mediates estrogen induction. Within this composite unit, the estrogen receptor (ER) and Sp1 bind noncooperatively in vitro. Synergistic binding in vivo could involve the chromatin configuration of DNA, since estrogen treatment induces a change in the chromatin structure of the promoter documented by the appearance of a prominent DNase I-hypersensitive site.

EXPERIMENTAL PROCEDURES

Plasmids—For the construction of the uteroglobin promoter-driven luciferase reporter plasmid, a HindIII (−395) to XhoI (+14) uteroglobin promoter fragment (9) was inserted into the pXP2 plasmid (10). Promoter linker-scanner mutants were generated from similar constructs (9). Further mutations were introduced by oligonucleotide-directed mutagenesis (11). The following expression plasmids for insect cells were used: for the expression of Oct, pPacOct (kindly supplied by C. Mows (12)); for human ER (13), pPacER (constructed and provided by G. Sasse); for Sp1, pPacSp1 (14); and for Sp3, pPacUbSp3 (15).

Genomic Dimethyl Sulfate (DMS) Footprinting in Vivo and Ligation-mediated Polymerase Chain Reaction—DMS footprinting was performed according to Ref. 16. In brief, endometrial epithelium or liver cells were exposed to 0.2% DMS in Dulbecco’s modified Eagle’s medium for 5 min. The reaction was stopped by washing several times with phosphate-buffered saline. Epithelial cells were separated, and genomic DNA was prepared, cleaved with piperidine, and submitted to a ligation-mediated polymerase chain reaction as described (17). The following gene-specific oligonucleotides were used: for the upper strand, ERA1 (GATCCTGTGGTTCCTCT), ERA2 (TCAACGCACTGTGGCCT-CACG), and ERA3 (GGCCTAGCTTCTCTTGACAGG); for the

1 The abbreviations used are: ERE, estrogen-responsive element; ER, estrogen receptor; DMS, dimethyl sulfate; EMSA, electrophoretic mobility shift analysis; hCG, human chorionic gonadotropin.
lower strand, ER1 (ACTGCTATTATTTACTGGG), ER2 (CATTGACTTGTTGGGATAAGTAATATTTCC), and ER3 (TTCCCTTTTCTCAATCCAGGTGCCATTTTCC). 

Electrophoretic Mobility Shift Analysis (EMSA) and Methylation Protection Analysis in Vitro—Nuclear extracts for EMSA were prepared according to Ref. 18. The following double-stranded DNA oligonucleotides were used: GTI, named Sp, containing a uteroglobin Sp-binding site (~232 to ~223) (6); a uteroglobin promoter (Pvu4II–HpaII) fragment comprising an ER and Sp-binding site (~304 to ~207) or the respective linker-scanner mutants (9); and a consensus ER (19). The gel-purified oligonucleotides were 32P-labeled by the Klenow filling-in reaction, and unincorporated nucleotides were removed through gel filtration. Recombinant human ER was expressed in COS-7 cells by transient transfection with the expression plasmid HEGO (13). Anti-bodies against Sp1 (20) and ER (21) were preincubated with nuclear extracts for 15 min at room temperature. Poly(dI-dC) and calf thymus DNA were added as nonspecific competitor, and binding buffers were as described in Ref. 22 but containing 3 mM ZnCl2. The binding reaction was incubated at room temperature for 15 min before loading on a 5% nondenaturating polyacrylamide gel. 10−7 M diethylstilbestrol was included in experiments with ER. Gels were run in 0.5-fold Tris borate/ethanolic solution immediately after transfection, and incubation was continued for 48 h. Diethylstilbestrol was used as estrogen agonist, and estrogen-induced Changes in the Occupancy of Putative Regulatory Elements—Expression of the rabbit uteroglobin gene in epithelial cells of the endometrium is induced by estrogen and progesterone (5). Using in vitro DNA binding experiments and transient gene transfer, we have defined a noncanonical ERE located around −258 (7) and three Sp-binding sites (also referred to as GC/GT boxes) located around −225, −200, and −65, respectively (9, 29) (Fig. 1A). To determine the role of these putative regulatory elements in hormone induction in vivo, we have studied their occupancy by the genomic footprinting technique (16). Since there are no suitable endometrial cell lines available, we have applied the DMS footprinting technique to the rabbit endometrial epithelium in situ after hormonal treatment of the animal. Ligation-mediated polymerase chain reaction analysis of the modified and piperidine-cleaved DNA revealed two hormone-dependent footprints in the promoter region between −300 and −200, which appeared in the endometrial epithelium but not in liver (Fig. 1B). Protection of three guanine residues over the ERE was found in both strands (open triangles), whereas a hypermethylated guanine residue was found in the lower strand (filled triangle). When compared with the liver lanes and taking as reference an unchanged band just upstream of the ERE, the protection in the upper strand was 30% in average for the three guanines. Over the adjacent GC/GT box, five guanine residues were protected in the lower strand and a single guanine in the upper strand. The corresponding residues are indicated in the nucleotide sequence of Fig. 1A. The footprints were observed in the hormonally induced endometrial epithelium but not in the uninduced endometrial epithelium from oestrous female rabbits (Fig. 1C, and see below). These footprints over the ERE and over the adjacent GC/GT box never appeared singly but always pairwise after various hormonal treatment leading to induction of the promoter. Interestingly, no prominent footprints were observed over the other putative GC/GT boxes located further proximally (data not shown).

The Distal Footprint Is Caused by the Estrogen Receptor, and the Adjacent Footprint Is Caused by a Member of the Sp Family of Transcription Factors—The distal footprint extended from −264 to −252. The pattern of protected guanines resembles an in vitro footprint formerly described for the ER (7). We verified that estrogens produced by the ovaries upon hCG stimulation are responsible for the induced footprint over the ERE by exposing the explanted uterus from oestrous animals to estrogen treatment. A footprint was induced when specific ligands of the ER, such as the synthetic estrogen diethylstilbestrol, were applied. The observed pattern resembled the footprints from pseudopregnant animals treated with hCG described above (Fig. 1, compare B and C). An estrogen-dependent in vivo footprint over the ERE was detectable as early as 30 min after hormone treatment (data not shown) and was visible for at least 4 h, suggesting a direct estrogen response. Similarly to the pairwise occurrence of footprints in hCG-induced endometrial epithelium, estrogen treatment of uteruses explants elicited the concomitant occupancy of the ERE and the adjacent GC/GT box (Fig. 1C).

An in vitro approach was chosen to identify the binding proteins at their respective sites. A DNA fragment encompassing both relevant regions was incubated with nuclear extracts of the endometrial epithelium from hCG-induced animals and subjected to EMSA. Two specifically retarded bands were observed (Fig. 2A, lane 5). The faster migrating band was supershifted by an antibody to ER and, therefore, corresponds to the bound ER (Fig. 2A, lane 1), whereas the slower band was...
supershifted by an antibody against Sp1 (Fig. 2A, lane 2; see below). Moreover, the faster band was competed by an excess of a consensus ERE oligonucleotide, while the slower band was competed by an oligonucleotide carrying a binding site for Sp factors (Fig. 2A, lanes 3 and 4, respectively). Consistently, a mutation in the ERE eliminated the faster band, whereas a mutation in the GC/GT box eliminated the slower band (Fig. 2A, lanes 7 and 6, respectively). Similar results were obtained in binding experiments using recombinant purified Sp1 expressed in vaccinia virus and recombinant human ER expressed in baculovirus-infected Sf9 cells or in COS-7 cells (Fig. 2B and data not shown).

The identity of the genomic footprints found in vivo was further proven by comparison with corresponding footprints generated in vitro. Both recombinant proteins, the baculovirus-expressed human ER and the vaccinia virus-expressed Sp1, protected virtually the same guanine residues as mapped in vivo (Fig. 1D). The same protection pattern was found when examining the retarded complexes obtained with extracts of induced endometrial epithelium that were immunologically

**Fig. 1.** DMS footprinting of the rabbit uteroglobin promoter *in vivo* and *in vitro*. A, schematic representation of putative regulatory elements in the uteroglobin gene promoter. The wild type nucleotide sequence of the elements is shown, and the observed methylation protection footprints *in vivo* are indicated by open triangles. The filled triangle indicates the observed hypermethylation at position −254. Below the wild type sequence, the upper strand of the linker-scanner mutants over the respective elements is shown. B, genomic DMS footprinting *in vivo* after hCG induction. Endometrial epithelium and liver of pseudopregnant rabbits were subjected to DMS treatment *in vivo*. Piperidine-cleaved genomic DNA was analyzed by ligation-mediated polymerase chain reaction. Panels show a representative result from the upper and corresponding lower strand comprising the distal promoter region from −270 to −200. Similar results were consistently found in repeated experiments. C, genomic DMS footprinting after short term estrogen induction. The uterus was explanted from an oestrus rabbit, and individual pieces were subjected to synthetic estrogen (diethylstilbestrol; DES) treatment or vehicle for 4 h. DMS was applied to the luminal surface of the intact uterus, and the endometrial epithelium cells were analyzed for resulting DNA modification. Protected guanine residues in the upper strand are indicated by open triangles (compare with left part of panel B). On the right of the gel, a quantitative evaluation of the observed methylation protection is shown. Bars represent the mean and S.D. calculated from three independent determinations, an earlier time point (1/2 h) after the addition of estrogen led to a similar result. D, methylation protection of the distal promoter region *in vitro*. Recombinant ER and Sp1 were incubated with a radioactively labeled DNA fragment covering the representative promoter region. Samples were treated with DMS and separated by EMSA. Specific retarded complexes were analyzed for guanine methylation (19). The autoradiograms show the upper and lower DNA strand; symbols are as in panel A.
identified as the endogenous ER and Sp1 (data not shown). The identity of contacts in both strands suggests that the genomic footprints originated from binding of ligand-activated ER and from Sp1.

**Functional Synergism between Sp1 and ER**—According to binding studies in vitro and gene transfer experiments, two additional putative Sp-binding sites in the uteroglobin promoter have been proposed (9, 29) (Fig. 1A). To reveal the functional significance of the various Sp-binding sites, we performed transient transfection experiments in primary epithelial cells from the endometrium. We selected linker-scanning mutations that affect Sp factor binding to the individual GC/GT boxes (9, 29) (Fig. 1A). The wild type uteroglobin gene promoter fragment spanning from −395 to +14 conferred moderate estrogen inducibility to the reporter (Fig. 3A, line 1), in accordance with the estrogen induction of uteroglobin transcription observed in intact animals (5). Mutation of the ERE completely abolished induction, confirming its function as a response element (Fig. 3A, line 2). Unexpectedly, mutation of the GC/GT box adjacent to the ERE drastically reduced estrogen induction (Fig. 3A, line 3), whereas mutations of the more promoter-proximal GC/GT boxes, at −195 and at −65, did not reduce estrogen induction but consistently resulted in slightly higher induction (Fig. 3A, lines 4 and 5, respectively). Combination of these individual mutants completely abolished estrogen induction (Fig. 3A, lines 6–8). This experiment demonstrates that estrogen-activated transcription requires not only binding of the activated receptor to its response element but also a synergistic interaction with another unrelated transcription factor, namely one of the Sp factors bound to the adjacent GC/GT box. Interestingly, the basal transcription rate was differently affected by these mutations. Mutation in the GC/GT box at −65 led to a strong decrease in basal activity, whereas the two more distal GC/GT boxes exhibited weaker effects, suggesting a differential role of these sites for basal and activated transcription.

Since the Sp family of transcription factors includes several members with similar affinities for GC/GT boxes (8, 15, 20, 29), we performed co-transfection experiments with ER in SL2 insect cells, which are devoid of endogenous Sp factors (14). The co-transfected ER alone conferred only weak estrogen induction to a reporter gene driven by the uteroglobin promoter; but estrogen induction was significantly enhanced by co-expression of Sp1, whereas a comparable co-expression of Sp3 had no such effect (Fig. 3B). Since Sp1 and Sp3 were expressed at similar levels in insect cells (20) and Sp1 is the most abundant GC/GT box binding activity in nuclear extracts of endometrial tissue (Fig. 2A, compare lanes 2 and 5), we tentatively conclude that Sp1 participates in the estrogen-dependent activation of the uteroglobin gene. The contribution of other GC/GT box-binding factors, such as Sp4 or BTEB (30), in the tissue-specific activation of the gene was not tested, since these proteins were not detectable in the tissue extracts by EMSA (8) (Fig. 2A).

**ER and Sp1 Bind to the Adjacent Binding Sites Simultaneously but Not Cooperatively**—The recruitment of Sp1 to its binding site triggered by the binding of the liganded ER could be due to cooperative DNA binding of the two factors. To test this hypothesis, we performed a titration experiment with the recombinant human ER and Sp1 proteins and a DNA fragment comprising the ERE and the adjacent GC/GT box. In the presence of sufficiently high concentrations of both factors, a ternary complex containing ERE and Sp1 was observed (Fig. 2B, lanes 8 and 11–16), as verified by methylation protection (data not shown). A similar gel retardation experiment was performed with DNA fragments mutated in either the ERE or the GT/GC box. As expected, the retarded band corresponding to the mutated site was not visible, and no ternary complex was detected (Fig. 2B, lanes 17 and 18). A quantitation of the different DNA-bound proteins as resolved by EMSA (Fig. 2B, lanes 13–16), reveals a linear function between the amount of added ER and the appearance of the ternary complex (Fig. 2C). These data exclude a significant cooperativity in binding of ER and Sp1 to the corresponding region in the promoter in vitro.

**The Nucleoprotein Organization of the Promoter Changes upon Hormone Induction**—An alternative explanation for the simultaneous binding of ER and Sp1 in vivo would be a hormone-induced alteration in chromatin structure, which could facilitate Sp1 binding. To assess this possibility, we measured the sensitivity of nuclear chromosomal DNA toward nucleolytic agents like DNase I or methidiumpropyl-EDTA. In nuclei treated with DNase I, already at the lowest enzyme concentration used, a narrow hypersensitive site was found at position −80 exclusively in the endometrial epithelium of hormonally induced animals (Fig. 4A). The same region was also hypersensitive toward methidiumpropyl-EDTA (data not shown). Thus transcriptional activation of the uteroglobin gene promoter is accompanied by an alteration of the nucleoprotein organization as indicated by the preferential accessibility toward nucleolytic agents at a precise position of the promoter.

**DISCUSSION**

*Both the ERE and the Adjacent GC/GT Box Are Essential for Estrogen Induction*—DNA regulatory elements can be identified in transfection experiments in cell culture, but the ultimate definition of sequences involved in the regulation of a particular gene can only be accomplished by studies in the intact tissue or even in the animal. One way to approach this goal is to analyze the regulatory regions of DNA using genomic footprinting techniques to identify sites that are occupied in vivo under physiologically relevant conditions (28). This type of experiment has usually been performed with cell lines in culture, with the well known limitations imposed by immortalization and artificial culture conditions. Here, we report the molecular analysis of steroid hormone effects in the native endometrial epithelium performed in an organ explant and applied to the rabbit uteroglobin gene. This methodology also allows us to monitor the pharmacological effects of related therapeutic agents in the complex background of the intact animal. The predictions derived from these studies have been experimentally tested via gene transfer in a homogenous and nearly authentic cellular system, i.e. primary cells from the endometrial epithelium.

Previous gene transfer experiments led to the independent identification of a noncanonical ERE and several GC/GT boxes in the rabbit uteroglobin promoter, but the contribution of these elements to gene regulation was unclear since the experiments were carried out in cells not expressing the endogenous uteroglobin gene (7, 9). In particular, it was not known whether the GC/GT elements participate in hormonal induction of the uteroglobin gene. The results of genomic footprinting experiments in the endometrial epithelium in situ demonstrate a selective behavior of the different GC/GT boxes, namely the simultaneous occupancy of the ERE and only the adjacent GC/GT box following induction of uteroglobin gene expression during early pseudopregnancy. A similar pattern was observed when animals were treated only with estrogens, although the extent of the observed changes was less pronounced, probably reflecting cooperative hormonal effects throughout early pseudopregnancy. Altogether, these findings suggest a permissive role for the liganded ER in the occupancy of the adjacent GC/GT box. Binding experiments with nuclear extracts from induced endometrial cells and with recombinant purified proteins suggest that the factors responsible for the observed in
Sp1 Recruitment Mediates Uteroglobin Gene Estrogen Activation

**Fig. 2.** ER and Sp transcription factors bind to the distal uteroglobin promoter in vitro. A, specific binding of nuclear proteins from hCG-induced endometrial epithelium to the uteroglobin promoter fragment comprising the putative ERE and Sp-binding site (−304 to −207; lanes 1–5). A gel retardation experiment was performed with either wild type fragment (lane 5) or fragments mutated at the Sp-binding site or in the ERE (lanes 6 and 7, respectively). Extracts were preincubated with antibodies against ER or Sp1 (lanes 1 and 2, respectively); arrowheads indicate supershifted antibody-transcription factor complexes. Competition with an excess of a bona fide ERE or Sp-binding site oligonucleotide was performed as control (lanes 3 and 4, respectively). B, noncooperative binding of recombinant human ER and recombinant human Sp1. A fragment comprising the ERE and Sp-binding site of the uteroglobin promoter (lanes 1–16) and the respective mutants (lanes 17 and 18) were used as in Fig. 2A. Titrations were performed applying geometrically increasing concentrations of the corresponding proteins (see Fig. 2C). Recombinant ER was added as a crude nuclear extract from baculovirus-infected Sf9 cells, and Sp1 was supplied as a vaccinia virus-expressed purified protein preparation (Promega, Madison, WI). For comparison with binding to single sites, a gel retardation experiment was performed under conditions of ternary complex formation (lane 11) but with the respective mutated oligonucleotides (lanes 17 and 18). Arrows mark the characteristic DNA-protein complexes, and ER-Sp1 indicates the ternary complex containing ER, Sp1, and the labeled DNA fragment. Filled circles denote unspecific or unidentified complexes from ER preparation; open circles indicate specific and pure Sp1-containing complexes. C, quantitation of the retarded complexes. Lanes 13–16 were quantitated. θ denotes the fraction of labeled DNA fragment in the corresponding band. Note the linear functions of the different DNA-protein complexes from ER concentration.

**vivo** footprints are the ER and members of the Sp family of transcription factors.

**ER and Sp1 Synergize Functionally but Do Not Bind Cooperatively to the Uteroglobin Promoter DNA**—In addition to the ERE, the integrity of the adjacent GC/GT box was essential for estrogen induction in primary endometrial cells. In transfection experiments in insect cells, which lack Sp factors, ER alone was insufficient for estrogen-dependent induction of the uteroglobin promoter. Since Sp1 was able to transcriptionally synergize with ER, while Sp3 is virtually inactive and represents only a minor fraction of GC/GT box-binding protein in endometrial epithelium extracts, we assume that Sp1 is the protein mediating the synergistic occupancy of ERE and GC/GT box. Sp3 has been shown to contain an inhibitory domain that represses transactivation mediated by Sp1 (15). Therefore, the possibility of modulating the estrogen response by changes in the cellular level of Sp3 relative to Sp1 should be considered (31).

The simultaneous occupancy of the adjacent ERE and GC/GT box could be due to protein-protein interactions, which would imply cooperative binding of the two proteins to their respective sites. However, although ER and Sp1 can bind to a promoter fragment simultaneously, quantitative binding experiments do not reveal a significant binding cooperativity in vitro.

**Molecular Mechanism of the Synergism between ER and Sp1**—Other factors could be involved in synergistic binding of ER and Sp1. Co-activators, such as CBP/p300, have been suggested to participate in Sp1 and ER transactivation and could therefore mediate, directly or indirectly, their synergism (32). Such multiple interactions between regulatory proteins could be difficult to reproduce in cell-free binding reactions, since the concentration of some partners in crude nuclear extracts might be limiting.

Multiple interactions of ER and Sp1 with components of the basal transcription machinery, such as TATA box binding protein-associated proteins, have been described (33–35), which could mediate the functional synergism (36). Their particular role in synergistic recruitment of the transcriptional preinitiation complex could be investigated in reconstituted in vitro transcribing systems.

An alternative explanation could involve the chromatin context of the DNA template. It is conceivable that ER and Sp1 do synergize for DNA binding on chromatin, although they do not synergize on free DNA, a behavior that has been described for other factors (37, 38). Experiments with nucleosomes assembled on uteroglobin promoter DNA would be required to clarify this issue.

Finally, hormone-dependent chromatin remodeling could possibly explain the observed synergism. Binding of ligand-activated ER to the uteroglobin ERE in chromatin could induce
Similar results were obtained without co-expressed Oct1. 200 ng of pPacER, and 10 ng of pPacSp1 or pPacSp3 per 60-mm dish. were used to avoid competition for limited factors (20): 10 ng of pPacOct, human ER, and either Sp1 or Sp3. Subsaturating amounts of plasmids plasmid was transfected together with expression vectors for Oct1, moter in transiently transfected SL2 cells. 5 
basal level (in the absence of estrogens).

A similar hormone-dependent binding of sequence-specific transcription factors to the vicinity of a steroid hormone-responsive element has been observed for the estrogen-inducible apo-very low density lipoprotein II promoter (41–43), the glucocorticoid-inducible tyrosine aminotransferase gene (44), and the glucocorticoid- or progesterone-inducible murine mammary tumor virus promoter (39). Thus, hormone-dependent recruitment of ubiquitous transcription factors to nearby and topologically restricted sites may be a crucial mechanism of hormonal gene regulation (45–49).

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REFERENCES
1. Beato, M., Herrlich, P., and Schütz, G. (1995) Cell 83, 851–857.
2. Felsenfeld, G., Boyes, J., Chung, J., Clark, D., and Studitsky, V. (1996) Proc. Natl. Acad. Sci. U. S. A. 93, 9384–9388.
3. Beier, H. M. (1968) Biochim. Biophys. Acta 160, 289–291.
4. Krishnan, R. S., and Daniel, J. C. J. (1967) Science 158, 490–492.
5. Muller, H., and Beato, M. (1980) Eur. J. Biochem. 112, 235–241.
6. Jantzen, C., Priton, H. P., Igo-Kemenes, T., Espel, E., Janich, S., Cato, A. C. B., Mugele, K., and Beato, M. (1987) Nucleic Acids Res. 15, 4535–4552.
7. Slater, E. P., Redeuilh, G., Thets, K., Suske, G., and Beato, M. (1999) Mol. Endocrinol. 4, 604–610.
8. Hagen, G., Muller, S., Beato, M., and Suske, G. (1992) Nucleic Acids Res. 20, 5519–5525.
9. Suske, G., Lorenz, W., Klug, J., Gazdar, A. F., and Beato, M. (1992) Gene Expr. 2, 339–352.
10. Nordheim, S. K. (1988) BioTechniques 6, 454–457.
11. Baretto, D., Fiegantzel, M., Vakarel, R., and Sturms, H. G. (1994) Nucleic Acids Res. 22, 541–542.
12. Sturms, R. A., Das, G., and Herr, W. (1988) Genes Dev. 12, 1582–1599.
13. Tora, L., Mullick, A., Metzger, D., Ponglikitmongkol, M., Park, I., and
Chambon, P. (1989) *EMBO J.* 8, 1981–1986
14. Courey, A. J., and Tjian, R. (1988) *Cell* 55, 887–898
15. Dennig, J., Beato, M., and Suske, G. (1990) *EMBO J.* 15, 5659–5667
16. Pfeifer, G. P., Steigerwald, S., Mueller, P. R., and Riggs, A. D. (1989) *Science* 246, 810–813
17. Truss, M., Bartsch, A., Schelbert, A., Haché, R. J. G., and Beato, M. (1996) *EMBO J.* 15, 5659–5667
18. Pfeifer, G. P., Steigerwald, S., Mueller, P. R., and Riggs, A. D. (1989) *Science* 246, 810–813
19. Truss, M., Chalepakis, G., Slater, E. P., Mader, S., and Beato, M. (1991) *Mol. Cell. Biol.* 11, 3247–3258
20. Hagen, G., Muñoz, S., Beato, M., and Suske, G. (1994) *EMBO J.* 13, 3843–3851
21. Greene, G. L., Sobel, N. B., King, W. J., and Jensen, E. V. (1984) *J. Steroid Biochem.* 20, 51–56
22. Sogawa, K., Imataka, H., Yamasaki, Y., Kusume, H., Abe, H., and Fujiikuriyama, Y. (1993) *Nucleic Acids Res.* 21, 1527–1532
23. Saceda, M., Grunt, T. W., Colomer, R., Lippman, M. E., Lupu, R., and Martin, M. B. (1996) *Endocrinology* 137, 4325–4330
24. Hanstein, B., Eckner, R., DiBenedetto, J., Halachmi, S., Liu, H., Searcy, B., Kurokawa, R., and Brown, M. (1996) *Proc. Natl. Acad. Sci. U. S. A.* 93, 11540–11545
25. Schippers, I. J., Klopper, M., van Waardenburg, R., and AB, G. (1994) *Eur. J. Biochem.* 221, 43–51
26. Strähle, U., Schmid, W., and Schütz, G. (1988) *EMBO J.* 7, 3389–3395
27. Eddy, E. M., Washburn, T. F., Bunch, D. O., Goulding, E. H., Gladen, B. C., Lubahn, D. B., and Korach, K. S. (1996) *Endocrinology* 137, 4796–4805
28. Schulte, R., Muller, M., Otuka-Murakami, H., and Renkawitz, R. (1988) *Nature* 332, 87–90
29. Schulte, R., Muller, M., Otuka-Murakami, H., and Renkawitz, R. (1988) *Science* 242, 1418–1420
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Uteroglobin Gene in Endometrial Epithelium
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