

# ***ANALYZING SEX STEROID PROFILES IN SERUM AND TARGET TISSUES: CHALLENGES AND OPPORTUNITIES***

**Matti Poutanen**

Institute of Biomedicine, University of Turku, Finland

Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Sweden



**Turku**



**Gothenburg**



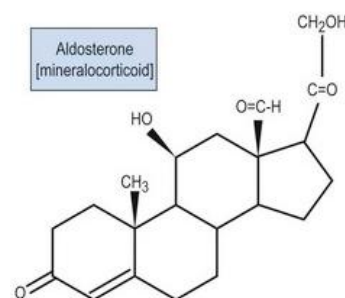
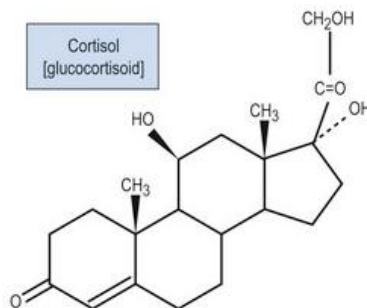
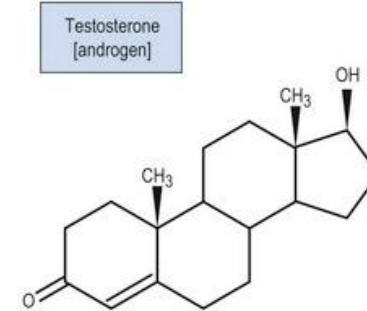
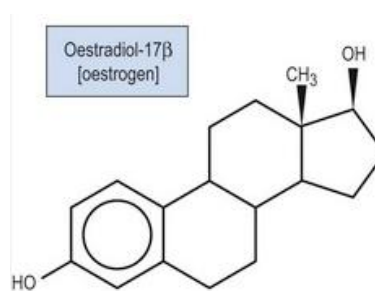
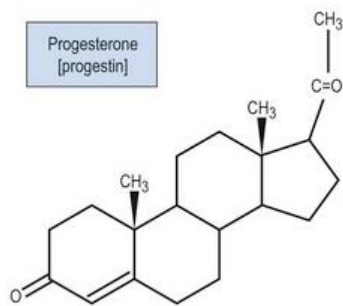
Google: using keyword steroids: ..... page  
after page pictures like those below



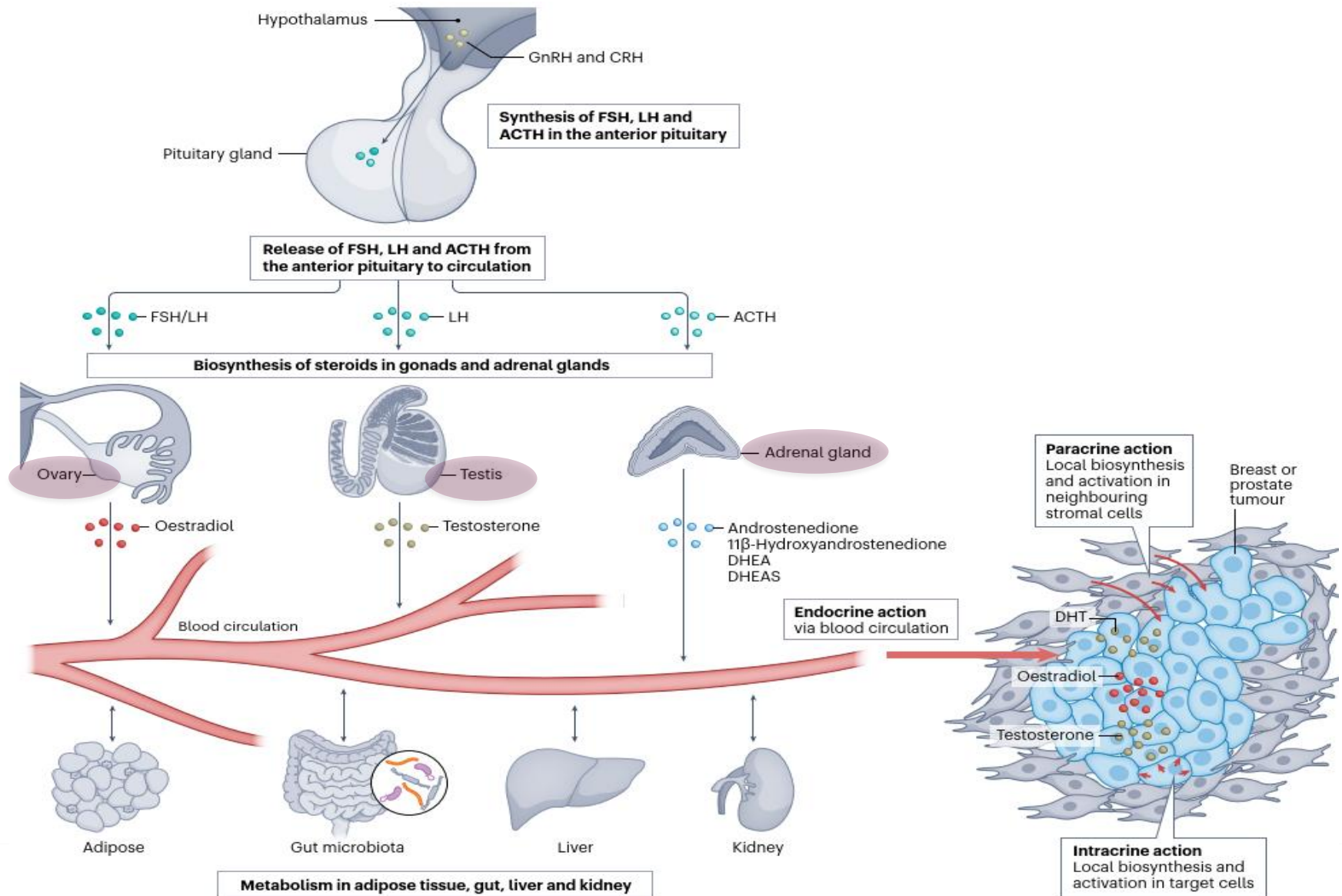
*These pictures do not have any relevance to the medical need  
to manipulate steroid hormone action pharmacologically*

# KEY STEROID HORMONES IN THE BODY

- Male sex hormones: **testosterone** and **dihydrotestosterone**
- Female sex hormones: **estradiol** and **progesterone**
- Glucocorticoids: **cortisol**, **cortisone**, **corticosterone**
- Mineralocorticoid: **aldosterone**

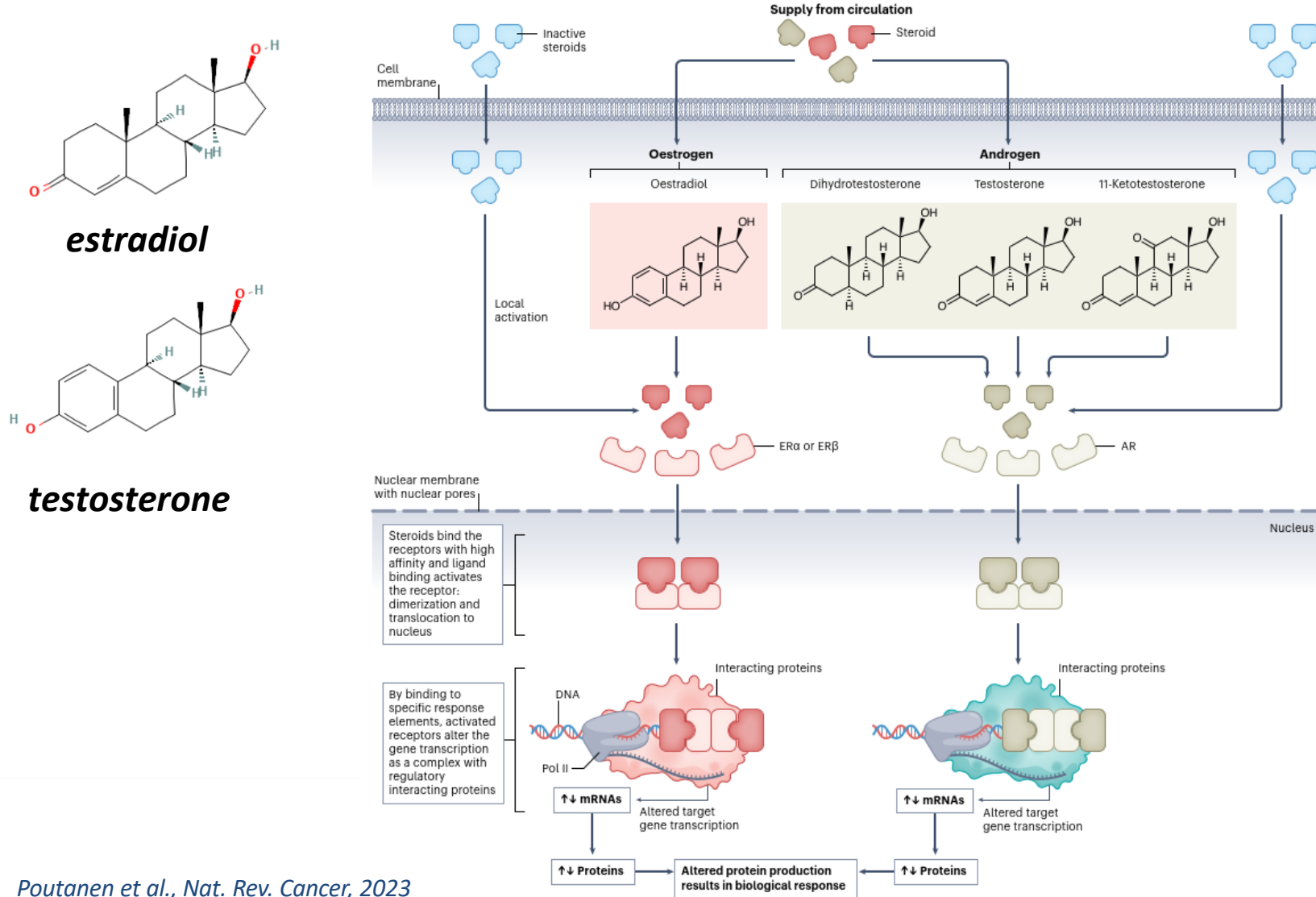


# STEROID SYNTHESIS: *Gonads and adrenal cortex*



# CLASSICAL SEX STEROID RECEPTORS ARE LIGAND (STEROID)-ACTIVATED TRANSCRIPTION FACTORS

- The amount and type of the ligand regulate the action



# WHY TO MEASURE SERUM STEROIDS

## TESTOSTERONE

- In men, hypogonadism, impotence, and disorders of spermatogenesis; in boys, pubertal disorders.
- In women, hirsutism, virilism, polycystic ovary syndrome (PCOS), menstrual disorders, and infertility. Additionally, adrenal hormone synthesis deficiencies and hormonally active tumors.

## ESTRADIOL

- Investigation of the menstrual cycle and its disorders. Evaluation of menopausal symptoms and amenorrhea.
- Suspicion of estrogen-producing tumors (granulosa cell tumors, testicular tumors). Monitoring of ovulation induction (IVF).

## CORTISOL

- Cortisol measurement is used to diagnose adrenal disorders and monitor treatment.

# Numerous over-the-counter and prescription medications modulate steroid hormone action



*Agonists: Compounds acting similarly to endogenous steroids*

**cortisol**



**ethinylestradiol (estrogen) +  
drospirenone (progestin)**  
*Oral contraceptive*



**levonorgestrel (progestin)**  
*Intra uterine device*



## Antagonists: compounds acting opposite to the endogenous hormones

### **Fulvestrant; antiestrogen**

- Treatment of breast cancer



### **Enzalutamide; antiandrogen**

- Treatment of prostate cancer



## Steroidisynthesin estäjät



### **Letrozol; aromatase inhibitor, inhibiting estradiol synthesis**

- Treatment of breast cancer



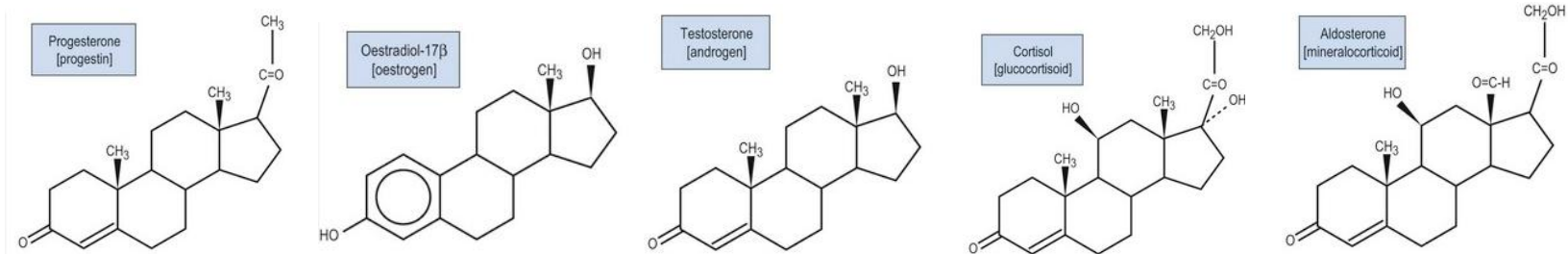
### **Finasteride; 5 $\alpha$ -reduktaase inhibitor, inhibiting DHT:n synthesis**

- Treatment of prostatic hyperplasia



# STRUCTURE OF STEROIDS

- Structurally very similar, despite having remarkably different effects in the body

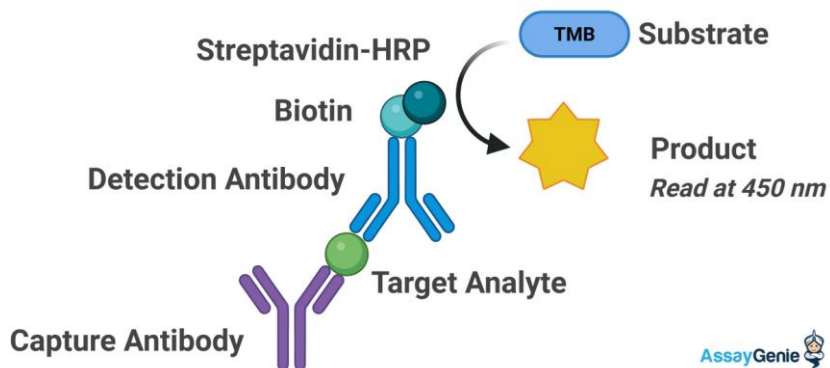


<https://www.ccdc.cam.ac.uk/structures/search?id=doi:10.5517/cc7p1mk&sid=DataCite>

<https://pubchem.ncbi.nlm.nih.gov/compound/5994>

# ANALYZING SEX STEROID CONCENTRATIONS: **IMMUNOASSAYS**

- Immunoassays were developed in the late 50s: originally for peptides but extended to steroids as well.
- Increasing demand for high-throughput steroid measurements** in clinical laboratories resulted in immunoassay simplification
- Method-specific biases and analytical non-specificity of steroid **immunoassays are worst at the low physiological range**
- Furthermore, the sex **steroid concentrations in preclinical models**, such as mice and rats, are even lower than in humans, due to the lack of SHBG.
- Issues to overcome with immunoassays:** Poor immunogenicity, structural similarity leading to cross-reactivity, and multianalyte profiling with immunoassays is difficult



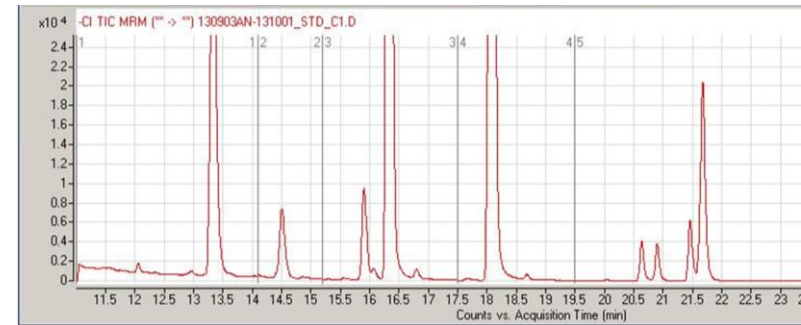
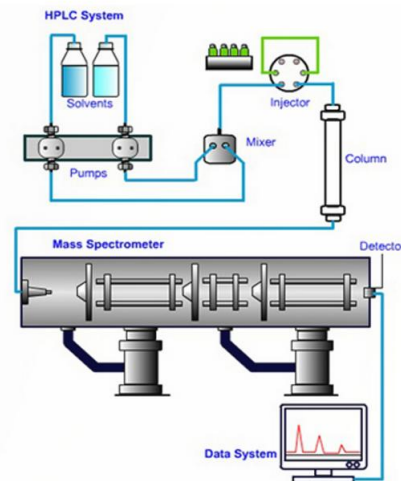
# ***ANALYZING SEX STEROID CONCENTRATIONS: MASS SPECTROMETRIC ASSAYS***

- MS-based steroid measurements **have been available for decades**, as have immunoassays
- They have always **remained the reference method** for steroid specificity and structure
- In the past, MS-based steroid assays **have been too expensive** for routine clinical laboratories and also for research, and have required highly skilled personnel and difficult-to-maintain equipment
- ...and many LC-MS methods **have presented inadequate sensitivity** for several steroids
- The currently available mass spectrometers have changed the field: **Now providing sensitivity as good/better as or better than the best immunoassays**, with reference-level specificity
- Multianalyte profiling with intra-tissue measurements also brings the possibility of **profiling steroid pathways**

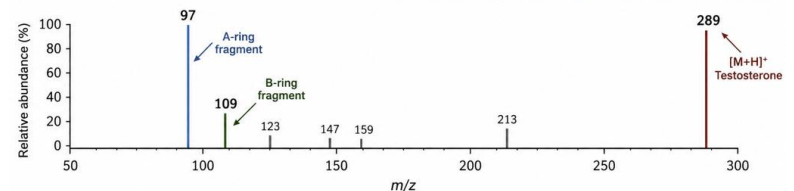
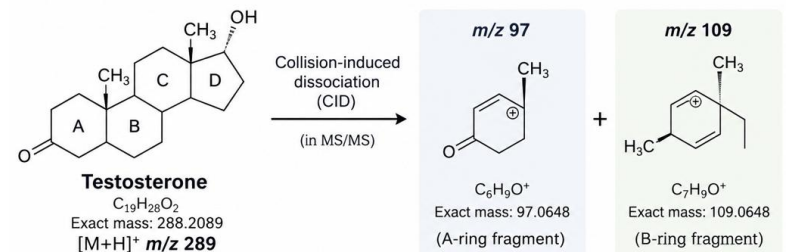
# ANALYZING SEX STEROID CONCENTRATIONS: **MASS SPECTROMETRIC ASSAYS**

**LC= Liquid chromatography:** the sample is pumped into a column with high pressure with a solid phase, and analytes have different affinities for the solid phase; thus, they elute with different retention times

**Tandem-mass spectrometry:** Analytes are transferred to mass spectrometry, where they are ionized; ions are detected by mass/charge ratio, and selected ions are further fragmented into daughter ions that are specific for the analyte



LC-MS/MS fragmentation of testosterone



# ***ANALYZING SEX STEROID CONCENTRATIONS: MASS SPECTROMETRIC ASSAYS***

## ***LC-MS is becoming the gold standard in steroid analysis***

- Clinical and research laboratories are replacing immunoassays with LC-MS
  - Superior selectivity and precision over immunoassays

## ***Still to remember:***

- Many LC-MS and especially GC-MS methods are still laborious and difficult to automate
- Our current multianalyte GC-MS/MS pipeline has a capacity of >50 samples/week, and the multianalyte LC-MS/MS about 200-400 samples/week
- Potentially different assay conditions are needed for different steroids
- In multianalyte procedures, prioritization is needed: Eg., to prioritize estradiol or DHT
- In common with immunoassays, proper validation is needed: eg., matrix effects need internal standards for signal correction.
- Matrix effects for each tissue of interest are important to be tested when intra-tissue concentrations are measured
- Internal standards needed

# ANALYZING SEX STEROID CONCENTRATIONS: MASS SPECTROMETRIC ASSAYS

*Sex steroid assays reporting task force (SSARTF)*

*Endocrinology, December 2014, 155(12):4603*



**CALL FOR PAPERS  
SUBMIT TODAY**



## Reporting of Steroid Hormone Measurements

- **Non-clinical studies** (*in vitro* or animal experiments): For commercial sex steroid assays typically validated for human serum in multiplex platform or kit formats used in non-clinical studies, **any change in species and/or matrix must be validated** by the assay laboratory to verify acceptable quantitative accuracy, precision, and specificity for each analyte.
- **Clinical studies:** Quantitative assay results must be verifiably traceable to a **common reference standard** where available. At present, these are available in matrix for testosterone and estradiol, but should be available in the future for major bioactive steroids.
- For example, the free testosterone analog assay is generally unacceptable, as reported results do not correspond to the reference dialysis-based methods.
- Similarly, **direct (unextracted) sex steroid immunoassays have unacceptable bias where sex steroid concentrations are low**, such as in samples from children, women, and hypogonadal men (for testosterone) and children, post-menopausal women, and men (for estradiol).

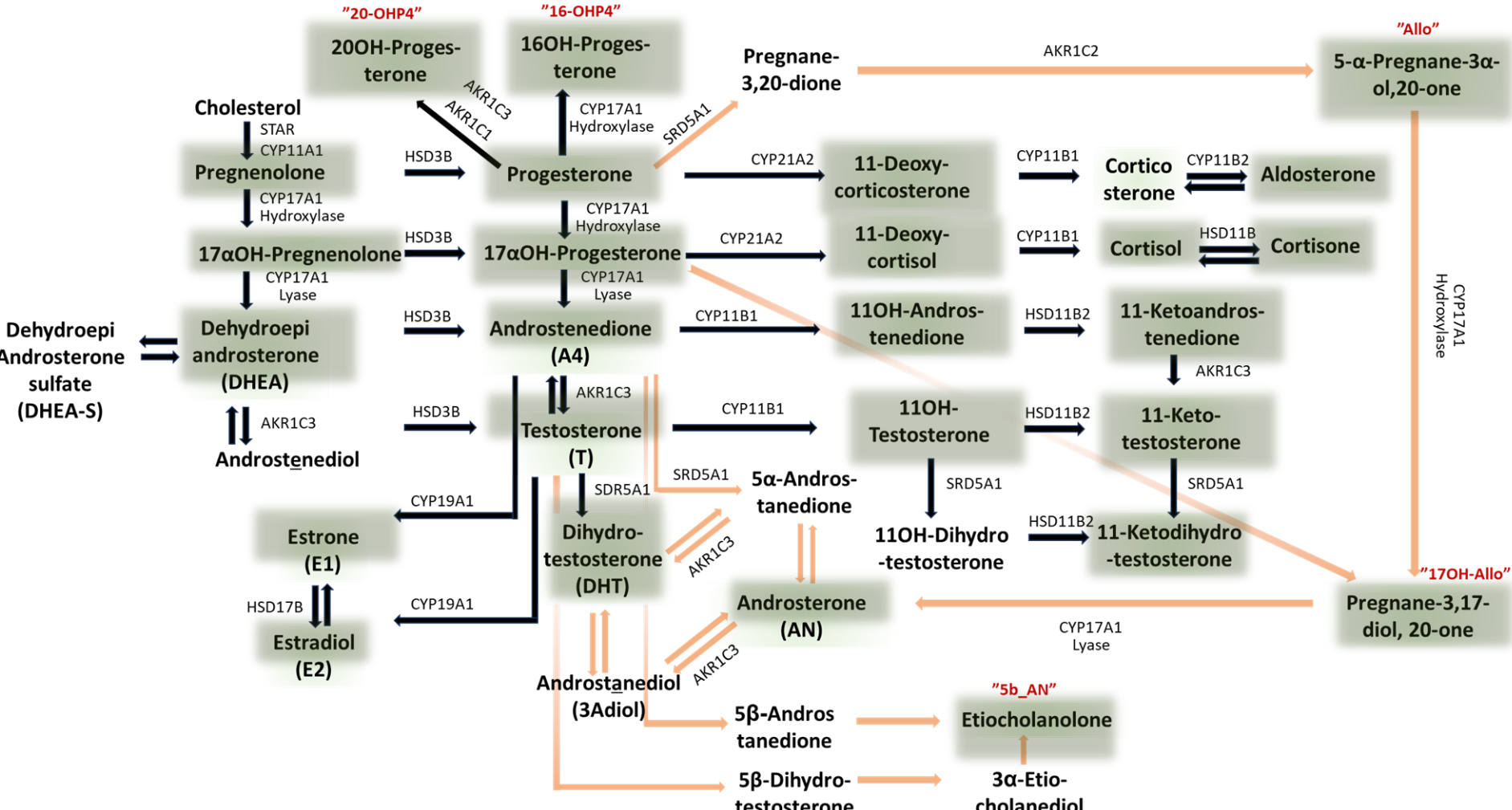
Immunoassay

Not categorically prohibited, but must satisfy the analytical requirements

LC-MS/MS

Not formally mandatory in every circumstance, but is the preferred approach when specificity/sensitivity of immunoassays is inadequate

## MEASUREMENT IN SERUM AND TISSUES: Analytes detected



# MASS SPECTROMETRIC METHODS APPLIED FOR STEROID MEASUREMENT IN SERUM AND TISSUES: **Sensitivity is a key feature**

| GC-MS/MS<br><i>Nilsson et al. 2015</i> |              |
|----------------------------------------|--------------|
| Steroid                                | LLOQ (pg/ml) |
| Estrone                                | 0.5          |
| Estradiol                              | 0.5          |
| Testosterone                           | 8            |
| DHT                                    | 2.5          |
| Androstenedione                        | 12           |
| Progesterone                           | 74           |
| DHEA                                   | 400          |
| 17 $\alpha$ -hydroxy-progesterone      | -            |
| 17 $\alpha$ -hydroxy-pregnenolone      | -            |

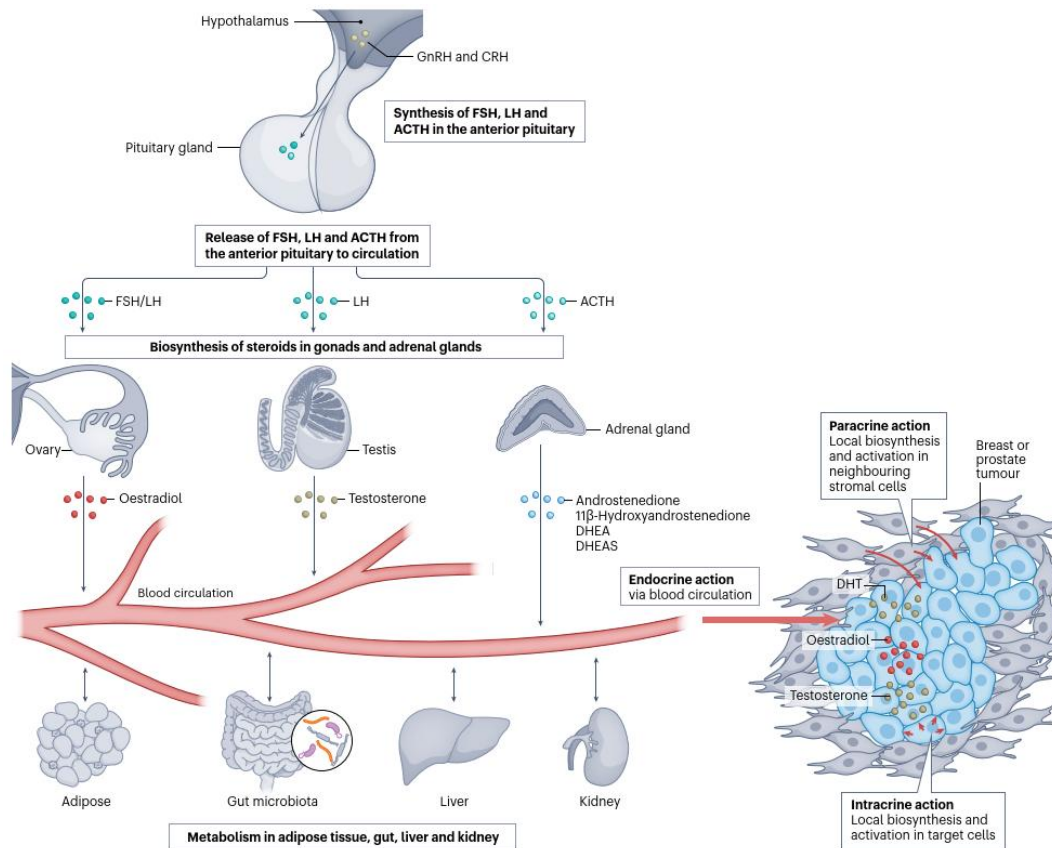
| LC-MS/MS<br><i>Ohlsson et al, unpublished</i> |              |
|-----------------------------------------------|--------------|
| Steroid                                       | LLOQ (pg/ml) |
| Estrone                                       | 1            |
| Estradiol                                     | 1            |
| Testosterone                                  | 10           |
| DHT                                           | 15           |
| Androstenedione                               | 10           |
| Progesterone                                  | 20           |
| DHEA                                          | 250          |
| 17 $\alpha$ -hydroxy-progesterone             | 20           |
| 17 $\alpha$ -hydroxy-pregnenolone             | -            |

| LC-MS/MS<br><i>Evstafev et al, unpubliuهد</i> |  |
|-----------------------------------------------|--|
| 11b-OH-Androstenedione                        |  |
| 11-Deoxycorticosterone                        |  |
| 11-Deoxycortisol                              |  |
| 11-Ketodihydrotestosterone                    |  |
| 11-Ketotestosterone                           |  |
| 17a-OH-Pregnenolone                           |  |
| 17a-OH-Progesterone                           |  |
| 11-Ketoandrostenedione                        |  |
| Aldosterone                                   |  |
| Androstenedione                               |  |
| Androsterone                                  |  |
| Corticosterone                                |  |
| Cortisol                                      |  |
| Cortisone                                     |  |
| Dehydroepiandrosterone                        |  |
| Dihydrotestosterone                           |  |
| Estradiol                                     |  |
| Estrone                                       |  |
| Pregnenolone                                  |  |
| Progesterone                                  |  |
| Testosterone / Epi-testosterone               |  |

| Seppo Auriola et al.,<br>University of Eastern Finland |            |
|--------------------------------------------------------|------------|
| Without derivatization                                 |            |
| LLOQ, pg/ml                                            |            |
| Estriol                                                | 3.6        |
| <b>Estradiol</b>                                       | <b>3.6</b> |
| Estrone                                                | 1.8        |
| Testosterone                                           | 3.6        |
| Androstenedione                                        | 9          |
| <b>DHT</b>                                             | <b>90</b>  |
| DHEA                                                   | 90         |
| Pregnenolone                                           | 90         |
| Progesterone                                           | 3.6        |
| 17-OH pregnenolone                                     | 36         |
| 17-OH progesterone                                     | 9          |
| 21-OH progesterone                                     | 3.6        |
| Aldosterone                                            | 9          |
| Androsterone                                           | 90         |
| Etiocholanolone                                        | 180        |
| Androstenediol                                         | 36000      |
| Cortisol                                               | 9          |
| Cortisone                                              | 9          |
| Corticosterone                                         | 3.6        |
| 11-deoxycortisol                                       | 1.8        |

3 pg/ml =10 pM

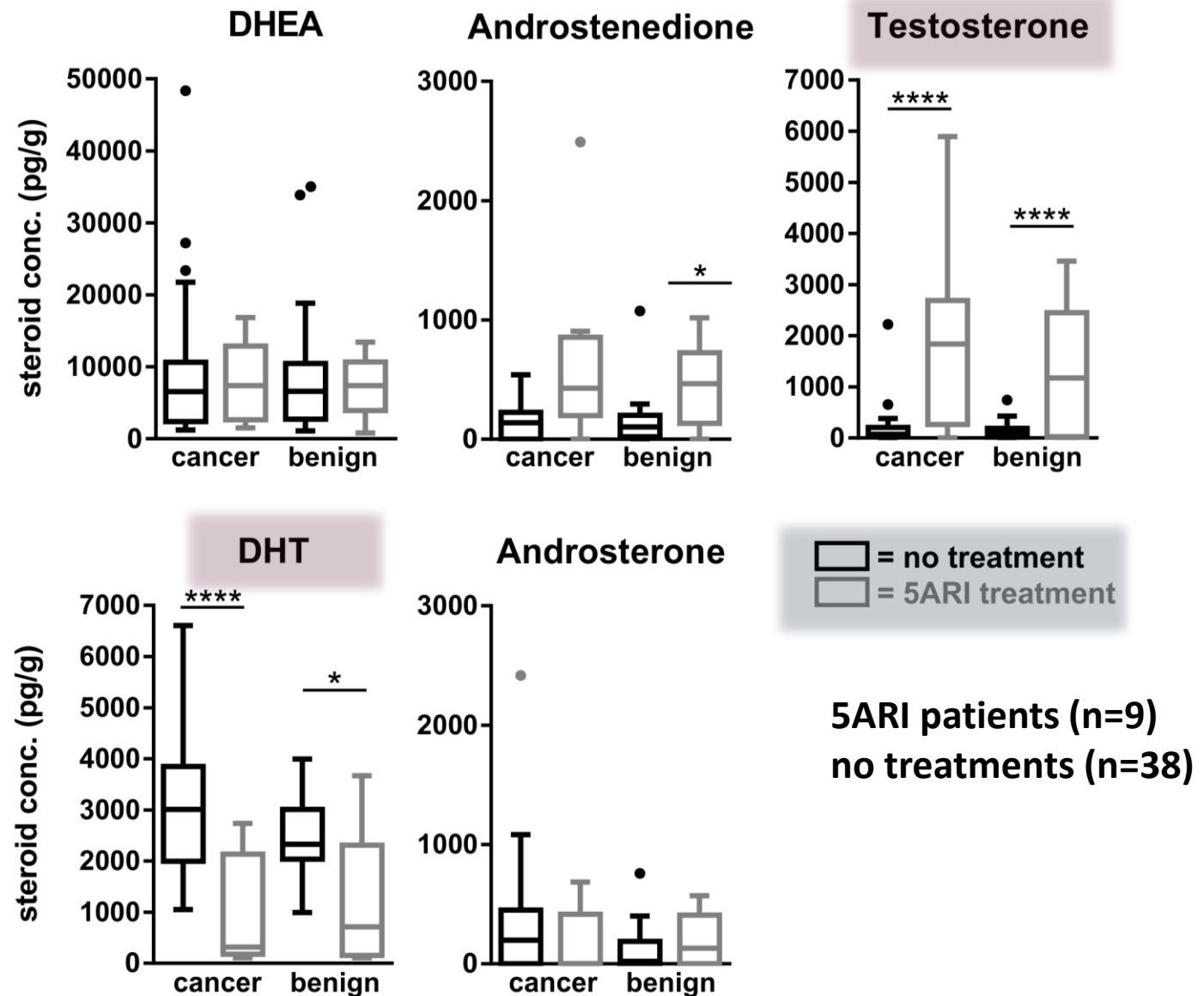
# STEROID PROFILING: TISSUE CONCENTRATIONS ARE NOT EQUAL TO SERUM CONCENTRATIONS



**SERUM CONCENTRATIONS DO NOT NECESSARILY REFLECT THE TARGET CELL CONCENTRATIONS**

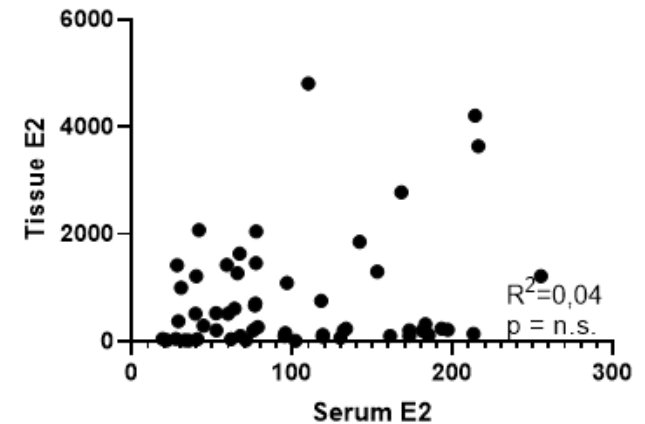
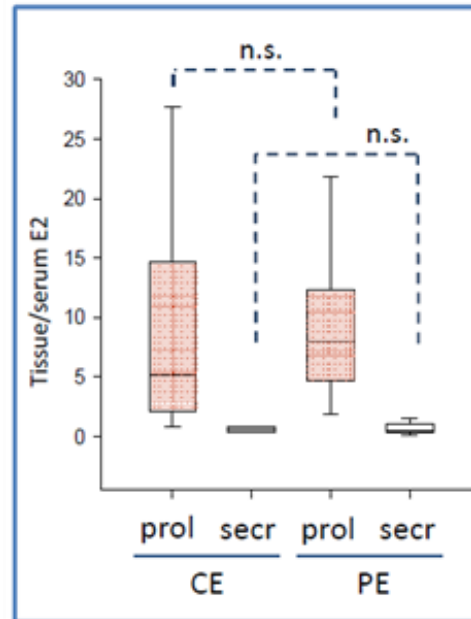
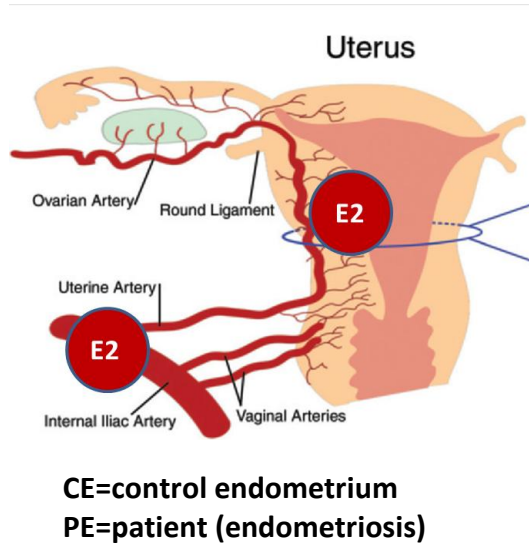
- **Testosterone activation to DHT in the prostate**
  - *SRD5A-inhibitors for BPH*
- **E2 production in postmenopausal breast cancer from adrenal precursors**
  - *CYP19A1 (Aromatase) inhibitors*
- **Androgen production from adrenal precursors in CRPC tissue during ADT**
  - *AR antagonists, CYP17A1 inhibitors*
- **Cortisol inactivation (kidney)**
  - *To facilitate mineralocorticoid action*

# 5 $\alpha$ REDUCTASE INHIBITOR EFFECT IS REFLECTING INTO INTRA TUMOR STEROID PROFILES



# TARGET TISSUE METABOLISM LIKELY REGULATES THE CONCENTRATION OF ESTROGENS ALSO IN PREMENOPAUSAL WOMEN

Huhtinen et al. JCEM, 2012



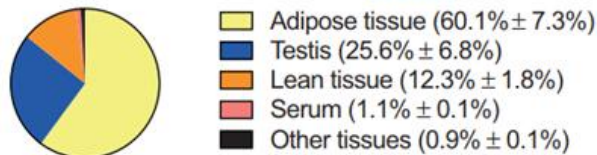
- High tissue/serum ratio of estradiol in proliferative-phase endometrium; not in secretory phase
- Not with progesterone

# MODIFICATION OF CIRCULATING SEX STEROIDS BY **ADIPOSE TISSUE**

➤ *Adipose tissue serves as a storage site for endocrine-acting steroids: male mouse as a model*

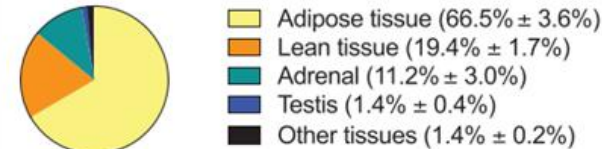
## Intact males: High **testosterone** pool in adipose

Sham pool  $68,534 \pm 24,727$  pg



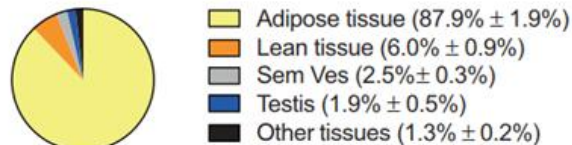
## Intact males: High **progesterone** pool in adipose tissue

Sham pool  $55,563 \pm 5,597$  pg

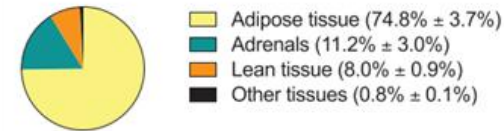


## Intact mouse: High **DHT** pool in adipose tissue

Sham pool  $27,443 \pm 6054$  pg



ORX pool  $121,094 \pm 28,854$  pg

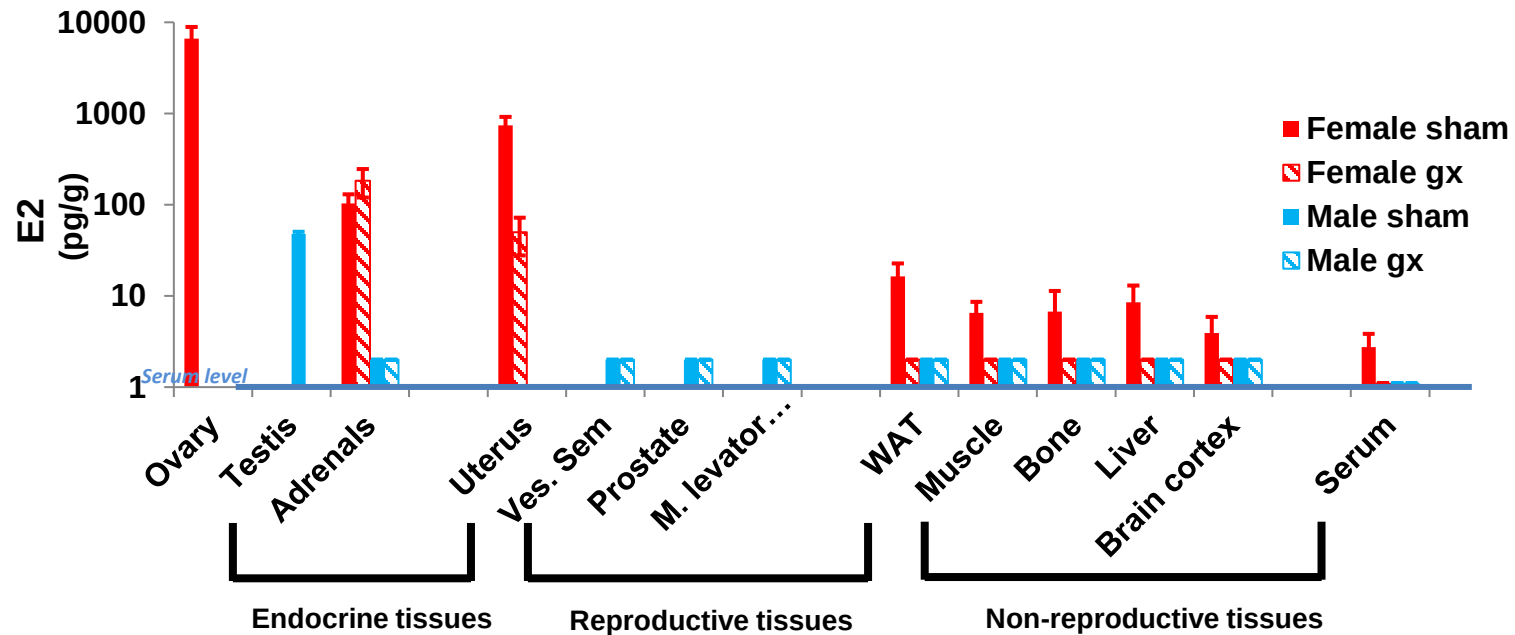


*In ORX mice, the progesterone pool is **1000-fold** larger than the pool of active androgens*

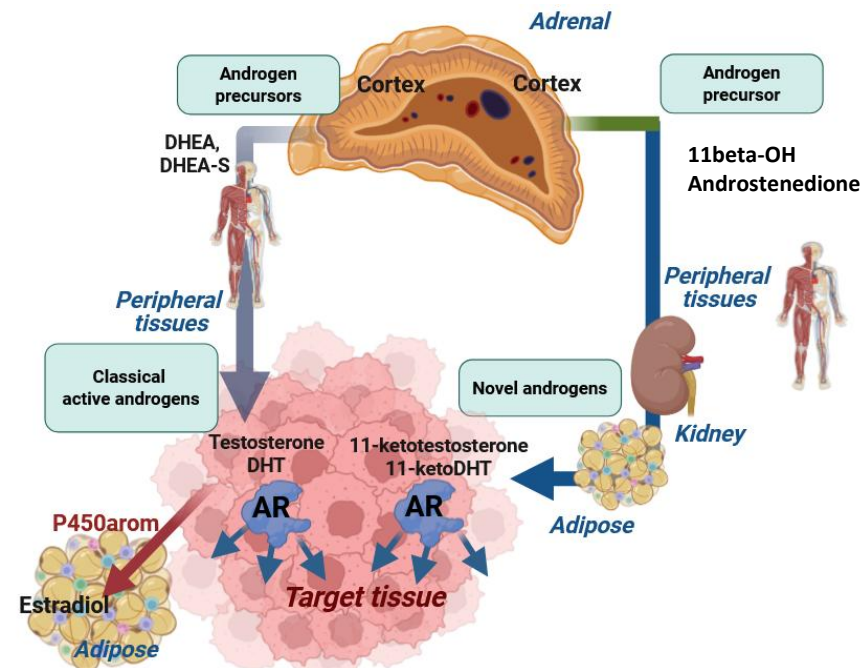
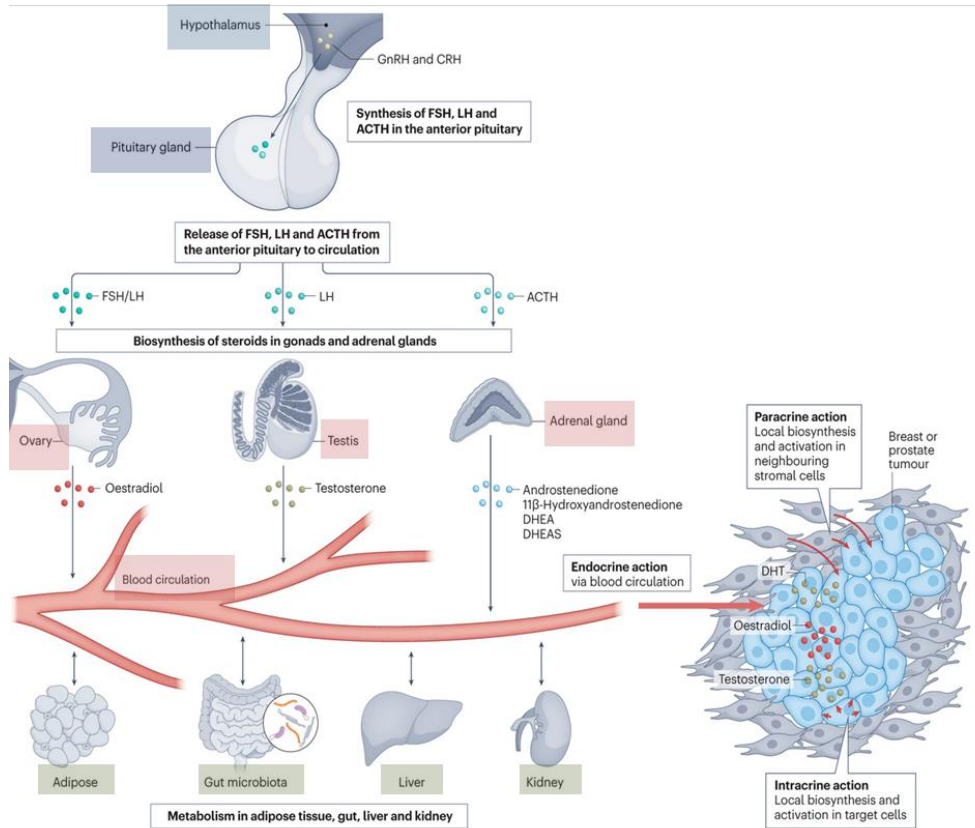


Colldén et al., *Endocrinology*. 2022 Mar 1;163(3):bqac001  
Colldén et al., *Endocrinology*. 2022 Oct 23;163(12):bqac163

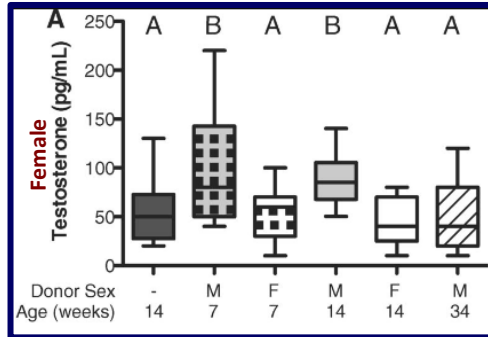
# HIGH RATIO TISSUE /SYSTEMIC ESTRADIOL IN MOUSE UTERUS; Various levels of E2 in mouse tissues



# CIRCULATING LEVELS ARE MODIFIED BY EXTRA-GONADAL TISSUES

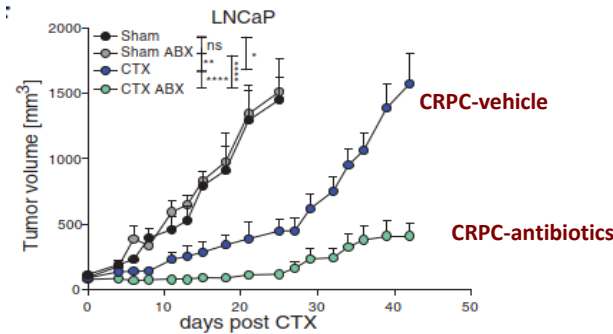


# GUT MICROBIOTA AFFECT CIRCULATING STEROID LEVELS: DATA ON PRECLINICAL MOUSE MODELS



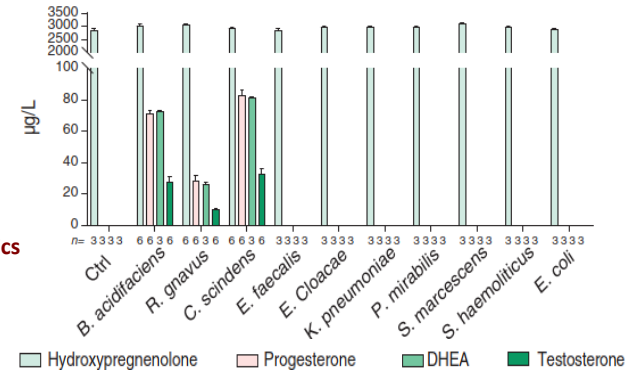
- Transplantation of the male microbiome in female mice results in hormonal and metabolic changes in the recipient females

*Science* 339, 1084-1088, 2013.



- Antibiotic treatment results to receded prostate cancer growth in a CRPC mouse model

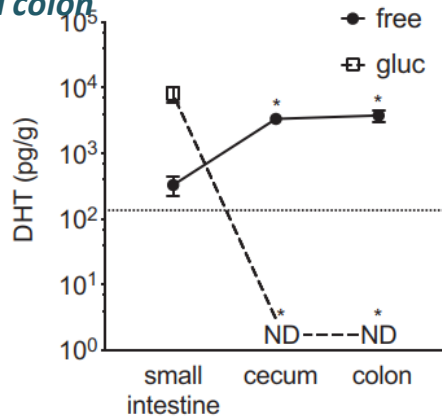
*Science*, 374, 216-224 2021.



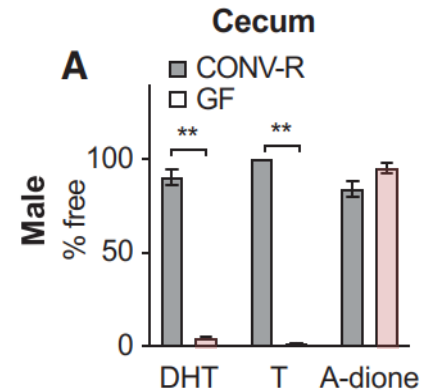
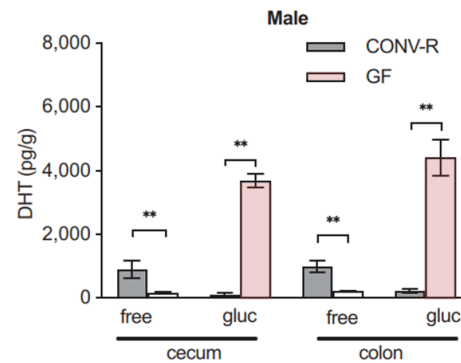
- Bacteria converting 17 $\alpha$ -hydroxypregnenolone to DHEA and testosterone identified

# ASSOCIATION BETWEEN MICROBIOTA CONTENT AND SEX STEROID-DEPENDENT PHENOTYPES EXISTS

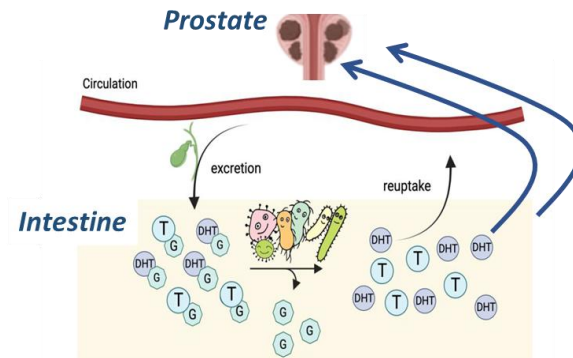
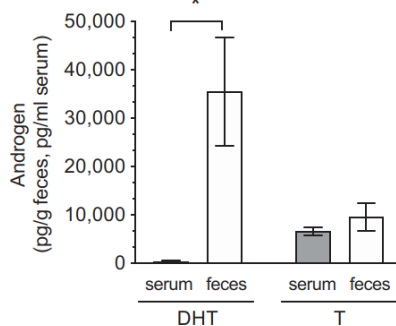
*DHT is unconjugated in mouse cecum and colon*



*Unconjugation is dependent on microbiota and specific for DHT and testosterone in mice*



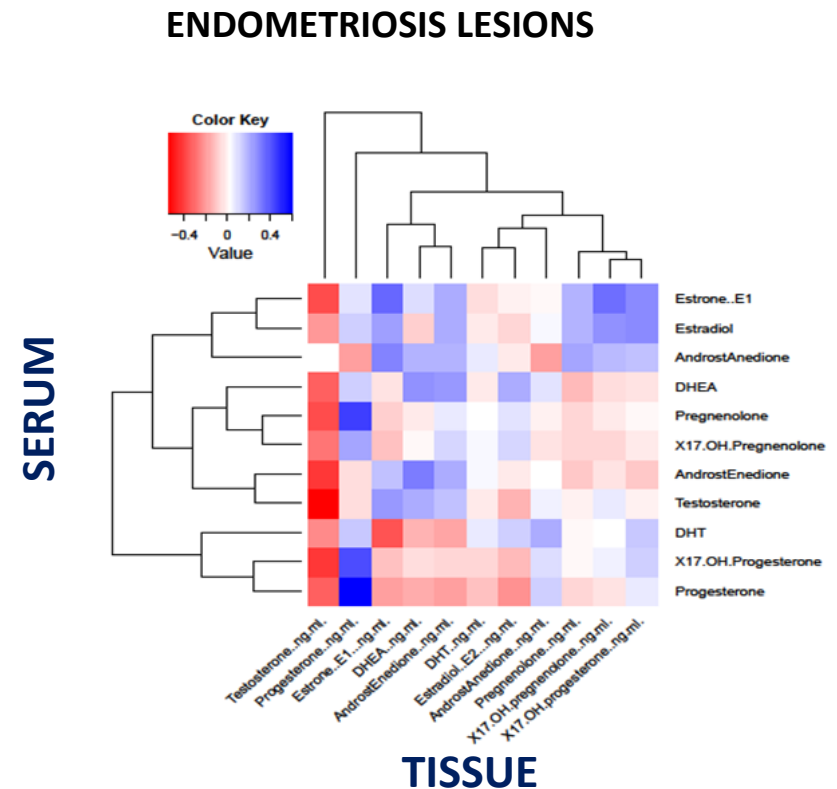
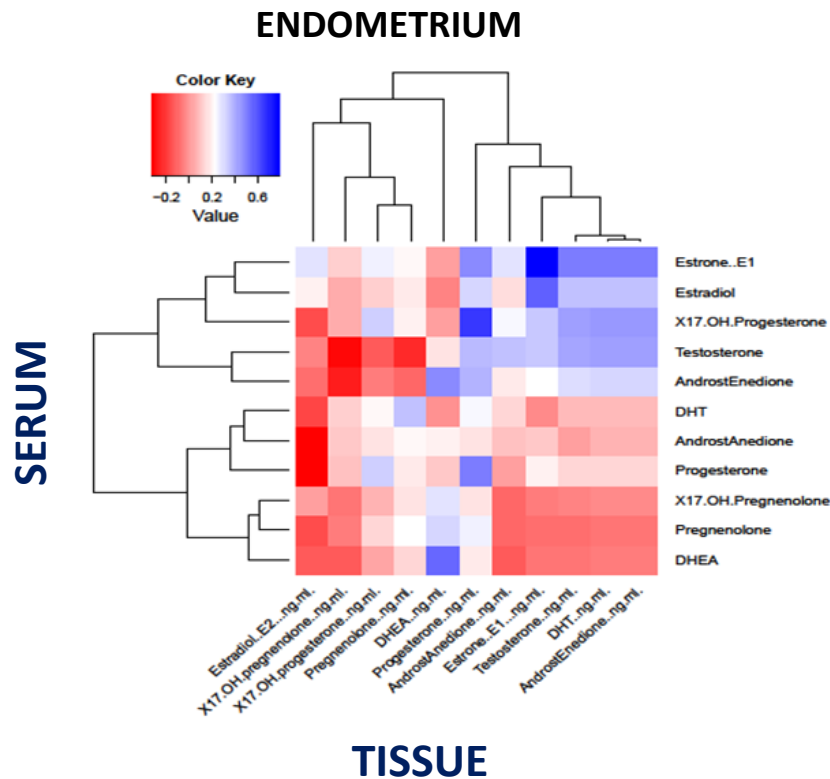
*Higher free DHT in feces compared to serum in young men*



Coll  n et al., *Endocrinology*. 2022 Mar 1;163(3):bqac001  
Coll  n et al., *Endocrinology*. 2022 Oct 23;163(12):bqac163

# TISSUE/SERUM RATIO IS STEROID-DEPENDENT, TISSUE-DEPENDENT, AND DEPENDENT ON THE PHYSIOLOGICAL STATE

*Example: Tissue to serum correlation of the steroids in healthy endometrium compared to endometriotic lesions of the same premenopausal women*



# **USE OF STEROID LC-MS/MS FOR BIOMARKER DISCOVERY**

# ARE 11-OXYGENATED C19 STEROIDS ARE THE PREDOMINANT ANDROGENS IN POLYCYSTIC OVARY SYNDROME?

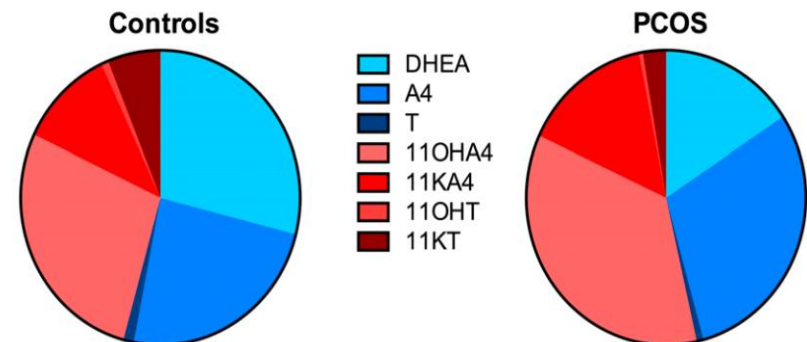
- The majority of studies report levels of 11KT equal to or higher than those of testosterone in women

*Eur J Endocrinol*, 2023, Vol. 188, No. 4, R98-R109, *Eur J Endocrinol*, 2023, 188, 86–100, *Nat Rev Endocrinol* 16, 284–296 (2020)

|                          | Controls (n = 49) | All PCOS (n = 114)            |
|--------------------------|-------------------|-------------------------------|
| Serum androgens (nmol/L) |                   |                               |
| T                        | 0.3 (0.2–0.5)     | 0.7 (0.5–1.0) <sup>a</sup>    |
| A4                       | 5.9 (3.3–9.2)     | 26.8 (16.9–35.2) <sup>a</sup> |
| DHEA                     | 7.1 (4.2–11.8)    | 14.1 (10.4–18.2) <sup>c</sup> |
| DHEAS (μmol/L)           | 6.0 (3.4–9.6)     | 8.1 (5.5–12.2) <sup>c</sup>   |
| FAI                      | 0.6 (0.3–0.9)     | 2.2 (1.4–4.0) <sup>a</sup>    |
| 11OHA4                   | 6.8 (4.9–12.5)    | 31.7 (16.8–47.8) <sup>a</sup> |
| 11KA4                    | 2.7 (2.0–3.9)     | 13.4 (8.5–18.8) <sup>a</sup>  |
| 11OHT                    | 0.2 (0.1–0.3)     | 0.4 (0.3–0.5) <sup>c</sup>    |
| 11KT                     | 1.5 (1.2–1.8)     | 2.4 (1.8–3.9) <sup>c</sup>    |

O'Reilly et al., *J Clin Endocrinol Metab*. 2017, 102:840–848.

Serum androgens (% contribution)



# ARE 11-OXYGENATED C19 STEROIDS ARE THE PREDOMINANT ANDROGENS IN POLYCYSTIC OVARY SYNDROME?

**Supplementary Table 2** Serum levels of classic androgens and 11-oxygenated C19 steroids in the polycystic ovary syndrome group

| Patients | Clinical symptoms of hyperandrogenism <sup>a</sup> | Body mass index (kg/m <sup>2</sup> ) | Classic androgens <sup>b</sup> |           |             | 11-oxygenated C19 steroids |                         |               |              | <i>11-KT/T</i> | <i>11-KT+T</i> |
|----------|----------------------------------------------------|--------------------------------------|--------------------------------|-----------|-------------|----------------------------|-------------------------|---------------|--------------|----------------|----------------|
|          |                                                    |                                      | $\Delta$ 4A (ng/mL)            | T (pg/mL) | DHT (pg/mL) | 11OH $\Delta$ 4A (pg/mL)   | 11K $\Delta$ 4A (pg/mL) | 11OHT (pg/mL) | 11KT (pg/mL) |                |                |
| 1        | +                                                  | 30.5                                 | 2.60                           | 499.3     | 63.0        | 1,484.9                    | 431.0                   | 300.7         | 1,068.6      | 2,14028056     | 1567           |
| 2        | +                                                  | 28.5                                 | 1.67                           | 571.5     | 98.3        | 1,787.3                    | 318.7                   | 157.6         | 870.6        | 1,52364273     | 1441           |
| 3        | +                                                  | 21.4                                 | 1.50                           | 410.8     | 77.1        | 990.4                      | 280.7                   | 134.0         | 462.7        | 1,12682927     | 872            |
| 4        | +                                                  | 32.6                                 | 1.06                           | 318.8     | 43.0        | 1,711.6                    | 350.2                   | 465.5         | 1,572.3      | 4,94339623     | 1890           |
| 5        | +                                                  | 21.9                                 | 2.22                           | 421.3     | 125.7       | 1,745.3                    | 611.8                   | 152.8         | 669.0        | 1,58907363     | 1090           |
| 6        | +                                                  | 39.1                                 | 2.02                           | 568.5     | 73.8        | 2,974.0                    | 563.5                   | 378.1         | 1,777.6      | 3,12852113     | 2345           |

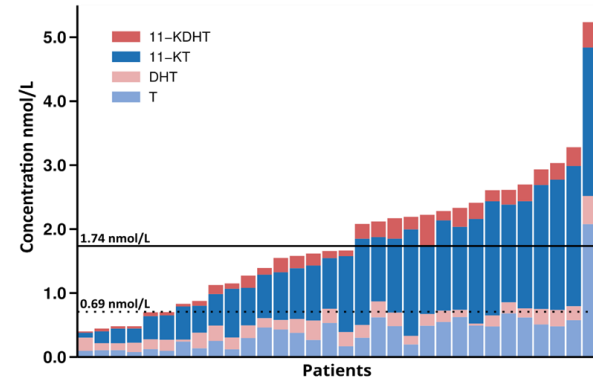
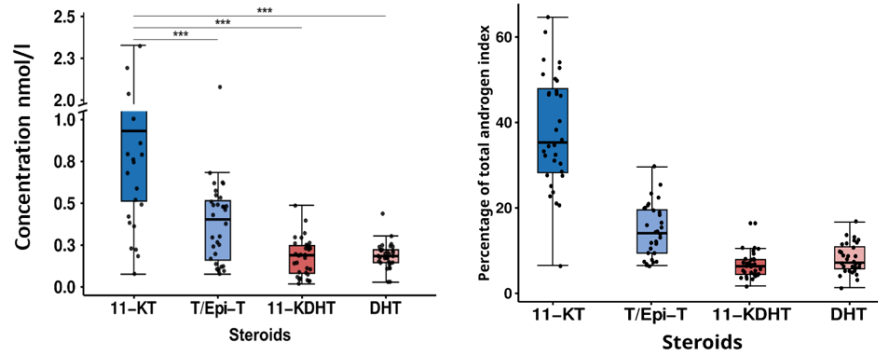
*Endocr J.* 2018 Oct 29;65(10):979-990

- **Machine learning-based steroid metabolome analysis reveals three distinct subtypes of polycystic ovary syndrome and implicates 11-oxygenated androgens as major drivers of metabolic risk:**
  - Women within the adrenal androgen excess cluster had a significantly higher prevalence of insulin resistance, impaired glucose tolerance, and type 2 diabetes. **Results implicate 11-oxygenated androgens as key drivers of metabolic risk in PCOS and suggest an androgen-based stratification that could guide future preventative and therapeutic strategies in women with PCOS.**

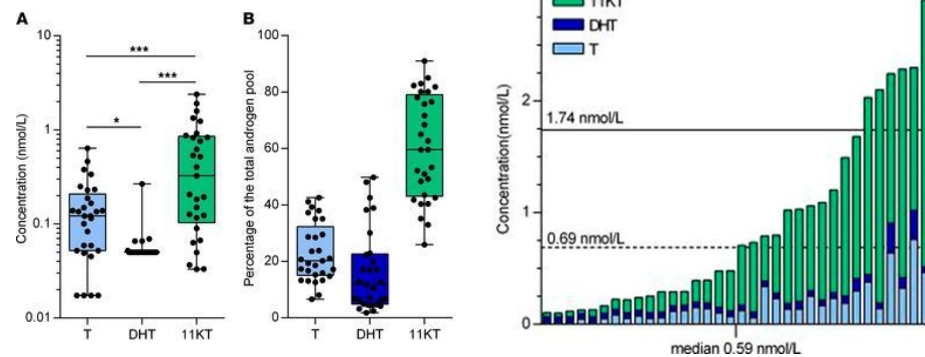
*Journal of the Endocrine Society*, Volume 7, Issue Supplement\_1, October-November 2023, bvad114.1653

# ADT DO NOT SUPPRESS 11-KETOTESTOSTERONE AND 11-KETODHT FORMATION

- 11-ketotestosterone is the most abundant circulating active androgen in chemically castrated men (ADT)
- High individual variation in 11-ketotestosterone concentrations



Akram, et al, unpublished

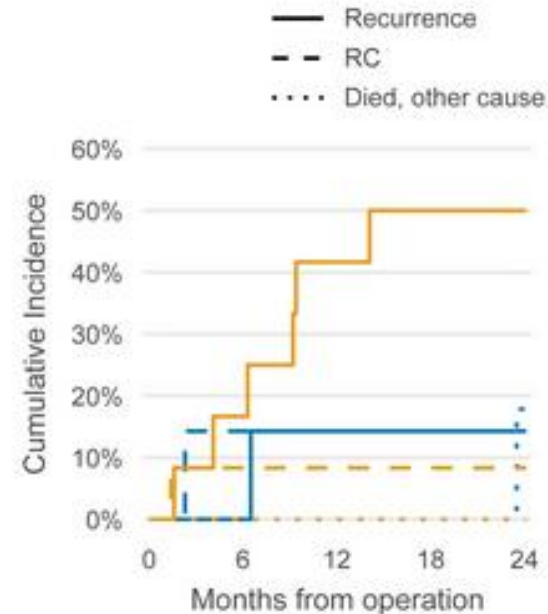
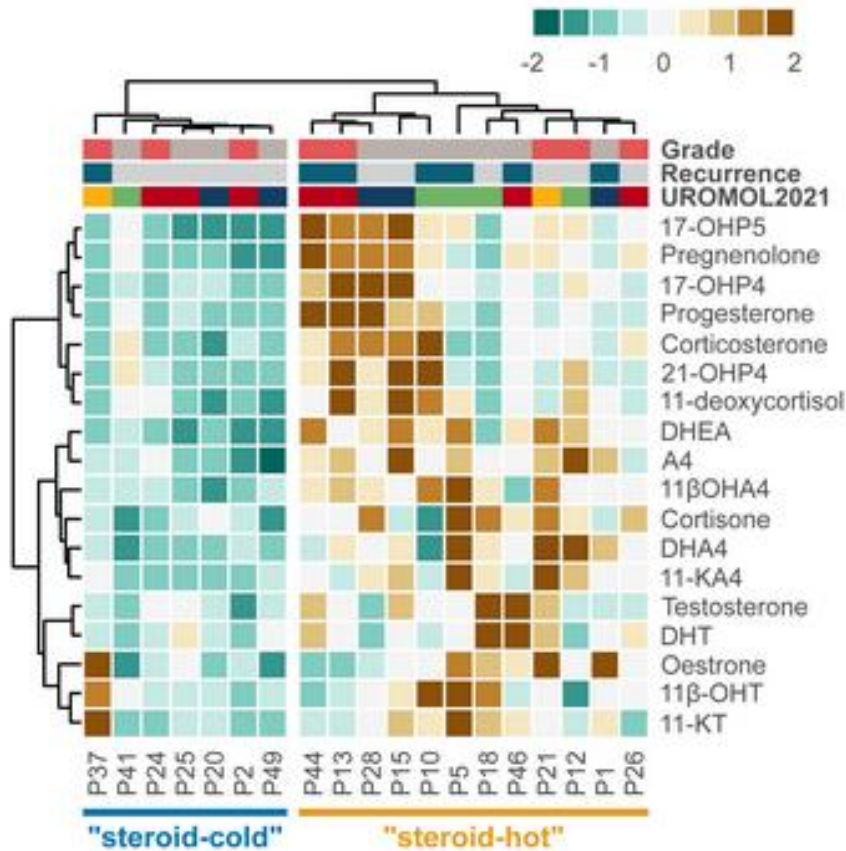


JCI Insight DOI: 10.1172/jci.insight.148507

# STERIOD PROFILING IN THE SERUM OF 19 PATIENTS WITH NON-MUSCLE-INVASIVE BLADDER CANCER

Clustering to **steroid-cold and steroid-hot groups**: One (1/7, 14%) had recurrence during follow-up in the steroid-cold group vs. six (6/12, 50%) in the steroid-hot group. **To be validated with a larger patient group**

**b**



**"steroid-cold"**

|             |   |   |   |   |   |
|-------------|---|---|---|---|---|
| At risk     | 7 | 6 | 4 | 4 | 3 |
| Censored    | 0 | 0 | 1 | 1 | 1 |
| Cum. Events | 0 | 1 | 2 | 2 | 3 |

**"steroid-hot"**

|             |    |   |   |   |   |
|-------------|----|---|---|---|---|
| At risk     | 12 | 9 | 6 | 5 | 5 |
| Censored    | 0  | 0 | 0 | 0 | 0 |
| Cum. Events | 0  | 3 | 6 | 7 | 7 |

|              |                   |                   |
|--------------|-------------------|-------------------|
| <b>Grade</b> | <b>Recurrence</b> | <b>UROMOL2021</b> |
| High-grade   | Yes               | Class 1           |
| Low-grade    | No                | Class 2a          |
|              |                   | Class 2b          |
|              |                   | Class 3           |

# SOME EXAMPLES WITH CLINICAL COHORTS

Journal of the Endocrine Society, 2024, 8, bvae179  
<https://doi.org/10.1210/jendso/bvae179>  
Advance access publication 16 October 2024  
Clinical Research Article



## Postnatal Dysregulation of Androgens in Extremely Preterm Male Infants

Anders K. Nilsson,<sup>1</sup> Ulrika Sjöbom,<sup>1,2</sup> Andreas Landin,<sup>3</sup> Mats X. Andersson,<sup>4</sup> Henrik Ryberg,<sup>3,5</sup> Aldina Pivodic,<sup>1,6</sup> Chatarina Löfqvist,<sup>1,2</sup> Karin Sävman,<sup>7,8</sup> Matti Poutanen,<sup>3,9</sup> Claes Ohlsson,<sup>10,11</sup> and Ann Hellström<sup>1</sup>

HPG axis is activated immediately after birth in extremely preterm infant males, resulting in an androgen pulse occurring several months earlier than during a normal pregnancy.

The Journal of Clinical Endocrinology & Metabolism, 2024, 109, 2967–2978  
<https://doi.org/10.1210/clinem/dgae197>  
Advance access publication 4 April 2024  
Clinical Research Article



## Sex Steroid Levels in Women With Hypopituitarism: A Case-controlled Observational Study

Catharina Olivius,<sup>1,2</sup> Kerstin Landin-Wilhelmsen,<sup>3,4</sup> Claes Ohlsson,<sup>3,5,6</sup> Matti Poutanen,<sup>3,5,7</sup> Penelope Trimppou,<sup>3,4</sup> Daniel S. Olsson,<sup>3,4,8</sup> Gudmundur Johannsson,<sup>3,4</sup> and Åsa Tivesten<sup>1,4</sup>

Women with HH and ACTH deficiency had markedly lower concentrations of all sex hormones than those without ACTH deficiency.

## Profiling steroid hormone landscape of bladder cancer reveals depletion of intratumoural androgens to castration levels: a cross-sectional study



Kimmo Kettunen,<sup>a</sup> Julia Mathlin,<sup>a,b</sup> Tarja Lamminen,<sup>c</sup> Asta Laiho,<sup>b</sup> Merja R. Häkkinen,<sup>d,e</sup> Seppo Auriola,<sup>e</sup> Laura L. Eklö,<sup>a,b</sup> Peter J. Boström,<sup>c,j</sup> Matti Poutanen,<sup>a,i,j</sup> and Pekka Taimen<sup>a,b,k</sup>



Underscoring the androgen-poor nature of the malignancy, it also identifies potential alterations in steroid profiles that are linked to disease aggressiveness

The Journal of Clinical Endocrinology & Metabolism, 2022, Vol. 107, No. 4, e1413–e1425  
<https://doi.org/10.1210/clinem/dgab867>  
Clinical Research Article



## Clinical Research Article

## Low Progesterone and Low Estradiol Levels Associate With Abdominal Aortic Aneurysms in Men

Claes Ohlsson,<sup>1,2,\*</sup> Marcus Langenskiöld,<sup>3,\*</sup> Kristian Smidfelt,<sup>3</sup> Matti Poutanen,<sup>1,4</sup> Henrik Ryberg,<sup>5</sup> Anna-Karin Norlén,<sup>5</sup> Joakim Nordanstig,<sup>3</sup> Göran Bergström,<sup>6,7</sup> and Åsa Tivesten<sup>6,8</sup>

Progesterone and estradiol are inversely associated with AAA in men, independent of known risk factors.

# CONCLUSIONS

- Serum steroids are commonly measured clinical biomarkers
- Mass-spectrometric assays are beneficial when low physiological levels are measured
- Multianalyte profiling of steroids or intra-tissue measurements has provided novel information on disease processes, but has not yet provided value as clinical biomarkers for diagnosis or as predictive/prognostic biomarkers

# PEOPLE INVOLVED

## Univ. of Turku

Michael Gabriel  
 Taija Heinosalo  
 Kaisa Huhtinen  
 Arttu Junnila  
 Guillermo Martinez  
 Nea Nygård  
 Oluwafemi Ojo  
 Petra Sipilä  
 Kalle Rytönen  
 Leena Staruss

Number of  
 technicians

## Univ. of Turku

### *Bioinformatics*

Laura Elo  
 Arfa Mehmood  
 Asta Laiho  
 Julia Mathlin  
 Sadia Akram  
 Sebastián Zúñiga Norman

### *Dpt of OBG/Pathology*

Antti Perheentupa  
 Pia Suvitie  
 Carita Edgren  
 Päivi Rosenberg  
 Harry Kujari

### *Turku Metabolomic Centre*

Alex Dickens  
 Ilia Evstafev

**FICANWest**  
 LÄNTINEN SYÖPÄKESKUS / VÄSTRA CANCERCENTRET  
 WESTERN FINLAND CANCER CENTRE

**TPCC**  
 Turku Prostate Cancer Consortium  
<https://tpcc.utu.fi/>

## Univ. of Turku

### *Dpt Urol + Pathol*

Peter Boström  
 Otto Ettala  
 Pekka Taimen  
 Tarja Lamminen  
 Mikael Högerman

## Univ. of Gothenburg

Claes Ohlsson  
 Malin Hagberg-Thulin  
 Hannah Colldén  
 Henrik Ryberg  
 Andreas Landin  
 Anna-Karin Norlén  
 Anna Lindkvist

## Univ. of Kuopio

Seppo Auriola  
 Merja Häkkinen

## Forendo Pharma/Organon

Risto Lammintausta  
 Janne Hakkarainen  
 Pasi Koskimies  
 Niina Saarinen-Aaltonen



## TREMENDO

Etiology, Prevention and Treatment of Metabolic, Endocrine and  
 Developmental Disorders

