Title	Classification of high and low androsterone UDP-glucuronyltransferase rats and their genetic expressions
Sub Title	
Author	松井, 道夫(Matsui, Michio) 渡辺, 宏(Watanabe, Hiroshi)
Publisher	共立薬科大学
Publication year	1981
Jtitle	共立薬科大学研究年報 (The annual report of the Kyoritsu College of Pharmacy). No.26 (1981.) ,p.109- 110
JaLC DOI	
Abstract	
Notes	学会講演要旨
Genre	Technical Report
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=AN00062898-00000026-0112

ラット肝 Δ^4-5 β-REDUCTASE

高橋美恵，松井道夫

〔日本薬学会　第101年会（1981年4月）で発表〕

〔目的〕　ヒトにおける *in vivo* 代謝研究から Testosterone (T) は 5α- および 5β-Steroids に還元されるのに対し Testosterone glucuronide (TGA) は選択的に 5β-Steroids に還元されることが知られている。演者らは以前にラット肝可溶性分画中に存在する Δ^4-5β-Reductase が T のみならず TGA および Testosterone sulfate (TS) の Δ^4 二重結合を還元して 5β-Steroids に変換すること，さらにこれらを基質とした場合の Δ^4-5β-Reductase の至適 pH は T および TS では約 6 であるのに対し，TGA を基質とした場合には約 11.5 とアルカリ性側であることを報告した。今回，Δ^4-5β-Reductase の性質を解明する目的で各至適 pH および生理的 pH 7.4 における Km および V_{max} 値を求めて比較検討した。

〔実験〕　Wistar 系雄性ラット肝可溶性分画と，基質 T, TGA または TS と NADPH 再成系の存在下で各 pH でインキュベートし，K_m および V_{max} 値を求めた。各基質の還元速度は先に開発した Isonicotinic acid hydrazide 法を応用し，酵素反応停止後，残存する T, TGA および TS をそのまま比色定量し，その基質残存量から求めた。一方 pH 7.4 における TGA の還元速度は，反応終了後抱合体を酵素水解し，得られた還元成績体 5β-Androstane-3α, 17β-diol 量を GC 法により定量した。

〔結果・考察〕　至適 pH における T, TGA および TS の K_m (V_{max}) 値はそれぞれ 24 μM (0.79 n mol/min/mg protein), 22 (0.68), 31 (0.49) であり，pH 7.4 における K_m (V_{max}) 値はそれぞれ 22 (0.86), 39 (0.87), 21 (0.53) であった。TGA は pH 7.4 で非常に強い基質阻害が認められ，Δ^4-5β-Reductase に対して他の基質と異なった反応様式を示した。

CLASSIFICATION OF HIGH AND LOW ANDROSTERONE UDP-GLUCURONYLTRANSFERASE RATS AND THEIR GENETIC EXPRESSIONS

松井道夫，渡辺　宏

〔5 th International Symposium on Microsomes and Drug Oxidations (July, 1981, Tokyo) で発表〕

Metabolism of androsterone in male and female Wistar rats is characterized by the discontinuous variations in biliary metabolites and hepatic microsomal UDP-glucuronyltransferase activity. More than 9-fold differences in the UDP-glucuronyltransferase activity were found in the native or detergent-activated microsomes. In contrast, no marked variation was observed in the rate of glucuronidation with bilirubin, testosterone,

4-nitrophenol and phenolphthalein between the high and low activity groups.

The specific activities of the hepatic microsomal UDP-glycuronyltransferase obtained by partial hepatectomy were in good accord with those obtained by decapitation 4 weeks after hepatectomy. Based on these results, classification of high and low transferase activity rats was carried out by partial hepatectomy.

All or 87% of the offspring from the cross between high activity rats showed high transferase activity, whereas all or 50% of the offspring from high activity rats crossed to low activity rats produced high transferase activity. All of the offspring from the cross between low activity rats gave low transferase activity. These data are consistent with the expected high and low activity ratios and provide evidence that the genetic expressions of the hepatic microsomal UDP-glucuronyltransferase activity toward androsterone are inherited as a single autosomal dominant trait. Postnatal changes in the transferase activity are under current investigation.

VARIABILITY OF ANDROSTERONE METABOLISM IN WISTAR RATS, WITH SPECIAL REFERENCE TO THE SULFATED AND GLUCURONIDATED METABOLITES

松 井 道 夫

〔Workshop on Sulfate Metabolism and Sulfate Conjugation (Sept., 1981. Noordwijkerhout, The Netherlands) で発表

Some striking features characterize the metabolism of androsterone in male and female Wistar rats. Androsterone was metabolized by several different pathways of biotransformations such as hydroxylation at C-2, C-7, C-11, C-15 and C-16, reduction of 17-oxo group, and conjugation with sulfuric acid and glucuronic acid; moreover, there were wide individual differences in biotransformation and biliary excretion. It was found that about half of the rats excreted large amounts of steroid monoglucuronides rapidly into bile, whereas the remaining rats excreted rather steroid mono- and disulfates slowly into bile in both sexes. Males provided more oxygenated steroid metabolites than females.

The studies on androsterone conjugates showed that metabolic fate of androsterone sulfate markedly differed from that of androsterone glucuronide. The injected androsterone sulfate was extensively metabolized to oxygenated steroid mono- and disulfates and excreted slowly into bile. In contrast, the injected androsterone glucuronide was eliminated rapidly into bile and behaved like a metabolic end-product.

In order to study the regulatory mechanism responsible for large variations in androsterone metabolism, we measured microsomal UDP-glucuronyltransferase and cytosolic