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GENERAL DISCUSSION

McGuire. I was a little surprised that you found progesterone receptor in all of your renal carcinomas and you made the comment that the affinity constant in the tumours was 10-fold lower than that in the normal tissues which is about 10^{-8} M so we're talking about binding at 10^{-7} M. Now people who work with SDS gel electrophoresis say that although you can separate SBG and receptors reasonably well CBG and progesterone receptor might be a little more difficult. My specific question is do you have unequivocal evidence that you are measuring progesterone receptor in these renal carcinomas?

Concolino. Yes, I think we have unequivocal evidence that we are dealing with progesterone receptor since our cytosol was preincubated with cortisol to saturate the binding sites of CBG and then the specificity was tested by the addition of cold progesterone which caused a decrease in binding.

McGuire. What was the exact affinity constant?

Concolino. In cytosol of human renal adenocarcinoma the K_D for progesterone ranged between 0.47×10^{-9} M and 5.16×10^{-8} M.

Bergink. Have studies been carried out using androgens as competitors for specific progesterone binding? Are you implying that there are 2 different receptors in the kidney or do you think that progesterone and androgens bind to the same binding site?

Concolino. I really do not know this. I think there are two different receptors, although from the recent studies of Bullock and Bardin it is known that progesterone in some animals seems to act through the androgen receptor. But I showed in one of the slides the attempts of treatment of advanced renal adenocarcinoma with both progesterone and androgens. Androgens were given in those patients who failed to respond to progestational therapy and the response to endocrine therapy was completely different. So our opinion is that kidney adenocarcinoma possess both receptors.

Jungblut. This slide shows the dissociation rates of various steroid–protein complexes during agargel electrophoresis at low temperature. There is virtually no dissociation of estradiol from its receptor during the 90 min run, while the complexes of progesterone and dihydrotestosterone with their respective receptors appear to be rather labile. In order to arrive at correct receptor concentrations one has to extrapolate to zero time. This is not necessary for the progesterone receptor assay, if the synthetic progestagen R 5020 is employed instead of the natural hormone.