DISCUSSION
The enzymes, acid and alkaline-phosphatases are of special significance in malignant condition. Alkaline phosphatase is known to participate in diverse biological functions like growth, differentiation and dedifferentiation (Moog, 1944; 1951; 1952; 1953; Johnson and Bevelander, 1947; Koning and Hamilton, 1954; Kabat and Furth, 1954; Hinsch, 1960; De et al., 1961; McWhinnie and Saunders, 1966) as well as in calcification and ossification processes (Horowitz, 1942; Lorch, 1949; Pranseen and McLean, 1935). Alkaline phosphatase is also known to participate in important metabolic functions (Barron, 1943; Dempsey and Wislocki, 1946; Johnson and Bevelander, 1947; Moog, 1952; Biesele and Biesole, 1944; Atkinson and Engle, 1947; Flock and Bollman, 1950; Schmidt-Matthiesen, 1963; Dominas, 1962). However, the metabolic role of acid-phosphatase is not very clear. Increased activity of this enzyme during liver regeneration in rats suggests a relationship of this enzyme with protein synthesis (Norberg, 1950).

The cervical tissue, except for the basal cell of epithelium, undergoes differentiation to perform its specialized function. The differentiated condition of this tissue in malignancy is accompanied by marked metabolic changes. This is in accordance with the loss of
differentiation and normal functionation, as well as gain in proliferative potency beyond homoeostatic principle. The proliferation of cells are simultaneously associated with necrosis and sloughing. Both the processes of cellular growth and dedifferentiation are beyond the limits of homoeostasis and characterize malignancy. While the peripheral sloughing of the tumour takes place uncontrolled proliferation of new cells simultaneously increases the size of the tumour and also spreads among the adjacent tissue as well as in distal organs. In the metabolic changes accompanying such expression, acid and alkaline phosphatase are expected to play important roles. To maintain the phenotypic expression of malignancy i.e. continuous production of new undifferentiated cells, it is of importance to explore how these two enzymes participate - whether any of their variants by way of isoenzymes are responsible for the maintenance of the same.

The enzymes alkaline and acid phosphatases catalyzes the hydrolysis of almost any phosphomonoester to give inorganic phosphate and the corresponding alcohol, or sugar. Both these enzymes distinguish themselves primarily by the range of pH dependence of their catalytic activity.
The existence of species, organ and even tumour specific variants of alkaline and acid phosphatases seem to be established without doubt. These isoenzymes differ in electrophoretic mobilities, heat stability, sensitivity to inhibition by amino acid and other chemical agents, pH optima, Km values and immunologic reactivity (Fishman et al, 1968; Haije and Dejong, 1963; Schlamowitz and Bodansky, 1953; Smith et al, 1960). The tissue specificity of phosphatase – isoenzymes are of growing importance due to its diagnostic value, but there is an astonishing gap in our information concerning the characteristics of this enzyme complex in malignancies and the possibilities of tracing possible tumour specific isoenzyme in the serum (Kellen and Lustig, 1971).

Fishman et al (1968) reported the presence of an isoenzyme of alkaline phosphatase in serum, and tumour of a patient with bronchogenic carcinoma which closely resembled the placental variants. They called this tumour isoenzyme as 'Hagan isoenzyme' which normally seemed to be produced by the placenta and not by the foetus. This is also produced by the neoplastic tumour cells in the adult by the depression of a genome in the neoplastic growth. Also the malignant cell of Hela is another example of cancer cells showing the characteristics of
placental alkaline phosphatase (Griffin, 1966). Warnock et al (1969) found isoenzymes of alkaline phosphatase in hepatic tumour which varies in their substrate specificity and molecular weight from the normal liver variants. Joplin and Jegatheesan (1962) suggested that in breast cancer tissue acid phosphatase activity increases considerably and it is higher than that of normal breast tissue.

Serum acid phosphatase is known to be elevated in carcinomas of the prostate, in primary tumours of bone and in metastatic tumours of the liver (Fishman, 1959). Babson, & Read (1959) demonstrated that Na-α-naphthyl phosphate was much more easily split by prostatic than red cell phosphatase. Thus substrate specific behaviour of acid phosphatase plays a great role in the diagnosis of prostatic cancer with respect to naphthyl phosphate as a substrate.

In the present study with malignant and non-malignant cervix, the enzymes alkaline and acid phosphatase show an interesting picture in their substrate specific behaviour. Alkaline phosphatase of premenopausal normal cervix shows least affinity towards Na-α-glycerophosphate among the substrate used, but the same enzyme
in malignant condition of same tissue shows highest affinity for the same substrate Na-\(\alpha\)-glycerophosphate. The result further reveals that glycerophosphate of \(\alpha\) and \(\beta\) configuration are inversely utilized in normal and malignant cases of pre-menopausal cervix. While alkaline phosphatase of normal cervix has greater affinity towards Na-\(\beta\)-glycerophosphate, the same enzyme in malignant condition has strikingly high affinity towards Na-\(\alpha\)-glycerophosphate. However, such relationship no longer exists when observed in case of post-menopausal condition (Fig. 2).

In malignant condition, acid phosphatase activity of cervix tissue shows higher preference for \(\beta\)-naphthyl phosphate, among the substrates used, but the activity is strikingly high in case of post-menopausal malignant cervix. While comparing the utilization of \(\beta\)-naphthyl phosphate as a substrate among alkaline and acid phosphatase activity of cervix tissue, it is noticed that alkaline phosphatase has lower preference for this substrate, but acid phosphatase has highest preference for the same. The inverse relationship of alkaline and acid phosphate is rather striking in cervical tissue with respect \(\beta\)-naphthyl phosphate as this manifestation is revealed in all the conditions studied—whether normal or malignant and whether in pre-menopausal or post-menopausal condition (Fig. 7).
This phenomenon of high affinity of acid phosphatase for β-naphthyl phosphate is highly accentuated in case of malignant cervix to the level of almost bearing diagnostic significance for cancer of the cervix.

The cervix is an endocrine target organ and its epithelium displays different stages of growth and differentiation under the influence of different sex hormones. The local steroidal milieu influencing the cellular phenotype as evidenced by its cytomorphic changes are associated with changes in the macromolecular pattern.

The enzymes participating in the adaptive changes of the biopolymers as a consequence of ovarian functions are of considerable interest particularly in respect of molecular variants of the enzyme under study.

The present result reveals that the substrate specific behaviour of the enzyme alkaline and acid phosphatase of cervix tissue depends upon the physiological condition of the tissue. In case of pre-menopausal condition, hormone influences the metabolism of the cervix tissue, often irrespective of normalcy and malignancy. The enzymes are the functional phenotype of the cell, and therefore exhibits the hormonal influence quite significantly in their behaviour. In post-menopausal
condition the direct effect of sex hormone has been withdrawn and therefore the behaviour pattern of enzymes under such circumstance appear different from that of pre-menopausal cervix tissue even under the influence of malignancy.

Utilization of naphthyl phosphate of \( \alpha \) and \( \beta \)-configuration by alkaline phosphatase demarcates pre- and post-menopausal condition irrespective of normalcy and malignancy. Alkaline phosphatase has lower preference for \( \text{Na-}\( \alpha \)-naphthyl phosphate \) both in normal and malignant cases of pre-menopausal condition compared to \( \beta \)-naphthyl phosphate as a substrate. Contrary to this higher preference of the same enzyme is noticed in post-menopausal condition towards \( \text{Na-}\( \alpha \)-naphthyl phosphate \) (Fig. 3).

In pre-menopausal condition, the utilization of \( \text{Na-}\( \alpha \) and \( \beta \)-glycerophosphate \) and \( \text{Na-}\( \alpha \)-naphthyl phosphate \) by acid phosphatase is less in malignant cervix than in normal cervical tissue. However, in post-menopausal condition the three substrates are inversely utilized, showing much higher rates of hydrolysis in malignancy and lower rate of hydrolysis in normal tissue. Hence these three substrates seems to demarcate pre- and post-menopausal status with respect to the acid phosphatase
activity under normal and malignant conditions.

Schmidt Matthiesen (1963) reported that apparently the activity of alkaline phosphatase is closely associated with the action of estrogen on the endometrium, although its function is still under study. Alkaline phosphatase most probably is important in protein synthesis and in the associated processes of growth and proliferation. There are series of reports indicating the effects of hormone on the alkaline phosphatase activity of the genital tract of many animals (Kamell and Atkinson, 1948; Pritchard, 1947; Talmadge, 1949; Bern, 1950; Ford, 1956). Studies in the human endometrium during the menstrual cycle, indicate that alkaline phosphatase is increased during the proliferative phase, reaches the peak shortly before or at the time of ovulation and then rapidly falls during the secretory phase (Nekay et al., 1956; Barbour, 1961; Fuhrmann, 1961; Hookerjee, 1961; Gross, 1964; Saksena et al., 1965; Taki et al., 1966; Filipe and Dawson, 1968). Herovici (1960) found the maximum alkaline phosphatase activity during ovulation and also observed the total disappearance of this enzyme after restraining the folliculine. Atkinson and Elftman (1946) have shown the influence of the sex hormone, singly or
in combination in many animals. It was observed by these workers that castration decreased the uterine alkaline phosphatase activity. Further, marked increase in the enzyme activity was observed following estrogen injection. The increase was not seen with progesterone or androgen or with progesterone administered simultaneously with estrogen.

Hormonal influence on acid phosphatase has been suggested, since the enzyme appears in the human prostate gland only after puberty (Gutman and Gutman, 1938). Reports on the activity of this enzyme during the hormonal fluctuation in different phases of the menstrual cycle are widely reported. It has been shown that acid phosphatase activity is low in human endometrium during the proliferative phase and rises continuously to reach its peak at the secretory phase (Hookerjee, 1961; Boutsolio, 1963; Fuhrmann, 1961; Vacek, 1965). Berger and Humprecht (1959) and Gracia-Brunel and Brandes (1966), however, found the highest activity of this enzyme at the time of ovulation. Others on the other hand, found no obvious difference in the activity of acid phosphatase between the follicular and luteal phase (Grose, 1964; Filipe and Dawson, 1968). Bitonski and Cohen (1965)
were able to demonstrate that acid phosphatase in the endometrium was located in the lysosomes. The reaction for the enzyme was positive only with permeable membranes since progesterone affects the permeability of lysosomal membranes. It is easy to understand that the activity of acid phosphatase might depend on the level of progesterone. But they failed to show any remarkable fluctuation of the enzyme during menstrual cycle.

Although the reports on the influence of sex hormones on the alkaline and acid phosphatase activity are highly contradictory, results of the present experiments indicate that estrogen increases the alkaline phosphatase activity of the uterine tissue of normal mice irrespective of substrates used. Progesterone seems to have a reverse effect from that of estrogen. In the non-oophorectomised normal, the enzyme activity is much less than that in oophorectomised mice, showing that in normal control progesterone effect on enzyme activity is more predominant than estrogen with the different substrate affinities except with Na-β-glycerophosphate. Compared to normal mice the enzyme activity of the uterus of tumour bearing mice is very much low with respect to Na-β-glycerophosphate as substrate.
The effect of estrogen and progesterone administration in the uterus of both types of tumor bearing mice reveals different degrees of enhanced or inhibited activity of the enzyme towards different substrates. Such effects do not seem to follow a definite pattern as is observed for normal mice. This might be due to the influence exerted by the tumor cells on the endocrine target organ modifying the response of the enzyme towards the hormone concerned in the light of hydrolysis of different substrates.

However, with respect to acid phosphatase, the picture is not so clearly defined in the uterus. The enzyme activity remains more or less unaltered in the tissue, in spite of transplantation of tumor cells either in oophorectomized mice or after exogenous hormonal stress. The results revealed that administration of exogenous estrogen influences the enzyme activity of uterus by way of enhancement in normal and carcinoma bearing mice. The effect particularly is significant with respect to the substrates β-naphthyl phosphate and phenyl phosphate. On the other hand, the same hormone decreases the activity in case of sarcoma 180 bearing mice. Progesterone offers exactly an opposite reaction to that
observed for estrogen. It decreases the enzyme activity in uterus of normal and carcinoma bearing mice but increases the enzyme activity in sarcoma 180 bearing mice. The substrate specific behaviour of acid phosphatase shows that not only in mouse uterine tissue but also in human cervix, the enzyme has highest preference for the substrate Na-β-naphthyl phosphate.

Contrary to reports on the presence of high alkaline phosphatase in different neoplastic tissue (Pesceotto, 1951; Koschino and Perisotto, 1952; Homburger and Fishman, 1953; Wachstein and Keisel, 1954; Gross et al., 1953) numerous investigators have revealed the presence of low alkaline phosphatase activity in certain malignant tumours (Foraker, 1956; Battuger et al., 1957; Feigin and Wolf, 1959; Monis and Rutenberg, 1960; Fishman et al., 1961). Monis and Rutenberg (1960) suggested that this enzyme had a limited role in metabolic processes of malignant tissues. Auerbach (1964) has also suggested that the decreased activity of hydrolytic enzymes in cancer cells may reflect a lack of differentiation and functional activity which is a fundamental feature of all malignancies.

The present result reveals that alkaline
phosphatase activity of Ehrlich's carcinoma and sarcoma 180 cells is quite low in comparison to the activity of this enzyme in other tissues of the host. It is also evident from the present study that by suppressing the ovarian function by oophorectomy, alkaline phosphatase activity appears to get elevated in both the tumor cells carcinoma and sarcoma 180 as compared to that in same tumor cells, transplanted in non-oophorectomized mice. This phenomenon seems to display uniformity with respect to all the types of substrates studied. The above picture is also true for acid phosphatase activity of tumor cells.

Administration of estrogen increases the alkaline phosphatase activity of carcinoma cells with respect to most substrates but decreases the acid phosphatase activity uniformly. In sarcoma 180 cells estrogen increases both alkaline and acid phosphatase activity. Progesterone enhances the activity of alkaline phosphatase in both types of tumor cells, with respect to all the substrates except β-naphthyl phosphate in Ehrlich's carcinoma. In this respect the affinity of the enzyme in the tumor cells towards α-naphthyl phosphate is particularly stronger than affinity towards the other
substrates. In sharp contrast to this, progesterone increases the affinity of acid phosphatase for \( \beta \)-naphthyl phosphate in Ehrlich's carcinoma and sarcoma 180 cells significantly greater than the increased activity with respect to the other substrates. It has also been shown that transplanted tumour cells, although not the so-called endocrine targets, are influenced by the ovarian hormones and is characterized by differential substrate affinities of alkaline and acid phosphatase.

With respect to the enzyme activity in different non-endocrine target organs, interesting results have been obtained in mice with or without the influence of the sex hormones. Regarding the alkaline phosphatase activity in different organs of normal mice, it appears that kidney, liver and intestine display high activity, as compared to that in lung, brain and uterus. The substrate specificity of the enzyme activity varies within a wide range. In kidney it is from 7 to 76, while in liver it is from 3 to 49, and in intestine from 12 to 65 units per gram of tissue. Uterus displays moderate amount of enzyme activity, the range varying from 3 to 15 units per gram of tissue. The variation of range denotes activities displayed with respect to utilization.
of different substrates. However, the maximum activity has been seen, with respect to Na-β-glycerophosphate. In comparison to the above mentioned organs, the alkaline phosphatase activity in lung and brain is very low. It varies within a range of 1 to 2 unit in normal mice.

Shtacher (1969) stated that alkaline phosphatase activity in kidney, intestine, liver and other tissues provide a sensitive biochemical index for monitoring any change in the cellular activities of these organs. The relationship between the various tissue alkaline phosphatase has been under discussion for many years (Belfanti et al., 1935). The organ specific behaviour of rat tissue phosphatase towards a variety of compounds was investigated by Fishman (1962). The heterogenic nature of kidney alkaline phosphatase was supported by many authors (Meloni, 1969; Fleioch and Bisaz, 1962; Moss et al., 1967; Femley et al., 1967). An extensive study of intestinal phosphatase activities during development has been made by Hoog (1962). In rat, a fat enriched diet has long been known to result in an increase in the alkaline phosphatase activity of the intestinal mucosa and serum (Ladesen, 1952; Gould, 1944). Inglis et al. (1967) reported that the intestinal isoenzyme contributes between
20-45\% of the total circulating alkaline phosphatase in the normal subjects. However, Longman (1966) and Glickman (1970) reported that the precise metabolic role of intestinal alkaline phosphatase is not understood; the enzyme may take part in the fat absorption or transportation.

In comparison to alkaline phosphatase, the acid phosphatase activity of kidney, liver and intestine is quite low in normal mice. On the contrary, the range of activity of enzyme becomes higher in lung and brain tissue. The substrate affinity of acid phosphatase is quite different from that of alkaline phosphatase. Instead of Na-\(\beta\)-glycerophosphate the enzyme shows higher preference for Na-\(\beta\)-naphthyl phosphate and phenyl phosphate in most of the organs of normal mice.

The acid phosphatase, although not as thoroughly investigated as alkaline phosphatase, is known to be widely distributed in animal tissues, the classical work in this line being those of Gomori (1941) and Wolf et al. (1943). The normal prostate is particularly known to have very high activity of acid phosphatase (Kutscher and Wolbergo, 1935).
Alkaline and acid phosphatases have been shown to vary greatly with malignancy of the tissues. The presence of high alkaline phosphatase in neoplastic tissue was first demonstrated by Franceen and McLean (1935) in osteogenic sarcoma and later in malignancy of liver (Homburger and Fishman, 1953), hydatid moles (Pescetto, 1951) ovarian carcinomas (Moschino and Parisotto, 1952), teratomas and embryonal carcinomas of the testis (Gomori, 1949; Homburger and Fishman, 1953; Sachstein and Keisel, 1954). Gross et al. (1959) also reported of elevated alkaline phosphatase in a number of neoplastic tissues.

Increased acid phosphatase activity in a heterogeneous group of malignancy have been clearly demonstrated (Gomori, 1949; Lemon and Wissman, 1949; Woodard, 1952; Glück, 1952; Lemon et al., 1954; Greenstein, 1956). Reiner et al. (1957) observed a wide variation in the concentration of acid phosphatase in identical tumors as well as in different tumor types. Serum acid phosphatase is known to be elevated in carcinoma of the prostate, in primary tumor of bone and metastatic tumor of liver (Fishman, 1959). Contrary to this Scarpelli et al., 1963 reported of decreased acid phosphatase activity in tumor cells.
The present investigation reveals that alkaline and acid phosphatase activity of Ehrlich's carcinoma and sarcoma 180 cells are rather low, although the activity of acid phosphatase are slightly greater than that of alkaline phosphatase. The activities of alkaline phosphatase vary from 0.04 to 0.4 in case of Ehrlich's carcinoma and 0.1 to 0.2, for sarcoma 180, while acid phosphatase values lie between 0.4 to 1 and 0.1 to 0.9 respectively. The substrate specific variations of activities reveal that in both the tumour cell types the highest range of alkaline phosphatase activity is with respect to Na-α-naphthyl phosphate as a substrate and not Na-β-glycero-phosphate as rated for different organs of normal mice. For acid phosphatase the affinity is highest for Na-β-naphthyl phosphate in both types of tumour cells as well as organs of the normal mice.

With respect to alkaline phosphatase activity, transplantation of tumour cells cause reduction of the enzyme activity in most of the host organs, including kidney where the highest activity comes down from 76 to 42 in carcinoma bearing mice and in case of sarcoma to 27.3. Greater affinity of the enzyme is still towards Na-β-glycero-phosphate. The lowering of enzyme activity due to tumour cell transplantation is also displayed in
the intestine and liver. However, transplantation of tumour cells has almost no effect on alkaline phosphatase activity of lung and brain. It appears that transplantation of tumour seem to exert an influence on kidney, liver and intestine resulting in lowering of alkaline phosphatase activity. The nature of influence is not clear at this stage of the experiment and could be due to metabolites from malignant cells. This influence though shown by both the tumour types taken, again may be tumour specific because Greenstein (1954) reported that along with many other enzymes the activities of alkaline and acid phosphatases were not altered remarkably in the liver, kidney, spleen and many other tissues of tumour bearing host.

In contrast to alkaline phosphatase, acid phosphatase activity observed in these organs due to tumour cell transplantation displays a strange reaction. Instead of two higher peaks of substrate affinity for 4a-6-naphthyl and phenyl phosphate in organs of the normal mice, the organs of tumour bearing host shows single peak either for 4a-6-naphthyl phosphate or phenyl phosphate. This strange phenomenon of abolition of one of the two sharp peaks of substrate utilization seem to characterize the influence exerted by the transplanted tumour cells, on
the acid phosphatase activity of these organs.

It is clear from the present experiments that most of the endocrine non-target organs behave quite differently from the target organ uterus, with respect to sex hormonal response. Withdrawal of the endogenous hormone by oophorectomy increases the activity of the alkaline phosphatase in most of the organs in normal condition. Unlike uterus, estrogen decreases the enzyme activity in these organs of normal mice with respect to all the substrates used. Substrate affinity of this enzyme in different organs varies with progesterone administration. While this hormone decreases the activity of alkaline phosphatase in normal uterus, it increases the same enzyme activity in kidney, liver and lung tissue of normal mice.

As already mentioned, it has been observed that transplantation of tumour cells exert influence over the endocrine target organ modifying its response towards the hormone concerned in the light of hydrolysis of different substrates by alkaline phosphatase. In the other organs studied although certain amount of reduction of enzyme activity is noticed, not much disturbance is caused with respect to the enzyme responsiveness towards the
two sex hormones.

Withdrawal of ovarian hormone causes increase of the acid phosphatase activity in most of the organs in both normal and tumour bearing mice. Exogenous estrogenic stress increases the activity of the enzyme further and progesterone has a variable effect in most of the organs of normal mice. But tumour cell transplantation seems to alter the responsiveness of acid phosphatase towards these two hormones in most of the organs of tumour bearing host. With external hormonal stress, the enzyme behaviour varies under a wide magnitude with respect to substrate affinity in different organs of both tumour bearing host.

It is evident from the various reports that the activities of alkaline and acid phosphatase in different tissues are profoundly influenced by the hormones (Kochakian 1946; Atkinson and Elftman, 1947; Atkinson and Engle, 1947; Born and Levy, 1952; Lang et al., 1954; Fishman et al., 1963; Filipe and Dawson, 1968; Dallonbach-Hellweg, 1971). The appearance of acid phosphatase in human prostate gland only after puberty (Gutman and Gutman, 1938) and its correlation with the estrous cycle of rats (Ring, 1950) indicate a definite hormonal influence on this enzyme. Besides alkaline
and acid phosphatase, there are extensive literature regarding the effect of sex hormones on many other enzymes. Both estrogen and androgen have been shown to increase RNA - polymerase activity. (Hancock et al., 1962; Gorski, 1964; Mandel, 1965) Administration of estrogen, progesterone and testosterone resulted in increased activity of lactic dehydrogenase (Goodfriend and Kaplan, 1964). Estrogen was also shown to influence the activities of adenosine triphosphatase (Karmakar, 1969) and alkaline phosphatase (Gautray et al., 1969). Existence of an estrogen dependent pyridine nucleotide transhydrogenase have been reported which is stimulated by this hormone (Abe et al., 1964). Hilf and his coworkers (1963; 1965; 1966; 1967) have made extensive studies on hormone dependent mammary tumours of intact and gonadectomized mice and have shown that estrogen treatment resulted in increased activities of certain enzymes accompanied by decrease in the activity of others. It has also been suggested that estrogen has direct effect on the metabolism of a particular tumour (Hilf et al., 1966) and that the elevation in enzyme activity was due to enhanced DNA mediated RNA and protein synthesis (Hilf et al., 1965). Sex hormonal dependence of thymidine kinase activity was also shown in rat adrenocortical carcinoma (Garland et al., 1971).
Estrogen, progesterone and testosterone were shown to inhibit bovine serum and pancreatic amylase, the effect of progesterone being most pronounced (Khayambashi, 1971) and inhibition of bovine liver glutamic dehydrogenase was shown by estrogen (Yielding and Tomkins, 1962) in purified enzyme preparation \textit{in vitro}. So it may be expected that changes in the enzyme activities either in the form of enhancement or reduction, as has been observed in the present study, might result following sex hormone administration. The changes in the substrate specificity of alkaline and acid phosphatase observed, may be explained in the light of the concept of Monod et al. (1963) which envisages the presence of at least two stereo-specifically different non-overlapping binding sites on the 'allosteric proteins'. The 'active site' binds the substrate and is responsible for the catalytic activity of the protein and the allosteric site bind to an allosteric effector specifically and reversibly, bringing about an allosteric transition - a discrete and reversible alteration in the structure of the protein molecule. Such binding can bring about a modification in the structure of the active site and so change one or several of the kinetic parameters characterizing the biologic activity of the protein. The hormone
may bind to one such allosteric site of alkaline phosphatase and bring about an altered preference for different substrates due to change in active site. This is however a mere speculation and remains to be experimentally proved. In spite of the various mechanisms suggested for sex hormone action, at the present state of our knowledge, it is rather difficult to explain how the different hormones exert their influence on the enzymes. The differences in the enzyme activity shown by sex hormone action may be an adaptive response towards hormonal stress indicating that the sensitivity of the enzyme or the enzyme variants are profoundly altered under different hormonal level, both in normalcy and in malignancy.