Androgen binding site in J111 cell line

Article *in* Medical science monitor: international medical journal of experimental and clinical research · August 2006

Source: PubMed

2 authors:

Kazem Ahmadi
Baqiyatallah University of Medical Sciences
52 PUBLICATIONS **156** CITATIONS
SEE PROFILE

Alan Burgess Mccruden
University of Strathclyde
13 PUBLICATIONS **338** CITATIONS
SEE PROFILE

© Med Sci Monit, 2006; 12(7): BR239-244
PMID: 16810130

Received: 2006.01.09
Accepted: 2006.05.06
Published: 2006.07.01

Androgen binding site in J111 cell line

Kazem Ahmadi[1ABCDEFG], **Alan B. McCruden**[2ACEG]

[1] Department of Immunology and Research Centre of Molecular Biology, Baqiyatallah University of Medical Sciences, Tehran, I.R. Iran
[2] Department of Immunology, University of Strathclyde, Glasgow, U.K.

Source of support: The study was financially supported by ministry of health and medical education of Islamic Republic of Iran

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Summary

Background: The finding of sex steroid receptor protein in non classical reproductive tissues suggested the possibility that sex steroids may have a relevance to the immune system.

Material/Methods: The J111 cells were maintained in RPMI 1640 complete medium at 37°C in 5% CO_2 in air. Cells were resuspended at 1×10^6cells in 0.2 ml complete medium in 1.5 ml eppendorf tubes. A single saturating concentration 1×10^{-9} M of [^{3}H]5α-DHT was added to the cells suspension. Unlabelled steroids (5α-DHT, 17-beta estradiol, or the synthetic glucocorticoid triamcinolone acetonid) were added over the range 1×10^{-8} to 1×10^{-9} M. Duplicate tubes were incubated at 37°C for 1h. For autoradiography, the supernatant was discarded and the pellet resuspended in 0.2 ml medium. For binding assay, Labeled cells were separated from unbound steroid by immunomagnetic bead using anti-CD68 antibody.

Results: In autoradiography, a population of approximately 96% of J111 cells that contain receptors for androgen has been demonstrated. The results of immunomagnetic showed that binding identified in the J111 cells was modest selective towards androgenic compounds. Schatchard analysis of data showed the KD value of 2.5×10^{-9} M and the number of receptor in each cell was found to be 257±1. Little competition was seen from 17 beta estradiol or the synthetic glucocorticoid triamcinolone acetonid.

Conclusions: These data indicate that androgen binding in J111 cells is of modest affinity and specific, due to the inability of 100-fold molar excess of estradiol to displace bound [^{3}H]-5αDHT.

key words: **J111 cells • androgen binding • KD • immunomagnetic bead and autoradiography**

Full-text PDF: http://www.medscimonit.com/fulltxt.php?IDMAN=8643
Word count: 2701
Tables: –
Figures: 4
References: 43

Author's address: Kazem Ahmadi, Department of Immunology, Baqiyatallah University of Medical Sciences. Tehran – I.R. Iran, e-mail: K.Ahmadi@bmsu.ac.ir

BACKGROUND

Recently attention has focused on the effect of sex and sex steroid hormones on the immune responses [1–7]. One of the points involved in the regulation of the immune system by steroid hormones could be the monocyte macrophage system. The mechanism by which steroid hormones exert their function on macrophages is generally thought to be mediated by the binding of hormone to specific intercellular proteins that may be termed receptor. Unlike peptide hormones, which have receptors on the cell membranes, the steroid hormones' receptors located in the nucleus and to some extent in the cytoplasm but not in the cell membrane [8–10].

In general, it is believed that testosterone exerts its effects through a common androgen receptor(AR) by translocation of cell-specific genes [11]. However, some evidences show that testosterone can act, after aromatization to estradiol, through the estrogen receptor (ER) [12]. In recent investigations, it has been shown that testosterone does exert its immunosuppressive activity neither through the ER nor through the classical AR responses [13,14].

While some evidences demonstrate that androgen aromatized to estradiol acts through the estrogen receptor in lymphocytes [12], Benten et al. concluded that androgens do not exert their immunosuppressive effect via the ER [14]. They demonstrated that testosterone-induced immuno-suppression can not be abolished by ER blockers when used in sufficient concentrations to prevent the suppressive effect of estradiol. Secondly, two different aromatize inhibitors cannot prevent the immunosuppressive action of testosterone. Also, treatment of mice with testosterone does not cause any significant increase in circulating estradiol. Thirdly, testosterone induced changes in spleen cells are totally different from those induced by estradiol. For example, testosterone leaves the percentage production of CD_4^+ T cells unaffected but induces an increase in CD_8^+T cells (15). Fourthly, the immunosuppressive effect of testosterone can be transferred adoptively by splenic T-cells, whereas T-cells cannot confer the estradiol-induced immuno-suppression. Therefore, it seems that androgens (testosterone) do not exert their immunosuppressive activity through the ER.

In addition, finding that there are no significant numbers of AR in T cell populations suggests that the immunosuppressive activity of testosterone, at least at high concentrations, is primarily a non-genomic effect [16]. However, Kuhnle et al. [17] reported the presence of a high affinity (Kd=1.3 nM) binding site for androgen in blood mononuclear cells containing 70% T-cells. Therefore, it appears that the immunosuppressive activity of androgens is a direct effect in contrast to what reported by Benten et al. [15]. There is now ample information indicating that steroid hormones and their metabolites can act in a variety of tissues via non-genomic mechanisms of action. The evidences supporting the non-classical actions of steroid hormones includes rapid effects and action in which entry into the cell and nuclear interaction has been precluded [18]. Brann et al. [19] reported a non-classical action of progesterone and its metabolites that occur within seconds or minutes and also actions which take place in an hour or longer but in a non-classical manner. There is evidence regarding steroid action which does not involve entry of the steroid into cells. Drouva et al. [20] showed that progesterone conjugated to bovine serum albumin (BSA), is still capable of stimulating LHRH release from hypothalamic *in vitro*. Rapid membrane effects of estrogens, androgens, glucocorticoid and vitamin D metabolite have also noted in a number of different sites within the brain [19,20].

Therefore, these proposed potential non-classical mechanisms of action of steroid hormones should be viewed not as a challenge to the classical mechanism of action but rather as an additional complementing layer of diversity. It is perhaps not surprising that such diverse modes of action for steroid hormones may exist as they confer the ability to mount rapid and/or prolonged responses depending upon the specific stimuli and/or challenge presented. The integration of these divers of action of steroids ultimately allows for a fine-tuned multi dimensional regulation of cellular, tissue and organ responses.

The aim of the present study was to investigate whether there is an androgen binding site in human monocyte\macrophage leukemia J111 cell line using autoradiography and also to identify the Kd value and the number of receptor by immunomagnetic bead.

MATERIAL AND METHODS

RPMI 1640, penicillin, streptomycin, glutamine, sodium bicarbonate solution, trypsin, the 17 beta estradiol (17β E2) and 5 alpha dihydrotestosterone (5α-DHT) and Feta calf serum (FCS were purchased from sigma Chemical Co.). [^{3}H]-5α DHT(250 ci/mMol), were purchased from Amersham. Liquid scintillation (Ultima TM MW 6013151) from packard. Kodak NTB photographic emulsion from Kodak, AGFA G33C X-ray fixer from AGFA, D19 Developer from X-ray itd. Depex mounting medium from Merk co. Giemsa's staining from BDH. Anti CD68 monoclonal antibody from (Biocare Medical) and Dyna bead® M-450 sheep anti IgG from Dynabead. All other chemicals were from Sigma Chemical Co, and BDH.

The J111 cells were maintained in RPMI 1640 complete medium at 37°C in 5%CO_2 in air. The cells were kept in the log phase of growth by passaging every week. Cells were then washed once with PBS to remove medium before adding 0.25% (W\V) trypsin and further 10 minutes incubation at 37°C. The cells were washed twice with fresh medium and plated into fresh flask at 1×10^6 cells per 25 cm^2 flask or $2–3\times10^6$ cells per 75 cm^2 flask. Stocks of J111 cells (1×10^6 cells/well) were kept in liquid nitrogen in freezing medium.

Sample of cell suspension was mixed with an equal volume of 0.4% (W/V) Trypan blue in PBS and incubated for 10 minutes. The cells failing to exclude the dye were counted and expressed as a percentage of the total cells present.

Cells were prepared as described above and resuspended at 1×10^6 cells in 0.2 ml complete medium in 1.5 ml eppendorf tubes. Cells were treated with ^{3}H-5αDHT (9.25 MBq) in the range of 1×10^{-7} to 1×10^{-9} M with and without a 100-fold excess of the corresponding non-radioactive steroid to correct

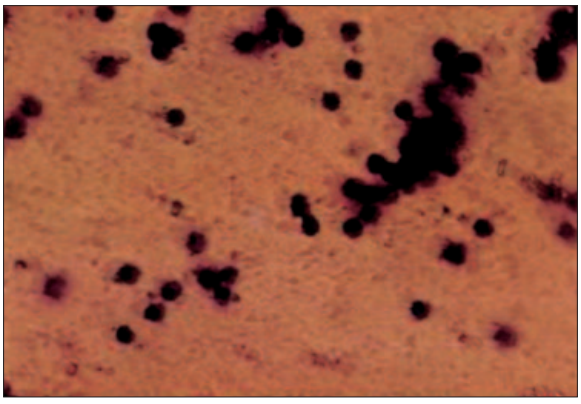

Figure 1. Cell autoradiography of J111 cell Line Cells were incubated with 1 nmol [^{3}H]-5αDHT as described in material and method. Slides were develop and stained with Giemsa and mounted in Depex. The slide was photographed at 40× magnification.

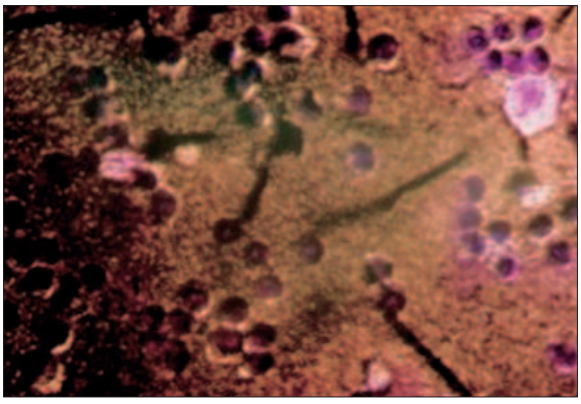

Figure 2. Cell autoradiography of J111 Cell Line Cells were incubated with 1 nmol [^{3}H]-5αDHT in the presence of 100 fold excess of non labeled 5α-DHT as described in material and method. Slides were develop and stained with Giemsa and mounted in Depex. The slide was photographed at 40× magnification.

for non specific binding. Cells were incubated for 2 hours at 4°C. At the end of incubation period, cells were washed three times and finally resuspended in 0.05 ml complete medium before smearing on a microscope slide, air dried and fixed in 100% methanol for 5 seconds. Slides were then dipped in Kodak NTB photographic emulsion at 45°C in a dark room and allowed to dry in a vertical position. Slides were sealed in light proof boxes over silica gel and left at 4°C for 6 weeks. Slides were warmed in room temperature, and developed for 5 minutes in Kodak D19 developer (8%W/V in water), washed in water for 1 minute, fixed in AGFA G33c x-ray fixer containing aditan hardener (2.5%V/V) for 5 minutes, washed in water for a further 5 minutes. After air drying, slides were stained with geimsa and then mounted in depex(BDH, company, England) and viewed with light microscope [21,22].

The radioactivity was measured by a method based on Chase and Rabinson [22]. They determined the amount of radioactivity by light microscope observation. A 96 percent confidence level has achieved at 1700 cells counts. Similarly, when a labelled cell was considered as a single event, the percentage of labelled cells is determined by counting labelled and unlabelled cells until a total of 1700 labelled cells were totaled. This method was based on photometric estimation, in fact the intensity of the auto radiographic label determined by estimating the intensity of the blackening of the emulsion overlying cells [23]. After counting the labelled cells under light microscope, the cells were photographed.

Cells in a volume of 0.2 ml (5×10^6 cells/ml) were placed in tubes and incubated for 1 h at 37°C with 1 mM protease inhibitor (phenyl methyl sulfonyl fluoride, PMSF) and increasing concentrations (2.5×10^{-9} M to 2.5×10^{-8} M) of the [^{3}H]-5αDHT with or without a one hundred fold-excess of unlabelled 5α-DHT (to measure total and non specific binding respectively). The use of protease inhibitor was based on a study by Sadi et al. [24] who showed that androgen receptor was higher in the presence of a protease inhibitor. After incubation, the immunomagnetic method was used to capture J111 cells for the receptor binding assay and to permit rapid washing of cells. The immunomagnetic method, also simplified the separation of the labelled cells from unbound steroid. Monoclonal antibody to CD68 (Biocare Medical) was used as first Ab and Dyna bead® M-450 sheep anti IgG as a second Ab. Tubes were replaced in the MPC-6 magnet, cells washed 3X with ice cold HBSS containing 0.1% (v/v) Triton x-100 and 1 mM PMSF at 4°C to remove unbound steroid. Finally, the cells were resuspended in 100 µl HBSS, transferred to a 5 ml tube and 1ml scintillation fluid (ULTIMA GOLD TMMW Packard company 6013159) added before transferring to the liquid scintillation counter.

Assay was also performed to examine the binding of 17β-Estradiol and triamcinilone acetonide to androgen receptor of J111 cells. 5×10^6 cells/tube was incubated with 1×10^{-9} M [^{3}H]-5αDHT in the presence of unlabelled competitors over the range of 1×10^{-9} M to 1×10^{-6} M. Cells were then incubated at 37°C for 1h, then washed 3 times with ice-cold HBSS containing 0.1% Triton x-100 and 1mM PMSF using magnet method. The percentage of binding inhibition by each concentration of competing ligand was determined in each case and compared with percentage inhibition induced by 100x DHT as reference for specific binding.

Statistical analysis

The results are expressed as the mean of experiments (n=6) ±the standard error (S.E) means or ±the standard deviation (S.D) means. An unpaired student t-test was used to determine the probability (p) of two sets of data from experiments being different from each other.

Results

In our quantitative study, based on published methods the higher grain density over cell nuclei was counted as positive for androgen binding [25, 26]. This was in comparison with negative and control and slides also containing a 100-fold excess of unlabelled 5α-DHT(Figures 1,2). The percentage of labelled cells was calculated according to the published method by counting the labelled and unlabelled cells until a total of 1700 cells have been tailed [22].

In our evaluation, the occurrence of 5α-DHT receptor in the J111 cells a population of approximately 96% of J111 cells

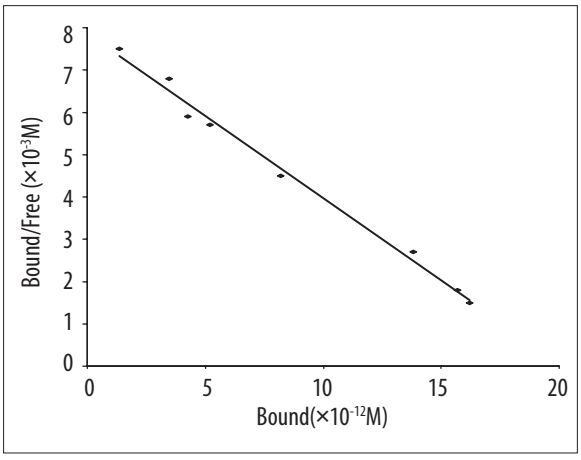

Figure 3. J111 cells were incubated with different concentrations of [³H]-5αDHT ranging between 2.5×10^{-9} M to 1×10^{-8} M in the presence of 100 fold excess of non labelled 5α-DHT. Scatchard analysis of [³H]-5αDHT binding indicated Kd=2.5×10^{-9} M. The number of receptors in each cell was 257±1.

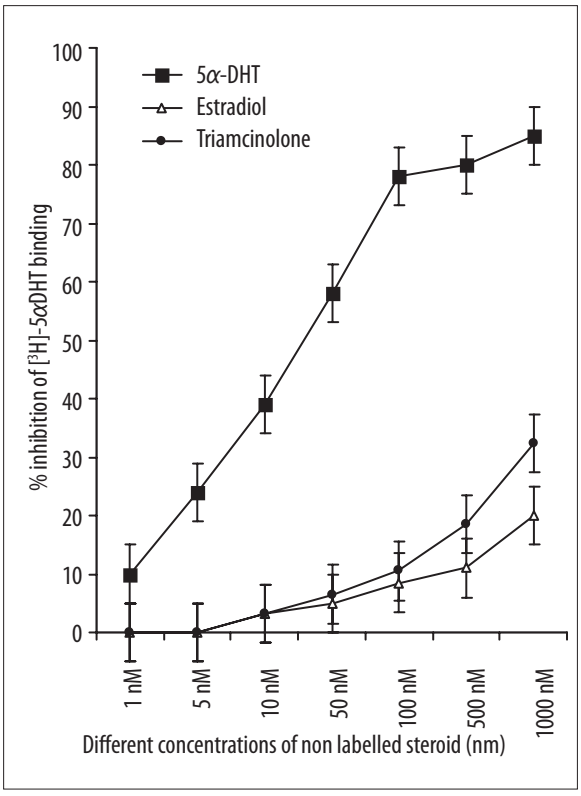

Figure 4. J111 Cell Line were incubated with 1 n.mol [³H]-5α-DHT in the presence of unlabelled competitors (5α-DHT, 17beta estradioland Triamcinolone) over the range of 1 n.mol to 1000 n.mol. The percentage of binding inhibition by each concentration of competing ligand was determined in each case and compared with percentage inhibition induced by 100 X DHT as reference for specific binding.

that contain receptors for androgen has been demonstrated (Figure 1). Saturation binding analysis over a wide range of [³H]-5αDHT concentrations with whole cells separated magnetically revealed a straight line slope indicating modest affinity for [³H]-5αDHT in J111 cells. The Scatchard plot is shown in Figure 3. The graph indicates the presence of one type of binding site with a Kd value of 2.5×10^{-9} M (Figure 3). The number of receptors per cell obtained in this study was 257±1 for J111 cells. Competition assay using 17β-estradiol and synthetic glucocorticoid triamcinolone acetonid were performed to determine the nature of androgen binding sites in J111 cells (Figure 4). These ligands did not inhibit specific binding, supporting binding for androgen.

Discussion

Several *in vitro* methods have been developed for determination of androgen receptor-binding activity. Most investigators have utilised dextran-coated charcoal to separate labelled cells from unbound steroid when assaying cytosolic androgen receptors. However, Kliman et al. [27] developed a receptor assay which utilised anti-5α-DHT Ab linked to sepharose in order to separate labelled cells from unbound steroid. Verhoeven et al. [28] used ammonium sulphate (35%) to precipitate androgen receptors. Similarly, Liao et al. [29] designed a rapid, economical and sensitive assay for androgen receptors that utilised hydroxylapatite adsorption of the radioactive steroid-receptor complex and washing of adducts on membrane filters instead of using tubes. In contrast to these biochemical assays of androgen-binding activity, autoradiographic methods for localization and quantitation of androgen receptors have been developed. Moreover, as with other classes of steroid hormone receptors, monoclonal Abs to the androgen receptor are now commercially available which allows extensive study of the structure and regulation of the receptor and its gene.

We previously demonstrated the presence of estrogen receptor in J111 cells but were unable to detect androgen receptor, which could be due to the limitation of the technique used [30]. Immunomagnetic beads used in our experiments had the important implications in helping to separate labelled cells from unbound steroid. Results obtained by the binding assay using magnetic beads were in line with results obtained from autoradiographic experiments in which specific binding for androgen in J111 cells was demonstrated.

Scatchard analysis of receptor-binding data for androgens showed a straight line for J111 cells (Figure 3) which indicates presence of androgen binding sites. It also indicates that [³H]-5αDHT binds to a single class of receptor with a modest affinity. This is in accordance with data for androgen receptor in other tissues reported previously. Our data support previously reports of presence of androgen binding site in human synoviocyte [31], human leukaemic cells, non Hodgkin's Lymphoma cells and human leukocytes [20]. McCruden [30] also reported a different pattern of binding between thymus and prostate. The nature of androgen binding site in J111 cells (Kd=2.5×10^{-9} M) seems also to be different from other tissues. Gulshan et al. [30] demonstrated the presence of two different estrogen binding species (type A and B). In J111 cells, type A estrogen receptors were found to have a Kd value of 8.7×10^{-11} M with 280 receptors per cell, while the Kd for type B was 2.5×10^{-9} M with 1130 receptors per cell. These data suggest a difference in receptors found in different tissues.

Our results are in accord with the results obtained by other investigators of the differential effects of androgens on the macrophage and on the immune response in general [32–37]. The number of androgen receptors found in J111 cells is relatively low compared to the both type A and B of estrogen receptors (280 and 1130 per cell) in these cells(30) but it was higher than androgen receptors in human mononuclear leukocytes (184±52) [19]. Moreover, with reference to competition experiment, it can be concluded that the binding identified in J111 cells is selective for androgenic compounds. Little competition was seen from estradiol (17β-E2) and synthetic glucocorticoid (Triamcinolone acetonide).

This affinity of 5α-DHT for androgen binding sites in CD68 positive cells as well as the degree of relative binding affinities for various steroid hormones is comparable to the androgen binding sites in other cells [38–42]. These experiments are also comparable to work described by Kuhnle et al. [20] who demonstrated high affinity (1.3 nM) androgen binding sites in peripheral mononuclear leukocytes (PML).

The presence of androgen binding site in J111 cells (Human monocyte- macrophage) for the first time, provides the experimental basis for an hypothesis of direct receptor-mediated effects of androgens on mature immunocompetent cells. This method provides a test for repeated quantitative receptor measurements in intact cells which are easily available, so that this whole cell assay can determine the androgen binding capacity under various physiological and clinical situations. The high or modest affinity, saturable capacity and specificity of the androgen binding sites fulfill the criteria for specific hormone receptors. Indeed, this method provides a non invasive technique for examining androgen binding sites in intact cells, thus minimising the interference caused by tissue or cell homogenisation or prolonged cell culture.

In Favor of these results, Brann et al. [19] reported a non-classical action of progesterone and its metabolites that occur within seconds or minutes and also actions which take an hour or longer but in a non-classical manner. There is evidence regarding steroid action which does not involve entry to cells. Willmer [43], proposed that steroids could be inserted vertically in the phospholipid bilayers of the membranes which would alter the fluidity of the membrane and block membrane ionic channels. Thus, while steroids may indeed alter membrane fluidity, it is unclear to what degree, if any, this effect would contribute to the overall biological action of these hormones.

CONCLUSIONS

Iit is conceivable from the findings reported in this study that the immunomodulatory action exerted by androgens may be at least partially realised through their interactions with respective receptors in macrophages. Also, further research on the androgen receptors in macrophage is required to establish whether the receptors are similar to the androgen receptor reported in other tissue or shows tissue variation as seen with estrogen [30].

Acknowledgement

Authors would also like to express appreciation to the people of department of Immunology, university of strathclyde.

REFERENCES:

1. McCrohon JA, Death AK, Nakhla S et al: Androgen receptor expression is greater in macrophages from male than from female donors. A sex difference with implications for atherogenesis. Circulation, 2000; 101(3); 224–26
2. Khan KN, Masuzaki H, Fujishita A et al: Estrogen and progesterone receptor expression in macrophages and regulation of hepatocyte growth factor by ovarian steroids in women with endometriosis. Hum Reprod, 2005; 20(7); 2004–13
3. Colton CA, Brown CM, Vitek MP: Sex steroids, APOE genotype and innate immune system. Neurobiol Aging, 2005; 26(3); 363–72
4. Ashcroft GS, Mills SJ: Androgen receptor-mediated inhibition of cutaneous wound healing. J. Clin Invest, 2002; 110(5); 615–24
5. Manolagas SC, Kousteni S, Jilka RL: Sex steroids and bone. Recent Prog Horm Res, 2002; 57; 385–409
6. Chen Q, Kaji H, Sugimoto T, Chihara K: Testosterone inhibits osteoclast formation stimulated by parathyroid hormone through androgen receptor. FEBs Lett, 2001; 491(1–2); 91–93
7. Gomez E, Ruiz P, Lopez R et al: Effects of androgen treatment on expression of macrophage Fc receptors. Clin Diagn Lab Immunol, 2000; 7(4); 682–96
8. Castagnetta L, Granata OM, Traina A et al: A role for sex steroids in autoimmune disease: a working hypothesis and supporting data. Ann NY Acad Sci, 2002; 966; 193–203
9. Cutolo M, Giusti M, Villaggio B et al: Testosterone metabolism and cyclosporine A treatment in rheumatoid arthritis. Br J Rheumatol, 1997; 36(4); 433–39
10. Pelfrey CM: Sexual dimorphism in autoimmunity: a focus on Th1/Th2 cytokines and multiple sclerosis. Clinical and Applied Immunology Reviews, 2001; 1: 331–45
11. Norman AW, Litwack G: Androgenes Hormones. Orlando: Academic Press Inc., 1987, 483–513
12. Sheridan PJ: Can a single androgen receptor fill the bill. Mol Cell Endocrinol., 1991; 76; C39–C45
13. Benten WPM, Wounderlich FM, Mossmann H: Testosterone-induced suppression of self-healing plasmodium chabaudi malaria: an effect not mediated by androgen receptors. J Endocrinology,1992; 135; 407–13
14. Benten WPM, Wunderlich F, Herrmann R, Kuhn-Velten WN: Testosterone-induced compared with oestradiol-induced immunosuppression against plasmodium chabaudi malaria. J Endocrinology, 1993; 139; 487–94
15. Benten WPM, Bettenhaeuser U, Wunderlich F et al: Testosterone-induced abrogation of self-healing of P.chabudi malaria: mediation by spleen cells. Infect Immun, 1991; 59: 4486–90
16. Wunderlich F, Benten WP, Lieberherr M et al: Testosterone signalling in T cells and macrophages. Steroid, 2002; 67(6); 535–38
17. Kuhnle U, Lindl U, Keller U et al: Androgen Binding sites in peripheral human mononuclear leukocytes of healthy males and Females. J Steroid Bioch Molec Biol, 1994; 48(4): 403–8
18. Benten WP, Guo Z, Krucken J, Wunderlich F: Rapid effects of anderogens in macrophages. Steroids, 2004; 68(8–9); 585–90
19. Brann DW, Hendry LB, Mahesh VB: Emerging diversities in the mechanism of action of steroid hormones. J Steroid Biochem Molec Biol, 1995; 52(2); 113–33
20. Drouva SV, Laplante E, Kordon C: Effects of ovarian steroids on *in vitro* release of LHRH from mediobasal hypothalamus. Neuroendocrinology, 1983; 37: 336–41
21. Baserga R, Malamud D: Modern methods in experimental pathology (Autoradiograpgy). Techniques and application. In hand book of autoradiography. P. 1-145. Edited by Harper & Row. New York, Publishers, 1969
22. Chase GD, Rabinowits JL: Principles of radioisotope methodology, ed. 3th. Burgess. Minneapolis, 1967
23. Blackett NM, Kember NF, Lamerton LF: The measurmrnt of radiation dosage distribution by autoradiographic means with reference to the effects of bone-seeking isotopes. Lab Invest, 1959; 8;171–74
24. Ojasoo T, Raynaud JP: Unique steroid congeners for receptors studies. Cancer Res, 1978; 38; 4186–98
25. Cunha GR, Shannon JM, Vanderslice KD et al: Autoradiographic demonstration of high afinity nuclear binding and finite binding capacity of [3H]-estradiol in mouse vaginal cells. Endocrinology, 1983; 113; 1427–30

26. Peters CA, Barrack ER: A new method for the labeling and autoradiographic localization of androgen receptors. J Histochem Cytochem, 1987; 35: 755–62
27. Kliman B, Maclaughlin RA, Prout GR: Measurment of androgen receptor in cytosol of human prostatic tissues with a sepharose-linked antibody system. Prog Clin Biol Res, 1979; 33: 85–96
28. Verhoeven G, Heyns W, Demoor P: Ammonium sulphate precipitation as a tool for the study of androgen receptor proteins in rat prostate and mouse Kidney Steroid, 1975; 26: 149–67
29. Liao S, Witte D, Schilling K, Chang C: The use of hydroxylapatite-filter steroid receptor assay method in the study of modulation of androgen receptor interaction. J Steroid Biochem, 1984; 20: 11–17
30. Gulshan S, McCruden AB, Stimson WH: Oestrogen recptors in macrophages. scand. J Immunol, 1990; 31: 691–97
31. Khalphali-Ellis Z, Handa RJ, PriceRH Jr et al: Androgen receptors in human synoviocytes and androgen regulation of interleukin-1-Beta) IL-1 beta) induced Il-6 production: a link between hypoandrogenicity and rheumatoid arthritis. J Rheumatol, 2002; 29(9); 1843–46
32. McCruden AB, Stimson WH: Androgen and other sex steroid cytosol receotors in the rat thymus. J Endocrinol, 1980; 85: 47–48
33. Liva SM, VoskuhlRR: Testosterone acts directly on CD4+ T lymphocytes to increase IL-10 production. I Immunol, 2001; 167(4); 2060–67
34. Friedl R, Brunner M, Moeslinger T, Spieckermann PG: Testosterone inhibits expression of inducible nitric oxide synthase in murine macrophages. Life Sciences, 2000; 68: 417–29
35. Posma E, Moes H, Heineman MJ, Faas MM: The effect of testosterone on cytokine production in the specific and non-specific immune response. Am J Reprod Immunol, 2004; 52(4): 237–43
36. Qiao Z, Guo Z, Yin G et al: Testosterone inhibits apoptosis of Leishmania donovani-infected macrophages. Zhongguo Ji Sheng Chong Xue Yue Ji Sheng Chong Bing Za Zhi, 1999; 17(1): 21–24
37. Cutolo M, Capellino S, Montagna P et al: Sex hormone modulation of cell growth and apoptosis of the human monocytic/macrophage cell line. Arthritis Res Ther, 2005; 7(5); R1124–32
38. Friedl R, Bruner M, Moeslinger T, Spieckermann PG: Testosterone inhibits expression of inducible nitric oxide synthase in murine macrophages. Life Sciences, 2000; 62: 417–29
39. Bryś M: Androgens and androgen receptor: do they play a role in breast cancer? Med Sci Monit, 2000; 6(2): 433–38
40. Kovacs WJ, Olsen NJ: Androgen receptors in human thymocytes. J Immunology, 1987; 139: 490–93
41. Ahmadi K, McCruden AB: Androgen receptor in macrophages of Male Rat is greater than in female. American Journal of Immunology, 2006; in press
42. Ahmadi K, McCruden AB: Macrophage may responses to androgen via its receptor. Med Sci Monit, 2006; 12(1): BR15–20
43. Willmer KF: Steroids and cell surfaces. Biol Rev, 1961; 36: 368–98

Index Copernicus

Global Scientific Information Systems for Scientists by Scientists

TM
INDEX
COPERNICUS
INTERNATIONAL

www.IndexCopernicus.com

- EVALUATION & BENCHMARKING
- PROFILED INFORMATION
- NETWORKING & COOPERATION
- VIRTUAL RESEARCH GROUPS
- GRANTS
- PATENTS
- CLINICAL TRIALS
- JOBS
- STRATEGIC & FINANCIAL DECISIONS

Index Copernicus integrates

IC Scientists

Effective search tool for collaborators worldwide. Provides easy global networking for scientists. C.V.'s and dossiers on selected scientists available. Increase your professional visibility.

IC Virtual Research Groups [VRC]

Web-based complete research environment which enables researchers to work on one project from distant locations. VRG provides:

- customizable and individually self-tailored electronic research protocols and data capture tools,
- statistical analysis and report creation tools,
- profiled information on literature, publications, grants and patents related to the research project,
- administration tools.

IC Journal Master List

Scientific literature database, including abstracts, full text, and journal ranking. Instructions for authors available from selected journals.

IC Patents

Provides information on patent registration process, patent offices and other legal issues. Provides links to companies that may want to license or purchase a patent.

IC Grant Awareness

Need grant assistance? Step-by-step information on how to apply for a grant. Provides a list of grant institutions and their requirements.

IC Conferences

Effective search tool for worldwide medical conferences and local meetings.

IC Lab & Clinical Trial Register

Provides list of on-going laboratory or clinical trials, including research summaries and calls for co-investigators.